

ISV ANNUAL CONGRESS

International
Society for
VACCINES

| 2026 |

12 - 14 OCTOBER
A ROOM WITH A ZOO
ANTWERP | BELGIUM



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ABSTRACTBOOK**

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WELCOME ADDRESS

Dear Colleagues,

It is my great pleasure to welcome you to the 2026 Annual Congress of the International Society for Vaccines in Antwerp, Belgium.

Belgium is a fitting host. For a small country, it has an outsized role in vaccines. Within a short distance of this venue you will find excellent vaccine centers, like the Institute of Tropical Medicine, which has worked on infectious diseases of global importance for more than a century, the University of Antwerp's Vaccine & Infectious Disease Institute and Vaccinopolis. There are also major vaccine research and manufacturing sites that supplied doses worldwide during the COVID-19 pandemic. Together with strong academic groups in Ghent, Leuven, Brussels, Liege and beyond, this ecosystem shows the full path from discovery through clinical trials to large-scale production and access.

Antwerp itself has always been a city of exchange. For centuries its port connected Europe to the rest of the world, and it remains a place where ideas, goods and people meet. We hope the congress works the same way. The programme covers preventive vaccination in both human and veterinary health. It follows vaccinology from start to finish: fundamental discovery, translational research, clinical development, regulatory science, manufacturing and implementation. Researchers and leaders from academia, industry, government and non-governmental organizations will meet here to take on shared challenges and set the direction for the next generation of vaccines. The programme also gives dedicated attention to biologicals. Monoclonal antibodies and other biologic interventions are increasingly used alongside vaccines to prevent and treat infectious disease. They also raise shared questions about design, manufacturing, regulation and access. The programme also takes on the practical problems of implementation, equity and public trust that decide whether scientific advances reach the people who need them.

I want to give a particular welcome to students and early-career researchers. You will find dedicated sessions, mentoring opportunities and networking events designed for you. We hope you leave Antwerp with new ideas and new collaborators.

My sincere thanks go to the organising and scientific committees, my fellow co-chairs, the session chairs, our sponsors, and the speakers who have given their time and expertise. Their work made this meeting possible.

Whether this is your first ISV Congress or one of many, I encourage you to make the most of the sessions, the conversations between them, and the city around us. If your schedule allows, take the chance to see more of Belgium. Major cities are all an easy train ride away, and each has its own history, architecture and, of course, its own culinary specialties.

Welcome to Antwerp.

THE ISV 2026 ANNUAL CONGRESS CHAIRS:



Michael Schotsaert

Icahn School of Medicine at
Mount Sinai, United States



Isabel Leroux-Roels

Ghent University, Belgium



Lakshmi Krishnan

National Research Council, Canada

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PROGRAM

MONDAY, 12 OCTOBER 2026

08:40-09:40	REGISTRATION & WELCOME COFFEE • sponsored by EuBiologics Co	ATRIUM
09:40-09:50	OPENING SESSION	OKAPI
	WELCOME BY ISV PRESIDENT: Manon Cox, NEXTWAVEBIO, USA CO-CHAIR REMARKS: Michael Schotsaert, ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, USA Lakshmi Krishnan, NATIONAL RESEARCH COUNCIL (NRC), CANADA Isabel Leroux-Roels, UNIVERSITY OF GHENT, BELGIUM	
09:50-10:35	STANLEY PLOTKIN LECTURE	OKAPI
	SESSION CHAIR: Manon Cox, NEXTWAVE BIO, USA / ISV PRESIDENT Yellow fever 17D live attenuated vaccine: A great vaccine but how does it work? Alan Barrett, THE UNIVERSITY OF TEXAS MEDICAL BRANCH (UTMB), USA	
10:35-11:55	PLENARY SESSION 1: Population Impact of Vaccination	OKAPI
	SESSION CHAIRS: Sarah Gilbert, UNIVERSITY OF OXFORD, UNITED KINGDOM Joon Haeng Rhee, CHONNAM NATIONAL UNIVERSITY MEDICAL SCHOOL, SOUTH KOREA	
10:35-11:00	Clinical Data for the RSVpreF Vaccine in Older Adults, At-Risk Adults Aged 18-59, and Immunocompromised Adults Kumar Ilangovan, PFIZER VACCINE R & D, USA	
11:00-11:25	Rotavirus Vaccines: Where We Are and What's Next Michelle Groome, UNIVERSITY OF WITWATERSRAND, SOUTH AFRICA	
11:25-11:40	Recombinant Staphylococcus Aureus Vaccine demonstrating 73.25% Protective Efficacy in Phase III clinical study in China Jingxin Li, CHENGDU OLYMVAX BIOPHARMACEUTICALS INC, PEOPLE'S REPUBLIC OF CHINA	
11:40-11:55	Safety and Immunogenicity of a Novel Trivalent Virus-Like Particle Poliovirus Vaccine (VPV): A Phase 1, Randomized, Observer-Blind Trial Qiaoling Yan, CANSINO BIOLOGICS INC., PEOPLE'S REPUBLIC OF CHINA	
11:55-12:05	Why Flanders is a Vaccine Development Hub Kristof Lowyck, DIRECTOR AMERICAS, FLANDERS INVESTMENT & TRADE, BELGIUM	OKAPI
12:05-13:30	LUNCH • sponsored by SANOFI	ATRIUM
12:30-13:30	LUNCH WORKSHOP Defining Immune Evidence Standards for Respiratory Vaccine Development SESSION CHAIR AND MODERATOR: Nnenna Chime, SANOFI, USA PANELISTS: François Beckers, SANOFI, FRANCE, Matthew Miller, MCMASTER UNIVERSITY, CANADA, Fabian Tibaldi, GSK, BELGIUM	OKAPI
13:30-15:05	PLENARY SESSION 2: Mucosal Vaccines	OKAPI
	SESSION CHAIRS: Michael Schotsaert, ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, USA Sandra Depelsenaire, VAXXAS, AUSTRALIA	
13:30-13:55	Trans-kingdom Effects on Immunity to Viruses Michael Diamond, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, USA	
13:55-14:20	Adjuvants - The Tool to Obtain the Required Immune Responses in Vaccination Dennis Christensen, CRODA PHARMA, DENMARK	
14:20-14:35	Charting Mucosal Immune Responses to Influenza using Human Immune-competent Organoids Martin Beukema, UNIVERSITY MEDICAL CENTER GRONINGEN, THE NETHERLANDS	
14:35-14:50	Environmental drivers of oral typhoid vaccine responses in Uganda: dissecting rural-urban differences and the role of Schistosoma mansoni Bridgious Walusimbi, MRC/UVRI AND LSHTM UGANDA RESEARCH UNIT, UGANDA	
14:50-15:05	Inhaled aerosol vaccination with an adenoviral-vectored TB vaccine induces robust respiratory mucosal immunity in humans Sam Afkhami, MCMASTER UNIVERSITY, CANADA	
15:05-15:30	COFFEE BREAK • sponsored by VisMederi	ATRIUM

15:30-17:35	CONCURRENT SESSION 1	CONCURRENT SESSION 2	CONCURRENT SESSION 3
	OKAPI	GORILLA 1	GORILLA 3
	Adjuvants	Vaccine Regulatory Science and Policy	“Bright Sparks” in Vaccinology PhD Student Session
	SESSION CHAIRS: • Ed Lavelle, TRINITY COLLEGE, DUBLIN • Lars Frelin, KAROLINSKA INSTITUTET, SWEDEN	SESSION CHAIRS: • Manon Cox, NEXTWAVE BIO, USA / ISV PRESIDENT • Xuefei Zhou, XZ GMP CONSULTING, USA	SESSION CHAIRS: • Jeffrey Ulmer, TECHIMMUNE LLC, USA • Martin Beukema, UNIVERSITY MEDICAL CENTER GRONINGEN, NETHERLANDS • Alejandra Capozzo, UNIVERSIDAD ABIERTA INTERAMERICANA, ARGENTINA
15:30-15:55	Open-access Adjuvants for Prophylactic Human Vaccines Marcelle Van Mechelen , VACCINE FORMULATION INSTITUTE, SWITZERLAND	Regulatory Acceptance of Immunological Biomarkers as Surrogate for Vaccine Efficacy – Ebola Zaire Vaccine Case Marie-Chantal Uwamwezi , PATH, BELGIUM	Cross-Reactive SARS-CoV-2 Antibodies in Pre-Pandemic Gambian Sera Exhibit Fc-Mediated Effector Activity Dawda Jobe , MRC UNIT THE GAMBIA AT LSHTM, GAMBIA <i>(15:30-15:40)</i> Seroepidemiology and serum bactericidal activity of IgG antibodies to Non Typhoidal Salmonella in healthy Children in Mukuru informal settlement in Kenya Schola Kamwethya , KENYA MEDICAL RESEARCH INSTITUTE, KENYA <i>(15:40-15:50) Switchover Break (15:50-15:55)</i>
15:55-16:20	From Empirical Adjuvants to Programmable Immunity Nathalie Garçon , N3J CONSULTING, BELGIUM	Beyond Efficacy: How Early Development Decisions Shape the Population Impact of Vaccines Beate Sander , UNIVERSITY OF TORONTO, CANADA	The Effect of Malaria Intermittent Preventive Treatment on Vaccine Responses and SARS-CoV-2 Seroprevalence in Adolescents: Findings from a Randomised Controlled Trial Ludoviko Zirimenya , MRC/UVRI & LSHTM UGANDA RESEARCH UNIT, UGANDA <i>(15:55-16:05)</i> APC-Mimetic Dendritic Cell-Derived Extracellular Vesicle Nanovaccine with STING Adjuvant Induces Long-Term Th1 Immunity and Immune Memory Against Dengue Virus Anindita Sengupta , INDIAN INSTITUTE OF TECHNOLOGY, INDIA <i>(16:05-16:15) Switchover Break (16:15-16:20)</i>
16:20-16:35	Antigen cross-presentation potentiating cancer vaccine adjuvant for T cell expansion and synergy with anti-PD-1 Giang Chau Dang , CHONNAM NATIONAL UNIVERSITY, SOUTH KOREA	Primary Healthcare Surveillance and Vaccination Challenges During the 2025 Meningococcal Serogroup C Outbreak Response in Sokoto State, Northern Nigeria Ikechukwu Nnaji , NIGERIA CENTRE FOR DISEASE CONTROL AND PREVENTION (NCDC), NIGERIA	Induction of influenza-specific immunity in pigs using dissolvable microneedle patches to deliver an adenovirus-based vaccine Inés Co Rives , UNIVERSITY COLLEGE CORK, IRELAND <i>(16:20-16:30) Switchover Break (16:30-16:35)</i>
16:35-16:50	Modulation of the bone marrow hematopoietic and immune cell landscape by vaccine adjuvants Eleanor Burgess , ICAHN SCHOOL OF MEDICINE, USA	Immunological assays and correlates of protection: the missing tool for next-generation influenza vaccines Emanuele Montomoli , VISMEDERI SRL, ITALY	Systemic response and short-term functional changes following infection with Necator americanus third-stage infective larvae: Insights from a control human hookworm infection trial in Lambarene, Gabon Therese Vanessa Amana Bokagne , CENTRE DE RECHERCHES MEDICALES DE LAMBARENE, GABONESE REPUBLIC <i>(16:35-16:45) Switchover Break (16:45-16:50)</i>

	CONCURRENT SESSION 1	CONCURRENT SESSION 2	CONCURRENT SESSION 3
	OKAPI	GORILLA 1	GORILLA 3
16:50-17:05	Neutrophils are the dominant early responders to a potent liposomal vaccine adjuvant Lee Sims , UNIVERSITY OF OXFORD, UNITED KINGDOM	Panel Discussion MODERATOR: Manon Cox , NEXTWAVE BIO, USA / ISV PRESIDENT PANELISTS: Emanuele Montomoli , VISMEDERI SRL, ITALY Beate Sander , UNIVERSITY OF TORONTO, CANADA Marie-Chantal Uwamwezi , PATH, BELGIUM Xuefei Zhou , XZ GMP CONSULTING, USA	Intranasal protein-based vaccines protect against 2.3.4.4b H5N1 infection in young and old BALB/C mice Gabriel Laghlali , ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, USA
17:05-17:20	GVX-PA-01, a novel <i>Pseudomonas aeruginosa</i> (Pa) vaccine Elodie Pastural , GLYCOVAX PHARMA, CANADA		A simplified and sensitive assay for tracking virus-specific T cell responses in the nasal cavity during SARS-CoV-2 human challenge studies Previtha Dawn Sakthi Vale , NATIONAL UNIVERSITY OF SINGAPORE, SINGAPORE
17:20-17:35	PIV5-Vectored Intranasal RSV Vaccine is Safe and Immunogenic in Infants and Young Children Biao He , BLUE LAKE BIOTECHNOLOGY, INC./ CYANVAC LLC, USA		AI-Driven Infodemic Surveillance and Its Impact on COVID-19 Vaccine Uptake in Sub-Saharan Africa: A Multi-Country Study Angyiba Serge Andigema , DEPARTMENT OF RESEARCH, BISONS' SCHOLARS, DOUALA, CAMEROON
17:35-20:00	POSTER SESSION 1 • sponsored by PFIZER		ATRIUM
17:35-20:00	WELCOME RECEPTION • sponsored by BHARAT BIOTECH		ATRIUM

TUESDAY, 13 OCTOBER 2026

08:00-08:30	WELCOME COFFEE • sponsored by MODERNA	ATRIUM
08:30-09:00	KEYNOTE SPEAKER	OKAPI
	SESSION CHAIR: Michael Schotsaert , ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, USA From Preclinical Insight to Clinical Evidence: Advancing the Next Generation of Pneumococcal Conjugate Vaccines Annaliesa Anderson , PFIZER, USA	
09:00-10:30	PLENARY SESSION 3: Vaccine Technology	OKAPI
	SESSION CHAIRS: Indresh Srivastava , NOVAVAX, USA Linda Lua , THE UNIVERSITY OF QUEENSLAND & THE GROWTH IMPACT, AUSTRALIA	
09:00-09:25	Beyond the Needle - Discussing the Future of Vaccine Technologies Tarit Mukhopadhyay , MERCK, USA	
09:25-09:50	Advancing Therapeutic Vaccines Through Clinically Validated LNP Delivery Technologies Xiangrong Song , WESTGENE BIOPHARMA, CHINA	
09:50-10:15	Exploring New Paradigms in Vaccine Landscape Emilio Fumero , MODERNA, SPAIN	
10:15-10:30	Safety, Reactogenicity and Immunogenicity of a Launch-IT Rabies Vaccine: A Randomized, Double-Blind, Placebo-Controlled, Dose-Escalation Phase 1 Study in Healthy Adults Lidia Oostvogels , ASTRIVAX THERAPEUTICS, BELGIUM	
10:30-11:00	KEYNOTE SPEAKER (VIRTUAL)	OKAPI
	SESSION CHAIR: Lakshmi Krishnan , NATIONAL RESEARCH COUNCIL (NRC), CANADA Entering the Vaccine Space During Uncertain Times Peter Marks , ELI LILLY AND COMPANY, USA	
11:00-11:20	COFFEE BREAK • sponsored by ARCTURUS THERAPEUTICS	ATRIUM

11:20-12:55	CONCURRENT SESSION 4 OKAPI	CONCURRENT SESSION 5 GORILLA 1	CONCURRENT SESSION 6 GORILLA 3
	Immunotherapies	Vaccines for Vector-borne Diseases	“Bright Sparks” in Vaccinology ECR Session
	SESSION CHAIRS: ▪ Lenny Moise, SEROMYX, USA ▪ Annie de Groot, EVA Therapeutics, USA	SESSION CHAIRS: ▪ Kai Dallmeier, KU LEUVEN, BELGIUM ▪ Alba Grifoni, LA JOLLA INSTITUTE FOR IMMUNOLOGY, USA	SESSION CHAIRS: ▪ Barbara Felber, NCI/NIH, USA ▪ Valentino D’Onofrio, GHENT UNIVERSITY, BELGIUM ▪ Denise Doolan, THE UNIVERSITY OF QUEENSLAND, AUSTRALIA
11:20-11:45	Unleashing our innate immune system as defense against disease Joost Kreijtz, TRAINED THERAPEUTIX DISCOVERY (TTXD), NETHERLANDS	From Efficacy to Impact: What We Can Learn About Dengue Vaccination From TAK-003, a Tetravalent Dengue Vaccine Liudmyla Budovska, TAKEDA PHARMACEUTICALS INTERNATIONAL AG, SWITZERLAND	Effectiveness of PCV10 and PCV13 against invasive pneumonia disease in vietnamese children prior to national introduction: a matched case-control study Cong Hieu Truong, PASTEUR INSTITUTE IN HO CHI MINH CITY, VIETNAM (11:20-11:30) Age-specific immunity gaps and residual susceptibility to measles and rubella before and after the measles-rubella supplementary immunisation campaign in South India Ramya Madhavan, CHRISTIAN MEDICAL COLLEGE, INDIA (11:30-11:40) Switchover Break (11:40-11:45)
11:45-12:10	Antibody effector functions in antiviral immunity Taia Wang, STANFORD UNIVERSITY SCHOOL OF MEDICINE, USA	Controlled human infection studies to accelerate vaccine development Meta Roestenberg, LEIDEN UNIVERSITY, NETHERLANDS	Antigen composition, not T-cell functionality, limits cross-reactivity to distant Coronaviruses after bivalent SARS2 Spike vaccination Ziyin Wang, LA JOLLA INSTITUTE FOR IMMUNOLOGY, USA (11:45-11:55) Implementation Effectiveness of a Community-Driven Vaccination Model at Boosting Immunization in Two Conflict-Affected Health Districts of Cameroon: A Quasi-Experimental Study Derrick Nebangwa, COMMUNITY-DRIVEN VACCINATION PROGRAMME (COVACC), CAMEROON
12:10-12:25	In situ cancer immunotherapy with modified MVdeltaC measles virus induces potent RIG-I-dependent tumor clearance and immune memory Frédéric Tangy, INSTITUT PASTEUR ONCOVITA, FRANCE	Structural Basis of 4G2-Induced Antibody-Dependent Enhancement in Flaviviruses Camilla Di Giulio, GLOBAL HEALTH INSTITUTE, EPFL, SWITZERLAND	Establishing a blood-stage Controlled Human Malaria Infection model in healthy Tanzanian adults with varying prior exposure to P. falciparum Omar Hassan, IFAKARA HEALTH INSTITUTE, TANZANIA (12:10-12:20)
12:25-12:40	Therapeutic HBV vaccine efficacy through ancestral mismatched T cell epitopes Nina Le Bert, DUKE-NUS MEDICAL SCHOOL, SINGAPORE	Rational design of live-attenuated West Nile virus vaccines that are non-transmissible by vector mosquitoes Gorben Pijlman, WAGENINGEN UNIVERSITY & RESEARCH, THE NETHERLANDS	An Intranasal Hemagglutinin Protein Booster After Intramuscular mRNA Vaccination Enhances Mucosal Immunity and Confers Protection Against Influenza Virus in Ferrets Seokchan Park, ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, USA
12:40-12:55	mRNA-Encoded HSV Monoclonal Antibody Based Immunotherapy Outperforms Acyclovir in a Murine Model of HSV-1 Encephalitis Sita Awasthi, UNIVERSITY OF PENNSYLVANIA, USA	Novel dengue virus non-structural protein vaccine that can prevent disease exacerbation caused by existing vaccines Kyoko Tsukiyama-Kohara, KAGOSHIMA UNIVERSITY, JAPAN	Divergent innate and humoral immune responses to 4CMenB vaccination in transgender individuals receiving gender-affirming hormone therapy Anthony Willems, CENTER FOR VACCINOLOGY (CEVAC), GHENT UNIVERSITY, BELGIUM

12:55-14:30	LUNCH • sponsored by GPN VACCINES	ATRIUM
13:30-14:30	CANADIAN VACCINE R&D SPOTLIGHT • sponsored by THE NRC	OKAPI
	Opening Remarks and Canada's Life Sciences and Commercialization Strategy Lakshmi Krishnan , NATIONAL RESEARCH COUNCIL (NRC) CANADA Advancing vaccine manufacturing platforms for rapid response to global health emergency Amine Kamen , MCGILL UNIVERSITY Canada's Public Health Agency Canada – From surveillance to vaccine preparedness Celia Lourenco , PUBLIC HEALTH AGENCY CANADA Stable CHO pools as a platform for rapid vaccine antigen manufacturing Yves Durocher , NATIONAL RESEARCH COUNCIL (NRC) CANADA	
14:00-15:30	POSTER SESSION 2 • sponsored by Merck Sharp & Dohme LLC	ATRIUM
14:30-15:30	ISV ANNUAL GENERAL MEETING	GORILLA 3
15:30-16:00	COFFEE BREAK • sponsored by VAXXAS	ATRIUM
16:00-17:50	PLENARY SESSION 4: Systems Vaccinology	OKAPI
	SESSION CHAIRS: Danilo Casimiro , SANOFI VACCINES R & D, USA Shan Lu , WORCESTER HIV VACCINE, USA	
16:00-16:25	Complexity from Simplicity: Using Systems Immunology to Define Conserved Innate Immune Mechanisms Mediating Diverse Effector Responses to Vaccines Jeffrey Tomalka , EMORY UNIVERSITY SCHOOL OF MEDICINE, USA	
16:25-16:50	Artificial Intelligence and Machine Learning (AI/ML) in the development of mRNA vaccines Fernando Ulloa-Montoya , SANOFI, FRANCE	
16:50-17:05	Induction of HIV broadly neutralizing antibodies by human vaccination Isabel Baken , AMSTERDAM UMC, THE NETHERLANDS	
17:05-17:20	Genome-guided identification and validation of novel T-cell vaccine targets for cross-species malaria protection Carla Proietti , THE UNIVERSITY OF QUEENSLAND, AUSTRALIA	
17:20-17:35	Novel DNA Delivery Method Using Lipid Nanoparticles Induces Durable Polyfunctional Immune Responses with Tier2 Neutralizing Antibody and Cytotoxic CD8 T Cells Barbara Felber , NCI/NIH, USA	
17:35-17:50	Immunological and transcriptomic profile of chimeric live-attenuated Zika vaccine linked to protection in non-human primates Kai Dallmeier , KU LEUVEN, BELGIUM	
18:30-23:00	GALA DINNER	MARBLE HALL

WEDNESDAY, 14 OCTOBER 2026

08:00-08:30	WELCOME COFFEE • sponsored by SpyBiotech	ATRIUM
08:30-09:00	KEYNOTE SPEAKER	OKAPI
	SESSION CHAIR: Isabel Leroux-Roels , UNIVERSITY OF GHENT, BELGIUM From Global Partnerships to Local Impact: Strengthening Vaccine Innovation Laura Palomares , INSTITUTO DE BIOTECNOLOGÍA UNAM, MEXICO	
09:00-10:35	PLENARY SESSION 5: One Health and Pandemic Preparedness	OKAPI
	SESSION CHAIRS: Albert Osterhaus , UNIVERSITY OF VETERINARY MEDICINE, GERMANY Laura Palomares , INSTITUTO DE BIOTECNOLOGÍA UNAM, MEXICO	
09:00-09:25	Active and Passive Mucosal Immunization Strategies for Improved Pandemic Preparedness Matthew Miller , MCMASTER UNIVERSITY, CANADA	
09:25-09:50	Antigenic evolution of H5 viruses and subtype-wide H5 vaccine development Mathilde Richard , ERASMUS MC, THE NETHERLANDS	

9:50-10:05	Safety of a bivalent Ebola virus and Sudan virus ChAdOx1 vectored vaccine in Tanzanian adults: an open-label, non-randomised phase 1 clinical trial Latipha Mohamed , IFAKARA HEALTH INSTITUTE, TANZANIA		
10:05-10:20	Single-visit rabies vaccination with a simian adenovirus vector elicits durable neutralising antibody responses indicating likely protection for >2 years: mid-term results from the RAB002 phase Ib/II clinical trial Alexander Douglas , UNIVERSITY OF OXFORD, UNITED KINGDOM		
10:20-10:35	Design, Development and Characterisation of Multivalent mRNA-LNP Vaccine Candidates for Mpox Hapiloe Maranyane-Tshililo , AFRIGEN BIOLOGICS & VACCINES, SOUTH AFRICA		
10:35-11:00	COFFEE BREAK • sponsored by CanSino Biologics ATRIUM		
11:00-12:35	CONCURRENT SESSION 7	CONCURRENT SESSION 8	CONCURRENT SESSION 9
	OKAPI	GORILLA 1	GORILLA 3
	Vaccine Confidence	Emerging Infections	Veterinary Vaccines
	SESSION CHAIRS: ▪ Linda Klavinskis , KING'S COLLEGE LONDON, UNITED KINGDOM ▪ Frédéric Tangy , INSTITUT PASTEUR ONCOVITA, FRANCE	SESSION CHAIRS: ▪ Jeffrey Ulmer , TECHIMMUNE LLC, USA ▪ Branka Grubor-Bauk , ADELAIDE UNIVERSITY, AUSTRALIA	SESSION CHAIRS: ▪ Amine Kamen , MCGILL UNIVERSITY, CANADA ▪ Denise Doolan , THE UNIVERSITY OF QUEENSLAND, AUSTRALIA
11:00-11:25	The State of Vaccine Confidence in 2026 Emilie Karafillakis , LONDON INSTITUTE FOR TROPICAL MEDICINE AND HYGIENE, UNITED KINGDOM	Preclinical and clinical development of a cellular immunity-based Covid-19 vaccine Helton Santiago , FEDERAL UNIVERSITY OF MINAS GERAIS, BRAZIL	Co-Infections and Immunomodulation: Hurdles and Drivers in Bovine Vaccinology ALEJANDRA CAPOZZO , UNIVERSIDAD ABIERTA INTERAMERICANA, ARGENTINA
11:25-11:50	Beyond Vaccine Hesitancy: Understanding and Rebuilding Trust in Vaccination in Complex Social Ecosystems Ève Dubé , LAVAL UNIVERSITY, CANADA	Safety and immunogenicity of EuHZV, an ECLS-based recombinant herpes zoster vaccine: a first-in-human Phase 1 study in adults aged 50–69 years Howard Her , EUBIOLOGICS CO., LTD, SOUTH KOREA	Developing Next Generation Broad-Spectrum Bacterial Vaccines Tim Hirst AND Chole Gates , GPN VACCINES, AUSTRALIA
11:50-12:05	Bridging the Mpox Vaccine Uptake Gap in Africa: Determinants of Acceptance and Hesitancy from a Systematic Review and Meta-Analysis Charles Ibeneme , TEXILA AMERICA UNIVERSITY ZAMBIA CAMPUS, ZAMBIA	Stabilized henipavirus fusion glycoproteins induce strong serum neutralizing antibody responses against of authentic virus and inform future vaccine design. Haye Nijhuis , AMSTERDAM UMC, THE NETHERLANDS	Selection and characterization of a contemporary respiratory syncytial virus subtype B strain for use in Controlled Human Infection Model (CHIM) studies Albert Osterhaus , UNIVERSITY OF VETERINARY MEDICINE HANNOVER, GERMANY
12:05-12:20	Panel Discussion MODERATOR: Michael Schotsaert , ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, USA PANELISTS: ▪ Emilie Karafillakis , LONDON INSTITUTE FOR TROPICAL MEDICINE AND HYGIENE, UNITED KINGDOM ▪ Ève Dubé , LAVAL UNIVERSITY, CANADA ▪ Chunlin Xin , CANSINO BIOLOGICS, PEOPLE'S REPUBLIC OF CHINA ▪ Igor Smolenov , ARCTURUS THERAPEUTICS, USA	CD4+ T cell-mediated immunity protects from VSV-SUD lethal challenge in a mouse model of Sudan virus infection Lara Kelchtermans , KU LEUVEN, BELGIUM	Development of a vaccine against deadly elephant endotheliotropic herpesvirus Xander De Haan , UTRECHT UNIVERSITY, THE NETHERLANDS
12:20-12:35		Characterization of the immune response to Fusobacterium nucleatum, an emerging pathogen associated with adverse pregnancy outcomes Tracy Lee , BC CANCER RESEARCH INSTITUTE, CANADA	Evaluation of the protective efficacy of foot-and-mouth disease vaccines against O/CATHAY topotype virus in pigs Yoon Hee Lee , ANIMAL AND PLANT QUARANTINE AGENCY, SOUTH KOREA
12:35-14:00	LUNCH • sponsored by HUMAN VACCINES & IMMUNOTHERAPEUTICS (HVI) and EXPERT REVIEW OF VACCINES (ERV) ATRIUM		
13:00-14:00	THE CAREER LAB: MANY PATHS, SHARED PURPOSE OKAPI An interactive workshop bringing together people across career stages to share experiences, exchange candid advice and lessons learned, and explore your next move towards a meaningful career in the vaccine ecosystem. Linda Lua , THE UNIVERSITY OF QUEENSLAND & THE GROWTH IMPACT, AUSTRALIA		
14:00-14:30	AWARD CEREMONY OKAPI		

14:30-14:55	ISV PAPER OF THE YEAR (VIRTUAL)	OKAPI
	SESSION CHAIR: Sita Awasthi, UNIVERSITY OF PENNSYLVANIA, USA A natural experiment on the effect of herpes zoster vaccination on dementia Pascal Geldsetzer, STANFORD UNIVERSITY, USA	
14:55-15:50	PLENARY SESSION 6: Challenge Studies	OKAPI
	SESSION CHAIRS: Isabel Leroux-Roels, UNIVERSITY OF GHENT, BELGIUM Baik-Lin Seong, YONSEI UNIVERSITY, SOUTH KOREA	
14:55-15:20	The Flu Air Shedding and Immune Monitoring (FLAIM) study, the first controlled human infection study at Vaccinopolis, Belgium Joren Raymenants, UNIVERSITY OF ANTWERP, BELGIUM	
15:20-15:35	Predicting West Nile Virus Outcomes: Insights and Limitations from Murine and Avian Models Byron Martina, ARTEMIS BIOSERVICES., THE NETHERLANDS	
15:35-15:50	SARS-CoV-2 humoral waning kinetics are reversed by inactivated vaccine boosting, restoring functional responses, durability and breadth Rafael Medina, EMORY UNIVERSITY SCHOOL OF MEDICINE, USA	
15:50-16:00	CLOSING SESSION & INTRODUCTION TO THE 2027 ISV ANNUAL CONGRESS	OKAPI
	Manon Cox, NEXTWAVE BIO / ISV PRESIDENT, USA Lakshmi Krishnan, NATIONAL RESEARCH COUNCIL (NRC), CANADA	
16:20-17:20	POST CONGRESS – A PANEL DISCUSSION BY BAVARIAN NORDIC New Insights on Mpox: Implications for Public Health and Clinical Practice	GORILLA 3

ISV ANNUAL CONGRESS

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VACCINES

| 2026

INVITED SPEAKERS

Alan Barrett

THE UNIVERSITY OF TEXAS MEDICAL BRANCH (UTMB), USA

Yellow fever 17D live attenuated vaccine: A great vaccine but how does it work?

Monday 12 October 2026 • 09:50-10:35 • Stanley Plotkin Lecture



BIOGRAPHY

Dr. Barrett obtained his PhD from the University of Warwick (1983) and completed a postdoctoral fellowship at the London School of Hygiene and Tropical Medicine (1983-1985). Subsequently, he was Lecturer, Senior Lecturer, and Head of the Molecular Microbiology Research Group at the University of Surrey (1985-1993). In 1993, Dr. Barrett moved to the University of Texas Medical Branch (UTMB) as an Associate Professor and was promoted to Professor in 1997. He became Director of the Sealy Center for Vaccine Development in 2008, which was re-designated the Sealy Institute for Vaccine Sciences, in 2017, and he was Director until September 2025, when he retired. He continues as an Adjunct Professor at UTMB. He was elected Fellow of the International Society for Vaccines in 2014 and Fellow of the American Academy of Microbiology in 2016. In 2018 he was awarded an honorary Doctor of Science Degree from the University of Warwick for his significant contributions to World Health Organization (WHO) vaccine research, development and implementation.

Dr. Barrett's research interests are the molecular basis of pathogenesis and vaccine development of orthoflaviviruses (dengue, Japanese encephalitis, West Nile, tick-borne encephalitis, yellow fever, and Zika). He has authored more than 385 papers, reviews, commentaries, and book chapters. He has served on many international committees for the United States (NIH and CDC), Singapore, and United Kingdom governments, plus the WHO and Coalition for Epidemic Preparedness Innovations (CEPI).

He is Founding Editor-in-Chief of Nature partner journal (*npj Vaccines*) (2015-present) and a member of the editorial boards of five journals: *Emerging Microbes and Infections*, *Journal of Medical Virology*, *Journal of Virological Methods*, *Journal of Virology*, and *Pan Amazonian Health Journal*. Finally, he has co-edited three books, including "*Vaccines for Biodefense and Emerging and Neglected Diseases*" and the first student textbook on vaccines, entitled "*Vaccinology: An Essential Guide*".

ABSTRACT

Yellow fever (YF) is a disease caused by yellow fever virus (YFV), a mosquito-borne orthoflavivirus found in 47 countries in Sub-Saharan Africa and tropical South America. The virus exists in a transmission cycle involving tree-hole breeding mosquitoes and non-human primates with the exact species of mosquito and primate varying by geographic location. The disease YF gets its name from virus-infection of the liver resulting in liver dysfunction such that the skin of those infected turns yellow. Severe disease by the virus causes hemorrhagic fever where the case-fatality rate can be as high as 40%. There are no treatments for YF other than supportive care, but there is a very effective live attenuated vaccine, termed 17D, which was developed empirically in the 1930s by Max Theiler and coworkers. Surprisingly, Theiler is the only scientist who has been awarded the Nobel Prize for medicine for development of a vaccine. The vaccine was first used in 1937. In the last 90 years approximately 1.2 billion doses of vaccine have been distributed. However, the vaccine is manufactured by only six producers who still produce vaccine in embryonated chicken eggs using technology that has changed little since the mid-1940s. Despite efficient utilization of vaccine, the last 10 years has seen the re-emergence of YFV as a major public health problem in both Africa and the South America. Vaccine supplies have been exhausted on multiple occasions and fractional dosing has been implemented on an emergency basis.

17D vaccine is characterized by loss of viscerotropism and neurotropism, plus loss of mosquito competence, and protective immunity is long-lived after a single dose. Reversion to virulence is rare with cases of yellow fever vaccine associated viscerotropic or neurotropic disease (YEL-AVD and YEL-AND), which are characterized by multiple organ failure or encephalitis, respectively, being reported. Thus, the vaccine has proved to be an excellent safe and efficacious vaccine with low reversion and long duration of protective immunity, often life-long. The mechanism of 17D attenuation and the mechanism of rare disease outcomes after vaccination are incompletely understood.

We have been investigating the mechanism(s) of protection and safety using a variety of tools, including reverse genetics, deep sequencing and monoclonal antibodies, and comparing vaccine from different sources and producers with wild-type strains from different genotypes. Surprisingly for a single-stranded RNA virus, the 17D vaccine is genetically very stable and the potential mechanism(s) for this will be discussed

Kumar Ilangovan

PFIZER VACCINE R & D, USA

Clinical Data for the RSVpreF Vaccine in Older Adults, At-Risk Adults Aged 18-59, and Immunocompromised Adults

Monday 12 October 2026 • 10:35-11:00 • Plenary Session 1: Population Impact of Vaccination



BIOGRAPHY

Dr. Kumar Ilangovan, MD, MSPH, MMCI is a physician specializing in internal medicine, pediatrics, and clinical informatics, with extensive experience in global vaccine development. He is a Director in Vaccines Clinical Research and Development at Pfizer, where he serves as the Global Development Lead for the adult respiratory syncytial virus (RSV) vaccine program. In this role, Dr. Ilangovan provides medical and scientific leadership across the full lifecycle of vaccine development, including clinical strategy, protocol design, trial execution, safety oversight, and the generation of high-quality clinical evidence to inform regulatory and public health decision making. He leads multidisciplinary global teams responsible for advancing adult RSV vaccines from early clinical development through late-stage trials. Prior to joining Pfizer, Dr. Ilangovan held senior medical leadership roles at a pediatric contract research organization, where he provided medical and scientific oversight for Phase I-IV clinical trials spanning neonatal through adolescent populations. Earlier in his career, Dr. Ilangovan was an academic physician and investigator with funded research in cancer prevention, health disparities, and health services research. He practiced as a dual trained internist and pediatrician and was actively involved in medical education and mentorship.

ABSTRACT

Introduction: The Pfizer bivalent respiratory syncytial virus prefusion F (RSVpreF) vaccine was approved for prevention of RSV-associated lower respiratory tract disease (LRTD) based on end-of-season 1 efficacy results from the pivotal RENOIR phase 3 efficacy study, which demonstrated a vaccine efficacy of 88.9% against RSV-LRTD with 3 or more symptoms, and sustained protection across two RSV seasons. Subsequent real-world effectiveness studies have further confirmed robust protection against RSV-related emergency department visits and hospitalizations.

The RSVpreF vaccine has undergone extensive late-phase clinical development to expand its indication to afford protection across diverse adult populations. The vaccine is currently licensed for use in older adults in more than 70 countries.

Recent studies aimed to evaluate its use in broader and more vulnerable populations, confirm the safety and immunogenicity of coadministration with other vaccines, and further characterize its overall safety profile. In addition, the clinical development program outlines future strategies to address implementation gaps and enable broader global access.

Methods: This summary integrates data from multiple late-phase clinical trials. Study designs included immunobridging trials evaluating adults 18–59 years old at high risk for severe RSV, as well as targeted analyses of highly vulnerable populations, specifically immunocompromised and renally impaired adults. To assess immune responses in common real-world implementation scenarios, co-administration studies were conducted to evaluate RSVpreF given concomitantly with COVID-19 (BNT162b2) and seasonal quadrivalent influenza (QIV) vaccines. Additionally, an integrated pooled safety analysis was performed using data from over 46,000 participants across eight distinct clinical trials.

Results: Recent immunobridging studies in high-risk adults (18–59 years) demonstrated noninferior neutralizing

immune responses and a safety profile comparable to that of the pivotal Phase 3 efficacy trial in older adults (≥ 60 years). Targeted analyses revealed that a single dose of RSVpreF elicited robust immune responses with no safety concerns in immunocompromised and renally impaired adults. Co-administration studies confirmed the safety and noninferior immunogenicity of RSVpreF when given concomitantly with COVID-19 and QIV vaccines. The integrated pooled safety analysis ($>46,000$ participants) affirmed a consistently favorable safety profile; reactogenicity was mild to moderate, and no newly identified safety signals were observed across non-pregnant, pregnant, and older adult demographics.

Conclusions: Collectively, these clinical updates underscore the robustness of the RSVpreF clinical program. The results demonstrate the vaccine can sufficiently boost RSV neutralizing titers in high-risk and vulnerable populations, while successful co-administration supports flexible, routine immunization practices. A well-established, pooled safety profile reinforces the vaccine's favorable safety and tolerability. Ongoing studies seek to inform the need for additional doses of RSVpreF to extend the duration of protection via revaccination. Furthermore, additional ongoing studies aim to address additional implementation gaps by broadening our understanding of co-administration with the herpes zoster vaccine and studying safety and immunogenicity in specific populations, which would allow for geo-expansion, providing greater access to this efficacious vaccine.

Michelle Groome

UNIVERSITY OF WITWATERSRAND, SOUTH AFRICA

Rotavirus Vaccines: Where We Are and What's Next

Monday 12 October 2026 • 11:00-11:25 • Plenary Session 1: Population Impact of Vaccination



BIOGRAPHY

Biosketch – Prof Michelle J. Groome

MBBCh (Wits), DCH (SA), MSc Med (Epi & Biostats; Wits), PhD (Wits)

Principal Researcher – Epidemiology, Wits Vaccines & Infectious Diseases Analytics (VIDA) Research Unit;
Reader (Associate Professor) – Faculty of Health Sciences, University of the Witwatersrand

Michelle Groome, a medical doctor and infectious disease epidemiologist, has over 20 years' experience in the field of infectious diseases and vaccinology, including conduct of clinical vaccine trials, respiratory and diarrheal disease surveillance programmes and observational studies assessing vaccine impact, effectiveness, immunogenicity and safety. Her most important public health contributions are in the field of enteric vaccines, particularly rotavirus vaccines. She is currently a Principal Researcher at the University of the Witwatersrand's Vaccines & Infectious Diseases Analytics Research Unit where she leads research programmes on maternal immunisation, antimicrobial resistance and diarrhoeal diseases. She holds a joint appointment as Reader in the Faculty of Health Sciences, University of the Witwatersrand, where she lectures and supervises post-graduate students. She has over 100 publications in peer-reviewed journals and has received several awards including the Emerging Global Leader Award from the Fogarty International Center, NIH, and the SAMRC Scientific Merit Award (silver medal). She has a National Research Foundation B2 rating and is a member of the Academy of Science of South Africa.

ABSTRACT

Rotavirus was first identified in 1973 and rapidly emerged as the leading cause of severe childhood diarrhoeal disease worldwide. The virus was responsible for a substantial burden of morbidity and mortality in the pre-vaccine era, accounting for approximately 25-33% of diarrhoeal hospitalisations and contributing significantly to deaths among children under five years of age. Surveillance efforts generated critical epidemiologic data on disease burden and circulating strains, strengthened laboratory capacity and provided evidence to support vaccine introduction. Phase 3 trials demonstrated that oral rotavirus vaccines (ORV) were safe and efficacious against severe rotavirus gastroenteritis, contributing to the World Health Organization recommendation that rotavirus vaccines be included in national immunisation programmes.

Today >140 countries have introduced rotavirus vaccines globally. Post-introduction evaluations have demonstrated major public health benefits, including substantial reductions in rotavirus hospitalisations, all-cause gastroenteritis hospitalisations, and diarrhoeal mortality. Despite these successes, important challenges remain. These include the small but measurable risk of intussusception, lower performance of oral rotavirus vaccines in low- and middle-income compared to high-income settings, vaccine financing and supply challenges, and incomplete understanding of rotavirus immunity and correlates of protection.

Development of parenteral non-replicating rotavirus vaccines represents a potential strategy to overcome challenges associated with oral vaccination. Initial evaluation of a monovalent P2-VP8-P[8] subunit vaccine demonstrated that the vaccine was safe and immunogenic against homologous P[8] strains in South African infants. Subsequently, a trivalent (TV) P2-VP8 (P[4],P[6],P[8]) vaccine, based on truncated VP8 subunit proteins, was developed. The vaccine was well-tolerated, elicited a robust serum immunoglobulin G binding

and virus-neutralising antibody response, and was associated with a reduction of challenge virus (Rotarix) shedding relative to placebo. However, in a Phase 3 efficacy study, TV P2-VP8 parenteral vaccine failed to demonstrate superiority for the prevention of severe rotavirus gastroenteritis when compared to standard of care (ORV, Rotarix®). The TV P2-VP8 vaccine was also evaluated in schedules where it was given concomitantly with ORV, or as a prime-boost regimen. Although well-tolerated, immunological superiority following ORV with TV P2-VP8 boosting or co-administration regimens compared to ORV only was not demonstrated for anti-rotavirus IgA antibodies.

Priorities for future research include developing and evaluating next generation parenteral vaccines, optimising vaccine delivery approaches, harmonising mucosal assays, identifying correlates of protection beyond serum IgA, and advancing platforms such as human intestinal enteroids and controlled human infection models.

Michael Diamond

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, USA

Trans-kingdom Effects on Immunity to Viruses

Monday 12 October 2026 • 13:30-13:55 • Plenary Session 2: Mucosal Vaccines



BIOGRAPHY

The Diamond laboratory investigates the molecular basis of infection and disease of globally emerging RNA viruses with a focus on the interface between pathogenesis and host immunity. His group studies positive-stranded RNA viruses from three important classes that infect humans: flaviviruses, alphaviruses, and coronaviruses. His laboratory develops and uses mouse models to identify mechanisms of viral immune evasion and host immune factors that restrict virus infection in different tissues. His group uses CRISPR-Cas9 screens to identify novel receptors required by viruses for entry, infection, tropism, and pathogenesis. His laboratory also has generated, characterized, and mapped thousands of mouse and human antibodies against flaviviruses (West Nile, Dengue, Zika, Powassan, yellow fever, and Japanese encephalitis viruses) alphaviruses (chikungunya, Mayaro, Venezuelan equine encephalitis, Eastern equine encephalitis, and Western equine encephalitis viruses), and coronaviruses (SARS-CoV-2) and studied their structure-function relationships to neutralization and Fc effector functions as well as their ability to prevent or treat infection and disease. His group developed mouse models of SARS-CoV-2 pathogenesis and used them to advance novel antibody-based therapeutics and mucosal vaccines, which are approved or in human clinical trials. His laboratory also investigates how trans-kingdom interactions (helminth co-infection, bacterial microbiota, and constituent metabolites) link with innate and adaptive immunity to modulate systemic viral infection and disease pathogenesis.

Dr. Diamond is an elected member of the American Society of Clinical Investigation, Association of American Physicians, American Association for the Advancement of Science, the National Academy of Medicine and the National Academy of Sciences. He is also a recipient of Stanley J. Korsmeyer Award of the American Society of Clinical Investigation and currently an elected Councilor for the Association of American Physicians.

ABSTRACT

Although helminth infections modulate host immune responses and can affect concurrent or subsequent viral infection outcomes in humans and vertebrate animals, the mechanistic basis for these effects remains uncertain. Here, we developed a coinfection model using the gastrointestinal (GI) tract-restricted helminth *Heligmosomoides polygyrus bakeri* (Hpb) and a pathogenic, mouse-adapted SARS-CoV-2 strain in C57BL/6J mice. Hpb infection protected mice from lethal SARS-CoV-2 challenge, and this effect occurred independently of adaptive immunity or canonical type 2 immune signaling. Despite limited effects on lung viral burden, coinfection preserved lung ventilatory function and had higher numbers of surfactant-producing alveolar type 2 (AT2) cells. Selective depletion of myeloid cell populations identified neutrophils and lung-resident macrophages as key cellular mediators of Hpb-dependent protection against SARS-CoV-2-induced morbidity, mortality, and AT2 cell injury. RNA sequencing of lung cells from coinfecting mice revealed that Hpb infection in the GI tract promotes a reparative transcriptional program in lung-resident and recruited macrophages while preserving antiviral immunity. Together, these findings suggest that a GI tract-restricted helminth can condition myeloid cells in the lung to enable recovery after SARS-CoV-2 infection.

Dennis Christensen

CRODA PHARMA, DENMARK

Adjuvants - The Tool to Obtain the Required Immune Responses in Vaccination

Monday 12 October 2026 • 13:55-14:20 • Plenary Session 2: Mucosal Vaccines



BIOGRAPHY

As Global Head of Research and Development for Adjuvant Systems, Dennis Christensen is leading the effort to expand Croda's offering of new and innovative vaccine delivery systems, immunostimulators and combined adjuvant systems. He has for more than 20 years been working with pharmaceutical and immunological aspects of vaccine adjuvants and delivery systems including targeted delivery of vaccines. In this period he has played a key role in the development of the CAF® series of adjuvants from Statens Serum Institut, of which the CAF®01 and CAF®09b are now being developed as commercial products by Croda Pharma. He is a key opinion leader in the vaccine adjuvant research field and has an extensive experience with international vaccine research and development programs. Dennis has a Master and PhD degree in Pharmacy from University of Copenhagen, Denmark. Besides his position at Croda, he holds an adjunct research professorship at Statens Serum Institut, Denmark.

ABSTRACT

Basically vaccination is all about presenting sufficient amounts of the right antigen, in the right conformation, to the right cell populations, while supporting with the right co-stimuli for a sufficient amount of time. Most of the modern vaccines constitute highly purified subunit antigens based on proteins, peptides, RNA or DNA and thus intrinsically contain little ability to facilitate uptake into and activation of professional antigen presenting cells. Vaccine adjuvants ensuring delivery and immunostimulation thus represent important tool for modern vaccines to induce the required immune responses to obtain protection upon vaccination. The COVID-19 pandemic clearly showed the need for access to vaccine delivery systems, immunostimulators and combined adjuvant systems where supplies are not at risk. The pandemic thus showed that the dependence of global supply chains and demand-supply to sourcing quality raw materials along with the stress on existing production capacities and platform-specific manufacturing challenges impeded vaccine development and access. With most of the novel adjuvant technologies used in vaccines today being either proprietary of Pharma Companies without motivation to grant access to the technologies or with limited production capacity, there is thus a clear need for strategic investments in scalable production capacity and commercial availability of novel vaccine delivery systems, immunostimulators and combined adjuvant systems.

This presentation will give an overview on the overall role for vaccine adjuvants, design of SoA adjuvant technologies and their mechanisms of action. I will also discuss what we can do better in the vaccine field to increase access to vaccine adjuvants for future vaccine technologies.

Marcelle Van Mechelen

VACCINE FORMULATION INSTITUTE, SWITZERLAND

Open-access Adjuvants for Prophylactic Human Vaccines

Monday 12 October 2026 • 15:30-15:55 • Concurrent Session 1: Adjuvants



BIOGRAPHY

Dr. Marcelle van Mechelen is an immunologist who began her scientific career as a Postdoctoral Fellow at Free University of Brussels and Erasmus Hospital in Belgium before joining GlaxoSmithKline's Vaccines. Over the course of 20 years, she led various multidisciplinary teams focused on preclinical R&D and clinical research, leading the development and implementation of preclinical and clinical immune monitoring tools for vaccines against infectious diseases such as Hepatitis B, HPV, Malaria, Zoster, and Tuberculosis. Her interest lies in particular on deciphering the links between innate and adaptive immune responses following vaccination and exploring the mechanism of action of adjuvants. Since 2015, Marcelle has worked as a senior scientific advisor in various fields including vaccine, autoimmunity, oncology, and regenerative medicine, and joined Vaccine Formulation institute in 2021 as Scientific Director.

ABSTRACT

The Vaccine Formulation Institute (VFI) is a Swiss-based institute dedicated to developing clinically relevant adjuvants that are made available to the vaccine community under open-access terms. VFI's portfolio includes three saponin-containing adjuvants: SQ (a squalene-in-water emulsion with QS-21 saponin), LQ (a liposome-based adjuvant with QS-21 saponin), and LMQ (a liposome-based adjuvant containing a synthetic TLR4 ligand and QS-21 saponin), as well as Sepivac SWE™ (a squalene-in-water emulsion). These adjuvants are compatible with diverse antigen types and have demonstrated consistent performance across multiple preclinical models.

The three saponin-containing adjuvants (LQ, SQ and LMQ) have been evaluated across a broad range of indications and preclinical models by VFI and its collaborative network. Studies led by VFI and partners have demonstrated that these adjuvants promote robust T-cell responses with a Th1 bias as well as functional antibody production when administered with various antigen platforms. Immunogenicity and /or protective efficacy has been documented for multiple vaccine candidates, targeting indications such as COVID-19, influenza, malaria, HIV/AIDS, MERS, tuberculosis, and Group A streptococcus.

Sepivac SWE™ has demonstrated safety and immunogenicity in Phase 1 and Phase 2 clinical trials, and a Phase 3 clinical study has recently been completed. Sepivac SWE™ is commercially available through Seppic and is provided by VFI under material transfer agreement for formulation and pre-clinical studies.

VFI's saponin-containing adjuvants (LQ, SQ, and LMQ) are all available at GMP grade, enabling their direct use in clinical-stage vaccine development under open-access terms.

Nathalie Garçon

N3J CONSULTING, BELGIUM

From Empirical Adjuvants to Programmable Immunity

Monday 12 October 2026 • 15:55-16:20 • Concurrent Session 1: Adjuvants



BIOGRAPHY

Dr Garçon is a PharmD, with an additional PHD in immunotoxicology, immunopharmacology. Over the past 40 years, my professional life has been driven by research and development at the interphase between immunology, pharmaceutical sciences and biology. After a postdoc at the royal free hospital in , London and a second one at baylor college of medicine, I joined GSK vaccine in 1990 to set up and led the adjuvant group. This led me to roles of increasing responsibility in the management of complex multi-disciplinary projects from discovery to life cycle management of vaccines, through staffs of scientists at international levels We have spearheaded the design, development and implementation of GSK's adjuvant strategy leading to the licensure of the first new adjuvanted vaccines worldwide. This gave me the opportunity to contribute and drive many aspect of adjuvants from research to manufacturing and production at a time when everything was to be invented. After some years, I joint a non for profit foundation as CEO/CSO where innovation where developed in vaccines, antimicrobial and diagnostics, to bridge the gap between research and development. I am now retired and support various entities working in the field of vaccines. I have written over 100 scientific papers in different language as well as chapters and book. I hold over a 100 patents and hold over 100 patents in the adjuvants and formulation field.

ABSTRACT

Adjuvants have played a central role in extending and improving vaccine performance, with technologies such as ASx, CpG-containing formulations and, more recently, mRNA platforms, demonstrating that sophisticated immune modulation can translate into major clinical impact. However, the next generation of vaccines will need to address increasingly complex challenges, including immune aging, substantial inter-individual variability and the need for rapid responses to emerging pathogens.

Despite major advances in immunology and biotechnology, translation remains a critical bottleneck. Numerous potential immune modulators are identified, yet relatively few progress into widely used vaccines. At the same time, vaccines and adjuvants have generally adopted emerging technologies more slowly than diagnostics and therapeutics.

Future adjuvant systems should therefore move beyond empirical enhancement of immune responses toward **controlled and programmable immune activation**, balancing potency with precision. This evolution will involve combinations of targeted innate sensing, advanced delivery systems, immune-modulatory molecules, genetic technologies and increasingly predictive approaches to vaccine design.

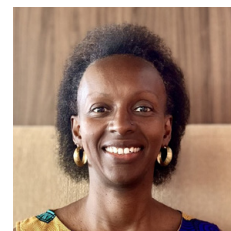
Looking toward 2030, the objective should be to develop adjuvant systems that are **targeted, tailored and timely**: targeting defined immune pathways, adapting responses to population and individual heterogeneity, and enabling rapid development against emerging threats. The transition from "one-size-fits-all" vaccination toward precision immunity represents a major opportunity to improve vaccine efficacy, durability and global preparedness.

Marie-Chantal Uwamwezi

PATH, BELGIUM

Regulatory Acceptance of Immunological Biomarkers as Surrogate for Vaccine Efficacy – Ebola Zaire Vaccine Case

Monday 12 October 2026 • 15:30-15:55 • Concurrent Session 2: Vaccine Regulatory Science and Policy



BIOGRAPHY

Marie-Chantal Uwamwezi is Senior Director of Regulatory Strategy at the Center for Vaccines Innovation and Access (CVIA) at PATH, a US nonprofit advancing global health innovation. She brings over 20 years of experience in global vaccine development and regulatory science, spanning early research through clinical development, licensure, and lifecycle management. She has contributed to several pioneering vaccine programs, including a leadership role in the regulatory review of RTS,S, the first malaria vaccine. This was also the first licensed vaccine against a parasitic disease using a novel adjuvant system. Her work focuses on translating scientific innovation into global health impact through robust and forward-looking regulatory strategies.

At PATH, Marie-Chantal leads regulatory strategy for vaccines addressing global health priorities, working closely with vaccine developers, funders, WHO and national regulatory authorities to enable efficient development pathways, including innovative clinical approaches and WHO prequalification. She is increasingly playing a key role in multi-stakeholder initiatives to address evidence and policy gaps, particularly for vulnerable populations.

Previously, she held senior leadership roles at Johnson and Johnson, MSD, and GSK, leading global regulatory strategies and interactions with major agencies worldwide. She is trained as a bioengineer with a specialization in biotechnology, and holds a post-graduate degree in biostatistics. Marie-Chantal is committed to advancing equitable access to vaccines globally.

ABSTRACT

Introduction/Background

Regulatory approval of vaccines developed for the prevention of infectious diseases requires adequate data to support their quality, safety and efficacy.

For new vaccines containing immunogens for which immune correlates of protection (ICPs) are established and accepted by regulators, efficacy is inferred by demonstrating that the ICP is achieved. Another type of vaccines for which demonstration of efficacy through a phase III randomized controlled trial would not be required are those for which vaccine efficacy can be inferred by demonstrating non-inferior immune responses between the candidate vaccine and a licensed vaccine for which efficacy and/or effectiveness has been established. However for novel vaccines, i.e. new immunogens, vaccine efficacy would be expected to be demonstrated through an adequately powered phase 3 double-blind randomized controlled study.

Regulators however acknowledge that demonstrating vaccine efficacy through randomized controlled trials is often infeasible for pathogens with sporadic outbreaks and high mortality, such as Ebola virus disease (EVD). Regulatory pathways have therefore evolved to allow immunological biomarkers to serve as surrogate endpoints reasonably likely to predict clinical benefit. This presentation analyzes the scientific and regulatory basis for this approach using an Ebola Zaire vaccine (Ad26.ZEBOV/MVA-BN-Filo) as a case study.

Material/Methods

The presentation reviews the regulatory guidelines and policy framework from WHO that enabled and supported alternatives to efficacy trials for the licensure of Ebola vaccines.

Salient elements from the EMA assessment report of the Ad26.ZEBOV/MVA-BN-Filo are discussed to highlight the considerations for accepting the proposed immunobridging approach to infer vaccine efficacy.

Results

EU approval of the Ad26.ZEBOV/MVA-BN-Filo vaccine under exceptional circumstances was based on immunobridging between human and NHPs. EBOV glycoprotein (GP)-binding antibodies measured by the standardized FANG ELISA assay were identified as the primary surrogate endpoint due to strong correlation with protection in NHP models. Binding antibodies showed high concordance with neutralizing antibodies but were preferred due to superior assay robustness, reproducibility, and broader applicability. This is a departure from the usual preference of regulators for functional immune responses as surrogate endpoints for efficacy.

Regulatory acceptance was enabled by standardized assays, quantitative modeling linking antibody levels to survival probability, and a totality-of-evidence approach. Residual uncertainties, including the absence of defined protective thresholds in humans, were meant to be through a post-authorization commitment to conduct a real-world effectiveness study/

Discussion/Conclusion

This case represents a seminal example of regulatory acceptance of immunological biomarkers as surrogates for vaccine efficacy. It demonstrates that integrating animal challenge data, human immunogenicity, and validated assays can support licensure when traditional efficacy trials are not feasible. GP-binding antibodies emerged as a scientifically and regulatorily acceptable surrogate, enabling timely access to a critical vaccine. This paradigm is highly relevant for other filoviruses and emerging pathogens facing similar development constraints. Several global health organizations are funding work to enable identification and building robust evidence base for immunological markers associated with protection against infectious diseases. This work is critical to accelerate the development of vaccines for epidemic-prone diseases.

Beate Sander

UNIVERSITY OF TORONTO, CANADA

Beyond Efficacy: How Early Development Decisions Shape the Population Impact of Vaccines

Monday 12 October 2026 • 15:55-16:20 • Concurrent Session 2: Vaccine Regulatory Science and Policy



BIOGRAPHY

Beate Sander, RN MBA MEcDev PhD, holds a Tier 1 Canada Research Chair in Economics of Infectious Diseases, is a Senior Scientist at the University Health Network (UHN), where she chairs the Health System and Policy Research Collaborative Centre, and Professor at the Institute of Health Policy, Management and Evaluation (IHPE), University of Toronto. She holds appointments as Adjunct Senior Scientist at ICES and Adjunct Scientist at Public Health Ontario (PHO).

Dr. Sander is an internationally recognized leader in infectious disease economics, with expertise in health economics and simulation modelling. Her research evaluates infectious disease interventions and estimates disease burden using population-based data, and advances methods to integrate equity, including inequality aversion, into economic evaluation. She leads a large, well-funded research program, coordinates transdisciplinary teams across countries, and has led linkage of laboratory, reportable disease, and administrative data to study infectious disease burden.

She has published >200 peer-reviewed articles and contributed to >140 reports and guidelines, with >220 citations in policy documents across 18 countries. Dr. Sander mentors a diverse group of trainees, many of whom hold competitive awards.

Dr. Sander serves as an expert to national and international advisory bodies and formerly to Canada's National Advisory Committee on Immunization (NACI), where she chaired the Economics Task Group and co-chaired the Economic Guidelines Task Group. During COVID-19, she co-chaired the Ontario COVID-19 Modeling Consensus Table and advised provincial and national decision makers. She is Past President of the Society for Medical Decision Making.

ABSTRACT

A vaccine that demonstrates strong efficacy in Phase 3 trials has cleared an important scientific milestone. Population impact, however, depends on more than efficacy. Regulatory approval is a critical step, but it is not the end of the pathway from innovation to population health impact. Following regulatory approval, vaccines enter a decision environment that includes recommendation processes, health technology assessment (HTA), funding decisions, implementation considerations, and increasingly, explicit consideration of equity. Together, these processes influence whether, how, and for whom a vaccine is used.

This presentation examines how decisions made early in vaccine development shape the evidence available for these later decisions. Vaccines are assessed across multiple domains, including clinical effectiveness, economic value, feasibility, ethics, and equity. As a result, development choices such as trial populations, endpoints, comparators, dosing schedules, delivery platforms, manufacturing strategies, and product characteristics can have implications that extend well beyond regulatory approval. Whether an efficacy trial enrolls older adults, people who are immunocompromised, or people who are pregnant, for example, determines whether a later recommendation can extend to them.

Drawing on experience in vaccine policy, economic evaluation, and health technology assessment, the

presentation traces the pathway from vaccine development to population use and explores how broader policy, implementation, and decision-making perspectives can inform development decisions. Particular attention is given to how development choices influence the evidence used in later decision-making, including the outcomes that are measured, the populations represented in the evidence base, and the ways product characteristics and manufacturing considerations shape implementation, access, recommendations, and use. For example, a thermostable, single-dose presentation can decide whether a vaccine reaches rural and lower-income settings or stays confined to well-resourced systems. Many of these issues can be considered while key development decisions remain open.

The presentation argues that population impact emerges from the interaction between scientific performance, evidence generation, implementation realities, and health system decision-making. Bringing these perspectives together earlier in development may help strengthen the evidence base, anticipate downstream decision needs, and support wider and more equitable use of effective vaccines.

Annaliesa Anderson

PFIZER, USA

From Preclinical Insight to Clinical Evidence: Advancing the Next Generation of Pneumococcal Conjugate Vaccines

Tuesday 13 October 2026 • 08:30-09:00 • Keynote Speaker



BIOGRAPHY

Annaliesa Anderson, PhD, D.Sc.h.c., FAAM, FIDSA, FMedSci

Dr. Annaliesa Anderson is Senior Vice President and Chief Vaccines Officer at Pfizer, where she leads the company's global vaccines research, development, and medical affairs organization. She oversees an end-to-end portfolio spanning discovery through post-licensure, with a focus on developing innovative vaccines to help prevent infectious diseases worldwide.

With more than 30 years of experience in the biopharmaceutical industry, Dr. Anderson has played a key role in the development of numerous vaccines, including vaccines for human papillomavirus (HPV), pneumococcal disease, meningococcal disease, COVID-19, and respiratory syncytial virus (RSV). During the COVID-19 pandemic, she also co-led the development of a licensed oral antiviral treatment for COVID-19.

Dr. Anderson earned her PhD in Biological Sciences from the University of Warwick in the United Kingdom and received an honorary Doctor of Science degree from Manchester Metropolitan University. She has authored more than 170 peer-reviewed publications and book chapters and holds an extensive patent portfolio in vaccines and anti-infective research and development.

A recognized scientific leader, Dr. Anderson has received awards for her contributions to mentoring and advancing diversity in science. In 2024, she was named among the Top 20 Women in Biopharma by *Endpoints News*.

She is an elected Fellow of the American Academy of Microbiology, the American Association for the Advancement of Science, the Infectious Diseases Society of America, and the Academy of Medical Sciences. She is also a Fellow of the Royal Society of Medicine and serves on multiple scientific and policy advisory boards.

Dr. Anderson is passionate about scientific education, mentorship, and developing the next generation of scientists. Her career has been dedicated to advancing innovations that improve public health and help protect people from infectious diseases around the world.

ABSTRACT

Pneumococcal conjugate vaccines have transformed the prevention of invasive pneumococcal disease and remain one of the clearest examples of how immunologic principles can be translated into major public health impact. By linking pneumococcal polysaccharides to carrier proteins, PCVs convert otherwise limited immune responses into T-cell-dependent responses with immune memory and boostability — properties that are particularly important for protection in infants and durable responses across age groups.

Despite this success, pneumococcal disease remains a meaningful public health challenge. More than 100 pneumococcal serotypes circulate globally, and residual disease reflects both serotypes not yet covered by existing vaccines and serotypes that remain difficult to protect against despite inclusion in licensed PCVs. As the field advances toward higher-valency vaccines, the challenge is therefore not only to broaden serotype coverage, but to preserve the quality of immune responses across every component of increasingly complex formulations.

This presentation will describe the scientific and clinical strategy guiding the evolution of Pfizer's pneumococcal conjugate vaccine platform from the original PCV7 through to potential higher valency vaccines such as PCV35. The transition from the current PCV20 to the potential future PCV25 was designed as a deliberate and carefully bridged advance, building from a clinically validated foundation while limiting changes to those needed to expand coverage and enhance responses to a selected challenging serotype. This approach has focused on maintaining conjugate design principles and polysaccharide-to-carrier ratios within ranges supported by prior extensive effectiveness and impact data, while preserving the ability to induce T-cell-dependent responses, immunologic memory, and booster responses across relevant age groups.

Within this framework, serotype 3 provides an important example of why next-generation PCV development must consider both breadth and immune quality. Although serotype 3 has been included in prior PCVs, it continues to contribute to disease burden. Targeted optimization of conjugation and carrier approaches has been evaluated with the goal of improving immune responses while maintaining the broader performance expected of a multivalent PCV.

The presentation will highlight how preclinical and clinical evidence can be integrated to guide the evolution of a proven vaccine platform. While expanding serotype coverage remains important, future advances in PCV design will depend equally on the ability to introduce and clinically validate targeted improvements that preserve the immunologic foundations of conjugate vaccine protection, particularly in infants. The experience with PCV25 provides one example of how such innovations may be evaluated as the field moves toward increasingly sophisticated next-generation PCVs.

Tarit Mukhopadhyay

MERCK, USA

Beyond the Needle - Discussing the Future of Vaccine Technologies

Tuesday 13 October 2026 • 09:00-09:25 • Plenary Session 3: Vaccine Technology



BIOGRAPHY

Tarit K. Mukhopadhyay, Vice President, Head of Infectious Disease and Vaccine Discovery, Merck

Tarit trained as a biochemical engineer and completed his undergraduate at University College London (UCL) in the United Kingdom. He conducted his doctorate in a joint venture between UCL and the Health Protection Agency, (now UK Health Security Agency), working on a novel Meningitis B vaccine and the UK licensed Anthrax vaccine.

As a former Professor in Vaccine Bioprocessing at the Department of Biochemical Engineering, UCL, he led the vaccine research portfolio. His work spanned Japanese Encephalitis virus vaccine, a novel tandem-core Hepatitis B virus like particle, influenza, rotavirus, and the use of lentiviruses for gene therapy. His work later focused on global health and access; with one grant from the Gates Foundation on low-cost vaccine manufacturing and the second from the UK Government to create a Future Vaccine Manufacturing Research Hub (VaxHub).

Tarit also chaired the Vaccine Development Working Group for the UK Vaccine Network established by the British Government to develop strategies and policies to tackle disease outbreaks of epidemic potential.

In 2019 he joined Merck as Head of Vaccine Process R&D at Merck Research Laboratories at West Point, PA, where he oversaw the development of Merck's pipeline vaccine projects including projects on Dengue, PCV and Covid vaccines. He is now currently Head of Infectious Disease and Vaccine Discovery at Merck.

ABSTRACT

In considering the future of vaccines certain trends remain clear: there will be a dwindling number of commercial opportunities for traditional prophylactic vaccines, however therapeutic opportunities will expand due to new technologies and approaches that will develop to enable these opportunities to grow. In the past few years we've seen small molecule interventions profess a 'vaccine-like image,' neoantigens therapy that reduce the incidence of certain cancers, and genetic medicines to address viral latency. In this talk we will discuss the recent advances of small-molecule long-acting injectables and how these images are being utilized in malaria in combination with a novel dual-plasmeprin inhibitor that can be utilized in both a treatment and vaccination setting using chemo-attenuated liver merozoites (CALM) or chemo-vaccination. Additionally, advances in personalized mRNA based cancer vaccines will also be discussed in the treatment of high-risk melanoma. Finally, we will examine the space of Hepatitis B and driving to a functional cure with a variety of genetic medicine approaches.

Xiangrong Song

WESTGENE BIOPHARMA, CHINA

Advancing Therapeutic Vaccines Through Clinically Validated LNP Delivery Technologies

Tuesday 13 October 2026 • 09:25-09:50 • Plenary Session 3: Vaccine Technology



BIOGRAPHY

Dr. Xiangrong Song is Professor and Ph.D. Supervisor at Sichuan University and Co-founder & CEO of WestGene Biopharma. She has extensive experience in mRNA therapeutics, vaccine development, nanomedicine, and targeted delivery systems. Her research focuses on the development of innovative lipid nanoparticle (LNP) delivery technologies and therapeutic mRNA platforms for oncology, infectious diseases, and metabolic disorders. Dr. Song has led multiple innovative drug programs into clinical development, including several IND-approved mRNA therapeutic vaccine programs in China and the United States. She has authored over 100 scientific publications and is inventor on numerous international patents in the fields of gene delivery and RNA therapeutics.

ABSTRACT

Messenger RNA therapeutics have shown significant promise across infectious diseases, cancer immunotherapy, and next-generation gene medicines. Among the key determinants of successful clinical translation, lipid nanoparticle (LNP) delivery systems play a central role in balancing delivery efficiency, safety, tolerability, and repeat dosing feasibility.

Our group has been focused on the development and translational evaluation of proprietary LNP systems for mRNA therapeutic applications, particularly in the field of therapeutic cancer vaccines. Through continuous optimization of ionizable lipids, formulation composition, and in vivo delivery characteristics, we have established a delivery platform capable of supporting efficient mRNA expression and favorable tolerability profiles in both preclinical and clinical settings.

These delivery systems have been evaluated in multiple therapeutic vaccine programs targeting virus-associated malignancies and solid tumors, with several programs advancing into clinical studies. Early translational and clinical findings support the feasibility of repeated administration and robust immune activation in therapeutic vaccine settings.

In this presentation, we will discuss the design considerations and translational experience associated with next-generation LNP systems for therapeutic mRNA vaccines. Selected case studies will be presented to illustrate how delivery optimization may influence antigen expression, immune activation, tolerability, and the feasibility of repeated administration in therapeutic cancer vaccine applications.

The presentation will also highlight future directions in targeted RNA delivery and immune modulation for oncology applications.

Emilio Fumero

MODERNA, SPAIN

Exploring New Paradigms in Vaccine Landscape

Tuesday 13 October 2026 • 09:50-10:15 • Plenary Session 3: Vaccine Technology



BIOGRAPHY

Emilio Fumero, MD, PhD, is a physician-scientist, internist, and infectious diseases specialist with more than 20 years of experience in virology, infectious diseases, and vaccinology. He trained in Internal Medicine at the Central University of Venezuela and specialized in Infectious Diseases at the University of Barcelona, Spain, where he also obtained his PhD in viral immunoregulation and vaccine development. Throughout his career, he has contributed to antiviral and vaccine research and development across academic research and the pharmaceutical industry. He currently serves as Scientific Director for Europe at Moderna.

ABSTRACT

Vaccinology is entering a new era in which vaccines are no longer defined solely as individual products targeting a single pathogen, but as outputs of adaptable platforms capable of responding to evolving public-health needs. Messenger RNA technology represents a major step in this transition. Its programmable, modular and scalable nature enables vaccines to be designed and updated rapidly, creating opportunities to address pandemic threats, antigenic evolution and increasingly complex prevention needs with greater precision.

Beyond speed, the mRNA platform expands the boundaries of antigen design. Multiple antigens can be encoded within a single formulation, including multicomponent or structurally complex antigens that may be difficult to produce using conventional technologies. By delivering the genetic instructions for antigen expression directly into host cells, mRNA vaccines can promote coordinated humoral and cellular immune responses. This immunological breadth has particular relevance for older adults and other vulnerable populations, in whom immunosenescence, comorbidities or immune compromise may diminish vaccine responsiveness. Although no platform can fully eliminate host-related variability, mRNA technology offers a compelling framework for designing vaccines capable of generating robust immune responses across diverse populations.

The platform may also open a new frontier in adult combination vaccination, particularly for the prevention of viral respiratory diseases. mRNA-1083, which combines influenza and COVID-19 antigens, illustrates the potential to move from pathogen-specific vaccination toward integrated respiratory protection. A combination approach could simplify vaccination pathways, reduce the number of separate appointments and injections, and help close the persistent gap between influenza and COVID-19 vaccine coverage. By making prevention more convenient for individuals and easier to implement for healthcare systems, combination vaccines may improve uptake among those at greatest risk of severe disease.

For influenza, the mRNA platform introduces an additional paradigm: enhanced strain and antigen fidelity. Its rapid design-to-production cycle may permit vaccine composition to be aligned more closely with strains circulating near the start of the vaccination campaign. Moreover, because antigen production does not depend on propagation in eggs, the encoded haemagglutinin sequence can preserve the intended viral antigen without the egg-adaptive changes that may arise during conventional manufacturing.

Taken together, these attributes position mRNA as more than a new vaccine technology. It is an enabling platform for rapid preparedness, sophisticated antigen engineering, broader protection of vulnerable populations and integrated adult immunisation. The emerging paradigm is one of programmable prevention: vaccines that can be updated, combined and tailored to the biological and public-health challenges of a changing world.

Peter Marks

ELI LILLY AND COMPANY, USA

Entering the Vaccine Space During Uncertain Times

Tuesday 13 October 2026 • 10:30-11:00 • Keynote Speaker (Virtual)



BIOGRAPHY

Peter Marks, M.D., Ph.D. received his graduate degree in cell and molecular biology and his medical degree at New York University and completed Internal Medicine residency and Hematology/Medical Oncology training at Brigham and Women's Hospital in Boston. He has worked in academic settings teaching and caring for patients and in industry on drug development. In 2012, he joined the Food and Drug Administration and served as Director of the Center for Biologics Evaluation and Research from 2016 to 2025. He is currently Senior Vice President for Molecule Development and Head of Infectious Disease at Eli Lilly and Company, has published extensively, and is a member of the National Academy of Medicine.

ABSTRACT

During the past two decades, anti-vaccine sentiment has increased, particularly in certain countries. This trend has accelerated during since the COVID-19 pandemic, as trust in public health agencies and vaccine manufacturers declined further. Uptake of commonly used childhood and adult vaccines has continued to decline in the United States, and in the 2025-2026 season, influenza vaccination rates fell to below 50% in individuals 75 years and older for the first time in many years. In that context, Lilly is reentering the infectious disease space with a significant investment in prophylactic vaccines. The long-term goal is to both to touch more lives and positively impact public health globally.

Joost Kreijtz

TRAINED THERAPEUTIX DISCOVERY (TTXD), NETHERLANDS

Unleashing our innate immune system as defense against disease

Tuesday 13 October 2026 • 11:20-11:45 • Concurrent Session 4: Immunotherapies



BIOGRAPHY

Joost Kreijtz is CEO (Europe) of Trained Therapeutix Discovery, a biotech company with its R&D headquarters in the Netherlands. TTxD develops nanomedicines that target innate immunity at its source to unlock the full potential of immunotherapy in oncology and inflammatory diseases. Trained as a biomedical scientist with a focus on immunology, Joost brings over 15 years of drug development experience, specializing in translating immunotherapies from concept to clinic and building high-performing biotech teams and companies.

ABSTRACT

Trained immunity is the functional reprogramming of innate immune cells and their progenitors through epigenetic and metabolic mechanisms. This was first discovered and described by Netea et al. based on studies using the BCG vaccine. Those studies showed that the vaccine inducing trained immunity through reprogramming myeloid progenitor cells in the bone marrow. This biology offers a therapeutic opportunity to act upstream of mature, short-lived innate immune cells. Particularly applicable in diseases where myeloid activation, inflammatory set points, or impaired anti-tumor innate immunity contribute to pathogenesis. Strategies that can selectively engage trained-immunity mechanisms within hematopoietic tissues remain limited.

Trained Therapeutix Discovery, Inc. is developing nanomedicine-based therapeutics, originally designed by Mulder et al, to modulate innate immunity at its origin. The company's RIDE nanoparticle platform is designed for progenitor-cell programming and downstream myeloid-lineage immune responses. Through epigenetic modulation of bone marrow progenitor cells, this approach seeks to recalibrate innate immune function in a disease-context-specific manner.

RIDE-001 is a first-in-class nanomedicine that trains myeloid progenitor cells to support anti-tumor innate immune responses. In oncology, this strategy induces durable innate immune activation, deploying pro-inflammatory myeloid cells to the tumor and mounting an anti-tumor response. This was first demonstrated in mouse tumor models including B16F10. Safety and tolerability was confirmed in rodent and non-human primate studies. RIDE-001 was well tolerated in both species and displayed the required pharmacological effects.

On the other side of the immunological coin, in inflammatory diseases, RIDE-002 modulates maladaptive inflammatory programs by intervening upstream at the myeloid progenitor cells with disease-modifying potential. In mouse models this was demonstrated with RIDE-002: treating inflammation by targeting myeloid progenitor cells.

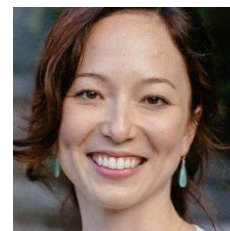
This platform-based novel class of immuno-modulatory drugs induces durable therapeutic responses in preclinical studies, warranting clinical validation.

Taia Wang

STANFORD UNIVERSITY SCHOOL OF MEDICINE, USA

Antibody effector functions in antiviral immunity

Tuesday 13 October 2026 • 11:45–12:10 • Concurrent Session 4: Immunotherapies



BIOGRAPHY

Taia Wang, MD, PhD, MSCI, is an Associate Professor of Medicine (Infectious Diseases) and of Microbiology and Immunology at Stanford University, and a primary faculty member of the Institute for Immunity, Transplantation, and Infection. Her laboratory studies antibody and effector cell biology to improve vaccine responses and outcomes in infectious and inflammatory disease. Her work is recognized for defining IgG Fc glycosylation as a functional determinant of human immunity and for identifying mechanisms by which antibody signaling regulates inflammation in the lung. Dr. Wang earned her MD and PhD at Mount Sinai School of Medicine, where her doctoral research with Dr. Peter Palese identified structural determinants of broad influenza virus immunity, and completed postdoctoral training with Jeffrey Ravetch at the Rockefeller University, where she studied human IgG and Fc receptor biology. She is a Burroughs Wellcome Fund Investigator, Searle Scholar, and a member of the American Society for Clinical Investigation.

ABSTRACT

Antibodies are among the immune system's most powerful tools for combating disease, yet fundamental principles governing how human antibody activity is naturally regulated remain incompletely understood. This talk will highlight ongoing work from our laboratory exploring underappreciated organizing principles in human antibody biology, including how antibody structure, glycosylation, and interactions with immune receptors shape function in health and disease. By uncovering the mechanisms that tune antibody activity, we seek to develop a more complete understanding of human humoral immunity and identify new opportunities to engineer and deploy antibodies as therapeutics and diagnostics across infectious, inflammatory, and other antibody-mediated diseases.

Liudmyla Budovska

TAKEDA PHARMACEUTICALS INTERNATIONAL AG, SWITZERLAND

From Efficacy to Impact: What We Can Learn About Dengue Vaccination From TAK-003, a Tetravalent Dengue Vaccine

Tuesday 13 October 2026 • 11:20-11:45 • Concurrent Session 5: Vaccines for Vector-borne Diseases



BIOGRAPHY

Liudmyla Budovska, MD, PhD is the Global Medical Lead for Vaccines (Travel Markets) at Takeda, where she leads global medical engagement and scientific exchange initiatives across international travel health markets. In her role, she works closely with healthcare professionals, scientific societies, researchers, and public health stakeholders to advance evidence-based vaccination practices and support informed healthcare decision-making.

Dr. Budovska brings more than 15 years of experience spanning clinical medicine, academic research, and global Medical Affairs. Prior to joining the pharmaceutical industry, she practiced and conducted research in Internal Medicine, Gastroenterology, and Allergy Medicine, earning both MD and PhD degrees. Throughout her career, she has been dedicated to translating scientific evidence into practical insights that support healthcare professionals and improve public health outcomes.

Her areas of interest include infectious diseases, vaccination, medical education, scientific communications, and the generation and application of real-world evidence. She is passionate about fostering scientific collaboration, advancing vaccine confidence, and promoting greater awareness of vaccine-preventable diseases and their impact on global health.

At the 2026 International Society for Vaccines (ISV) Congress, Dr. Budovska will present "From Efficacy to Impact: What We Can Learn About Dengue Vaccination From TAK-003, a Tetravalent Dengue Vaccine," highlighting how clinical trial and real-world evidence can inform dengue vaccination strategies and contribute to public health decision-making in dengue-endemic regions.

ABSTRACT

Background: Dengue is a rapidly expanding mosquito-borne viral disease and an increasing global public health challenge. Urbanization, climate change, population growth, and increased travel continue to expand its reach and the population at risk. With no specific antiviral treatment available, effective prevention relies on integrated strategies including surveillance, vector control, clinical management, and vaccination.

Methods: This presentation reviews the evolution of evidence supporting TAK-003, a live attenuated tetravalent dengue vaccine, and explores how clinical and real-world data can inform public health decision-making.

Results: The TAK-003 clinical development program included more than 28,000 participants across endemic and non-endemic regions. In the Tetravalent Immunization against Dengue Efficacy Study (TIDES), TAK-003 met the primary and key secondary endpoints for efficacy against virologically confirmed dengue and dengue-related hospitalization. Long-term follow-up through 4.5 years after the primary vaccination series has provided evidence of sustained protection, including reductions in hospitalized dengue, and continued favourable outcomes through seven years of observation, including booster assessments. Across the clinical data, no evidence of disease enhancement or increased hospitalization risk has been observed, and the vaccine has demonstrated a favourable safety profile irrespective of baseline serostatus. Post-authorization experience, encompassing more than 30 million distributed doses, has continued to support a positive benefit-risk profile. Real-world studies, including effectiveness analyses conducted during outbreak in Brazil, demonstrated

protection against symptomatic and hospitalized dengue. Observational studies in endemic and non-endemic settings provided additional safety and tolerability information.

Conclusion: The clinical and real-world evidence generated for TAK-003 provides an opportunity to assess effectiveness, safety, durability of protection, and implementation experience across diverse settings. By looking at the role of vaccination as part of a broader dengue prevention strategy, this presentation aims to provide insights into how evidence from clinical trials and real-world programs can support national immunization policy discussions and contribute to reducing the growing global burden of dengue

Keywords: Dengue vaccination; TAK-003; Public health impact

Meta Roestenberg

LEIDEN UNIVERSITY, NETHERLANDS

Controlled human infection studies to accelerate vaccine development

Tuesday 13 October 2026 • 11:45-12:10 • Concurrent Session 5: Vaccines for Vector-borne Diseases



BIOGRAPHY

Meta Roestenberg is an infectious diseases clinician, professor and head of the Leiden University Center for Infectious Diseases department at Leiden University Medical Center in the Netherlands where she leads a group of translational researchers in answering key questions related to host-pathogen interaction by making use of controlled human infection models (CHIM). Her team pioneered the clinical testing of a genetically attenuated sporozoite vaccine against malaria and established CHIMs for schistosomiasis and hookworm. She then started to collaborate with Ingrid de Visser to expand the portfolio of CHIM trials to include outpatient RSV, non-toxicogenic and toxicogenic *Clostridioides difficile*, chikungunya virus, influenza and rhinovirus. To more effectively collaborate in the public-private interface, Meta and Ingrid founded INFECTA to facilitate the early-phase clinical testing of novel products for infectious diseases including CHIM studies. Recognising the ethical complexity of such healthy volunteer studies, the team is active in establishing ethical frameworks for such CHIM trials, contributing to generating guidelines and leading discussions. Moreover, the team has tackled many regulatory hurdles and has an active volunteer engagement program.

ABSTRACT

Vaccines are one of the safest and most cost-effective interventions in global health, yet vaccine development is an endeavor that carries inherent risks of failure. Many of such failures occur late in clinical development, when phase 3 efficacy trials do not deliver on the promise provided by preclinical data.

Controlled Human Infection Models (CHIMs), also known as human challenge models, are carefully managed medical research studies in which healthy adult volunteers are deliberately exposed to well-characterized strains of infectious agents under controlled conditions. These studies take pivotal roles in vaccine development, providing early clinical evidence of protection in healthy volunteers and providing valuable insights into disease mechanisms, pathogenesis, and host factors contributing to susceptibility for infection.

The establishment of CHIMs requires several key components, including safe and accurate monitoring of participants to ensure their safety. Endpoint measurements, which can be clinical or microbiological should be well established to ensure detectability of the infection.

To ensure that the methodology of CHIMs is made more widely available, a the not-for-profit CRO INFECTA was established as a joint effort from academic centers in The Netherlands. INFECTA offers full service early phase clinical trials and CHIMs according to regulatory requirements for product registration.

Jeffrey Tomalka

EMORY UNIVERSITY SCHOOL OF MEDICINE, USA



Complexity from Simplicity: Using Systems Immunology to Define Conserved Innate Immune Mechanisms Mediating Diverse Effector Responses to Vaccines

Tuesday 13 October 2026 • 16:00-16:25 • Plenary Session 4: Systems Vaccinology

BIOGRAPHY

Dr. Tomalka's research applies Systems Immunology combined with molecular and cellular validation to define mechanisms that drive protective immunity to infection and vaccination, with a focus on how innate immune signaling (IL-1/NF- κ B, AP-1, IRF/IFN) shapes downstream cellular and humoral responses. His group studies these signaling cascades in the context of myeloid and lymphoid cells, first identifying signatures in human cohorts and using pre-clinical studies to validate and model mechanisms.

To define how complex and diverse vaccine responses are regulated by the combined activity of a limited number of transcription factors, we integrate bulk and single-cell Omics – RNA-seq, ATAC-seq, proteomics, metabolomics, and high-dimensional flow cytometry – to generate datasets that span all levels of biological regulation. Within this framework, one can track how metabolites (host and microbiome) induce the expression of cytokines in innate immune cells to drive autocrine and paracrine activation of signaling cascades in myeloid and lymphoid cells that promote transcriptional changes leading to altered function and induce epigenetic changes (memory) that permanently alter how those cells respond to future challenge.

A central contribution of his work is the discovery of CREB1 as a mechanistic driver of HIV vaccine efficacy: identified through unbiased analysis of NHP and human ALVAC/RV144 trial data, a 43-gene CREB1 signature correlates with V1V2 antibody responses, CD4⁺ T cell polyfunctionality, and protection from SHIV challenge. In total, this CREB1 signature has now been confirmed seven independent vaccine studies, with generalizability shown to other viral vectors (Ad5, VSV) and adjuvants (Alum, 3M-052). In addition to identifying innate immune signatures of efficacy in vaccine trials, his lab works on adjuvant discovery and development designing next generation adjuvants targeted to activate specific immunological cascades/signatures of protective vaccine responses. This work includes specifically modulating T cell differentiation status to improve cellular effector responses, in addition to improving neutralizing and non-neutralizing antibody responses.

ABSTRACT

The immune system drives diverse responses to vaccination, microbial pathogens, and even tissue dysfunction, yet all of that diversity is built using the same “blocks” arranged differently: complexity from simplicity. The innate immune system stands as the beginning and the end, the alpha and the omega, of coordinated immune responses in vaccines. Adjuvants and/or immunogenic vaccines target the innate immune system to increase antigen presentation and produce cytokines, directing the development of T and B cell responses. Those antigen specific T and B cell responses then produce effector cytokines and antibodies after future exposures which function to activate and mobilize innate immune responses (macrophages, neutrophils, NK cells) to eliminate the infection. My lab uses Systems Immunology tools to define the mechanistic role for three critical innate immune signaling axes in generating protective vaccine responses: 1) NF- κ B, 2) IRF/IFN, and 3) CREB1. We have found that CREB1 is a master regulator of HIV vaccine responses: functionally priming DCs to induce enhanced lymphocyte activation, activating co-stimulatory and cytokine signaling and MHC II in CD4⁺ T cells, and driving chemotaxis and protein synthesis in B cells. At the core of CREB1 regulation of vaccine responses is that it sits upstream of NF- κ B, IFN, and AP-1 (FOS/JUN) responses, orchestrating

a balance of these signals. We have new evidence that acquisition of a trained NF- κ B and IFN state after vaccination leads to production of high levels of antibody, while a trained IFN state promotes T cell responses. We can use adjuvants, or combinations of adjuvants, to mimic the natural balance that drives protective immune response, leading to more effective vaccines and even dose sparing to reduce cost. Collectively, this work highlights how Systems Immunology allowed us to identify how integration of three ancestral innate signaling cascades after vaccination mechanistically defines the adaptive immune response and subsequent protection.

Fernando Ulloa-Montoya

SANOFI, FRANCE

Artificial Intelligence and Machine Learning (AI/ML) in the development of mRNA vaccines

Tuesday 13 October 2026 • 16:25-16:50 • Plenary Session 4: Systems Vaccinology



BIOGRAPHY

Fernando Ulloa Montoya, PhD

Head Data and Computational Sciences
Vaccines R&D, Sanofi

Fernando is the Head of Data and Computational Sciences in Vaccines R&D at Sanofi. He leads a global team of data and computational scientists integrating and leveraging data, AI and computational methods across the entire pharmaceutical value chain—from vaccine design and pre-clinical studies to clinical trials, process development and manufacturing. Previously, he was leading the Data Science team at Sanofi's mRNA Center of Excellence.

Before joining Sanofi in 2021, he held various positions of increasing responsibilities at GSK. Leading translational research and data science teams focused on predictive biomarkers and companion diagnostics for cancer immunotherapy, identifying vaccine correlates of protection and utilizing genomics and computational methods to deepen the understanding of vaccine adjuvants' mechanisms of action.

He has a degree in Biochemical Engineering from the Instituto Politécnico Nacional in Mexico, an M.S. degree in Chemical Engineering at Washington State University and a Ph.D. degree in Chemical Engineering from the University of Minnesota.

ABSTRACT

First-generation mRNA vaccines (mRNA 1.0) have demonstrated clinical efficacy across three targets (SARS-CoV-2, RSV, influenza), favorable immunogenicity with induction of functional antibodies and CD4/CD8 T cell responses, and a platform approach that accelerates time to clinic. However, mRNA 1.0 falls short on key vaccine attributes: reactogenicity can exceed that of non-mRNA comparators in an antigen-dependent manner and thermostability remains inferior to conventional platforms. Addressing these gaps to deliver mRNA 2.0 requires navigating a vast, multi-parameter design space—spanning mRNA sequence, lipid nanoparticle (LNP) formulation, and manufacturing—that is intractable to conventional one-parameter-at-a-time optimization.

This presentation describes how Sanofi's integrated mRNA Center of Excellence applies AI/ML across the value chain to enable this transition. On sequence design, we developed CodonBERT, a foundational large language model trained on 10 million mRNA sequences across species and fine-tuned for protein expression, which outperforms published models including in flu antigen expression prediction. In parallel, RiboNN, a deep neural network trained on over 2,000 mammalian Ribo-seq datasets, predicts translational efficiency directly from RNA sequence, identifying the 5' UTR and ORF as the most information-dense regions for translational output. Combining generative algorithms with predictive oracles including RiboNN and massively parallel screenings, we have generated novel UTRs that outperform our baseline.

On reactogenicity, we leveraged ML with data from Sanofi's proprietary MIMIC® system, an in vitro immune construct platform, to rank LNP candidates by biological signals resulting from different cell types: dendritic cells, monocytes, macrophages, and endothelium ahead of clinical testing. This forward-translation approach shows high concordance with clinical reactogenicity outcomes across multiple trials, enabling preclinical

down-selection of candidates. For manufacturability, mechanistic, and data-driven modeling of drug substance and LNP drug product processes are being used to link process parameters (flow rate ratio, mixing, pH, temperature) to critical quality attributes and immunogenicity, moving toward manufacturability-by-design.

Collectively, this translational AI/ML ecosystem—integrating high-throughput data generation, predictive and generative modeling, and active learning—represents a paradigm shift from trial-and-error, single-parameter approaches to data-driven, multi-parameter optimization. Key open questions remain around biomarkers predictive of efficacy and reactogenicity, translatability of preclinical models across diverse LNP formulations, and structure-function relationships governing LNP performance. This comprehensive strategy positions mRNA technology for systematic, AI/ML-enabled advancement toward safer, more stable, and more effective vaccines for patients.

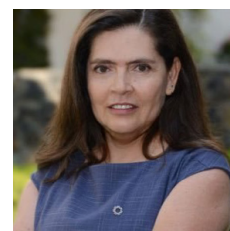
Disclosure: This work has been funded by Sanofi. Fernando Ulloa Montoya is a Sanofi employee and may hold shares or stock options in the company.

Laura Palomares

INSTITUTO DE BIOTECNOLOGÍA UNAM, MEXICO

From Global Partnerships to Local Impact: Strengthening Vaccine Innovation

Wednesday 14 October 2026 • 08:30-09:00 • Keynote Speaker



BIOGRAPHY

Laura A. Palomares is Chair of the Scientific Advisory Committee of the Coalition for Epidemic Preparedness Innovations (CEPI), contributing scientific guidance to advance CEPI's mission of accelerating vaccine development and strengthening global preparedness for epidemic and pandemic threats. An internationally recognized biotechnology leader, she brings expertise in vaccine innovation, biopharmaceutical development, and the translation of research into manufacturing capabilities.

As Director and Principal Investigator of the Institute of Biotechnology at the National Autonomous University of Mexico (UNAM), she leads strategic research, industry partnerships, and technology translation to strengthen Mexico's biotechnology ecosystem. Her work has advanced recombinant vaccine manufacturing through collaborations with domestic and global companies, successful technology transfer initiatives, and licensed influenza vaccine programs.

She founded a GMP-certified National Laboratory that supports biopharmaceutical characterization, regulatory activities, and clinical-stage development, including monoclonal antibody programs. Her advisory and governance roles with CEPI, COFEPRIS, and the Mexican Pharmacopoeia connect scientific innovation with regulatory strategy and public health priorities.

Recognized for scientific excellence, innovation leadership, and talent development, Palomares builds bridges across academia, industry, and public health to advance vaccine and biopharmaceutical development.

ABSTRACT

Vaccine innovation achieves its full potential when scientific advances translate into accessible products, sustainable capabilities, and tangible public health benefits. Global partnerships are essential to this process, but their success depends on how effectively they respond to local needs and strengthen the institutions, expertise, and infrastructure required to develop and manufacture vaccines. Connecting global ambition with local implementation is therefore central to both epidemic preparedness and long-term health resilience.

Drawing on perspectives from the Scientific Advisory Committee of the Coalition for Epidemic Preparedness Innovations (CEPI) and leadership at the Institute of Biotechnology of the National Autonomous University of Mexico (UNAM), this lecture will examine how international collaboration can support vaccine innovation while building durable national and regional capacity. It will consider the complementary roles of global health organizations, academic institutions, industry, and regulatory authorities in advancing promising technologies and creating pathways from research to clinical development and manufacturing.

A central theme is that technology transfer must extend beyond the delivery of a production process. Meaningful local impact requires the transfer and development of knowledge, analytical capabilities, quality systems, and problem-solving expertise. It also depends on sustained investment in people and institutions, early engagement with regulatory requirements, and partnerships that align scientific objectives with public health priorities. Experiences in recombinant vaccine development, academic-industry collaboration, and the establishment of infrastructure for biopharmaceutical characterization will illustrate the opportunities and practical challenges involved.

The presentation will also explore how preparedness goals can inform capacity building between emergencies. Efforts to accelerate vaccine development must be accompanied by strategies that enable local partners to adapt technologies, maintain operational readiness, and contribute scientific solutions of their own. In this context, local institutions are essential contributors to a more responsive and geographically diverse vaccine innovation ecosystem.

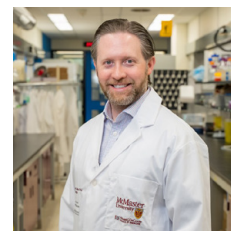
Ultimately, strengthening vaccine innovation requires partnerships that connect discovery with implementation and shared global objectives with locally defined priorities. This lecture will offer a framework for considering partnership success through both scientific progress and the capabilities that remain: skilled teams, stronger institutions, credible development pathways, and the ability to respond to future health threats. These enduring outcomes are what turn global collaboration into lasting local impact.

Matthew Miller

MCMASTER UNIVERSITY, CANADA

Active and Passive Mucosal Immunization Strategies for Improved Pandemic Preparedness

Wednesday 14 October 2026 • 09:00-09:25 • Plenary Session 5: One Health and Pandemic Preparedness



BIOGRAPHY

Dr. Matthew S Miller is Executive Director of NexusHealth, and Scientific Director of the M.G. DeGrootte Institute for Infectious Disease Research at McMaster University. He also serves as Co-Director of Canadian Pandemic Preparedness Hub (CP2H). He is a Professor in the Department of Biochemistry and Biomedical Sciences and was granted the title of University Scholar in 2025. Dr. Miller holds a Canada Research Chair in Viral Pandemics.

Dr. Miller completed his PhD in Microbiology and Immunology at the University of Western Ontario, followed by a postdoctoral fellowship in Virology at the Icahn School of Medicine at Mount Sinai in New York, NY under the mentorship of Dr. Peter Palese. He was recruited to McMaster University in 2014 and has authored over 100 peer-reviewed publications in leading journals. He has received several major awards and distinctions, including a CIHR New Investigator Award, the CIHR Bhagirath Singh Early Career Award in Infection and Immunity, and an Early Researcher Award from the Government of Ontario, a Distinguished Alumni Award for Excellence in Basic Science from Western University, the Canadian Society for Virology Grandvaux-McCormick Award for Service to Canadian virology, and the CIHR Leadership Award for Excellence in Vaccine Research. He was elected to the Royal Society of Canada College of New Scholars in 2024. Dr. Miller is featured in the book *"Canadians Who Innovate: The Trailblazers and Ideas That are Changing the World"* by Roseann O'Reilly Runte (ISBN13: 9781668023853).

Dr. Miller's research program is focused primarily on pandemic prevention, especially the development of broadly-protective vaccines, antibodies, therapeutics, and diagnostics. His team is also interested in understanding the way that viral infections and the immune response contribute to genetic and neurodegenerative conditions (e.g., ALS). He sits the scientific advisory board of several major pharmaceutical companies. He is a member of the Canadian National Advisory Committee on Immunization (NACI) COVID-19 Working Group and the H5Nx Highly Pathogenic Avian Influenza Working Group. He serves on the Public Health Agency of Canada Expert Panel on H5Nx Highly Pathogenic Avian Influenza (HPAI) and the PHAC Expert Advisory Panel on Hantavirus and Ebolavirus. He was elected Secretary-Treasurer of the Canadian Society for Virology from 2021-2022. Dr. Miller is co-founder and Chief Scientific Officer of AeroImmune Inc.

ABSTRACT

Influenza virus and coronaviruses have caused major pandemics and pose a serious threat for future human outbreaks. Additionally, these viruses circulate endemically in humans and pose a formidable challenge to vaccine-mediated protection due to their rapid ability to select for mutations that evade pre-existing immunity. In order to more effectively protect the human population from future pandemics and the endemic circulation of these viruses, new vaccine strategies are needed that can provide broader and more durable protection. Mucosal vaccination has become particularly attractive as a means of more effectively preventing respiratory virus infections. In addition to stimulating more potent adaptive immune responses at the site of infection, mucosal immunization can also elicit local innate responses that contribute to the breadth of protection that these vaccines can offer. Our team has developed complementary next-generation approaches to broadly protective "active" and "passive" immunization. First, we have developed a next-generation inhaled chimpanzee

adenovirus-vectored vaccine capable of broad protection against coronavirus infection. We have shown that this vaccine elicits broadly-protective humoral and cellular immunity – along with local trained innate immunity capable of mediated heterologous protection. This vaccine has recently successfully completed Phase I clinical trials and is now being evaluated in Phase II trials. We have also complementary “passive” immunization strategies that use antibodies and aptamers delivered to the respiratory mucosa to provide broad protection. Passive immunization strategies are often overlooked but are critical to providing protection to vulnerable populations who fail to mount effective adaptive immune responses. Together, these novel platforms provide the opportunity to protect the human population more effectively from current endemic virus circulation, and against future pandemics.

Mathilde Richard

ERASMUS MC, THE NETHERLANDS

Antigenic evolution of H5 viruses and subtype-wide H5 vaccine development

Wednesday 14 October 2026 • 09:25-09:50 • Plenary Session 5: One Health and Pandemic Preparedness



BIOGRAPHY

Mathilde Richard is a biochemical engineer and molecular virologist. She completed her PhD in France in 2010 under the supervision of Prof. Bruno Lina, studying the resistance of influenza A viruses to neuraminidase inhibitors. She then joined the Department of Viroscience for her postdoctoral studies, which focused on the pathogenesis, virulence, and transmissibility of influenza A viruses, with a particular emphasis on the genetic and phenotypic viral factors involved in the emergence of new pandemics. Since 2018, she has been a principal investigator in the Department of Viroscience. Her team's research focuses on understanding the genesis, emergence, and pathogenesis of highly pathogenic avian influenza viruses, as well as on developing new vaccination strategies to address antigenic diversity in the context of pandemic preparedness.

ABSTRACT

Highly pathogenic avian influenza A(H5) viruses globally impact wild and domestic birds and have caused severe infections in mammals, including humans, underscoring their pandemic potential. The antigenic evolution of the A(H5) hemagglutinin (HA) poses challenges for pandemic preparedness and vaccine design. We will present our recent work characterizing the global antigenic evolution of the A(H5) HA using antigenic cartography. The A(H5) antigenic map was used to develop a novel concept of broad reactivity: antigenic centrality. We developed an antigenically central vaccine, eliciting antibody responses that broadly cover the A(H5) antigenic space. We will also show how this high-resolution A(H5) antigenic map is used as a tool to further monitor the antigenic evolution of emerging A(H5) viruses and to understand the breadth of immune responses in individuals sequentially immunized with A(H5) vaccines. This work showcases how understanding antigenic evolution can inform the development of vaccine strategies conferring subtype-wide influenza A(H5) immunity and demonstrates the value of antigenic maps for evaluating vaccine-induced immune responses using antibody profiles and landscaping approaches.

Emilie Karafillakis

LONDON INSTITUTE FOR TROPICAL MEDICINE AND HYGIENE, UNITED KINGDOM

The State of Vaccine Confidence in 2026

Wednesday 14 October 2026 • 11:00-11:25 • Concurrent Session 7: Vaccine Confidence



BIOGRAPHY

Dr Emilie Karafillakis, is an Assistant Professor and the European Director of the Vaccine Confidence Project at the Vaccine Confidence Project™, at the London School of Hygiene & Tropical Medicine and the University of Antwerp. She is a senior social scientist with more than 10 years of experience in international research and teaching in academia. With a background in public health, infectious disease control, and health systems and policies research, her work focuses on understanding individual and group beliefs, attitudes and confidence in health interventions and assess how these can influence public health control measures and health promotion strategies, including vaccination. She has extensive experience on issues of vaccine confidence in Europe, including among parents, adolescents, pregnant women and healthcare professionals.

ABSTRACT

Drawing on the latest data from the Vaccine Confidence Project, this talk provides an overview of vaccine confidence today, across the life course and including trends in gender and age differences. Key forces reshaping the landscape of vaccine confidence will be explored, including the politicization of vaccination and the way information systems have changed around us.

Ève Dubé

LAVAL UNIVERSITY, CANADA

Beyond Vaccine Hesitancy: Understanding and Rebuilding Trust in Vaccination in Complex Social Ecosystems

Wednesday 14 October 2026 • 11:25-11:50 • Concurrent Session 7: Vaccine Confidence



BIOGRAPHY

Ève Dubé is a professor of Anthropology at Laval University in Quebec City, Canada and a researcher at the *Centre de recherche du CHU de Québec-Université Laval*. Her field of expertise is anthropology of public health. She is particularly interested in the social, cultural, historical, and religious dimensions of infectious disease prevention. She holds a Canadian Institute of Health Research Applied Public Health Chair on the Anthropology of Vaccination. As an expert on vaccine acceptance, she sits on different national and international committees, including Canada's National Advisory Committee on Immunization. She chairs the Social Science and Humanities Network of the Canadian Immunization Research Network and is the scientific co-director of the Bridge Research Consortium.

ABSTRACT

Trust has become central to vaccination efforts, yet public health responses often rest on outdated assumptions about how trust is built and lost. This presentation will examine the key factors that shape trust in vaccination and challenge common misconceptions that continue to guide intervention design. Drawing on research conducted in Canada, including with Indigenous and religious communities, it will show that what is often labelled "vaccine hesitancy" frequently reflects deeper issues: historical trauma, strained relationships with health institutions, and practical barriers to access. Rebuilding trust therefore requires understanding these root causes and designing context-specific, multicomponent strategies, rather than relying on more information alone.

Helton Santiago

FEDERAL UNIVERSITY OF MINAS GERAIS, BRAZIL

Preclinical and clinical development of a cellular immunity-based Covid-19 vaccine

Wednesday 14 October 2026 • 11:00-11:25 • Concurrent Session 8: Emerging Infections



BIOGRAPHY

Helton Santiago is graduated in Medicine (1995-2001) with master's and doctorate degrees in Biochemistry and Immunology from the Federal University of Minas Gerais (2001-2002), a post-doctorate from George Washington University (Washington, DC, USA, 2007 -2008) in vaccine development and post-doctorate by the National Institutes Of Health (Bethesda, MD, 2008-2012) in the study of the interaction between allergies and helminth infections. He is currently an associate professor in the Department of Biochemistry and Immunology at UFMG working in clinical research, and basic research with emphasis on the human immune response to viral infections, operational tolerance in transplants, and cancer immunology. He also serves as clinical director of the Vaccine Technology Center of UFMG and specialist in the Brazilian National Ethics Instance.

ABSTRACT

SARS-COV-2 is a coronavirus showing constant emergency of variant and subvariants, which presses the update of Covid-19 vaccines regularly. The antigen that most of vaccines target is the Spike Protein, which is also the most variable antigen of the vaccines. SpiN-Tec is a chimeric protein combining RBD and Nucleocapsid that showed promising protection in animal models inducing strong cellular immunity, but no neutralizing antibodies. Vaccination with SpiN-Tec was able to prevent mortality, pulmonary pathology and control virus load in K18-ACE-2 mice and hamsters when challenged with Wuhan, Delta and Omicron (BA1, JN1 and KP2). We vaccine was evaluated for safety and immunogenicity in healthy Brazilian adults in a phase I/II study. The study was double-blind, randomized, controlled with active comparator (Covishield in the phase I and Comirnaty Bivalent in phase II). The study was tested 3 doses in the phase I and the intermediate (60 ug) was selected to move forward to phase II. In the phase II, 318 individuals were randomized, being 158 in the Cormirnaty and 160 in the SpiN-Tec group. Median age was 41 yo (IQR 27-55), 53.5% were female. SpiN-Tec was considered safe causing mild to moderate pain, swelling and erythema at injection site, headache, fatigue, myalgia and nausea, SpiN-Tec induced robust anti-N IgG and IFNg in response to both N and S antigens but no neutralizing antibodies. During follow-up, we observed 39 breakthrough infections after 28 days of vaccination, 24 (15.2%) in the Comirnaty and in 15 (9.3%) in the SpiN-Tec group. Despite the study was not powered for efficacy, we observed a relative reduction of 44% in the number of SpiN-Tec group, although not statistically significant (log-rank $p=0.11$). This results indicate that SpiN-Tec is safe, immunogenic and provides a protection against SARS-COV-2 independently of neutralizing antibodies against a variety of SARS-COV-2 variants.

Alejandra Capozzo

UNIVERSIDAD ABIERTA INTERAMERICANA, ARGENTINA

Co-Infections and Immunomodulation: Hurdles and Drivers in Bovine Vaccinology

Wednesday 14 October 2026 • 11:00-11:25 • Concurrent Session 9: Veterinary Vaccines



BIOGRAPHY

Dr Alejandra V. Capozzo is Director of the Centre for Advanced Studies in Health Sciences (CAECIHS) at Universidad Abierta Interamericana (UAI) in Buenos Aires, Argentina, and a Professor and Principal Researcher at the National Scientific and Technical Research Council (CONICET). She obtained her PhD in Biological Sciences from the University of Buenos Aires, specialising in vaccinology and applied immunology, with a particular focus on foot-and-mouth disease. She completed her postdoctoral training in neonatal immunology at the University of Maryland, United States.

With more than 25 years of experience in applied veterinary immunology and vaccine development, Dr Capozzo's work focuses on immune responses to infectious diseases of major animal health and economic importance. Her research combines fundamental and translational approaches, with particular emphasis on the development, evaluation and quality control of veterinary vaccines, the design and validation of serological tools, and the study of biological and environmental factors that influence vaccine performance under field conditions.

Her scientific contributions have been especially significant in the field of foot-and-mouth disease, where she has worked on vaccine-induced immunity, correlates of protection, diagnostic and serological methods, and the impact of coinfections and host-related factors on vaccine efficacy. She has also contributed to research on bovine viral diseases, helminth infections, neonatal immunity and novel immunomodulatory strategies for livestock.

Dr Capozzo currently serves as Chief Executive Officer of the Global Foot-and-Mouth Disease Research Alliance (GFRA). She is also Chair of the Veterinary Immunology Committee of the International Union of Immunological Societies (VIC-IUIS), a member of the Board of Directors of the International Society for

Vaccines (ISV), and Coordinator of the Latin American Veterinary Immunology Network (RedLatInmVet). In addition, she contributes as an expert and consultant to international initiatives in animal health, vaccinology, disease surveillance and research coordination.

Her work includes strong engagement with industry and technology transfer. She has contributed to the development and implementation of tools for veterinary vaccine production and quality control, including an in-process control kit for foot-and-mouth disease vaccines and immunomodulatory approaches designed to improve vaccine responses in livestock. She is also committed to mentoring early-career scientists, strengthening regional research capacity, and fostering interdisciplinary networks that connect veterinary immunology, vaccinology and One Health priorities across Latin America and beyond. Throughout her career, she has promoted collaboration between academia, industry, regulatory agencies and international organisations, with the aim of translating scientific knowledge into practical solutions for animal health, food security and sustainable livestock production.

ABSTRACT

Veterinary vaccine evaluations are typically conducted in healthy animals under controlled settings, contrasting

with the complex epidemiological and immunological landscapes of natural grazing environments. In endemic regions, concurrent and persistent immunoregulatory infections dynamically shape host immunity, hindering disease control. Over the last decade, our laboratory has investigated how chronic endemic pathogens, specifically *Fasciola hepatica* and Bovine Leukemia Virus (BLV), compromise the protective efficacy of foot-and-mouth disease virus (FMDV) vaccines and novel mRNA platforms. By combining controlled experimental protocols in cattle and murine models with field surveillance in livestock and water buffalo (*Bubalus bubalis*) populations, we study the mechanisms driving parasite-mediated vaccine interference. Our findings reveal that the timing of co-infection is a critical determinant of immune outcomes. While animals infected prior to vaccination preserve germinal center dynamics and affinity maturation, those infected post-vaccination display a distinct “quality gap.” This chronic, parasite-driven immunoregulation selectively impairs the qualitative maturation of the humoral response, significantly reducing antibody avidity indices and abrogating the booster effect, while leaving absolute antibody quantities and conventional titers unaltered. This qualitative deficit correlates with diminished cell-mediated immunity, evidenced by reduced IFN- γ production. Furthermore, our field studies in naturally infected water buffaloes provide the first systemic evidence of herd-wide degradation across all evaluated serological parameters, including neutralizing titers. We demonstrated that immunotolerance is platform-dependent; while viral and mRNA platforms are highly susceptible, bacterial vaccines heavily engage alternative Pattern Recognition Receptors (PRRs) that partially circumvent helminth-induced suppression. To counteract this parasite-immunity cycle, we explored strategic interventions, showing that targeted anthelmintic therapy with triclabendazole restores antibody avidity, and that co-administering pro-inflammatory PRR agonists (such as Dectin-1 beta-glucans) at the time of vaccination may rescue compromised immunity by driving a balanced immune shift. Together, this body of work support that vaccine performance under field realities depends heavily on herd-health status, highlighting the necessity of integrating advanced diagnostic matrices, strategic management and next-generation adjuvants into global livestock health planning.

Key Words: Foot-and-Mouth Disease; *Fasciola hepatica*; Antibody Avidity

Tim Hirst and Chloe G

GPN VACCINES, AUSTRALIA

Developing Next Generation Broad-Spectrum Bacterial Vaccines

Wednesday 14 October 2026 • 11:25-11:50 • Concurrent Session 9: Veterinary Vaccines



BIOGRAPHY

Dr Tim Hirst is the Chairman and CEO of GPN Vaccines Inc., a US biotechnology company with an Australian subsidiary conducting clinical trials of a new vaccine against the world's foremost bacterial pathogen, *Streptococcus pneumoniae*. He is an entrepreneur and investor with extensive expertise in the life sciences, executive management and venture capital investment. He was previously the Vice President and Deputy Vice Chancellor for Research & Innovation at The University of Sydney and Professor & Head of Microbiology at the University of Bristol, UK.

Dr Chloe Gates is the Associate Director of Early Phase Development at GPN Vaccines. She completed her PhD on streptococcal vaccine development at the University of Adelaide in 2024 and has received recognition for her work in vaccine immunology at international conferences. She is a co-inventor on a patent filed on pneumococcal vaccine development and was awarded the Derrick Rowley Prize in Microbiology and Immunology in 2019.

ABSTRACT

GPN Vaccines is a clinical-stage biotechnology company developing a new generation of broadly protective bacterial vaccines. Its lead product, Gamma-PN is an investigational, serotype-independent pneumococcal vaccine designed to address a fundamental limitation of currently available serotype-specific vaccines. More than 100 serotypes of *Streptococcus pneumoniae* exist, yet currently available vaccines provide protection against only a subset, requiring manufacturers to continually develop vaccines incorporating additional serotypes. Gamma-PN is a non-encapsulated whole cell vaccine designed to generate immune responses against protein antigens shared across all pneumococcal strains, offering the potential to elicit protection independent of capsular serotype. GPN is building a broader bacterial vaccine portfolio beyond Gamma-PN. This includes Gamma-SU, a vaccine designed to prevent post-weaning meningitis in pigs, which is a globally endemic disease responsible for significant economic losses to the pig industry. It is also an emerging zoonotic pathogen of humans. Like *Streptococcus pneumoniae*, *Streptococcus suis* has multiple serotypes; however, the only commercially available vaccine Porcilis® produced by MSD Animal Health is designed to prevent infection by just one serotype, serotype 2. Gamma-SU is designed to offer serotype-independent protection against all serotypes. Porcine trials have demonstrated that Gamma-SU elicits functional serotype-independent opsonophagocytic antibodies that kill a diversity of *Streptococcus suis* serotypes. These data support GPN Vaccines' approach to developing whole cell vaccines with broad platform potential for overcoming the limitations of serotype-specificity.

Pascal Geldsetzer

STANFORD UNIVERSITY, USA

A natural experiment on the effect of herpes zoster vaccination on dementia

Wednesday 14 October 2026 • 14:30-14:55 • ISV Paper of the Year (Virtual)



BIOGRAPHY

Pascal Geldsetzer is an Assistant Professor of Medicine at Stanford University and a Biohub Investigator. His research focuses on identifying and evaluating the most effective interventions for improving health at older ages. In addition to leading several randomized trials, his methodological emphasis lies on the use of natural experiments to ascertain causal effects in large observational datasets, particularly in electronic health record data. He has won an NIH New Innovator Award, the Pershing MIND Prize, a Biohub investigatorship, and three NIH R01 grants as Principal Investigator. In 2026, he was named one of the 100 most influential people in health and medicine globally by TIME Magazine (The TIME100 Health list) for his work on the link between shingles vaccination and dementia.

ABSTRACT

Neurotropic herpesviruses may be implicated in the development of dementia^{1,2,3,4,5}. Moreover, vaccines may have important off-target immunological effects^{6,7,8,9}. Here we aim to determine the effect of live-attenuated herpes zoster vaccination on the occurrence of dementia diagnoses. To provide causal as opposed to correlational evidence, we take advantage of the fact that, in Wales, eligibility for the zoster vaccine was determined on the basis of an individual's exact date of birth. Those born before 2 September 1933 were ineligible and remained ineligible for life, whereas those born on or after 2 September 1933 were eligible for at least 1 year to receive the vaccine. Using large-scale electronic health record data, we first show that the percentage of adults who received the vaccine increased from 0.01% among patients who were merely 1 week too old to be eligible, to 47.2% among those who were just 1 week younger. Apart from this large difference in the probability of ever receiving the zoster vaccine, individuals born just 1 week before 2 September 1933 are unlikely to differ systematically from those born 1 week later. Using these comparison groups in a regression discontinuity design, we show that receiving the zoster vaccine reduced the probability of a new dementia diagnosis over a follow-up period of 7 years by 3.5 percentage points (95% confidence interval (CI) = 0.6–7.1, $P = 0.019$), corresponding to a 20.0% (95% CI = 6.5–33.4) relative reduction. This protective effect was stronger among women than men. We successfully confirm our findings in a different population (England and Wales's combined population), with a different type of data (death certificates) and using an outcome (deaths with dementia as primary cause) that is closely related to dementia, but less reliant on a timely diagnosis of dementia by the healthcare system¹⁰. Through the use of a unique natural experiment, this study provides evidence of a dementia-preventing or dementia-delaying effect from zoster vaccination that is less vulnerable to confounding and bias than the existing associational evidence.

Joren Raymenants

UNIVERSITY OF ANTWERP, BELGIUM



The Flu Air Shedding and Immune Monitoring (FLAIM) study, the first controlled human infection study at Vaccinopolis, Belgium

Wednesday 14 October 2026 • 14:55-15:20 • Plenary Session 6: Challenge Studies

BIOGRAPHY

I'm a general internist working as postdoctoral researcher on controlled human infection model studies at Vaccinopolis, Belgium. My background is in internal medicine, infectious disease epidemiology, public health and clinical trial conduct. For the FLAIM study, I authored the protocol, took the role of project manager and PI, and analyzed the clinical and virological data. Immunological analyses continue in collaboration with partners

ABSTRACT

The Flu Air Shedding and Immune Monitoring (FLAIM) study is the first controlled human infection model (CHIM) study to have taken place at Vaccinopolis, a state of the art clinical research facility with 30 BSL3 participant rooms, an ambulatory trial unit and research labs in Antwerp.

This presentation will be the first to present FLAIM study results. The study aims to disentangle the factors that determine whether an individual sheds Influenza virus and poses an infection risk to their surroundings, by assessing a range of viral shedding, exhaled breath particle and (mucosal) immunity parameters.



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ORAL ABSTRACTS

PLENARY SESSION 1: POPULATION IMPACT OF VACCINATION

Monday 12 October 2026 • 11:25–11:40 • Okapi 1, 2, 3

Recombinant Staphylococcus Aureus Vaccine demonstrating 73.3% Protective Efficacy in Phase 3 clinical study in China

JinXin LI

Nanjing Medical University, China

Background: Staphylococcus aureus (S. aureus), including methicillin-resistant S. aureus (MRSA), is a leading cause of perioperative infection and hospital-acquired infections. No licensed vaccine against S. aureus infection exists.

Methods: We conducted a multicenter, randomized, double-blind, placebo-controlled phase 3 trial of rFSAV, a recombinant five-antigen alum-adjuvanted vaccine, in adults 18 to 70 years of age undergoing elective closed-fracture orthopedic surgery from 66 hospitals, in China. Participants were randomly assigned in a 1:1 ratio to receive rFSAV or placebo, with two priming doses on day 0 and a booster dose on day 7. The primary objective was to evaluate the protective efficacy against invasive S. aureus infection within 42 days after surgery.

Results: From August 29, 2022 through May 23, 2025, 6326 participants were screened and 6014 were randomized. rFSAV demonstrated a protective efficacy of 73.3% (95% CI, 46.2 to 86.7) against invasive S. aureus infection within 42 days after surgery. Vaccine-induced functional antibody responses peaked by day 14 and waned after day 42. Adverse events were more frequent with rFSAV than placebo but were predominantly mild or moderate. Serious adverse events occurrence in participants in the rFSAV and placebo groups were comparable, with no difference observed between the groups.

Conclusions: rFSAV provided substantial perioperative protection against S. aureus infection after elective orthopedic surgery and an acceptable safety profile, supporting its potential to prevent invasive S. aureus infection in surgical patients.

PLENARY SESSION 1: POPULATION IMPACT OF VACCINATION

Monday 12 October 2026 • 11:40–11:55 • Okapi 1, 2, 3

Safety and Immunogenicity of a Novel Trivalent Virus-Like Particle Poliovirus Vaccine (VPV): A Phase 1, Randomized, Observer-Blind Trial

Jinbo GOU, Qiaoling YAN

CanSino Biologics Inc., China, People's Republic of

Non-infectious, scalable virus-like particle (VLP) based polio vaccine offers a promising alternative for global polio eradication.

In a randomized, observer-blind, Phase 1 trial, the safety and immunogenicity of a trivalent VLP-based vaccine (VPV) were evaluated in 72 healthy adults across low, medium, and high doses compared to conventional IPV (cIPV). The safety profiles for all VPV formulations were comparable to cIPV; adverse events were exclusively mild-to-moderate, with no serious adverse events reported.

By day 29, VPV induced substantial neutralizing antibody titers across all three serotypes, with a clear dose-dependent response observed. Responses for serotypes 1 and 2 were comparable to cIPV, and while serotype 3 titers were lower, they remained well above the protective threshold through day 180. In conclusion, VPV is a safe, highly immunogenic candidate for advancing global polio eradication.

PLENARY SESSION 2: MUCOSAL VACCINES

Monday 12 October 2026 • 14:20–14:35 • Okapi 1, 2, 3

Charting Mucosal Immune Responses to Influenza using Human Immune-competent Organoids

Martin BEUKEMA¹, Jacqueline DE VRIES¹, Nilima DINESH KUMAR¹, Nils DOESBURG¹, Barbro MELGERT^{2,3}, Anke HUCKRIEDE¹

¹ University Medical Center Groningen, Netherlands, The

² Groningen Research Institute for Pharmacy, Department of Molecular Pharmacology, University of Groningen, Groningen, Netherlands

³ Groningen Research Institute for Asthma and COPD, University Medical Center Groningen, University of Groningen, Groningen, Netherlands

Background: Understanding the early immune events that determine protection against influenza virus infection remains a major challenge for mucosal vaccine design. Given that influenza infection is rapidly initiated at the respiratory mucosa, we hypothesize that early epithelial-immune cell interactions are determinants of both susceptibility and antiviral immunity to the influenza virus.

Methods: To mechanistically dissect these early mucosal immune responses in a human-relevant context, we developed an immune-competent, apical-out airway organoid model as New Approach Methods to enable direct modelling of how macrophages, neutrophils, and monocytes modulate early infection dynamics and host responses.

Results: Apical-out organoids recapitulate key features of the human upper airway epithelium, including ciliated cell predominance and α 2,6-linked sialic acid expression, and supported productive influenza A replication. Influenza virus infection triggered modest epithelial cytokine responses dominated by CXCL8 and type III interferons. Incorporation of individual innate immune cell populations revealed strikingly distinct antiviral programs. Macrophages potently suppressed viral titers (>10-fold), restricted infection in the organoids, and amplified type I/III interferons and pro-inflammatory cytokines. Neutrophils reduced viral titers but did not constrain viral replication in organoids. Instead, neutrophils dampened interferon responses and increased MPO levels, suggesting primarily non-cytokine-mediated antiviral mechanisms. Monocytes exerted moderate antiviral activity, limiting dissemination with minimal cytokine induction.

Conclusion/discussion: This study established a physiologically relevant platform for modelling epithelial-immune interactions at the respiratory mucosa and identifies immune cell-type-specific innate strategies that govern early influenza control. This preclinical system provides a foundation for defining mucosal correlates of protection and for guiding immune-driven strategies in next-generation influenza therapeutics and vaccine design.

PLENARY SESSION 2: MUCOSAL VACCINES

Monday 12 October 2026 • 14:35–14:50 • Okapi 1, 2, 3

Environmental drivers of oral typhoid vaccine responses in Uganda: dissecting rural–urban differences and the role of *Schistosoma mansoni*

Bridgious WALUSIMBI^{1,2}, Agnes NATUKUNDA^{1,2}, Rebecca AMONGIN¹, Victoria HEYROUD⁵, Claire BAINE¹, Jacent NASSUNA¹, Emily L WEBB³, Alison M ELLIOTT⁴, Gyaviira NKURUNUNGI^{1,2}

¹ MRC/UVRI and LSHTM Uganda Research Unit, Uganda

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⁵ Edinburgh Napier University, UK

Introduction/Background: Oral vaccines often perform suboptimally in high-exposure settings, yet the underlying drivers remain poorly defined. Environmental factors, including helminth infections and enteric exposures, are hypothesised to shape mucosal immunity and vaccine responsiveness. We investigated rural–urban differences in immune responses to oral typhoid vaccination in Uganda and evaluated the contribution of *Schistosoma mansoni* within this broader environmental context.

Materials/Methods: We analysed 697 adolescents (9–17years) from POPulation differences in VACcine responses (POPVAC) programme, a set of randomised controlled trials, in two contrasting settings, in Uganda: schistosomiasis-endemic rural Lake Victoria islands and urban Entebbe municipality. Participants received oral typhoid vaccine (Ty21a). Salmonella Typhi O-lipopolysaccharide (O:LPS)-specific plasma IgA, copro-IgA and copro-IgG were quantified by ELISA four weeks post-vaccination. *S. mansoni* infection was defined by plasma circulating anodic antigen and/or stool PCR. Adjusted linear regression assessed rural–urban differences and infection associations. Causal mediation analysis was used to estimate the contribution of *S. mansoni* to setting-specific differences.

Results: *Schistosoma mansoni* prevalence was substantially higher in rural than urban participants (71% vs 43%, $p < 0.001$). Urban participants elicited stronger post-vaccination responses across compartments: plasma IgA (adjusted geometric mean ratio [aGMR] 1.44, 95% CI 1.12–1.84), copro-IgA (1.71, 1.09–2.69) and copro-IgG (1.26, 1.05–1.51). In contrast, total copro-IgA did not differ, indicating preserved baseline mucosal IgA production but selective impairment of antigen-specific responses.

Associations between *S. mansoni* infection and vaccine responses were context-dependent. In rural participants, infection was associated with reduced plasma IgA (0.79, 0.65–0.97), whereas in urban participants it was associated with reduced copro-IgA (0.64, 0.44–0.93).

Mediation analysis demonstrated that rural–urban differences in systemic responses were largely independent of *S. mansoni*. However, reduced mucosal IgA responses in the rural setting were partially mediated by infection (natural indirect effect 1.15, 95% CI 1.02–1.30), accounting for approximately one-quarter of the total effect.

Discussion/Conclusion: These data demonstrate pronounced rural–urban differences in immune responses to oral typhoid vaccination, characterised by stronger systemic and mucosal *S. Typhi*-specific antibody responses in urban participants. Our causal mediation analyses suggest that while rural–urban differences in systemic Ty21a responses are predominantly driven by other factors, the helminth does contribute to differences in antigen-specific mucosal IgA responses. By integrating antigen-specific systemic and mucosal antibody responses and causal mediation analyses, this study provides a comprehensive evaluation of Ty21a immunogenicity and highlights environmental exposures as key determinant of heterogeneity in oral vaccine responses.

PLENARY SESSION 2: MUCOSAL VACCINES

Monday 12 October 2026 • 14:50–15:05 • Okapi 1, 2, 3

Inhaled aerosol vaccination with an adenoviral-vectored TB vaccine induces robust respiratory mucosal immunity in humans

Sam AFKHAMI, Mangalakumari JEYANATHAN, Dominik FRITZ, Emilio AGUIRRE, Karen HOWIE, Anna ZGANIACZ, Anna DVORKIN-GHEVA, Michael THOMPSON, Richard SILVER, Ruth CUSACK, Brian LICHTY, Paul O'BYRNE, Martin KOLB, Maria Fe MEDINA, Myrna DOLOVICH, Imran SATIA, Gail GAUVREAU, Zhou XING, Fiona SMAILL

McMaster University, Canada

Background: Tuberculosis remains a leading cause of death from a single infectious agent, and BCG, the only licensed TB vaccine, provides inconsistent protection against pulmonary disease in adults. Most next-generation candidates have been designed for parenteral, intramuscular (i.m.) delivery, yet this route consistently fails to improve on BCG and induces poor immunity at the site where infection is established: the lung. Protection against pulmonary TB depends on respiratory mucosal immunity, including airway tissue-resident memory T cells and trained innate immunity in alveolar macrophages. Critically, induction of these airway responses requires vaccine delivery directly to the respiratory mucosa rather than via the periphery. Inhaled aerosol vaccination offers a needle-free means of achieving this, but its ability to induce mucosal immunity with an adenovirus-vectored vaccine in humans had not been previously demonstrated. We conducted a phase I trial to evaluate the safety and immunogenicity of a human serotype-5 adenovirus-vectored TB vaccine (AdHu5Ag85A) delivered by inhaled aerosol versus i.m. injection in previously BCG-vaccinated adults.

Methods: BCG-vaccinated adults were assigned to receive a single dose of AdHu5Ag85A by either inhaled aerosol or i.m. injection. Aerosol vaccine was delivered to the respiratory tract through the inhaled route using the Aerogen Solo vibrating-mesh nebulizer with tidal breathing. Safety and lung function were monitored following vaccination. Systemic immunity was assessed in peripheral blood, and airway mucosal responses were assessed in bronchoalveolar lavage fluid obtained by bronchoscopy before and after vaccination, using intracellular cytokine staining, multiplex cytokine analysis, and transcriptomic profiling of alveolar macrophages.

Results: Both aerosol and i.m. vaccination were safe and well tolerated, with only infrequent, mild, and transient adverse events and no serious adverse events; lung function remained unchanged from baseline. Aerosol vaccination markedly induced antigen-specific, polyfunctional CD4⁺ and CD8⁺ T cell responses in the airways, whereas i.m. injection failed to elicit airway responses, confirming that mucosal immunity is induced only through inhaled delivery. These airway T cells acquired a tissue-resident memory phenotype, co-expressing the residency markers CD69 and CD103 along with the lung-homing integrin CD49d, again only after aerosol vaccination. Aerosol delivery further drove persisting transcriptional reprogramming of alveolar macrophages consistent with trained innate immunity, a feature not seen following i.m. injection. Both routes induced comparable systemic T cell responses in the blood.

Conclusions: Inhaled aerosol delivery of an adenovirus-vectored vaccine safely induces the hallmarks of respiratory mucosal immunity in humans which i.m. injection cannot achieve. These findings support inhaled aerosol vaccination as a route for next-generation TB vaccines.

CONCURRENT SESSION 1: ADJUVANTS*Monday 12 October 2026 • 15:30–15:55 • Okapi 1, 2, 3***Open-access adjuvants for prophylactic human vaccines****Marcelle Paulette VAN MECHELEN***Vaccine Formulation Institute, Switzerland*

The Vaccine Formulation Institute (VFI) is a Swiss-based institute dedicated to developing clinically relevant adjuvants that are made available to the vaccine community under open-access terms. VFI's portfolio includes three saponin-containing adjuvants: SQ (a squalene-in-water emulsion with QS-21 saponin), LQ (a liposome-based adjuvant with QS-21 saponin), and LMQ (a liposome-based adjuvant containing a synthetic TLR4 ligand and QS-21 saponin), as well as Sepivac SWE™ (a squalene-in-water emulsion). These adjuvants are compatible with diverse antigen types and have demonstrated consistent performance across multiple preclinical models.

The three saponin-containing adjuvants (LQ, SQ and LMQ) have been evaluated across a broad range of indications and preclinical models by VFI and its collaborative network. Studies led by VFI and partners have demonstrated that these adjuvants promote robust T-cell responses with a Th1 bias as well as functional antibody production when administered with various antigen platforms. Immunogenicity and /or protective efficacy has been documented for multiple vaccine candidates, targeting indications such as COVID-19, influenza, malaria, HIV/AIDS, MERS, tuberculosis, and Group A streptococcus.

Sepivac SWE™ has demonstrated safety and immunogenicity in Phase 1 and Phase 2 clinical trials, and a Phase 3 clinical study has recently been completed. Sepivac SWE™ is commercially available through Seppic and is provided by VFI under material transfer agreement for formulation and pre-clinical studies.

VFI's saponin-containing adjuvants (LQ, SQ, and LMQ) are all available at GMP grade, enabling their direct use in clinical-stage vaccine development under open-access terms.

CONCURRENT SESSION 1: ADJUVANTS

Monday 12 October 2026 • 16:20–16:35 • Okapi 1, 2, 3

Antigen cross-presentation potentiating cancer vaccine adjuvant for T cell expansion and synergy with anti-PD-1Giang Chau DANG¹, Vandara LOEURNG¹, Paopachapich PA¹, Chheng Y SENG¹, Shee Eun LEE^{1,2}, Joon Haeng RHEE^{1,2}¹ Chonnam National University, Korea, Republic of (South Korea)² FlagImmune, Republic of Korea.

Therapeutic cancer vaccines (TCVs) face challenges in preferentially stimulating CD8+ cytolytic T lymphocytes. The combination of immune checkpoint inhibitors (ICIs) and TCVs became a dominant trend for more efficacious tumor suppression. TCV adjuvants that strongly drive the cross-presentation of protective antigens and expand the CD8+ T cell population responsive to ICIs will surely bring much better outcomes. The specialized dendritic cell subset cDC1 is proficient in cross-presenting antigens and maintaining precursor-exhausted T cell (Tpex) cell population, which are robustly reinvigorated by anti-PD-1/PD-L1 ICIs. In this study, we introduce a novel hybrid adjuvant, Flt3L-FlaB (FB), designed to enhance the efficacy of TCVs by integrating FMS-like tyrosine kinase 3 ligand (Flt3L) with the immune-stimulating flagellin B (FlaB), a Toll-like receptor 5 (TLR5) agonist. In a preclinical immune-cold mouse tumor model, FB potently expanded and activated cross-presenting cDC1s. The cDC1 expansion and activation were accompanied by a rise in CD8+ T cells exhibiting stem-like memory (Tscm) and Tpex phenotypes in tumor tissue and draining lymph nodes, resulting in sustained efficacious anti-tumor immune responses. The combination of FB-adjuvanted TCV with anti-PD-1 therapy manifested significantly enhanced tumor eradication, which rendered treated mice persistently immune to metastasis and higher dosage cancer cell rechallenge with long-lasting immune memory. Multiple murine tumor models, including those of colon, cervical, and breast cancer, were employed to demonstrate the robust and broad-spectrum antitumor efficacy of the FB-adjuvanted TCV. Given the clinical challenges of achieving robust tumor-eradicating immune responses against poorly immunogenic tumor antigens, these findings suggest that FB could contribute to enhancing the therapeutic efficacy of TCVs in clinical practices, particularly as a powerful combination partner for ICI regimens.

CONCURRENT SESSION 1: ADJUVANTS

Monday 12 October 2026 • 16:35–16:50 • Okapi 1, 2, 3

Modulation of the bone marrow hematopoietic and immune cell landscape by vaccine adjuvants**Eleanor BURGESS^{1,2,3}, Moataz NOUREDDINE^{1,2,3}, Farah EL-AYACHE^{1,3}, Gabriel LAGHLALI^{1,3}, Johanna VANDEKERCHOVE^{1,3}, Lauren CHANG^{1,2,3}, Jeffrey DOWNEY⁴, Michael SCHOTSAERT^{1,3,5,6}**¹ Department of Microbiology, Icahn School of Medicine, New York, NY, United States² Graduate School of Biomedical Sciences, Icahn School of Medicine, New York, NY, United States³ Global Health and Emerging Pathogens Institute, Icahn School of Medicine, New York, NY, United States⁴ Cardiovascular Research Institute and the Department of Medicine, Cardiology, Icahn School of Medicine, New York, NY, United States⁵ Marc and Jennifer Lipschultz Precision Immunology Institute, Icahn School of Medicine, New York, NY, United States⁶ Icahn Genomics Institute, Icahn School of Medicine, New York, NY, United States

Vaccination against influenza virus is currently the best strategy to lessen disease burden. The low immunogenicity of the subunit vaccines and variation in effectiveness highlight the need for vaccine adjuvants. Rational vaccine design over the past decades has produced novel adjuvants, such as TLR7/8 agonists, aimed at eliciting Type 1 immune responses, like host responses against viral infections. TLR7/8 agonists induce type 1 IFNs which can have profound effects on hematopoietic stem and progenitor cells (HSPCs) in bone marrow. We aimed to evaluate how the TLR7/8 agonist, IMDQ-PC, designed to adjuvant the inactivated influenza vaccine, affects HSPCs and hematopoietic output. C57BL/6 mice were vaccinated via the intramuscular route with the quadrivalent inactivated influenza vaccine (QIV) with or without IMDQ-PC or with PBS, and HSPCs in bone marrow were characterized using flow cytometry. We found that vaccination with IMDQ-PC significantly lowers the frequency of monocytes in bone marrow while increasing their frequency in the blood at day 4, indicative of increased egress into the periphery. Vaccination with IMDQ-PC induces phenotypic changes by upregulating Sca-1 expression on HSPCs for up to 14 days post vaccination, suggesting type 1 IFN signaling in the bone marrow. Adjuvanting QIV with IMDQ-PC also increased the proportion of downstream granulocyte/monocyte progenitors at 4- and 7-days post vaccination. Furthermore, mice vaccinated with IMDQ-PC displayed a transient drop in phenotypically quiescent long-term HSCs compared to QIV or PBS vaccinated mice. These results suggest that IMDQ-PC triggers a type 1 IFN response that reaches HSPCs in the bone marrow, altering surface marker expression and inducing emergency myelopoiesis. Whether IMDQ-PC itself enters the bone marrow and whether HSPCs are being directly or indirectly signaled by type 1 IFNs is the focus of ongoing research. These findings provide insight into the working mechanism of vaccine adjuvants and their potential safety considerations.

CONCURRENT SESSION 1: ADJUVANTS

Monday 12 October 2026 • 16:50–17:05 • Okapi 1, 2, 3

Neutrophils are the dominant early responders to a potent liposomal vaccine adjuvant

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Introduction: Neutrophils are the most abundant circulating leukocytes which rapidly respond to infection and inflammation, yet their role in vaccine-induced immunity is poorly understood. Using a mouse model, we investigated the early neutrophil response following intramuscular administration of LMQ – a liposome-based vaccine adjuvant containing a synthetic TLR4 agonist and QS-21 saponin. We further examined the mechanisms that contribute to adjuvant uptake and activation of neutrophils in vaccination.

Methods: Female BALB/c mice were injected intramuscularly with PBS or LMQ to assess cell-specific adjuvant uptake. At defined time points, the site of injection (SOI) was analysed by spectral flow cytometry to quantify immune cell recruitment and adjuvant uptake across distinct cell populations. To evaluate the contribution of neutrophils to vaccine-induced adaptive immunity, their recruitment to the SOI was blocked using an anti-CXCR2 antibody (Ab) prior to immunisation with LMQ-adjuvanted ovalbumin (OVA). Mechanisms underlying neutrophil-adjuvant interactions were further investigated in vitro by stimulating neutrophils isolated from naïve mouse spleens with fluorescently-labelled LMQ, or control liposomal formulations (liposomes alone (L) or containing the TLR4 agonist (LM) or QS-21 (LQ)), in the presence or absence of TAK242 (TLR4 inhibitor) and anti-CD11b (CR3 blockade). Adjuvant uptake and expression of antigen-presentation associated markers were quantified by spectral flow cytometry.

Results: Within 6 h of fluorescent-labelled LMQ administration, neutrophils accounted for ~60% of CD45+ cells at the SOI and represented the predominant adjuvant-positive population during the first 24 h post-vaccination. Blocking neutrophil recruitment with an anti-CXCR2 antibody reduced their numbers at the SOI by ~6-fold with a concomitant decrease in activated CD86+ myeloid cells; analysis of the impact on adaptive immune responses is ongoing. In vitro, neutrophils efficiently internalised LMQ and liposomal formulations containing either TLR4 agonist or QS-21, whereas the uptake of liposomes alone (L) was significantly lower. LMQ exposure in vitro induced a marked upregulation of CD11b on neutrophils along with increased CD86 and MHCII expression, consistent with an activated, antigen-presenting phenotype. Inhibition of TLR4 signaling markedly reduced uptake of immunostimulant-containing adjuvant formulations (LM, LQ, LMQ), while CD11b blockade caused a modest but significant reduction across all formulations, indicating that both pathways contribute to neutrophil-adjuvant interaction.

Conclusions: Neutrophils are the predominant early responders to LMQ adjuvant, rapidly accumulating at the injection site and serving as the primary adjuvant-uptaking population within the first 24 h post-vaccination. Our findings show that both TLR4 signaling and CD11b contribute to neutrophil-adjuvant interactions, and illustrate the key role of individual immunostimulatory adjuvant components in promoting neutrophil activation. Collectively, these data highlight the critical role of neutrophils in early response to vaccination with LMQ – an adjuvant compositionally similar to GSK's AS01TM – and provide mechanistic insights into innate immune activation during the initial hours following immunisation.

CONCURRENT SESSION 1: ADJUVANTS

Monday 12 October 2026 • 17:05–17:20 • Okapi 1, 2, 3

GVX-PA-01, a novel *Pseudomonas aeruginosa* (Pa) vaccine

Elodie PASTURAL, Tze Chieh SHIAO, Serge MOFFETT

Glycovax Pharma, Canada

Introduction: *Pseudomonas aeruginosa* (Pa) is one of the ESKAPE pathogens identified by WHO as increasingly resistant to antimicrobial treatments, specifically to carbapenem. Pa is responsible for many chronic and progressive respiratory diseases and is the leading cause of nosocomial pneumonia and respiratory failure in hospitals, particularly in cystic fibrosis patients. Several Pa vaccine candidates, mostly based on well-characterized virulence factors, progressed to clinical trials; however, none reached market authorization, emphasizing the need for novel strategies.

The National Research Council of Canada (NRC) had identified a specific glycan antigen in the bacterium's type A liposaccharide that is common to several clinical strains and therefore a potential target for vaccine development. This novel antigen was characterized as a methylated rhamnan (MeRha) oligosaccharide. When MeRha was conjugated to the CRM197 carrier protein and adjuvanted with Sigma Adjuvant, intramuscular administration of the vaccine candidate proved immunogenic in both mice and rabbits, and the sera reacted with the Pa strain the oligosaccharide was identified from, as well as with various Pa clinical isolates and serotypes. Glycovax licensed the technology to develop it further to clinical stage.

Methods:

Vaccine design

Glycovax applied GlycoForge, its versatile conjugate vaccine platform, to design the GVX-PA-01 vaccine candidate. More specifically, GVX-PA-01 is the combination of the glycoconjugate antigen, consisting of the CRM197 protein carrier covalently coupled with the oligosaccharide through a proprietary linker, with the Sulfated Lactosyl Archaeol (SLA) archaeosome adjuvant.

SLA is a sulfated glycolipid based on archaebacterial polar lipids developed by NRC. The unique nature of SLA's lipid creates a multi-prong vigorous immune response when combined with an antigen. Glycovax elaborated an entirely new fully chemical synthesis process to improve manufacturability at commercial scale and streamline the regulatory path.

Production of vaccine candidates

Glycovax manufactures both CRM197 and SLA for its own vaccine candidates and for commercialization. SLA is prepared as a ready-to-use liposome suspension.

Four MeRha oligosaccharides (di- to pentamer) were chemically synthesized and conjugated to CRM197. Before administration, each glycoconjugate was formulated with SLA or a comparator adjuvant.

Animal studies

Mouse studies were conducted to determine the optimal GVX-PA-01 formulation among the different combinations of oligosaccharides and adjuvants.

Pig and mouse studies were then initiated to assess the protection conferred by the selected candidate against challenge by PAO1 strain.

Results: All MeRha antigens were reactive to MeRha-specific 1B1 antibody, confirming the composition and structure of the synthetic glycan epitopes.

Mouse studies were then conducted to determine the optimal GVX-PA-01 candidate. The MeRha tetrasaccharide conjugate adjuvanted with SLA was the best candidate, as determined by criteria of immunogenicity and levels of serum binding to killed PAO1 strain and other strains. An opsonophagocytic killing assay on the same sera will further functionally characterize GVX-PA-01.

Conclusion: Novel strategies are needed to successfully develop an effective vaccine against Pa. Targeting a methylated saccharide conserved across Pa strains and formulating its conjugate with a novel adjuvant has shown promising preliminary results in terms of immunogenicity and protection. Glycovax is committed to pursuing the clinical development of GVX-PA-01.

CONCURRENT SESSION 1: ADJUVANTS

Monday 12 October 2026 • 17:20–17:35 • Okapi 1, 2, 3

PIV5-Vectored Intranasal RSV Vaccine is Safe and Immunogenic in Infants and Young Children

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Background: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infection in young children. Protection of infants against RSV can be achieved through maternal immunization or administration of recombinant monoclonal antibodies nirsevimab or clesrovimab. However, no vaccine is currently available to prevent RSV-associated morbidity and mortality following waning of passive immunity. Vaccines using parainfluenza virus 5 (PIV5) as a vaccine vector have been developed for respiratory pathogens including SARS-CoV-2, mumps, and RSV, and have been evaluated clinically in a total of more than 500 participants. BLB201, a PIV5-vectored intranasal RSV vaccine, expresses the RSV fusion (F) protein, replicates efficiently in serum-free Vero cells, is genetically stable, and protects against viral challenge in multiple animal models. BLB201 is currently the only pediatric RSV vaccine in clinical development in the United States. Here we report the preliminary results from an ongoing Phase 1/2a study of this intranasal RSV vaccine in infants and young children.

Methods: The Phase 1/2a study is a double-blind, randomized, placebo-controlled clinical trial evaluating two ascending intranasal dose levels of BLB201 (10^6 PFU and 10^7 PFU) in children aged 8–59 months (NCT05655182). More than 160 RSV-seropositive and RSV-seronegative children have been enrolled to date to assess the safety, tolerability, and immunogenicity of BLB201. Blood and nasal samples were collected before and after vaccination to evaluate vaccine viral RNA levels in nasal swabs, as well as serum antibody and cellular immune responses to RSV antigens.

Results: In an interim analysis, BLB201 has been well tolerated, with no serious adverse events due to vaccination. RSV-seronegative infants and young children developed both mucosal and systemic antibody responses following a single intranasal dose of BLB201. Remarkably, BLB201 was also immunogenic in RSV-seropositive children, demonstrating significant boosting of neutralizing antibodies in serum and protective against symptomatic RSV infection. A comparison of placebo recipients versus vaccine recipients demonstrated fewer medically-attended RSV infections and fewer lower respiratory tract infections due to RSV in vaccinees. Vaccine virus was detected transiently in some vaccinated children, and sequencing analysis showed no changes in the RSV F gene, demonstrating genetic stability of BLB201.

Conclusion: BLB201 is a promising RSV vaccine candidate moving forward in phase 2 development. Current data indicate substantial immune responses following a single intranasal dose and a suggestion of clinical efficacy in preventing symptomatic RSV infection.

CONCURRENT SESSION 2: VACCINE REGULATORY SCIENCE AND POLICY

Monday 12 October 2026 • 15:30–15:55 • Gorilla 1

Regulatory acceptance of immunological biomarkers as surrogate for vaccine efficacy – Ebola Zaire vaccine case

Marie-Chantal UWAMWEZI

PATH, Belgium

Introduction/Background: Regulatory approval of vaccines developed for the prevention of infectious diseases requires adequate data to support their quality, safety and efficacy.

For new vaccines containing immunogens for which immune correlates of protection (ICPs) are established and accepted by regulators, efficacy is inferred by demonstrating that the ICP is achieved. Another type of vaccines for which demonstration of efficacy through a phase III randomized controlled trial would not be required are those for which vaccine efficacy can be inferred by demonstrating non-inferior immune responses between the candidate vaccine and a licensed vaccine for which efficacy and/or effectiveness has been established. However for novel vaccines, i.e. new immunogens, vaccine efficacy would be expected to be demonstrated through an adequately powered phase 3 double-blind randomized controlled study.

Regulators however acknowledge that demonstrating vaccine efficacy through randomized controlled trials is often infeasible for pathogens with sporadic outbreaks and high mortality, such as Ebola virus disease (EVD). Regulatory pathways have therefore evolved to allow immunological biomarkers to serve as surrogate endpoints reasonably likely to predict clinical benefit. This presentation analyzes the scientific and regulatory basis for this approach using an Ebola Zaire vaccine (Ad26.ZEBOV/MVA-BN-Filo) as a case study.

Material/Methods: The presentation reviews the regulatory guidelines and policy framework from WHO that enabled and supported alternatives to efficacy trials for the licensure of Ebola vaccines.

Salient elements from the EMA assessment report of the Ad26.ZEBOV/MVA-BN-Filo are discussed to highlight the considerations for accepting the proposed immunobridging approach to infer vaccine efficacy.

Results: EU approval of the Ad26.ZEBOV/MVA-BN-Filo vaccine under exceptional circumstances was based on immunobridging between human and NHPs. EBOV glycoprotein (GP)-binding antibodies measured by the standardized FANG ELISA assay were identified as the primary surrogate endpoint due to strong correlation with protection in NHP models. Binding antibodies showed high concordance with neutralizing antibodies but were preferred due to superior assay robustness, reproducibility, and broader applicability. This is a departure from the usual preference of regulators for functional immune responses as surrogate endpoints for efficacy.

Regulatory acceptance was enabled by standardized assays, quantitative modeling linking antibody levels to survival probability, and a totality-of-evidence approach. Residual uncertainties, including the absence of defined protective thresholds in humans, were meant to be through a post-authorization commitment to conduct a real-world effectiveness study/

Discussion/Conclusion: This case represents a seminal example of regulatory acceptance of immunological biomarkers as surrogates for vaccine efficacy. It demonstrates that integrating animal challenge data, human immunogenicity, and validated assays can support licensure when traditional efficacy trials are not feasible. GP-binding antibodies emerged as a scientifically and regulatorily acceptable surrogate, enabling timely access to a critical vaccine. This paradigm is highly relevant for other filoviruses and emerging pathogens facing similar development constraints. Several global health organizations are funding work to enable identification and building robust evidence base for immunological markers associated with protection against infectious diseases. This work is critical to accelerate the development of vaccines for epidemic-prone diseases.

CONCURRENT SESSION 2: VACCINE REGULATORY SCIENCE AND POLICY

Monday 12 October 2026 • 16:20–16:35 • Gorilla 1

Primary Healthcare Surveillance and Vaccination Challenges During the 2025 Meningococcal Serogroup C Outbreak Response in Sokoto State, Northern NigeriaIkechukwu NNAJI¹, Aminu DOGONDAJI², Micheal POOPOLA¹, Chidiebere OPARA¹, Amos DANGANA¹, Olajumoke BABATUNDE¹, Emmanuel EZEH¹, Jide IDRIS¹¹ Nigeria Centre for Disease Control and Prevention (NCDC), Nigeria² Sokoto State Ministry of Health, Nigeria

Backgrounds/Introduction: Meningococcal meningitis remains a major public health threat across the African meningitis belt, with recurrent outbreaks causing substantial morbidity and mortality. In Nigeria, outbreaks of *Neisseria meningitidis* continue to occur, particularly in northern states such as Sokoto. Effective outbreak control depends on timely surveillance, laboratory confirmation, and adequate vaccination coverage. Primary healthcare centres (PHCs), as the first point of contact within the health system, play a critical role in case detection, reporting, and implementation of vaccination interventions. This study assessed surveillance performance and vaccination-related challenges during the 2025 meningococcal serogroup C (NmC) outbreak response in Sokoto State.

Materials/Method: A descriptive cross-sectional analysis was conducted from March to June 2025 across fourteen affected Local Government Areas of Sokoto State. A total of 845 suspected cerebrospinal meningitis cases meeting the national case definition were identified through PHC-based surveillance systems. Demographic and epidemiological data were collected using standardized Case Investigation Forms, and cerebrospinal fluid (CSF) samples were obtained where feasible for laboratory confirmation. Samples were tested using real-time polymerase chain reaction at the National Reference Laboratory of the Nigeria Centre for Disease Control and Prevention (NCDC). Data were analyzed using SPSS version 16.

Results: Among the 845 suspected cases, 456 (54.0%) were males and 389 (46.0%) were females. Only 113 (13.4%) cases had CSF samples tested, highlighting significant limitations in specimen collection and laboratory access. Of the tested samples, 74 (65.5%) were confirmed positive for *Neisseria meningitidis* serogroup C. Vaccination history was poorly documented, with vaccination status recorded for only 30 (3.6%) cases. Among those with documented status, 26 (86.7%) were unvaccinated. Epidemiological trends demonstrated sustained transmission throughout the outbreak period, with cases peaking between epidemiological weeks 10 and 17. Gaps in surveillance documentation, delayed laboratory confirmation, and limited availability of vaccination records constrained timely public health decision-making and outbreak response.

Discussion/Conclusion: The 2025 NmC outbreak in Sokoto State exposed critical weaknesses in PHC-level surveillance systems, laboratory diagnostic capacity, and vaccination documentation. These challenges limited effective outbreak monitoring and evidence-based vaccination response efforts. Strengthening PHC surveillance, improving access to lumbar puncture and laboratory confirmation, enhancing immunization record systems, and expanding meningococcal vaccination coverage are essential to improving preparedness and reducing the impact of future outbreaks in Nigeria's meningitis belt.

CONCURRENT SESSION 2: VACCINE REGULATORY SCIENCE AND POLICY

Monday 12 October 2026 • 16:35–16:50 • Gorilla 1

Immunological assays and correlates of protection: the missing tool for next-generation influenza vaccines

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When the influenza community gathered in Siena in 2019 to discuss immunological assays and correlates of protection for next-generation vaccines, the conclusion was sobering: substantial progress had been made in developing and standardising assays, yet seasonal vaccine design had not been meaningfully changed by it. Seven years on, that assessment deserves revisiting. More than fifty years after Hobson and colleagues showed that a serum haemagglutination inhibition (HI) titre in the range of 1:18–1:36 conferred roughly 50% protection in challenged volunteers, the HI assay remains the reference correlate of protection and continues to underpin regulatory decision-making. The convenience of this threshold has obscured its limitations. It was established in healthy adults using a partially attenuated challenge virus, in subjects whose antibodies were often derived from natural infection rather than vaccination. It performs poorly in the population that carries most of the influenza burden: adults aged 65 and older, in whom a titre of 1:40 is not necessarily predictive of protection and in whom enhanced formulations “high-dose, adjuvanted, and recombinant vaccines” are now preferentially recommended.

Several immune markers now have solid evidence as correlates independent of the serum HI titre. Neuraminidase inhibition (NI) antibodies have been identified as independent correlates in field studies and controlled human infection models, and appear more broadly cross-reactive than HI antibodies across drifted strains. Antibodies targeting the conserved HA stalk domain correlate, in cohort studies, with protection against both infection and symptomatic disease. Cross-reactive CD4+ and CD8+ T cells, nasal IgA, antibody effector functions measured by ADCC and ADCP, and systems-immunology signatures are all under investigation. Crucially, randomised comparisons in older adults show that enhanced vaccines induce markedly stronger NI responses than standard-dose vaccine, with poor correlation between NI and HA-specific neutralizing responses, evidence that HA-based readouts capture only part of the protection these products confer.

Novel correlates are useful only if the assays measuring them are reproducible across laboratories. Collaborative studies within the FLUCOP consortium have demonstrated that consensus protocols, shared critical reagents and pooled post-vaccination serum standards substantially reduce inter-laboratory variation in HI testing, and that normalization against a study standard improves agreement for microneutralisation. A harmonised, validated ELLA-NI standard operating procedure for anti-neuraminidase antibodies is now freely available and performs consistently with influenza A and B antigens. Yet neuraminidase content remains unstandardized in licensed vaccines, formulated and released on HA content alone even as mRNA candidates encoding both HA and NA advance through early clinical evaluation.

Defining correlates of protection is therefore not an academic exercise: it determines whether next-generation and broadly protective vaccines reach the market on immunogenicity data rather than large efficacy trials, and whether product changes can be supported by comparability studies.

CONCURRENT SESSION 3: "BRIGHT SPARKS" IN VACCINOLOGY – PHD STUDENT SESSION

Monday 12 October 2026 • 15:30–15:40 • Gorilla 3

Cross-Reactive SARS-CoV-2 Antibodies in Pre-Pandemic Gambian Sera Exhibit Fc-Mediated Effector Activity

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Introduction: Pre-existing cross-reactive antibodies to SARS-CoV-2 have been reported in several African populations prior to the COVID-19 pandemic. However, the functional properties of these antibodies and their potential relevance to vaccine-induced immunity remain poorly understood. Thus, we aimed to understand the evolution of SARS-CoV-2 binding, neutralizing and Fc-mediated effector antibody response in pre-pandemic and COVID-19 pandemic samples from The Gambia.

Methods: SARS-CoV-2 anti-spike (S) and nucleocapsid (N) specific binding antibody responses were quantified in pre-pandemic (n=825) and COVID-19 pandemic samples (n=914) collected longitudinally across three 6-monthly sampling timepoints (2021-2022). Neutralising activity was assessed using a pseudovirus neutralisation assay, while ADCC activity was measured using a functional reporter assay. Associations between IgG subclass composition and ADCC activity were evaluated using correlation analyses.

Results: 21% of pre-pandemic samples were reactive to SARS-CoV-2 N protein, compared to 4% reactivity to S protein. Pre-pandemic N-reactivity increased with age, with 28% of adults >50 years showing seropositivity. No neutralising activity was detected in S IgG cross-reactive pre-pandemic sera. However, N IgG cross-reactive pre-pandemic samples displayed measurable ADCC activity that were moderately higher than those observed in pandemic sera. The response in pre-pandemic samples is associated with relative predominance of IgG3, whereas pandemic N-specific antibodies were largely IgG1 driven.

Conclusion: Repeated exposure to coronaviruses and other viral infections may explain why many adults had cross-reactive anti-N IgG antibodies even before COVID-19 emerged. Although these pre-existing antibodies cannot neutralise SARS-CoV-2, they can still trigger Fc-dependent effector activities. This highlights the potential contribution of non-neutralising functional antibodies to antiviral immunity and underscore the importance of considering Fc-mediated responses when evaluating vaccine-induced immunity and immune correlates of protection.

CONCURRENT SESSION 3: "BRIGHT SPARKS" IN VACCINOLOGY – PHD STUDENT SESSION

Monday 12 October 2026 • 15:40–15:50 • Gorilla 3

Seroepidemiology and serum bactericidal activity of IgG antibodies to Non Typhoidal Salmonella in healthy Children in Mukuru informal settlement in KenyaSchola KAMWETHYA¹, Mercy NGETICH¹, Cecilia MBAE¹, Hellen DALE^{2,3}, Robert ONSARE¹, Tonney NYIRENDA⁴, Melita GORDON^{2,3}, Sam KARIUKI^{1,5,6}¹ Centre for Microbiology Research, Kenya Medical Research Institute, Nairobi, Kenya² Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, United Kingdom³ Clinical Research, Malawi-Liverpool-Wellcome Clinical Research-Program, Blantyre, Malawi⁴ Pathology Department, Kamuzu University of Health Sciences, Blantyre, Malawi⁵ Wellcome Sanger Institute, Hinxton, United Kingdom⁶ Drugs for Neglected Diseases initiative, Nairobi, Kenya

Background: Invasive non-typhoidal Salmonella (iNTS) infections, particularly caused by Salmonella enterica serovars Typhimurium (STm) and Enteritidis (SEn), remain a major cause of morbidity and mortality in sub-Saharan Africa affecting children under five years of age. Understanding the seroprevalence and functional immunity in this population is critical for informing vaccine development and public health interventions. This study assessed the seroprevalence, age-related exposure patterns, and the functional bactericidal activity of naturally acquired antibodies among apparently healthy children in Mukuru informal settlement, Nairobi, Kenya.

Methods: A cross-sectional study was conducted among 1000 apparently healthy children under five years of age residing in Mukuru informal settlement of Nairobi. Sampling was done between April 2021 and November 2021. IgG seroprevalence against serovars S. Typhimurium and S. Enteritidis was assessed using Enzyme-Linked Immunosorbent Assay (ELISA), while the correlates of protection of the IgG antibodies was evaluated using a serum bactericidal assay (SBA). The chi-square test, odds ratio and logistic regression models were used to analyze age-related trends and correlates of protection.

Results: The overall seroprevalence of IgG antibodies was 96.29% for S. Typhimurium and 93.58% for S. Enteritidis, with exposure increasing significantly with age ($p < 0.05$). Peak exposures were detected in children aged 25–36 months and above. However, functional serum bactericidal activity was low, detected in only 9.13% of children for S. Enteritidis and 0.3% for S. Typhimurium. A weak correlation ($p = 0.014$ for SEn, $p = 0.1898$ for STm) between IgG levels and bacterial killing was observed, suggesting that naturally acquired antibodies lack protective bactericidal activity.

Discussion/ Conclusion: The high seropositivity observed suggests widespread early exposure to NTS in Mukuru. Seropositivity is relatively higher than for a study conducted in Uganda (seropositivity of 82% and 70% for S. Typhimurium and S. Enteritidis respectively Stockdale et al 2019). Seroprevalence increased with age - due to repeated exposure to NTS bacteria and immune system activation. This trend aligns with findings reported by Peter et al (2023) and Tonney et al (2014). Despite high seropositivity, there was no strong correlation between IgG levels and SBA - with no differences between different age groups. This weak functional response suggests that passively acquired and naturally acquired IgG antibodies may not be protective against NTS disease, reinforcing the need for effective vaccination strategies.

Promising candidates, including Generalized Modules for Membrane Antigen (GMMA), glycoconjugate, and live attenuated vaccines, could help reduce NTS-related morbidity. Additionally, interventions to improve sanitation, water quality, and hygiene are essential in mitigating transmission risk.

CONCURRENT SESSION 3: "BRIGHT SPARKS" IN VACCINOLOGY – PHD STUDENT SESSION

Monday 12 October 2026 • 15:50–16:00 • Gorilla 3

The Effect of Malaria Intermittent Preventive Treatment on Vaccine Responses and SARS-CoV-2 Seroprevalence in Adolescents: Findings from a Randomised Controlled Trial

Ludoviko ZIRIMENYA^{1,2}, Gyaviira NKURUNUNGI^{1,2}, Jacent NASSUUNA¹, Agnes NATUKUNDA¹, Doreen NAYEBARE¹, Claire BAINE¹, Alison ELLIOTT^{1,2}, Emily WEBB^{1,2}

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Background: Vaccine immunogenicity varies across populations, particularly in malaria-endemic settings. Malaria may alter immune responses to unrelated vaccines and pathogens such as SARS-CoV-2. We evaluated whether intermittent preventive treatment (IPT) with dihydroartemisinin-piperazine (DP) modifies vaccine responses, including to BNT162b2, and influences SARS-CoV-2 seroprevalence in adolescents from a malaria-endemic setting.

Methods: We conducted a randomised, double-blind trial among adolescents aged 9–17 years in Jinja district, Uganda (ISRCTN62041885). Participants were randomised 1:1 to monthly IPT with DP or placebo. A three-day course of oral DP or an identical placebo (weight-based dosing) was administered monthly, including two courses before the first immunisation. Participants received BCG at week 0; yellow fever, oral typhoid, and HPV at week 4; and tetanus–diphtheria with an HPV booster at week 28. The primary outcome was vaccine response at week 8 and, for tetanus/diphtheria, at week 52 (intention-to-treat analysis). Malaria parasitaemia was measured retrospectively by PCR.

A nested longitudinal study assessed SARS-CoV-2 seroprevalence and response to BNT162b2, which was administered during the national rollout. SARS-CoV-2 seroprevalence was determined using pre-COVID-19 vaccination spike and nucleocapsid IgG antibodies at weeks 0, 4, and 8. Vaccine responses were assessed using pre-vaccination (week 8) and post-vaccination (week 52) antibody concentrations. Outcomes were compared using logistic and linear regression.

Results: A total of 341 participants were enrolled in the trial (56% female, 170 DP and 171 placebo). 145 (85%) DP and 140 (82%) placebo participants were followed up to week 52. At enrolment, 64% in the DP and 58% placebo arm were malaria PCR positive, decreasing to <6% at all follow-up visits in the DP arm. There was no effect of DP versus placebo on primary outcomes: BCG-specific IFN- γ ELISpot response (geometric mean ratio 1.09 (95%CI 0.93–1.29)); yellow fever neutralising antibody (1.19 (0.91–1.54), $p=0.20$ for plaque reduction neutralising reference tests (PRNT50) titres and 1.24 (0.97–1.58), $p=0.09$ for PRNT90 titre); Ty21a IgG (1.09 (0.81–1.46), $p=0.58$), HPV-16 IgG (0.72 (0.44–1.77), $p=0.19$), HPV-18 IgG (0.71 (0.47–1.09), $p=0.11$); tetanus toxoid IgG (1.22 (0.91–1.62), $p=0.18$), and diphtheria toxoid IgG (0.97 (0.83–1.13), $p=0.72$). There was some evidence that DP reduced waning of the yellow fever response.

In the nested study, SARS-CoV-2 seroprevalence was assessed in 283 participants (142 DP, 141 placebo), and vaccine responses in 187 vaccinated participants (95 DP, 92 placebo). Pre-COVID-19 vaccination SARS-CoV-2 seropositivity and antibody concentrations did not differ between the arms at any time point. Post-vaccination mean N-antibody concentrations were comparable between the arms. Among participants who were seronegative at week 8 and subsequently vaccinated with BNT162b2, the fold change in S-antibody concentrations from week 8 to 52 was higher in the DP group compared to placebo (adjusted mean difference: 0.32, 95% CI 0.04–0.60; $p=0.02$).

Conclusion: Monthly malaria IPT reduced malaria prevalence but did not improve peak responses to routine vaccines or affect SARS-CoV-2 seroprevalence. However, DP was associated with reduced waning of the yellow fever response and enhanced humoral responses following BNT162b2 vaccination.

CONCURRENT SESSION 3: "BRIGHT SPARKS" IN VACCINOLOGY – PHD STUDENT SESSION

Monday 12 October 2026 • 16:00–16:10 • Gorilla 3

APC-Mimetic Dendritic Cell-Derived Extracellular Vesicle Nanovaccine with STING Adjuvant Induces Long-Term Th1 Immunity and Immune Memory Against Dengue VirusAnindita SENGUPTA^{1,2}, Jayanta BHATTACHARYYA^{1,2}¹ Centre for Biomedical Engineering, Indian Institute of Technology, Delhi, New Delhi 110016, India.² Department of Biomedical Engineering, All India Institute of Medical Science, Delhi, New Delhi 110029, India.

Introduction/Background: Dengue virus (DENV) vaccine development remains a major challenge due to cross-reactive antibodies, limited neutralizing antibody responses, and insufficient cellular immune memory. Effective vaccines require efficient antigen presentation and strong Th1-biased cellular immunity. Dendritic cells (DCs) are the most potent antigen-presenting cells capable of cross-presentation and T-cell activation. However, DC vaccines are limited by the complexity of cell-based therapies. To address this, we developed an APC-mimetic nanovaccine based on dendritic cell-derived extracellular vesicles (DEVs) that integrates trained innate immune activation with controlled antigen presentation from licensed dendritic cells to promote efficient and rapid antigen presentation, Th1-biased immune responses, and durable cellular and humoral immunity. The DEV nanovaccine was combined with a STING agonist to further enhance antigen presentation, immune memory formation, and virus neutralization.

Materials/Methods: Bone marrow-derived dendritic cells (BMDCs) were pulsed with heat-inactivated DENV-2 antigen to generate antigen-loaded DEVs. Vesicles were characterized for size, morphology, and expression of antigen presentation and co-stimulatory molecules (MHC-I, MHC-II, CD40, CD86). In vitro uptake, dendritic cell maturation, cytokine production, and T-cell activation assays were performed. Mice were immunized using a prime-boost strategy with the DEV nanovaccine, with or without a STING agonist. Immune responses were evaluated in secondary lymphoid organs, spleen, and lymph nodes at early and memory time points (Day 30 and Day 45). Flow cytometry was performed to evaluate dendritic cell activation, CD4+ and CD8+ T-cell responses, central and effector memory T cells, memory B cells, plasma cells, Tfh cells, and germinal centre responses. Antigen-specific recall responses were measured using ex vivo restimulation assays, and virus neutralization was evaluated using the focus reduction neutralization test (FRNT).

Results: DEV nanovesicles retained antigen-presenting and co-stimulatory molecules and were efficiently internalized by antigen-presenting cells, inducing dendritic cell maturation and pro-inflammatory cytokine production (IL-6, TNF- α), resulting in Th1-biased T-cell activation (IFN- γ , IL-2). In vivo immunization induced strong immune activation and enhanced antigen presentation. Vaccination increased CD8+ central memory T cells by approximately 2–3-fold at Day 30 and expanded CD4+ central memory (CD44+ CD62L+) T cells up to five-fold at Day 45. Memory B cells (CD19+ CD27+), plasma cells (B220+ CD138+ TACI+), Tfh cells (CD4+ CXCR5+), and germinal centre structures were also increased, accompanied by strong antigen-specific recall responses and potent virus neutralization (FRNT50: 10³).

Discussion/Conclusion: These findings demonstrate that APC-mimetic DEV nanovaccines, combined with STING adjuvant, can induce durable Th1-biased cellular and humoral immunity and long-term immune memory. This platform represents a promising next-generation vaccine strategy for tetravalent dengue virus and other infectious diseases requiring strong cellular immunity and durable immune protection with multiple serotypes.

CONCURRENT SESSION 3: "BRIGHT SPARKS" IN VACCINOLOGY – PHD STUDENT SESSION

Monday 12 October 2026 • 16:10–16:20 • Gorilla 3

Induction of influenza-specific immunity in pigs using dissolvable microneedle patches to deliver an adenovirus-based vaccineInés CÓ RIVES¹, Katherine ACEVEDO¹, Imane ALLAOUI¹, Emery G. DORA², Grace COPITHORNE³, Edgar GARCIA MANZANILLA³, Kelly A. S. DA COSTA⁴, Nigel J. TEMPERTON⁴, Sean N. TUCKER², Ann Ying-An CHEN¹, Anne C. MOORE¹¹ School of Biochemistry and Cell Biology, University College Cork, T12 XF62 Cork, Ireland² Vaxart Inc., 170 Harbor Way Suite 300, South San Francisco, CA 94080, USA³ Pig Development Department, The Irish Food and Agriculture Authority, Teagasc, Moorepark, P61 C996 Fermoy, Co Cork, Ireland⁴ Viral Pseudotype Unit, Medway School of Pharmacy, The Universities of Kent and Greenwich at Medway, Chatham ME4 4BF, UK

Global vaccine access is often hindered by cold-chain distribution requirements and the need for trained healthcare workers. New injection-free, thermostable vaccine formats are urgently needed to address these issues. Easy-to-administer dissolvable microneedle skin patches (DMN) offer promising potential in this field. We previously incorporated and stabilised several vaccine platforms into DMN and demonstrated their immunogenicity in rodents. However, mice can be a poor predictor of function in larger animals and humans. Pigs represent a highly relevant, yet under-utilised, model for vaccine research due to their anatomical and immunological similarity to humans and their role as a host for many relevant pathogens. Here, we examined the anatomical breadth and cross-reactivity of antibody responses in pigs, when vaccinated with an adenovirus-based influenza virus vaccine by skin-based DMN administration, compared to intramuscular injection. A higher, pig-relevant vaccine dose was needed compared to the lower doses used in mice, and it was successfully incorporated into DMN patches. Similar serum IgG and neutralising responses were observed in both immunised groups. We present results on mucosal IgG and IgA titres, as well as B and T cell responses induced by skin-patch and IM-based vaccination. Interestingly, patch-based vaccination skewed the antibody response towards stronger antigen specific and lower vector-specific antibodies, compared to IM injection. In mucosal tissues, IgG predominated over IgA across both immunised groups. Further research into the glycosylation profile and Fc-effector functions of antibodies was conducted. Overall, our study contributes to increased understanding of how the vaccine delivery technology and the route of immunisation impact on the magnitude and quality of the systemic and mucosal humoral immune responses to an adenoviral-vectored vaccine. Furthermore, it demonstrates the potential of novel, stabilising vaccine technologies to elicit broad immunity in a translatable large-animal model, highlighting the strong potential for needle-free, thermostable alternatives to injection-based immunisation.

CONCURRENT SESSION 3: "BRIGHT SPARKS" IN VACCINOLOGY – PHD STUDENT SESSION

Monday 12 October 2026 • 16:20–16:30 • Gorilla 3

Systemic response and short-term functional changes following infection with *Necator americanus* third-stage infective larvae: Insights from a control human hookworm infection trial in Lambarene, GabonTherese Vanessa AMANA BOKAGNE^{1,2}, Kossiwa Clarisse KOKOU¹, Ayodele ALABI^{1,3}, Christine NDONG EMGOME¹, Edlom Pelagie TCHADIE^{1,2}, Augustin BOUEYA BOUEYA¹, Eddy MABICKA¹, Peter KREMSNER^{1,2}, Selidji T AGNANDJI^{1,4}¹ Centre de Recherches Medicales de Lambarene, Gabonese Republic² Institute of Tropical Medicine, Travel Medicine and Human Parasitology, Competence Centre for Tropical Medicine Baden-Württemberg, Universitätsklinikum Tübingen, Germany³ Department of Parasitology, Leiden University Medical Center, The Netherlands⁴ Institute of Medical Microbiology, University Hospital Münster, Germany

Background: Hookworm infection caused by *Necator americanus* remains a significant public health concern, particularly in low- and middle-income countries, where mass drug administration has failed to prevent reinfection. Developing a vaccine is therefore crucial to complement current control measures, which necessitates a thorough understanding of host immune responses. However, most data on the immune response to *Necator americanus* infection have been obtained from naïve populations using laboratory animal-derived strains, which do not fully mirror the infections experienced in people living in high-endemic settings or involve local strains. Here we report findings from a control human hookworm infection (CHHI) trial conducted in Lambaréne, the first of its kind on the African continent, using local strains from local donors. By leveraging the CHHI models, we investigated the systemic response and short-term functional changes following infection with 50 *Necator americanus* L3 (NaL3) stage in healthy volunteers over 16 weeks of follow-up and compared the immune response in people from non-endemic areas and naturally infected individuals.

Method: NaL3 infective stage was cultured from local donor stools following good manufacturing procedure. Approximately 50 NaL3 infective stages were used to infect 10 healthy adult volunteers, including 8 endemic individuals and 2 non-endemic Caucasians. 5 participants were included as placebo. Type 1 (TNF- α , IFN- γ , IL-2, IL-1 β) and Type 2 cytokines (IL-5, IL-4, IL-6, GM-CSF), including chemokines (IL-8) and T regulatory cytokines (IL-10), were measured in volunteers' plasma at baseline, 1 week, 4 weeks, 8 weeks and 16 weeks post-infection using a Luminex bead assay. Additionally, peripheral blood mononuclear cells were isolated and stimulated overnight with Dengue peptide, heat-killed *S. aureus*, heat-killed *Mycobacterium tuberculosis*, *Plasmodium falciparum* infected red blood cells and the toll-like receptor agonist Pam3Cys to assess the cellular functionality of the cells in response to heterologous antigen.

Results: The results indicate a mixed cytokine response in infected individuals, characterised by a transient but robust Type 2 immune response (elevated IL-5 and eosinophils) during the parasite migration and establishment in the gut, and an initial downregulation of Type 1 and T regulatory cytokines during the acute phase, followed by an increase in IFN- γ and TNF- α in the early chronic stage of the infection. No significant differences in cytokine profiles were observed between endemic and non-endemic volunteers, but baseline cytokine levels appeared to influence the intensity of parasite-induced immune modulation. Notably, cellular responses to heterologous antigens showed a stimuli independent transient tolerance in the early intestinal adult stage for all inflammatory cytokines IL-6, TNF- α , IL-10, and IL-1 β which is speculated to be driven by epigenetic reprogramming of innate cells towards a tolerant phenotype.

Conclusion: These findings highlight a distinct immunological profile elicited by the *N. americanus* local strain, contributing to our understanding of helminth-induced immune modulation in people living in endemic settings.

CONCURRENT SESSION 3: "BRIGHT SPARKS" IN VACCINOLOGY – PHD STUDENT SESSION

Monday 12 October 2026 • 16:30–16:40 • Gorilla 3

Intranasal protein-based vaccines protect against 2.3.4.4b H5N1 infection in young and old BALB/C mice

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Since the beginning of 2020, a massive outbreak of H5N1 virus infection in wild birds and poultry was associated with an increased rate of infection in mammals such as seals or dairy cattle, suggesting mammalian adaptation of H5N1 viruses. Furthermore, a higher incidence of mammalian H5N1 infections poses an increased risk of mutations associated with mammalian adaptation. This would increase the risk of human to human transmission, thereby enhancing the threat of a potential epidemic of high pathological H5N1 virus. Currently, few vaccines are available against H5N1 influenza virus, and all of them are to be administered intramuscularly. There is therefore a strong interest in developing efficient mucosal vaccines against the currently circulating H5N1 strains, that could prevent not only infection but also potential human to human transmission. To that end, we previously demonstrated the combination adjuvant NE/IVT, consisting of a nanoemulsion (NE) and an RNA-based RIG-I agonist (IVT) induced potent systemic and mucosal immune responses in protein-based influenza vaccines, which protected from disease and H1N1 virus transmission in a guinea pig model. NE/IVT-adjuvanted SARS-Cov2 protein vaccines administered intranasally, both as homologous vaccination, and as a heterologous vaccination following intramuscular vaccination with mRNA vaccine. In this work, we demonstrated that vaccination with NE/IVT in combination with recombinant H5 and/or N1 from recent 2.3.4.4b H5N1 induces strong mucosal and systemic antibody responses in the mouse model and an efficient neutralization against vaccine matching and drifted H5N1 viruses. Furthermore, our mucosal strategy efficiently protects against lethal H5N1 challenge, leading to no detectable titer in both upper and lower respiratory tract. In addition to young BALB/c, intranasal NE/IVT vaccine allows strong protection in 18-month-old BALB/c. Together, our data demonstrate the efficacy of an intranasal adjuvanted recombinant vaccine against H5N1 virus, and this in young and old animals.

CONCURRENT SESSION 3: "BRIGHT SPARKS" IN VACCINOLOGY – PHD STUDENT SESSION

Monday 12 October 2026 • 16:40–16:50 • Gorilla 3

A simplified and sensitive assay for tracking virus-specific T cell responses in the nasal cavity during SARS-CoV-2 human challenge studies

Previtha Dawn SAKTHI VALE, Natalene Hui Shan YUEN, Joey Ming Er LIM, Adeline CHIA, Huiwen ZHENG, Yirong DAI, Anthony Tanoto TAN, Antonio BERTOLETTI, Nina LE BERT

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Background: The nasal cavity is the primary entry site for respiratory viruses, including SARS-CoV-2, and a critical frontline of immune defence. Understanding antibody and T cell responses at the site of infection is essential for early-stage screening of novel vaccines and antivirals. Virus-specific T cells can be detected in the human nasal cavity from mid-turbinate swabs followed by ELISpot or activation-induced marker (AIM) assays, but assay complexity and limited lymphocyte yields constrain broader application. We hypothesised that a simple, rapid cytokine release assay (CRA) could reliably capture virus-specific nasal T cell responses and enable longitudinal tracking during controlled human infection.

Methods: We developed a nasal CRA based on overnight stimulation of nasal cells with peptide pools spanning viral proteins or control anti-CD3/CD28 activation, followed by quantification of IFN- γ and CXCL10. Candidate biomarkers were identified by NanoString transcriptomics and Olink proteomics of stimulated healthy-donor nasal samples, and CXCL10 was validated against IFN- γ ELISpot. Assay sensitivity was benchmarked using serial dilution of a defined HLA-A*11:01-restricted influenza NP-specific T cell response across CRA, ELISpot, AIM, and dextramer readouts. We then applied the CRA using peptide pools spanning SARS-CoV-2 Spike, Nucleoprotein, NSP12, and bystander antigens influenza A Nucleoprotein and CMV UL123, to freshly collected nasal samples from seronegative volunteers (n=17) in a SARS-CoV-2 Delta controlled human infection model (CHIM), sampled longitudinally from day -1 to day 14 with paired blood analysis.

Results: Multi-omic screening identified CXCL10 as the most sensitive biomarker of nasal T cell activation, and combined IFN- γ /CXCL10 measurements improved assay sensitivity. CRA readouts correlated with ELISpot in paired samples while being more sensitive than ELISpot or AIM assays at lower lymphocyte counts. In the CHIM cohort, only 2/17 participants developed confirmed infection, yet all showed rapid lymphocyte recruitment to the nasal cavity as early as day 1 post-challenge. In contrast to natural primary infection, where nasal SARS-CoV-2-specific T cells persist for months, the response following experimental challenge was transient and modest, returning to baseline or below detection within days in nearly all participants. Bystander T cells were also recruited: 10/16 individuals showed strong influenza NP-specific responses after day 1, indicating co-recruitment of tissue-resident memory T cells (Trm) alongside antigen-specific responses, likely reflecting the larger pool of influenza-specific nasal Trm from greater cumulative exposure. Critically, this recruitment was not peripheral in origin: CMV-specific responses were absent despite circulating CMV-specific T cells in blood, indicating that recruited cells were locally tissue-resident rather than blood-derived. Across stimulations and timepoints, secreted IFN- γ and CXCL10 were strongly correlated.

Conclusion: We describe a simple, rapid nasal CRA that reliably captures virus-specific T cell responses from minimal nasal material, with dual IFN- γ /CXCL10 readout enhancing sensitivity. Applied within a SARS-CoV-2 CHIM, the assay revealed that nasal T cell dynamics following controlled challenge differ fundamentally from natural infection, with transient rather than persistent responses, and that bystander Trm are co-recruited from a tissue-resident rather than circulating pool. These findings inform interpretation of mucosal immunity in CHIM studies and support nasal T cell monitoring in vaccine and antiviral development.

CONCURRENT SESSION 3: "BRIGHT SPARKS" IN VACCINOLOGY – PHD STUDENT SESSION

Monday 12 October 2026 • 16:50–17:00 • Gorilla 3

AI-Driven Infodemic Surveillance and Its Impact on COVID-19 Vaccine Uptake in Sub-Saharan Africa: A Multi-Country Study

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Background: Vaccine hesitancy remains a major barrier to immunisation success, exacerbated by digital misinformation ecosystems. Recent advances in AI-driven social listening tools enable real-time detection of vaccine-related misinformation and behavioural trends. However, empirical evidence linking these systems to vaccination outcomes in low-resource settings remains limited.

Methods: We conducted a prospective mixed-methods study (2023–2025) across Cameroon, Niger, and Burkina Faso (n = 12,457 participants).

- Data sources:
 - Social media datasets (Twitter/X, Facebook; ~4.2 million posts analyzed)
 - National immunisation records
 - Household surveys
- Intervention:

Deployment of an AI-based infodemic monitoring system (deep learning NLP classifier; F1-score = 0.91) to:

- Detect misinformation clusters
- Trigger targeted public health messaging campaigns
- Outcome measures:
 - Vaccine uptake (primary)
 - Confidence scores (secondary)
 - Misinformation exposure index

Results:

- Misinformation prevalence peaked at 38.4% of vaccine-related content during outbreak waves
- Exposure to misinformation was associated with:
 - –27% reduced likelihood of vaccination (OR: 0.73; 95% CI: 0.69–0.78)
- AI-guided interventions led to:
 - +18.6% increase in vaccine uptake (p < 0.001)
 - +24% improvement in confidence scores
- Regions receiving targeted messaging showed:
 - 2.3× faster recovery in vaccination rates

Discussion: This study demonstrates that AI-enabled infodemic surveillance can significantly improve vaccine uptake by enabling precision public health responses. These findings align with emerging digital health frameworks leveraging machine learning for real-time vaccine sentiment tracking and response systems.

Conclusion: Integrating AI-driven infodemic monitoring into national immunisation programs represents a scalable strategy to counter vaccine hesitancy and strengthen health system resilience in LMICs.

PLENARY SESSION 3: VACCINE TECHNOLOGY

Tuesday 13 October 2026 • 10:15–10:30 • Okapi 1, 2, 3

Safety, Reactogenicity and Immunogenicity of a Launch-iT Rabies Vaccine: A Randomized, Double-Blind, Placebo-Controlled, Dose-Escalation Phase 1 Study in Healthy Adults

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Introduction/Background: The ongoing need for new (prophylactic and therapeutic) vaccines could be addressed by the Launch-iT vaccine platform, which uses DNA plasmids to launch live-attenuated viral vectors upon administration, thereby combining the practical advantages of DNA immunization with the potency of live-attenuated viral vector vaccines. The live-attenuated YF17D vaccine strain of the yellow fever virus was selected as viral vector because of its ability to trigger broad and polyfunctional immune responses in combination with having an excellent long-term safety record. Here, we present the first clinical data with Launch-iT Rabies, which encodes the YF17D genome with the sequence of the rabies glycoprotein (RabG) inserted.

Materials/Methods: Launch-iT Rabies was evaluated in a randomized, double-blind, placebo-controlled, dose-escalation Phase 1 study (SAFYR). In the study, healthy adults aged 18–40 years received a single vaccination with Launch iT Rabies 30µg, 100µg or 300µg, or with placebo (N = 12 per group). Safety was evaluated through the collection of solicited adverse events (AEs) during the 14-day post-vaccination period, unsolicited AEs during a 1-month period, and adverse events of special interest (AESIs) and serious adverse events (SAEs) throughout the 1-year study period. Viremia and shedding of the launched viral vector was evaluated in blood, buccal swabs, urine and feces samples collected from a subset of the participants at the Day 5, Day 8, Day 15 and Month 1 visits. Rabies-specific humoral and cellular immune responses were evaluated throughout the study. (ClinicalTrials.gov Identifier: NCT06998004; EUCT number: 2024-511194-29-00).

Results: Launch-iT Rabies had an favorable safety profile with limited reactogenicity. There were no AESIs, vaccine-related SAEs, or AEs leading to discontinuation from the study. All vaccine-related solicited AEs, and most vaccine-related unsolicited AEs were mild or moderate in intensity, and resolved without treatment. Viraemia (presence of YF17D viral vector RNA) was detected in a single blood sample collected at Day 5 from a participant in the 300µg group. No shedding was detected. Rabies-specific neutralizing antibodies were induced across all Launch-iT Rabies dose groups. The highest response rate was seen in the 100µg group, in which 45.5% of the participants achieved rabies-specific neutralizing antibody levels (RFFIT) ³ 0.3 IU/mL after a single injection. The humoral immune response had a promising durability profile with antibody titers remaining above the detection level for at least 6 months in all seroconverted participants, and above the seroprotective level (³ 10 IU/mL) in most. Moreover, rabies-specific polyfunctional CD4+ T cell responses that persisted for at least 6–12 months were induced in a subset of participants across all dose groups. In addition, 2 participants in the 300 µg group also induced durable rabies-specific polyfunctional CD8+ T cell responses.

Discussion/Conclusion: The obtained data provide initial clinical validation of the novel Launch-iT concept, supporting the feasibility of the in situ launching of viral vectors from a DNA plasmid, and the subsequent induction of broad and durable immune responses against selected target antigens. Our results support the further development of a second-generation Launch-iT, for which we have early preclinical evidence of improved response rates.

CONCURRENT SESSION 4: IMMUNOTHERAPIES

Tuesday 13 October 2026 • 12:10–12:25 • Okapi 1, 2, 3

In situ cancer immunotherapy with modified MVdeltaC measles virus induces potent RIG-I-dependent tumor clearance and immune memoryFrederic TANGY¹, Aleksandr BARINOV¹, Heidy VERA-PERALTA¹, Joëlle NADER², Valérie NAJBURG¹, Jens HOFFMANN³, Jean-François LE BIGOT¹, Jean-François FONTENEAU², Nicolas BOISGERAULT², Anastassia KOMAROVA¹¹ Institut Pasteur Oncovita, France² CRCI2NA / INSERM UMR 1307 / CNRS UMR 6075, Nantes, France³ EPO Experimental Pharmacology & Oncology Berlin-Buch GmbH, Berlin, Germany

Introduction: Oncolytic viruses can destroy tumors directly or by activating antitumor immunity, but balancing safety with potent immune stimulation remains challenging. Live-attenuated measles virus (MV) selectively infects cancer cells through CD46 entry receptor, a membrane inhibitor of the complement cascade which is commonly overexpressed on tumor cells surface to protect them from complement-dependent attacks by the innate immune system (NK cells, ADCC). This enveloped negative-stranded RNA virus replicates preferentially in cells with impaired type I interferon (IFN-I) responses. To enhance innate and adaptive immune stimulation to the tumors, we engineered a C protein-deficient MV, in which a key viral antagonist of innate immunity was eliminated. We evaluated the anticancer properties of this MVdeltaC and its mechanism of action.

Material and methods: The recombinant modified virus was cloned and rescued by reverse genetics. Its anticancer properties were evaluated both in vitro in many human cancer cells and in vivo in different PDX and syngeneic models in immunocompetent mice.

Results and discussion: MVdeltaC exhibited potent oncolytic activity in a panel of human tumor cell lines, with 70% of them showing high sensitivity, including mesothelioma, lung, liver, breast, bladder, ovarian, and cervical cancers. We demonstrated that this enhanced killing activity is driven by the accumulation of 5' copy-back defective viral RNA molecules that activate RIG-I/MAVS signaling and trigger robust type I interferon and pro-inflammatory cytokine/chemokine responses. Transcriptomic analysis of infected human tumor cells showed a strong activation of pathways involved in cancer inflammation, such as TNFα signaling, inflammatory response, INFα and IFNγ responses, apoptosis. Intratumoral vaccination in immunocompetent mice bearing syngeneic neuroblastoma induced complete tumor regression in 90% of animals and established long-term antitumor memory. Antitumor responses were dependent on infiltrating CD8⁺ T and NK cells and were further enhanced by anti-CTLA-4 therapy or CD4⁺ T-cell depletion. Prior measles immunization accelerated tumor clearance, indicating vaccine-boosted responses. MVdeltaC also controlled the growth of human mesothelioma, melanoma, and triple-negative breast cancer xenografts and patient-derived tumors in immunodeficient models. MVdeltaC infection induced immunogenic cell death and the release of tumor antigens, activating dendritic cells and promoting cross-presentation to autologous T cells.

Conclusion: These findings establish MVdeltaC as a clinically ready, broad-spectrum immunotherapeutic that links RIG-I activation by defective viral genome generation to elicit potent and durable antitumor immunity. MVdeltaC is currently under GMP manufacturing and phase 1/2a FIH clinical trial should start in patients with pleural mesothelioma and triple negative breast cancer.

CONCURRENT SESSION 4: IMMUNOTHERAPIES

Tuesday 13 October 2026 • 12:25–12:40 • Okapi 1, 2, 3

Therapeutic HBV vaccine efficacy through ancestral mismatched T cell epitopes

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Background: Therapeutic vaccines for the treatment of chronic viral infections, such as chronic hepatitis B infection, have been mainly designed to target conserved viral regions and to preferentially restore dysfunctional virus-specific CD8 T cells. Such vaccines have failed to deliver clinical benefit, but a recent trial combining siRNA Elabsiran and PEG-IFN- α reported a remarkable ~50% HBsAg loss rate in chronic HBV patients who responded to BRIL-179, a therapeutic vaccine composed of recombinant HBV envelope proteins, administered prior to the trial. (Wong, G. L.-H. et al. Elabsiran and PEG-IFN α for chronic hepatitis B infection: a partially randomised, open-label, phase 2 trial. *Nat. Med.*(2026), 35: 151-159). We conducted a study to define the underlying immunological mechanisms induced by therapeutic vaccinations that lead to increased HBsAg loss rates.

Methods: We studied CHB patients on nucleo(t)side analogue therapy who received BRIL-179 plus siRNA (n=77), with a subset subsequently treated with siRNA and PegIFN- α (n=31). We performed T cell epitope mapping, functional characterization and longitudinal tracking of vaccine-induced T cells, quantification and phenotyping of HBs-specific B cells, and sequence analysis comparing vaccine and infecting HBV strains.

Results: We found that BRIL-179-mediated modulation of HBV-specific immunity did not result from recovery of pre-existing dysfunctional T cells. Instead, the vaccine primed novel IL-2-producing CD4⁺ T cells targeting epitopes that were largely mismatched to patients' infecting HBV strains. These responses were driven by a PreS1 N-terminal domain sequence within the vaccine's large S protein that shows homology to prehistoric HBV lineages that predominated in Eurasia until the late 2nd millennium BCE.

The vaccine-induced CD4⁺ T cells were detected in most vaccinated patients across diverse HLA class II backgrounds and persisted with stable functionality for more than two years. Despite their lack of cross-reactivity with contemporary HBV genotypes, the presence of these epitope-mismatched CD4⁺ T cells was associated with marked, progressive maturation of HBs-specific B cells during PEG-IFN- α /siRNA treatment, consistent with intramolecular T cell help.

Conclusions: We conclude that the ability of BRIL-179 to increase HBsAg loss is associated with the induction of epitope-mismatched CD4⁺ T cells that persist and promote HBs-specific B cell maturation during PEG-IFN- α treatment. These findings challenge current therapeutic vaccine strategies for chronic viral infections that focus on conserved viral regions and CD8⁺ T cell responses, and suggest that ancestral HBV epitopes lost during viral evolution may represent potent targets for inducing therapeutically effective antiviral immunity.

CONCURRENT SESSION 4: IMMUNOTHERAPIES

Tuesday 13 October 2026 • 12:40–12:55 • Okapi 1, 2, 3

mRNA-Encoded HSV Monoclonal Antibody Based Immunotherapy Outperforms Acyclovir in a Murine Model of HSV-1 EncephalitisSita AWASTHI¹, Edward KREIDER¹, Doina ATANASIU², John LUBINSKI¹, Lauren HOOK¹, Briyenna MCWILLIAMS¹, Manaswini GOPALAKRISHNAN¹, Bahiyah WATSON¹, Valerie BROMBERG¹, Sarah SON¹, Justin SU¹, Drew WEISSMAN¹, Gary COHEN², Harvey FRIEDMAN¹¹ Perelman School of Medicine, University of Pennsylvania, United States of America² School of Dental Medicine, University of Pennsylvania, United states

HSV-1 infection can cause encephalitis, a devastating neurological disease associated with substantial morbidity and mortality, despite antiviral therapy. Antibody-based immunotherapies, including bispecific antibodies, have transformed the treatment of cancer and autoimmune disorders, but their application in infectious diseases has lagged. To improve current HSV encephalitis treatment outcomes, we developed a panel of mRNA-encoded anti-herpesvirus antibodies targeting key functional domains of glycoproteins B and D, which achieved potent cross-neutralization of HSV-1 and HSV-2. The antibodies were expressed using mRNA technology as full-length monoclonal antibodies, single-chain variants (ScFv), or bispecific constructs. A single administration of the various mRNA encoding HSV antibodies generated robust systemic ELISA antibody expression detectable up to 28 days and high serum neutralizing antibody titers.

We used a murine model of HSV-1 encephalitis, characterized by rapid disease progression within 96–120 h after intranasal infection and death within 120–172 hours. We determined that prophylactic administration of antibody-encoding mRNAs provided complete protection when delivered 24 h before lethal viral challenge. We next evaluated the efficacy of antibody administered as therapy. Mice were infected intranasally with a lethal dose of HSV-1 and 72 h later, they were either left untreated, treated with daily acyclovir for two weeks, or given a single dose of mRNA encoding a type common ScFv to gB. Remarkably, the antibody treatment eliminated detectable HSV-1 replication in the olfactory bulb, brain, and trigeminal ganglia of 100% of treated animals, a result not achieved in naïve animals, or those receiving prolonged acyclovir therapy. The therapeutic administration of the ScFv gB antibody at 72 h reduced HSV-1 DNA by 4 to 5 log₁₀ in the olfactory bulbs, brain, and trigeminal ganglia compared with untreated controls.

These findings demonstrate the extraordinary therapeutic potential of mRNA-encoded antibody immunotherapy for treatment of severe herpesvirus infections and establish a compelling framework for the developing the next-generation of antiviral biologics capable of improving treatment outcomes.

CONCURRENT SESSION 5: VACCINES FOR VECTOR-BORNE DISEASES

Tuesday 13 October 2026 • 12:10–12:25 • Gorilla 1

Structural Basis of 4G2-Induced Antibody-Dependent Enhancement in Flaviviruses

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Introduction: Flaviviruses, including dengue (DV) and yellow fever (YFV) viruses, represent a major global health threat, causing an estimated 400 million infections annually. A critical challenge in developing effective flavivirus vaccines is the complex immune response these viruses elicit, which can increase disease severity through a phenomenon named antibody-dependent enhancement (ADE). During ADE, sub-neutralizing antibodies bind to the viral surface and promote Fc receptor-mediated internalization and viral replication, thereby increasing viremia and disease severity. This effect is particularly well-documented in dengue, where sequential infection with a heterologous serotype represents a major risk factor for severe disease, especially in seronegative vaccinated individuals (Wells et al., 2025). The monoclonal antibody 4G2 has become a standard tool for measuring ADE in vitro and represents one of the best-characterized examples of this phenomenon. 4G2 binds to the fusion loop on the envelope protein, a highly conserved epitope across flaviviruses, making it a broadly neutralizing antibody with potential for pan-flavivirus vaccine design. Yet this same conserved epitope is also responsible for 4G2-mediated ADE, highlighting a fundamental paradox in flavivirus vaccine development (Kotaki et al., 2021). Understanding how 4G2 simultaneously mediates viral neutralization and enhancement is therefore essential for elucidating the mechanistic basis of ADE and designing safe and effective flavivirus vaccines.

Methods: To elucidate the mechanism behind 4G2-induced ADE, we employed a comprehensive experimental approach combining structural and functional analyses. We generated immunocomplexes by incubating 4G2 first with dengue envelope dimers and then with yellow fever virions, progressively increasing the biological complexity of the system. Structural characterization was performed using cryo-electron microscopy (cryoEM) to visualize at high resolution the interactions between epitopes and paratopes. We validated these structural observations through complementary functional assays, such as RNA protection assays, using YFV pre-incubated with 4G2 antibodies at different concentrations and timepoints.

Results: CryoEM analysis revealed that 4G2 binds exclusively to monomeric dengue E proteins, with clear Fab density associated only with E monomers, while binding to E dimers was not observed. This selectivity likely reflects restricted accessibility of the fusion loop epitope within the dimeric conformation. When full YFV virions were treated with 4G2, cryoEM showed dose-dependent disruption of viral architecture, with particles appearing damaged or collapsed. These structural observations were supported by RNA protection assays, which demonstrated dose-dependent reduction in protected viral RNA following 4G2 treatment, indicating compromised virion integrity.

Discussion: Our data reveal a mechanistic model of 4G2-induced ADE based on a concentration-dependent switching mechanism. At low antibody concentrations, 4G2 binding to viral surfaces facilitates Fc receptor-mediated internalization and viral replication, thus promoting ADE. Conversely, at higher antibody concentrations, 4G2 binding induces E dimer dissociation, exposing the fusion loop epitope and destabilizing the overall viral architecture, thereby preventing ADE. This mechanism is explained by the mutually exclusive nature of 4G2-E protein interactions and E-E dimer interactions. These structural insights into the molecular dynamics of ADE have important implications for flavivirus vaccine design, specifically highlighting the need to elicit protective antibody responses while avoiding sub-neutralizing concentrations that enhance infection.

CONCURRENT SESSION 5: VACCINES FOR VECTOR-BORNE DISEASES

Tuesday 13 October 2026 • 12:25–12:40 • Gorilla 1

Rational design of live-attenuated West Nile virus vaccines that are non-transmissible by vector mosquitoesKristel DOETS, Barry ROCKX, Monique VAN OERS, Gorben PIJLMAN*Wageningen University & Research, Netherlands, The*

West Nile virus (WNV) is a highly pathogenic flavivirus transmitted by mosquitoes. All flaviviruses produce abundant quantities of small non-coding viral RNA required for pathogenicity in vivo. This so-called subgenomic flavivirus RNA (sfRNA) is the product of incomplete viral genomic RNA degradation by the cellular exoribonuclease XRN1, which stalls at conserved RNA structures in the 3' untranslated region (UTR). SfRNA-deficient WNV mutants are hypothesized to be promising live-attenuated vaccines. However, a first generation of sfRNA mutants appeared genetically unstable: mutations in the 3'UTR either reverted to wildtype sequence or induced deletions. Here we engineer genetically stable WNV variants through random mutagenesis of three-dimensional RNA structures within the 3'UTR that are essential for sfRNA biogenesis, followed by high-throughput phenotypical selections. WNV mutants that were genetically stable for at least 10 passages were analysed for failure to induce cytopathic effect in cell culture and the (in)ability to produce sfRNA. The sfRNA-deficient WNV mutants showed significantly reduced viral spread in midguts observed by immunofluorescence and lower infection rates of *Culex pipiens* mosquitoes. Four live-attenuated vaccine candidates were evaluated in safety studies to monitor the level of attenuation in mice. We were able to select a genetically stable vaccine candidate, deficient in sfRNA expression and sufficiently attenuated, that confers full protection against WNV challenge in a wildtype C57/BL6 model of WNV disease.

CONCURRENT SESSION 5: VACCINES FOR VECTOR-BORNE DISEASES

Tuesday 13 October 2026 • 12:40–12:55 • Gorilla 1

Novel dengue virus non-structural protein vaccine that can prevent disease exacerbation caused by existing vaccines

Kyoko TSUKIYAMA-KOHARA¹, Jun-ichiro TAKANO², Bouchra KITAB¹, Mohammad EH KAYESH¹, Asako TAKAGI³, Fumihiko YASUI³, Tomoko HONDA³, NT M MYATT⁴, Ryosuke SUZUKI⁵, Atsushi YAMANAKA⁶, Koji ISHII⁵, Yasuhiro YASUTOMI², Kouichi MORITA⁴, Michinori KOHARA³

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Epidemics of the dengue virus (DENV) primarily occur in tropical regions, infecting around 400 million people each year. Of these, approximately 100 million develop dengue fever. Therefore, there is an urgent need for a safe and effective vaccine that does not induce antibody-dependent enhancement (ADE) and that addresses the link between vaccine-induced disease exacerbation. We constructed a recombinant vaccinia virus (VV) that has inserted nonstructural protein 2-5 regions of DENV (rDIs-DENV2C-NS25) using the attenuated VV DIs strain as a vector. This strain can provide lifelong immunity.

The rDIs-DENV2C-NS25 significantly induced IFN γ and IL-2 in response to NS protein peptides, indicating its potential to induce cellular immunity to DENV in mice. In Type I Interferon-receptor knockout (A129) mice, immunization of rDIs-DENV2C-NS25 and/or rDIs-DENV4-NS25 provide anti-viral response to DENV1~4, almost similar to or more than the existing recombinant DENV vaccines against DENV infection. The ADE activity was detected in mouse sera after immunization with existing vaccines and further DENV challenge, as shown by a single-round infectious particle (SRIP) assay. In contrast, ADE activity was not induced by immunization of rDIs-DENV-NS25 alone, nor after DENV challenge.

The effect of rDIs-DENV2C-NS25 was further examined with the non-human primate model. The immunization of rDIs-DENV2C-NS25 significantly induced IFN γ in response to peptides from NS2b and NS4b by ELISPOT assay. It can significantly suppress DENV2C infection in the liver and spleen tissues of the macaque monkey. Significant induction of IFN γ responsive monokine, MIG (CXCL9), and significant suppression of inflammatory chemokine, Eotaxin-1 (CCL11), in liver tissues after 7 days of DENV-2 challenge were observed. ADE activity was not induced by rDIs-DENV2C-NS25 immunization.

Thus, rDIs-DENV2C-NS25 constitutes a safe and effective novel vaccine candidate for DENV, which does not induce ADE and demonstrates antiviral efficacy across all DENV serotypes through cell-mediated immunity.

CONCURRENT SESSION 6: "BRIGHT SPARKS" IN VACCINOLOGY – ECR SESSION

Tuesday 13 October 2026 • 11:20–11:30 • Gorilla 3

Effectiveness of PCV10 and PCV13 against invasive pneumonia disease in vietnamese children prior to national introduction: a matched case-control study

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Background: Evidence on the effectiveness of pneumococcal conjugate vaccines (PCVs) in Vietnam remains limited, despite the availability of 10-valent (PCV10) and 13-valent (PCV13) conjugate vaccines in the private sector since 2014 and 2019. We evaluated the effectiveness of PCVs against invasive pneumococcal disease (IPD) among Vietnamese children prior to national introduction.

Method: We conducted a matched case-control study between February 2022 and January 2025 in southern Vietnam. Cases were children aged 2–59 months hospitalized with culture-confirmed IPD from normally sterile sites at three tertiary pediatric hospitals. Four age- and neighborhood-matched community controls were enrolled per case. Vaccine effectiveness (VE) was estimated using conditional logistic regression as $(1 - \text{adjusted odds ratio}) \times 100\%$.

Results: We enrolled 72 IPD cases and 288 matched controls; 37.5% of cases had received ≥ 1 PCV dose. The most frequent clinical syndromes were meningitis (36.1%) and pneumonia-associated sepsis (30.6%). Serotype 19A predominated (26.4%), followed by 6A (13.9%) and 19F (11.1%); 77.8% of cases were caused by serotypes included in PCV13. For vaccine-type IPD (VT-IPD), adjusted VE of PCV10 against PCV10-type IPD was 86.3% (95% CI: 13.3–97.9) for ≥ 1 dose and 89.5% (95% CI: 16.1–98.7) for ≥ 2 doses; VE of PCV13 against PCV13-type IPD was similarly high. Against all-serotype IPD, adjusted VE was 65.1% (95% CI: 21.8–84.4) for ≥ 1 PCV10 dose and 84.4% (95% CI: 20.0–97.0) for ≥ 1 PCV13 dose. No significant effectiveness was observed against non-PCV10-type IPD. VE was highest against serotype 6A and declined with increasing time since vaccination.

Conclusion: This first Vietnamese evidence demonstrates that PCV10 and PCV13 provide substantial protection against VT-IPD and overall IPD in young children despite low vaccine coverage. The predominance of serotype 19A and waning protection over time emphasize the importance of selecting 19A-containing formulations and booster schedules to inform timely national PCV introduction in Vietnam.

CONCURRENT SESSION 6: "BRIGHT SPARKS" IN VACCINOLOGY – ECR SESSION

Tuesday 13 October 2026 • 11:30–11:40 • Gorilla 3

Age-specific immunity gaps and residual susceptibility to measles and rubella before and after the measles–rubella supplementary immunisation campaign in South India

Ramya MADHAVAN, Akilandeswari ESWARAN, Vaishnavi GANDHI, Tintu VARGHESE, Poornima SARAVANAN, Lakshmi RAJ, Reshma RAJU, Julian Vivek LEANDER XAVIER

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Background: Monitoring population immunity to vaccine-preventable diseases (measles, rubella) is essential for guiding elimination and control strategies. Over the past decade, India has implemented major public health interventions, notably the national measles-rubella (MR) supplementary immunization activity (2017–2020). Despite these national initiatives, regional evidence on their population-level impact remains sparse. This study aimed to evaluate age- and gender-stratified seropositivity patterns for MR in 2013 and 2022 in a South Indian community based cross sectional study, providing localized data to inform policy and identify potential immunity gaps.

Methods: Biobanked serum samples collected in 2013 and 2022 as part of other studies, were tested for IgG antibodies to measles and rubella by ELISA. Serostatus was defined using disease-specific optical density (OD) cut-offs. Close to 800 samples with ~200 samples in each age-strata (1-5 years, 6-15 years, 16-40 years and >40years) were tested for the IgG antibody. Age and gender stratified descriptive statistics and density plots were generated to assess antibody distributions 5 years before and 5 years after the MR campaign. In addition, two-component normal mixture model was fitted to log-transformed antibody titre/ OD data to estimate the seronegative proportion and effective reproduction number (R_e). Multilevel generalised linear mixed-effects models (GLMER) were fitted with year, age, and gender as fixed effects, and geographic cluster as a random effect, to identify predictors of seronegativity.

Results: Descriptive analysis showed a substantial increase in seroprevalence for measles and rubella between 2013 and 2022 across all age groups and gender. Mixture modelling indicated that the measles, the seronegative proportion declined from 26.7% to 18.9%, with R_e falling from 3.20 to 2.27; despite improvement, R_e remained above 1, suggesting ongoing outbreak potential. For rubella seronegative proportion declined from 28.0% to 7.0%, reducing R_e to 0.49 in 2022, consistent with herd immunity. Multilevel modelling further clarified these patterns. For measles and rubella, year and age were highly significant predictors of seronegativity. Gender had no effect for measles but was significant for rubella, with males less likely to be seronegative. Cluster-level variation was minimal for measles and modest for rubella.

Conclusion: This study demonstrates the strong impact of India's MR vaccination campaign, achieving herd immunity for rubella and improving measles immunity, though additional efforts are needed to eliminate measles transmission. The findings highlight the distinct pathways through which vaccination and exposure shapes population immunity profiles, and the continued need for surveillance to identify immunity gaps in specific age strata.

CONCURRENT SESSION 6: "BRIGHT SPARKS" IN VACCINOLOGY – ECR SESSION

Tuesday 13 October 2026 • 11:40–11:50 • Gorilla 3

Antigen composition, not T-cell functionality, limits cross-reactivity to distant Coronaviruses after bivalent SARS2 Spike vaccinationZiyin WANG, Nematullah WASEEM, Naomi PEISAJOVICH, Aaron SUTHERLAND, April FRAZIER, Alessandro SETTE, Alba GRIFONI*La Jolla Institute for Immunology, United States of America*

The COVID-19 pandemic highlighted the need for vaccines strategies that elicit broad T cell-mediated immunity against emerging viral families. BetaCoronaviruses, including severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome (MERS-CoV), pose significant pandemic risks due to their zoonotic potential and genetic diversity. While current vaccines have been highly effective at reducing severe disease and mortality, they are primarily designed to enhance antibody responses to the Spike protein and remain susceptible to viral evolution. In contrast, T-cell immunity- particularly when directed against conserved regions of viral proteins – offer a promising avenue for achieving broader and more durable protection. We have previously identified Conserved Spike T cell epitope regions (CTERs) within the ancestral Wuhan Spike protein that exhibit strong cross-reactive potential across multiple BetaCoronavirus subgenera.

In this study, we investigated whether bivalent Spike-based vaccination (Beta + Omicron) enhances T cell responses targeting CTERs and improves cross-reactive immunity across BetaCoronavirus. Peripheral blood mononuclear cells (PBMCs) were collected from 56 adult participants enrolled in the COVAIL trail at baseline (day 0) and 90 days post-vaccination. Antigen-specific CD4+ and CD8+ T cell response were assessed using a combined activation-induced marker (AIM) and intracellular cytokine staining (ICS) assay within a 25-color flow cytometry panel. We compared responses elicited by peptide pools spanning CTER and nonCTER regions derived from SARS-CoV-2, SARS-CoV-1 and MERS-CoV.

At the population level, bivalent vaccination did not increase the magnitude, breadth, or functional quality of cross-reactive T-cell responses, nor did it preferentially enrich CTER-specific responses within the Spike-directed repertoire. Although individual donors exhibited heterogeneous changes in cross-reactive responses, these variations did not translate into a consistent population-wide shift. Despite the absence of enhanced cross-reactivity, CTER-specific T cells exhibited elevated IFN γ production, preserved memory differentiation, and showed no evidence of increased expression of exhaustion markers following vaccination. These results indicate that conserved epitope-specific T cells remain functionally competent and are not intrinsically limited in their capacity to mediate cross-reactive immunity.

Collectively, our findings suggest that repeated exposure to Spike alone is insufficient to redirect established T-cell immunity toward conserved epitopes capable of broad BetaCoronavirus recognition. Instead, the limited enhancement of cross-reactivity appears to reflect constraints imposed by antigen composition rather than T-cell functionality. These results highlight a key limitation of Spike-focused vaccine strategies and support the development of next-generation vaccines that incorporate conserved epitopes from multiple viral proteins. Such approaches may better harness the full potential for T-cell-mediated immunity to achieve durable, cross-protective responses against diverse and emerging coronaviruses.

CONCURRENT SESSION 6: "BRIGHT SPARKS" IN VACCINOLOGY – ECR SESSION

Tuesday 13 October 2026 • 11:50–12:00 • Gorilla 3

Implementation Effectiveness of a Community-Driven Vaccination Model at Boosting Immunization in Two Conflict-Affected Health Districts of Cameroon: A Quasi-Experimental Study

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Background: Childhood vaccination coverage remains suboptimal in humanitarian and resource-limited settings, with community-level barriers significantly impeding immunization uptake. This study evaluated the implementation effectiveness of a community-driven vaccination (CDV) model at improving vaccination coverage in conflict-affected regions of Cameroon characterized by frequent lockdowns, population displacement, high socioeconomic burden, and limited health infrastructure.

Methods: The study employed a quasi-experimental design with non-random allocation conducted between August and November 2025 in Bafut and Tombel health districts. Four intervention health areas within the districts were sampled using paper-based cluster sampling and matched with four control areas. The intervention comprised local stakeholder engagement and Community Health Worker (CHW)-led household sensitization, identification, and referral of zero-dose and undervaccinated children. Pre- and post-intervention surveys were conducted to assess reductions in the number of children with incomplete vaccination schedules as the primary outcome; while changes in CHW engagement, caregiver vaccination attitudes, trust, and barriers as secondary outcome measures. Difference-in-differences analysis was used to estimate intervention's net effects.

Results: The study surveyed 1,364 caregiver-child pairs across 144 communities (quarters) in the two health districts including 779 pre-intervention participants (285 control, 494 intervention) and 585 postintervention participants (256 control, 329 intervention). The intervention achieved a 33.6% relative reduction in the number of children with incomplete schedules as the primary outcome, declining from 34.8% to 23.1% in the intervention arm ($p=0.0004$) versus 35.1% to 32% in controls ($p=0.5092$), with a net effect of -8.6 pp attributable to the intervention. Coverage of the pentavalent vaccine (Diphtheria-Pertussis-Tetanus-Hepatitis B- Haemophilus influenzae type b vaccines combined) was 97.7% (95% CI: 96.8–98.4) among the intervention group vs. 95.1% (95% CI: 90.4–97.6) among the control group. Similarly, coverage was 85.7% (95% CI: 76.8–91.5) vs. 81.7% (95% CI: 76.4–86.0) for the measles-rubella vaccine, and 87.1% (95% CI: 81.8–91) vs. 82.4% (95% CI: 79.7–84.9) for vitamin A supplement across the intervention versus the control arms, respectively. In the intervention arm, CHW engagement increased significantly from 35.1% to 73.8% ($p<0.001$), representing a net effect of +24.4 pp. Significant improvements in the intervention group were also observed in vaccination attitudes: low trust decreased by 90.6% (12.8% to 1.2%, $p<0.001$), negative perceptions declined by 82.9% (10.5% to 1.8%, $p<0.001$), and fear of side effects reduced by 71.4% (18.2% to 5.2%, $p<0.001$).

Conclusions: CHW-led interventions represent an effective and scalable strategy for improving vaccination coverage. These findings, therefore, support integration of the CDV model into national immunization programmes, particularly in humanitarian and resource-limited settings.

CONCURRENT SESSION 6: "BRIGHT SPARKS" IN VACCINOLOGY – ECR SESSION

Tuesday 13 October 2026 • 12:00–12:15 • Gorilla 3

Establishing a blood-stage Controlled Human Malaria Infection model in healthy Tanzanian adults with varying prior exposure to *P. falciparum*Omar HASSAN, Florence MILANDO, Latipha MOHAMED, Nassoro LILOLIMWE, Neema BALIGE, Ally OLOTU*Ifakara Health Institute, Tanzania*

Controlled human malaria infection (CHMI) studies play a crucial role in assessing potential interventions and understanding immune protection to inform malaria vaccine development. Blood-stage CHMI offers a more precise means for proof-of-concept testing of blood-stage interventions like vaccines and drugs through bypassing the pre-erythrocytic stages of malaria infection. Unlike sporozoite CHMI, blood-stage CHMI has not been utilized in malaria-endemic countries prior to this trial.

For the first time, we aimed to establish a blood-stage CHMI model in an endemic region in a clinical trial involving healthy adults aged 18–45 residing in Bagamoyo, Tanzania. Based on *P. falciparum* anti-schizont IgG serology, twelve participants meeting eligibility criteria were enrolled into "low" (n=6) and "high" (n=6) prior malaria exposure groups. The groups comprised individuals with anti-schizont IgG levels below the 25th percentile and above the 75th percentile of the population scale, respectively. Participants were challenged with approximately 1000 chloroquine-sensitive *P. falciparum* 3D7 clone-infected erythrocytes on day of challenge (C+0) and closely monitored for 28 days at the IHI clinical trial facility in Bagamoyo. Participants underwent twice daily clinical assessments where Malaria associated Adverse events (AEs) were also solicited. Unsolicited adverse events were collected throughout study participation. Blood samples were collected for safety and immunology assessments at designated times points, with venous blood samples for *P. falciparum* qPCR collected once on day C+1 then twice daily up to C+28. Malaria associated Adverse events were solicited when malaria qPCR parasitemia reached a threshold of ≥ 500 parasites/ μ L, if a volunteer showed signs or symptoms of malaria with a previous qPCR result of ≥ 200 parasites/ μ L or on day C+28 if none of the former criteria were met, treatment with artemether-lumefantrine and a single low dose of primaquine was administered. Participants were then sampled daily and discharged at the discretion of the investigators once two consecutive negative daily qPCR results were attained. Before treatment, blood samples were collected for direct membrane feeding assay (DMFA) to assess *P. falciparum* transmission.

AEs collected during the trial were mostly mild and rarely moderate, there were no severe AEs and no serious AEs. AEs were more frequently reported in the low prior malaria exposure group. There were no serious adverse events. 10 of the 12 participants developed parasitemia detectable by qPCR. There was no significant difference between the median asexual parasite densities at first positive between the two groups. Median time to detectable parasitemia and pre-defined treatment criteria was longer in high prior malaria exposure group compared to low prior malaria exposure group. Abnormal safety laboratory results were observed for transaminases, neutrophils, lymphocytes and platelets. These changes were transient and ranged from mild to moderate before resolving completely.

The challenge inoculum was found to be safe with frequency and severity of AEs in keeping with previous challenge studies. Participants reached 50-fold higher parasite densities with fewer AEs compared to naïve UK adults who underwent challenge with a similar dose of the inoculum. These data support the onward use of this model in assessing Malaria interventions

CONCURRENT SESSION 6: "BRIGHT SPARKS" IN VACCINOLOGY – ECR SESSION

Tuesday 13 October 2026 • 12:15–12:30 • Gorilla 3

An Intranasal Hemagglutinin Protein Booster After Intramuscular mRNA Vaccination Enhances Mucosal Immunity and Confers Protection Against Influenza Virus in FerretsSeokchan PARK^{1,2}, Vivian YAN^{1,2,3}, Gabriel LAGHLALI^{1,2}, Juan GARCÍA-BERNALT DIEGO^{1,2,4}, Farah EL-AYACHE^{1,2}, Kaijun JIANG^{1,2,3}, Adolfo GARCÍA-SASTRE^{1,2,5}, Miyu MORIYAMA⁶, Akiko IWASAKI^{6,7,8}, Michael SCHOTSAERT^{1,2}¹ Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY, USA² Global Health Emerging Pathogens Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA³ Graduate School of Biomedical Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA⁴ Department of Microbiology, Instituto de Investigación Hospital Universitario 12 de Octubre (Imas12), Madrid 28041, Spain⁵ Department of Medicine, Division of Infectious Diseases, Icahn School of Medicine at Mount Sinai, New York, New York 10029, United States⁶ Department of Immunobiology, Yale School of Medicine, New Haven, CT 06510⁷ Center for Infection and Immunity, Yale School of Medicine, New Haven, CT 06510⁸ HHMI, Chevy Chase, MD 20815

Influenza viruses remain a major global public health concern, causing substantial morbidity and mortality despite widespread vaccination efforts. Currently licensed parenteral influenza vaccines primarily induce systemic antibody responses that reduce disease severity but are limited in their ability to generate robust mucosal immunity at the primary sites of viral entry. Consequently, intranasal vaccination strategies have been proposed to elicit both mucosal and systemic immune responses. However, to date, only a single live attenuated intranasal influenza vaccine has been licensed, and its use remains restricted in certain age groups due to platform-specific limitations. To overcome these challenges, a heterologous prime–boost (prime–pull) strategy—consisting of intramuscular priming followed by an intranasal boost—has emerged as a promising approach. This strategy is particularly attractive given that most licensed vaccines are administered parenterally and has been shown to effectively enhance mucosal immunity even after systemic priming. Here, we evaluated an intranasal booster strategy using unadjuvanted recombinant hemagglutinin (HA) following primary messenger RNA–lipid nanoparticle (mRNA–LNP) vaccination in a ferret model. Experimental groups included a PBS control, an LNP–luciferase control (LNP), a currently licensed influenza vaccine (QIV), a three-dose mRNA regimen (mRNA), and a heterologous regimen consisting of two mRNA doses followed by an intranasal HA boost (mRNA–HA). The mRNA-only regimen elicited the highest levels of circulating HA-specific serum antibodies, underscoring the strong systemic immunogenicity of the mRNA platform. In contrast, the mRNA–HA regimen induced significantly enhanced mucosal antibody responses compared with both the mRNA and QIV groups, demonstrating the effectiveness of the prime–pull strategy. Importantly, the mRNA–HA regimen conferred superior protection against homologous H1N1 influenza virus infection in both the upper and lower respiratory tracts, as evidenced by reduced viral replication and attenuated lung pathology relative to QIV. Transcriptomic analysis further revealed that this regimen did not induce excessive early interferon-stimulated gene (ISG) responses, while maintaining balanced IFN- γ levels, consistent with efficient viral control without excessive inflammation or immunopathology. Collectively, these findings demonstrate that an adjuvant-free intranasal HA booster following mRNA priming is a safe and effective strategy for enhancing mucosal immunity and protection against influenza virus infection. The efficacy of this prime–pull approach in preventing viral transmission is currently under investigation in a ferret transmission model.

CONCURRENT SESSION 6: "BRIGHT SPARKS" IN VACCINOLOGY – ECR SESSION

Tuesday 13 October 2026 • 12:30–12:45 • Gorilla 3

Divergent innate and humoral immune responses to 4CMenB vaccination in transgender individuals receiving gender-affirming hormone therapy

Anthony WILLEMS¹, Sharon PORREZ¹, Marjolein VERSTRAETE¹, Thoma VANNIEUWERKE¹, Gwenn WAERLOP¹, Azhar ALHATEMI², Bart JACOBS², Simon DE GUSSEM², Fien DE BOEVER², Jeroen VERVALCKE³, Guy T'SJOEN³, Geert LEROUX-ROELS¹, Isabel LEROUX-ROELS^{1,2}, Valentino D'ONOFRIO^{1,2}

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Introduction: Sexual dimorphism significantly influences immune responses, with men and women exhibiting distinct immune reaction patterns to vaccination or infection. While sex chromosomes contribute to these differences, sex hormones provide an additional, dynamic layer of regulation in immune function. We investigated immune responses following vaccination in transgender persons receiving gender-affirming hormone therapy (GAHT) and compared them to cisgender persons not receiving exogenous hormone therapy. The goal is to study the influences of sex hormones on vaccine-induced immune responses in different chromosomal backgrounds.

Methods: This ongoing, open-label clinical study evaluates immune responses in healthy adults (18-50 years) following vaccination with 4CMenB (Bexsero®). Participants are stratified into four cohorts: cisgender men (CM; n = 17), cisgender women (CW; n = 19), transgender men (TM; n = 17), and transgender women (TW; n = 15). Blood samples were collected at baseline (D0), before the second dose (D28), and at multiple post-vaccination time points (D1, D29, D56).

Innate immune responses were evaluated by measuring serum cytokine concentrations at D0, D1, D28, and D29 using U-PLEX kits on the Meso Scale Discovery platform. Humoral immunity was assessed using the human serum bactericidal antibody (hSBA) assay on serum samples collected at D0, D28, and D56, with antibody responses summarized as log₁₀-transformed geometric mean titres (GMT).

Results: Several chemokines involved in monocyte, and dendritic cell recruitment showed significantly elevated median concentrations (pg/ml) in CM (XY) and TM (XX and testosterone treated) one day after each vaccine administration (D1, D29). Notably, MCP-4 levels were significantly higher in TM compared to TW (D29: 1076.37 vs. 700.70, p=0.001), as well as elevated MCP-1 levels in TM compared to TW (D29: 2492.48 vs. 1771.77, p=0.028). In addition, several other chemokines and cytokines were significantly different between cohorts on D29, including MIP-1β, eotaxin, IL-18, as well as pro-inflammatory (IL-15) cytokines. Comparable trends were observed on D2 across gender groups. Additional cytokines were also assessed, but no significant differences between cohorts were observed.

One month after the second dose (D56), GMT analyses revealed distinct responses: TW (XY and estrogen treated) exhibited the highest GMTs overall, particularly against the NZ98/254 strain (97.01 [66.99-140.48]), exceeding those observed in CM (46.19 [19.15-111.40]), CW (44.44 [24.61-80.25]), and TM (37.67 [19.58-72.46]), although not significantly. For strain 44/76, non-significant higher GMTs were observed in participants with an XY chromosomal background (CM: 75.34 [37.99-149.39], TW: 80.63 [47.71-136.28]) vs. an XX chromosomal background (CW: 38.40 [20.27-72.77], TM: 46.19 [27.75-76.87]). Strain 5/99 elicited higher GMTs in CM (156.95 [93.50-263.44]) and TM (testosterone treated) (122.89 [58.57-257.85]) vs. CW (64.00 [31.16-131.46]) and TW (70.20 [32.09-153.57]).

Conclusion: Distinct vaccine-induced innate and humoral immune responses were observed across gender groups, with increased early chemokine responses in testosterone-high genders (CM and TM), and stronger hSBA responses in XY individuals (CM and TW) against two of three 3 reference strains. These findings suggest that hormonal and chromosomal backgrounds differentially modulate early innate activation and subsequent humoral immune responses following vaccination. Ongoing cellular and multi-omics analyses will further elucidate mechanisms underlying these differences.

PLENARY SESSION 4: SYSTEMS VACCINOLOGY

Tuesday 13 October 2026 • 16:25–16:50 • Okapi 1, 2, 3

Artificial Intelligence and Machine Learning (AI/ML) in the development of mRNA vaccines

Fernando ULLOA MONTOYA

Sanofi, Belgium

First-generation mRNA vaccines (mRNA 1.0) have demonstrated clinical efficacy across three targets (SARS-CoV-2, RSV, influenza), favorable immunogenicity with induction of functional antibodies and CD4/CD8 T cell responses, and a platform approach that accelerates time to clinic. However, mRNA 1.0 falls short on key vaccine attributes: reactogenicity can exceed that of non-mRNA comparators in an antigen-dependent manner and thermostability remains inferior to conventional platforms. Addressing these gaps to deliver mRNA 2.0 requires navigating a vast, multi-parameter design space—spanning mRNA sequence, lipid nanoparticle (LNP) formulation, and manufacturing—that is intractable to conventional one-parameter-at-a-time optimization.

This presentation describes how Sanofi's integrated mRNA Center of Excellence applies AI/ML across the value chain to enable this transition. On sequence design, we developed CodonBERT, a foundational large language model trained on 10 million mRNA sequences across species and fine-tuned for protein expression, which outperforms published models including in flu antigen expression prediction. In parallel, RiboNN, a deep neural network trained on over 2,000 mammalian Ribo-seq datasets, predicts translational efficiency directly from RNA sequence, identifying the 5' UTR and ORF as the most information-dense regions for translational output. Combining generative algorithms with predictive oracles including RiboNN and massively parallel screenings, we have generated novel UTRs that outperform our baseline.

On reactogenicity, we leveraged ML with data from Sanofi's proprietary MIMIC® system, an in vitro immune construct platform, to rank LNP candidates by biological signals resulting from different cell types: dendritic cells, monocytes, macrophages, and endothelium ahead of clinical testing. This forward-translation approach shows high concordance with clinical reactogenicity outcomes across multiple trials, enabling preclinical down-selection of candidates. For manufacturability, mechanistic, and data-driven modeling of drug substance and LNP drug product processes are being used to link process parameters (flow rate ratio, mixing, pH, temperature) to critical quality attributes and immunogenicity, moving toward manufacturability-by-design.

Collectively, this translational AI/ML ecosystem—integrating high-throughput data generation, predictive and generative modeling, and active learning—represents a paradigm shift from trial-and-error, single-parameter approaches to data-driven, multi-parameter optimization. Key open questions remain around biomarkers predictive of efficacy and reactogenicity, translatability of preclinical models across diverse LNP formulations, and structure-function relationships governing LNP performance. This comprehensive strategy positions mRNA technology for systematic, AI/ML-enabled advancement toward safer, more stable, and more effective vaccines for patients.

Disclosure: This work has been funded by Sanofi. Fernando Ulloa Montoya is a Sanofi employee and may hold shares or stock options in the company.

PLENARY SESSION 4: SYSTEMS VACCINOLOGY

Tuesday 13 October 2026 • 16:50–17:05 • Okapi 1, 2, 3

Induction of HIV broadly neutralizing antibodies by human vaccination

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Introduction/Background: An effective HIV vaccine will likely require the induction of broadly neutralizing antibodies (bnAbs), ideally targeting multiple conserved sites of vulnerability on the HIV envelope (Env) glycoprotein. These specialized antibodies can overcome the great genetic diversity of HIV by targeting the most conserved regions of Env. However, no HIV vaccine has yet succeeded in inducing even a single bnAb lineage in humans, in part because inferred germline precursor B cells with bnAb potential typically fail to recognize native-like Env and require extensive affinity maturation to acquire neutralization breadth. The germline-targeting (GT) vaccine approach aims to guide the maturation process of such precursor B cells towards becoming broadly neutralizing, and depends on an engineered priming immunogen to activate and expand bnAb precursor B cells. One such priming immunogen is germline-targeting trimer BG505 SOSIP GT1.1 gp140 (GT1.1), designed to activate precursor B cells that target the conserved CD4bs epitope, in particular those of the VRC01-class.

Material/Methods: Three doses of 300 µg GT1.1 adjuvanted with AS01B was evaluated in 19 healthy participants in a phase I clinical trial IAVI C101 (NCT04224701) performed in the Netherlands and the United States. Peripheral blood mononuclear cells (PBMCs) from GT1.1 recipients were collected two weeks post-vaccination, and GT1.1-induced CD4bs-directed MBCs were single cell sorted. Two doses of BG505 SOSIP.664 adjuvanted with Alum/3M-052 were evaluated in 12 C101 participants in two related follow-up trials IAVI C107/IAVI C110 (NCT05863585/NCT05983874), also conducted in the Netherlands and the United States, respectively.

Results: GT1.1 successfully primed VRC01-class responses in most participants, while also engaging diverse non-VRC01-class CD4bs-directed B cells through improved CD4bs accessibility. We characterized this diverse memory B cell (MBC) response and show that GT1.1 activates a functional CD4bs-directed MBC response that shares features with infection-induced bnAbs such as longer-than-average CDRH3 lengths. GT1.1 induced multiple independent B cell lineages capable of neutralizing wild-type viruses, with some IGHV4-encoded lineages showing cross-clade HIV neutralization. A subset of GT1.1-induced CD4bs-directed lineages persisted for over 80 weeks after the final GT1.1 immunization before they were boosted by fully glycosylated BG505 SOSIP.664. Notably, one lineage, referred to as VINCA1, included 223 members, showed great expansion upon boosting and displayed up to 56% breadth on a 119-strain multi-clade panel designed to represent the global diversity of HIV, thereby presenting itself as the first human HIV vaccine-induced CD4bs-directed B cell lineage. Two cryo-EM structures with wild-type trimers revealed that the VINCA1 lineage displays a CDRH3-dominated binding type, and that it interacts with the CD4bs using a novel and conserved epitope within the CD4bs "supersite". The CDRH3 includes non-templated nucleotide additions that encode for residues that drive neutralization breadth. These residues were conserved throughout the whole lineage, including members

isolated at early timepoints. Together, these results highlight that VINCA1 is a unique lineage, with intrinsic or early adopted characteristics that allow for bnAb development.

Discussion/Conclusion: Our work expands the understanding of CD4bs-directed B cells after vaccination and provides proof-of-concept that we can steer bnAb development using sequential immunization with increasingly more complex trimers in humans

PLENARY SESSION 4: SYSTEMS VACCINOLOGY

Tuesday 13 October 2026 • 17:05–17:20 • Okapi 1, 2, 3

Genome-guided identification and validation of novel T-cell vaccine targets for cross-species malaria protectionCarla PROIETTI¹, Anouschka AKERMAN¹, Margaret KING¹, Roos VAN SCHUIJLENBURG¹, David J PATTINSON², Jonathan TAN¹, Sarah DRAPER³, Lauren Holz HOLZ⁴, Ian F HERMANS⁵, William R HEATH⁴, Gavin F PAINTER³, Denise L DOOLAN¹¹ The University of Queensland, Australia² James Cook University, Cairns, Australia³ Victoria University Wellington, Wellington, New Zealand⁴ The University of Melbourne, Melbourne, Australia⁵ Malaghan Institute of Medical Research, Wellington, New Zealand.

Introduction/Background: Malaria remains a major global health challenge despite recent deployment of first-generation malaria vaccines. The licensed RTS,S and R21 vaccines both target the sporozoite surface protein, the circumsporozoite protein (CSP), and provide only partial, strain-specific protection, highlighting the need for vaccines capable of inducing broad, durable immunity. Effective vaccines against the pre-erythrocytic (sporozoite/liver) stage of the parasite life cycle would stop disease and prevent transmission, making vaccines that induce durable liver-stage immunity a global health priority. T-cell responses directed against antigens expressed in the infected hepatocytes are implicated as critical effectors, and preclinical studies show that vaccine-induced responses against specific liver-stage malaria can provide cross-species immunity. However, the Plasmodium parasite expresses more than 5,300 proteins, and the optimal antigen targets of protective T-cell responses against liver stage malaria are unknown.

Methods: To address this knowledge gap, we implemented a systematic genome-guided, human-informed antigen discovery strategy to identify the optimal Plasmodium targets for a cross-species malaria vaccine. Cellular and humoral immune responses against the complete Plasmodium falciparum proteome were comprehensively profiled in malaria-exposed individuals with immunity to malaria. Antigens were ranked according to T-cell and antibody immunogenicity, conservation across Plasmodium species, and genomic and physicochemical characteristics. Analysis of 97 features identified determinants of T-cell immunogenicity, enabling the development of machine-learning models that predicted immunogenicity directly from genomic sequence data. An eight-feature predictive signature was subsequently applied across the Plasmodium proteome to prioritise the top 25 vaccine candidates for experimental validation. Lead antigens were evaluated in vivo using liver-targeting vaccine platforms, including mRNA-lipid nanoparticle (mRNA-LNP) and DNA-adenovirus prime-target immunisation strategies designed to induce robust T-cell responses in the liver.

Results: Proteome-wide profiling revealed distinct and largely non-overlapping repertoires of T-cell and antibody targets. Unexpectedly, highly immunogenic T-cell antigens exhibited minimal antibody recognition and significantly greater conservation across Plasmodium species than dominant antibody targets. In vivo testing demonstrated that all lead candidates induced robust CD8⁺ T-cell responses and liver-resident memory T-cell (TRM) populations, with distinct antigen- and platform-specific immune profiles. Several lead antigens generated strong antigen-specific IFN- γ responses and were highly conserved across species. The most immunogenic candidates also conferred significant protection against P. yoelii 17XNL sporozoite challenge, reducing both liver-stage and blood-stage parasite burden. Together, these findings support the potential of conserved T-cell-targeted antigens as candidates for next-generation malaria vaccines.

Discussion/Conclusion: These findings validate a genome-guided, human data-driven approach for malaria vaccine antigen discovery. By integrating systems immunology, computational prediction, and experimental validation, we identified a new class of conserved T-cell vaccine targets capable of inducing protective immunity against malaria. The strong conservation of these antigens across Plasmodium species and their ability to generate protective liver-focused T-cell responses support their potential for development as next-generation malaria vaccines with broad, cross-species protective capacity.

PLENARY SESSION 4: SYSTEMS VACCINOLOGY

Tuesday 13 October 2026 • 17:20–17:35 • Okapi 1, 2, 3

Novel DNA Delivery Method Using Lipid Nanoparticles Induces Durable Polyfunctional Immune Responses with Tier2 Neutralizing Antibody and Cytotoxic CD8 T Cells

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Background: We developed a new vaccine platform combining DNA with lipid nanoparticle (LION), resulting in a simple, refrigerator-stable, PEG-free formulation, administered by IM injection that stays at the injection site. Spike DNA/LION was highly immunogenic, inducing durable (>4.1 years) cellular and humoral immunity, along with prolonged lymph node (LN) activation and germinal center (GC) expansion (PMID40230522). Here, we evaluated a DNA/LION vaccine expressing stabilized HIV SOSIP Env in macaques.

Methods: Immune responses were monitored with serology, CBC count, plasma proteomics, flow cytometry, scRNA-seq.

Results: The LION/DNA vaccine induced transient innate and robust, durable (>1.7yrs) adaptive immune responses. LION/DNA elicited difficult-to-achieve Tier2 neutralizing antibodies targeting the CD4-binding site in four of six macaques, unlike DNA delivered by electroporation (EP). LION/DNA induced mainly CD8+ T cell responses with a polyfunctional, cytotoxic (PRF-1+GzmB+CD107a+), non-exhausted (TIGIT-PD-1+CXCR5-), and stem-like (TCF-1+) profile. This contrasts with the CD4-focused responses obtained by DNA/EP vaccination. LION/DNA vaccination induced strong early, transient type I- and type II-driven interferon-stimulated gene responses, and cytokine responses, resulting in activation of pathways involving platelets, neutrophils, myeloid, T, B, and NK cells. Network analysis predicted engagement of myeloid cells in ligand-receptor interactions via SLAMF7/CD48, MIF/CXCR4-CD74, and BAFF/BAFF-R resulting in activation of NK, T, and B cells in both blood and LN, and the enhancement of NK's ADCC function via FCER1G-FcRg engagement, further corroborated by the correlation between ADCC and antibody levels. Network communications mediated by CD40LG, BAFF, and MIF promoted NF-κB signaling and regulated critical steps in GC activation and the prolonged survival of high-affinity B cells and Tfh. A pan-lymphocyte program across CD4, CD8, and B cells upon DNA/LION exposure showed upregulation of JUNB, YBX1, BCL3, and KLF2, and downregulation of TGFB1, JUND, AKT3, BRAF, TRAF3, FOXO1, BACH2, reflecting coordinated lymphocyte activation and differentiation in LN as a result of the IFN response.

Conclusion: Our data showed that LION/DNA vaccination triggered complex immune responses in LN, including innate-to-adaptive signaling, myeloid-lymphocyte communication, and increased GC activation resulting in Tier2 NAb production and induction of CD8 T cells with memory, stemness, and cytotoxicity features.

Together, DNA/LION vaccination induced robust cellular and humoral responses, supporting its potential as simple and promising nucleic acid vaccine method with broad applications, providing simultaneously NAb, CD8 cytotoxic T cells and long-lasting immunity.

PLENARY SESSION 5: ONE HEALTH AND PANDEMIC PREPAREDNESS

Wednesday 14 October 2026 • 09:50–10:05 • Okapi 1, 2, 3

Safety of a bivalent Ebola virus and Sudan virus ChAdOx1 vectored vaccine in Tanzanian adults: an open-label, non-randomised phase 1 clinical trial.Latipha MOHAMED¹, Omary HASSAN¹, Florence MILANDO¹, Neema BALIGE¹, Safiness DAUDI¹, Janeth KAMAGE¹, Hania MSAMI¹, Theresa LAMBE², Daniel JENKINS², Ally OLOTU¹¹ Ifakara Health Institute, Tanzania² University of Oxford

Background: Four orthoebolavirus species are known to cause Ebola disease, with Ebola virus (species Orthoebolavirus zairense) and Sudan virus (species Orthoebolavirus sudanense) responsible for the majority of outbreaks and cases. Currently, no licensed vaccines are available for orthoebolaviruses other than Ebola virus. Therefore, this study aimed to evaluate the safety and immunogenicity of a non-replicating single-adenoviral vector vaccine (ChAdOx1 biEBOV) encoding glycoproteins from both Ebola virus and Sudan virus.

Methods: This was a single-centre, open-label, phase 1 dose-escalation clinical trial conducted among healthy Tanzanian adults aged 18–55 years with no clinically significant comorbidities and no prior exposure to adenovirus-vectored vaccines. Participants were non-randomly enrolled into four groups: a low-dose group (5×10^9 viral particles [vp]), a medium-dose group (2.5×10^{10} vp), a high-dose group (5×10^{10} vp), and a preferred-dose group selected based on safety and tolerability data from the previous groups. All doses were administered intramuscularly. A protocol amendment was introduced after completion of recruitment in the high-dose group, which reduced the number of participants in the preferred-dose group and introduced a second vaccine dose administered 12 weeks after the first dose.

The primary outcomes included assessment of solicited adverse events within 7 days after vaccination, unsolicited adverse events within 28 days after vaccination, changes in clinical laboratory parameters within 28 days, and serious adverse events and adverse events of special interest throughout the study period. This study is registered with ClinicalTrials.gov (NCT05301504).

Findings: A total of 48 participants were enrolled: six in the low-dose group, six in the medium-dose group, eleven in the high-dose group, and twenty-five in the preferred-dose group. Twenty-five participants in the high-dose group received one vaccine dose, and twenty-one participants received two vaccine doses.

Thirteen (27%) of 48 participants reported at least one local adverse event, and nine (19%) of 48 participants reported at least one systemic adverse event. All solicited adverse events were mild in severity. Two serious adverse events were reported but were unrelated to the vaccine. Unsolicited adverse events were mild to moderate and short-lived. No adverse events of special interest were observed. Transient mild lymphopenia and neutropenia were observed in participants in the high-dose and medium-dose groups, respectively.

Interpretation: The ChAdOx1 biEBOV vaccine was safe and well tolerated in healthy Tanzanian adults. The safety and tolerability profile was consistent with other vaccines using the same adenoviral vector platform. These findings support further clinical development and evaluation of this vaccine.

PLENARY SESSION 5: ONE HEALTH AND PANDEMIC PREPAREDNESS

Wednesday 14 October 2026 • 10:05–10:20 • Okapi 1, 2, 3

Single-visit rabies vaccination with a simian adenovirus vector elicits durable neutralising antibody responses indicating likely protection for >2 years: mid-term results from the RAB002 phase Ib/II clinical trialAdam RITCHIE¹, Omary HASSAN², Nsiande URASA², Rinter KIMATHI¹, Paschal APANGA¹, Wilmina KALINGA², Sanne TERRY³, Hildegund ERTL⁴, Ally OLOTU², Alexander DOUGLAS¹¹ University of Oxford, United Kingdom² Ifikara Health Institute, Tanzania³ Sciensano, Belgium⁴ Wistar Institute, USA

Background: Current rabies vaccines require multiple doses and are expensive, resulting in poor access in endemic countries and tens of thousands of deaths per year. Despite encouraging real-world effectiveness evidence and use among wealthy travellers, pre-exposure prophylaxis (PrEP) is often considered cost-ineffective for use in endemic settings.

Development of new rabies vaccine regimes benefits from availability of an internationally-standardised assay of virus neutralising antibody (VNA), for which results ≥ 0.5 IU/mL indicate an adequate response to vaccination.

Methods: We developed ChAdOx2 RabG, primarily with a view to its use as PrEP in rabies-endemic areas. We enrolled healthy Tanzanian adults and children (2–6 years old) in a Phase Ib/II clinical trial and are following them up for five years. Adults received single-visit vaccination with intramuscular ChAdOx2 RabG (n=45) or an intradermal inactivated rabies vaccine (IRV) (n=15). Children received one of these single-visit regimens (n=45 and n=30 respectively), or a two-visit, WHO-recommended intradermal PrEP regimen (n=30).

Results: We recently reported one year follow-up data. ChAdOx2 RabG was safe and well tolerated. All participants receiving single-visit ChAdOx2 RabG vaccination attained VNA ≥ 0.5 IU/mL. Seroconversion was more rapid than anticipated: consistent seroconversion by day 14 suggested additional potential as single-visit post-exposure prophylaxis.

We have now completed three years of follow-up, with immunogenicity data up to two years available at the time of writing. Geometric mean VNA among ChAdOx2 RabG recipients remained 3.8 IU/mL at year 2 follow-up, significantly higher than single-visit IRV recipients (GMT 1.1 IU/mL, $p=1 \times 10^{-5}$ by Mann-Whitney) and trending higher than recipients of the WHO-recommended two-visit ID IRV regime (GMT 2.7 IU/mL, $p=0.08$ by Mann-Whitney). 38/40 paediatric ChAdOx2 recipients attending year 2 follow-up maintained VNA ≥ 0.5 IU/mL. Initial modelling suggests VNA half-life measured in years; we anticipate year 3 immunogenicity data will be available before the Congress and will allow more precise estimation of the duration of maintenance of VNA ≥ 0.5 .

Discussion: Single-visit vaccination with ChAdOx2 RabG induces durable responses suggestive of maintenance of protection for several years, superior to single-visit vaccination with licensed vaccine and comparable to a WHO-recommended regime. More broadly, and relevant also to use of the ChAdOx platform for emergency response, this data strengthens understanding of both the speed and the durability of virus neutralising antibody induced in adults and children by single-dose simian adenovirus-vectored regimes.

PLENARY SESSION 5: ONE HEALTH AND PANDEMIC PREPAREDNESS

Wednesday 14 October 2026 • 10:20–10:35 • Okapi 1, 2, 3

Design, Development and Characterisation of Multivalent mRNA-LNP Vaccine Candidates for Mpox

Hapiloe MARANYANE-TSHILO¹, Nnini OBONYE¹, Andani MULELU¹, Shannon WILSON¹, Thalia NAIDOO¹, Bianca ARENDSE¹, Edwina FORTUIN¹, Ruqaiyah ADAMS¹, Astrid TRIMMEL¹, Gerhardt BOUKES¹, Roanne KEETON², Nicola DOUGLASS², Ben GABRIEL³, Anne DE GROOTE⁴, Wendy A BURGERS², Caryn FENNER¹

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Background: The emergence of Mpox in immunologically naïve populations and recurrent outbreaks in Africa highlight the urgent need for safe, scalable vaccines capable of inducing durable protective immunity. Currently countermeasures rely on legacy smallpox vaccines, which have limitations in supply, reactogenicity, and long-term protection. To address these challenges a multivalent mRNA vaccine program was established leveraging the rapid adaptability of mRNA technology for outbreak preparedness. Conserved intracellular mature virion (IMV; M1R and A29L) and extracellular enveloped virion (EEV; A35R and B6R) antigens were selected based on sequence conservation in monkeypox virus (MPXV) isolates and their ability to elicit neutralising antibody responses. To enhance cellular immunity, a synthetic multi-epitope construct comprising of conserved vaccinia CD4+ T-cell epitopes, previously shown to provide 100 % protection against lethal vaccinia virus Western Reserve challenge in mice (Moise et al., 2011) was incorporated.

Materials/Methods: Multi-antigen B-cell target configurations were identified in silico using antibody-accessible surface area (AbASA) analysis and structural modelling to optimize co-expression, immunogenicity and manufacturability. Plasmid DNA templates encoding monovalent and multivalent constructs were synthesised and used for in vitro transcription (IVT) to generate capped, polyadenylated mRNA drug substance (DS) with optimised untranslated regions for enhanced translation. Analytical characterisation assessed RNA integrity, size, concentration, poly(A) tail length and capping efficiency. Purified mRNA was formulated into lipid nanoparticles (LNPs) using the NanoAssemblr™ Ignite™. These were characterized for particle size, polydispersity, mRNA content, encapsulation efficiency, lipid composition, N:P ratios, mRNA integrity, and in vitro expression.

Results: Optimal antigen configurations were identified for bivalent (M1R_A29L) and quadrivalent (B6R_A35R_M1R_A29L) fusion constructs. Reverse-translated DNA sequences were successfully assembled into plasmid templates and used to generate IVT-derived mRNA at laboratory scale. Resulting transcripts exhibited expected sizes, high integrity ($\geq 70\%$), intact poly(A) tails (>100 nucleotides), and minimal double-stranded RNA contamination (< 10 ng/mg RNA). HEK293T transfection confirmed expression of multiple encoded MPXV antigens, including at least three antigens in the different constructs. Formulation yielded mRNA-LNPs with suitable particle sizes (~ 70 nm), low polydispersity indices (< 0.2) and high RNA encapsulation efficiency ($> 90\%$). In vitro evaluation confirmed antigen expression from both monovalent and multivalent mRNA-LNP formulations.

Discussion/Conclusion: This work demonstrates an integrated workflow for rapid development of multivalent MPXV mRNA-LNP vaccine candidates, spanning antigen design, mRNA manufacturing, formulation, and analytical characterisation. The successful generation and characterisation of multiple construct permutations enables systematic optimisation of antigen composition and supports the down-selection of lead candidates for immunogenicity, efficacy, and challenge studies.

CONCURRENT SESSION 7: VACCINE CONFIDENCE

Wednesday 14 October 2026 • 11:50–12:05 • Okapi 1, 2, 3

Bridging the Mpox Vaccine Uptake Gap in Africa: Determinants of Acceptance and Hesitancy from a Systematic Review and Meta-AnalysisCharles IBENEME^{1,2}, Olaiya Paul ABIODUN¹, Glory ONYEUGO², Lilian MALIRO³, Titilola MUNKAIL², Folake Abiola ABIODUN⁴, Omogoye Tosin SAMUEL⁴¹ Department of Public Health, Texila America University Zambia Guyana Online Campus² Africa Centers for Disease control and Prevention, Addis Ababa Ethiopia³ Expanded Programme on Immunization Department, Ministry of Health, Malawi⁴ ARETE Global Health Initiative, Abuja, Nigeria

Introduction / Background: The resurgence of mpox in Africa and the 2024 declaration of a Public Health Emergency of International Concern highlighted an urgent need to strengthen vaccination strategies across the continent. While the Africa CDC and WHO-led Access and Allocation Mechanism delivered nearly two million mpox vaccine doses to African countries, vaccine uptake has remained uneven and frequently below target coverage. Demand-side barriers such as vaccine hesitancy, misinformation, and trust deficits may significantly influence program performance. This study synthesizes available evidence to quantify mpox vaccine acceptance and hesitancy in Africa and identify the key determinants influencing uptake.

Materials / Methods: A systematic review and meta-analysis was conducted in accordance with PRISMA 2020 guidelines. Searches were performed across PubMed/MEDLINE, Embase, Scopus, Web of Science, Global Health, and African Index Medicus, complemented by grey literature from WHO, Africa CDC, and UNICEF (2016–2026). Studies reporting quantitative data on vaccine acceptance, hesitancy, or uptake among African populations were included. Random-effects meta-analysis using the DerSimonian–Laird method and Freeman–Tukey double arcsine transformation was applied to pool proportions. Subgroup analyses examined regional patterns and outbreak phases, while meta-regression assessed determinants of vaccine acceptance.

Results: Eighteen studies were included in the quantitative synthesis, with fourteen contributing acceptance and hesitancy estimates. Pooled vaccine acceptance across African populations was 58% (95% CI: 52–64%), while pooled hesitancy was 32% (95% CI: 27–38%), indicating substantial demand-side barriers. Acceptance varied across subregions, with the highest levels observed in East Africa (64%) and the lowest in Central Africa (49%). Uptake increased significantly during peak outbreak phases (67%) compared with early outbreak periods (49%). Meta-regression identified trust in health authorities (OR 2.1), prior vaccination history (OR 1.8), and higher education (OR 1.5) as positive determinants of acceptance, while exposure to misinformation (OR 0.6) significantly reduced vaccine willingness.

Discussion / Conclusion: Mpox vaccine acceptance across Africa remains moderate and highly context-dependent, with approximately one-third of populations expressing hesitancy. These findings highlight that vaccine supply alone cannot ensure successful outbreak control. Strengthening trust-based communication, community engagement, and misinformation management will be essential to closing the administration–uptake gap. Integrating behavioral insights into vaccination strategies and leveraging trusted community networks may significantly improve vaccine utilization during future mpox responses and other emerging infectious disease outbreaks.

CONCURRENT SESSION 8: EMERGING INFECTIONS

Wednesday 14 October 2026 • 11:25–11:50 • Gorilla 1

Safety and immunogenicity of EuHZV, an ECLS-based recombinant herpes zoster vaccine: a first-in-human Phase 1 study in adults aged 50–69 yearsHoward HER^{1,2}, ChanKyu LEE¹, JeMin HAN¹, JoonYoung KIM¹, Jonathan LOVELL⁴, JungHyun CHOI³, YeongOk BAIK^{1,2}¹ EuBiologics Co., LTD, Korea, Republic of (South Korea)² EuPOP Life Sciences Inc., Buffalo, NY, USA³ The Catholic University of Korea Eunpyeong St. Mary's Hospital, Seoul, Republic of Korea⁴ POP Biotechnologies Inc., Buffalo, NY, USA

Background: Herpes zoster causes substantial morbidity in older adults. The licensed AS01B-adjuvanted recombinant subunit vaccine established VZV glycoprotein E (gE) combined with a saponin-containing adjuvant as the benchmark, and additional recombinant zoster vaccine options with scalable manufacturing and diversified supply may help broaden global access. EuHZV is built on ECLS, a combined liposomal platform integrating EcML, an Escherichia coli-derived monophosphoryl lipid A TLR4 agonist filed with the US FDA as Type IV Drug Master File 44350, with CoPoP, a cobalt-porphyrin-phospholipid that allows recombinant gE to be displayed on the liposome surface without chemical conjugation. The platform is therefore designed to co-display and co-deliver antigen, a TLR4 agonist, and a saponin adjuvant on a single liposomal particle.

Methods: This first-in-human, randomized, observer-blinded, active comparator-controlled Phase 1 study (NCT06409494) assigned 72 healthy Korean adults aged 50–69 years 1:1:1 to low-dose EuHZV (25 µg gE), high-dose EuHZV (50 µg gE, adjuvant scaled proportionally), or licensed AS01B-adjuvanted recombinant zoster vaccine, administered intramuscularly at weeks 0 and 8. The primary objective was safety and tolerability. Secondary immunogenicity objectives were anti-gE IgG by ELISA (VRR, GMT, GMFR) and cell-mediated immunity by IFN-γ ELISpot and intracellular cytokine staining. Safety analyses used the safety set (n=72); immunogenicity analyses used the per-protocol set (n=69).

Results: Results reported here derive from the pre-specified interim analysis conducted after database lock of the main study period. All 72 participants received both doses and completed the main study period through 4 weeks after dose 2. Through that period, no SAEs, AESIs, immediate adverse events or grade 3/4 adverse events were reported; during subsequent follow-up, one grade 2 SAE considered unrelated to vaccination was reported. Solicited local reactions occurred in 100%, 100% and 91.7%, and systemic reactions in 87.5%, 100% and 95.8% of low-dose, high-dose and comparator recipients; fever ≥38°C occurred in 8.3%, 25.0% and 16.7%, and all resolved. Four weeks after dose 2, VRR was 100% in all three groups. Anti-gE IgG geometric mean titres rose markedly from baseline in all three groups, with overlapping 95% confidence intervals across the two EuHZV dose levels and the licensed comparator; antigen-specific IFN-γ ELISpot and intracellular cytokine staining responses likewise increased from baseline in all groups. Quantitative immunogenicity estimates are not presented here pending final database lock. Database lock for the 52-week follow-up and the integrated final CSR are planned for late September 2026; complete final safety and week-4, week-26 and week-52 immunogenicity data will be presented for the first time at this congress.

Conclusions: Both EuHZV dose levels were well tolerated, with no grade 3/4 adverse events through 4 weeks after dose 2, and both achieved a VRR of 100% with humoral and cellular immune responses in all groups. This exploratory Phase 1 study was not designed or powered to establish superiority, equivalence or non-inferiority between groups. The findings support further clinical development of EuHZV and continued evaluation of the ECLS platform and informed a three-arm dose-ranging Phase 2 study to select a dose for subsequent pivotal evaluation.

CONCURRENT SESSION 8: EMERGING INFECTIONS

Wednesday 14 October 2026 • 11:50–12:05 • Gorilla 1

Stabilized henipavirus fusion glycoproteins induce strong serum neutralizing antibody responses against of authentic virus and inform future vaccine design.Haye NIJHUIS^{1,2}, Ilja BONTJER^{1,2}, Tim BEAUMONT^{1,2}, Sabine DE RUITER^{1,2}, Nathalie DEREUDDRE-BOSQUET³, Rogier SANDERS^{1,2,4}, Marit VAN GILS^{1,2}¹ Department of Medical Microbiology and Infection Prevention, Laboratory of Experimental Virology, Amsterdam UMC, University of Amsterdam, 1105 AZ, Amsterdam, Netherlands² Amsterdam Institute for Infection and Immunity, Infectious Diseases, 1105 AZ, Amsterdam, Netherlands³ Center for Immunology of Viral, Auto-immune, Hematological and Bacterial diseases (IMVA-HB/IDMIT), Université Paris-Saclay, Inserm, CEA, Fontenay-aux-Roses, France⁴ Department of Microbiology and Immunology, Weill Medical College of Cornell University, New York NY, 10065, USA

Each year highly pathogenic zoonotic viruses cause many outbreaks. Among them are two Henipaviruses, Hendra and Nipah virus, that are known to cause fatal disease in humans. Nipah and Hendra virus cause a little over ten cases a year with a case fatality rate between 40-70%. Besides imposing a great burden on local communities, these BSL-IV pathogens could be used as bioweapons and as such are designated priority pathogens by the WHO. No specific treatment or vaccines against Henipaviruses are commercially available, underscoring the need for better therapeutic or preventative options against these viruses. Here, we designed, produced and characterized recombinant Hendra and Nipah glycoproteins (GP) using rational design. These recombinant surface glycoproteins are native-like when assessed with known quaternary-specific antibodies by ELISA. Genetic fusion facilitated utilizing a two-component nanoparticle platform for immunization with the benefit of presenting only properly folded, quaternary structured proteins, and also enhancing the immunogenicity of the antigens through multivalent display. Immunization of non-human primates (NHPs) with nanoparticles presenting the Hendra and Nipah GP proteins elicited serum neutralization of authentic Hendra and Nipah viruses efficiently, indicating that an effective humoral immune response was induced. Subsequently, using our stabilized Henipavirus fusion glycoproteins as bait, we have isolated NHP-derived monoclonal antibodies targeting these viruses. Taken together our results justify moving forward Hendra and Nipah GPs presented on nanoparticles as vaccine candidates. Furthermore, antibodies isolated from immunized NHPs should reveal epitopes of vulnerability, advancing our understanding of the fusion glycoprotein structure and functionality. Finally, selected antibodies with exceptional potency and breadth will be explored as therapeutics, to be used, for example, in an outbreak setting, greatly diminishing the burden these viruses pose upon local communities and mitigating the potential risk they pose as biological weapons.

CONCURRENT SESSION 8: EMERGING INFECTIONS

Wednesday 14 October 2026 • 12:05–12:20 • Gorilla 1

CD4+ T cell-mediated immunity protects from VSV-SUD lethal challenge in a mouse model of Sudan virus infection

Lara KELCHTERMANS, Katrien GEERTS, Cuong THI PHAM, Vanshika MALVIYA, Winston CHIU, Carolien DE KEYZER, Elias BROECKHOVEN, Johan NEYTS, Susan SCHLENNER, Yeranddy A. ALPIZAR, Kai DALLMEIER

KU Leuven, Belgium

Introduction/Background: Recurring outbreaks of filoviruses, including Sudan virus, highlight the need to better define the immune mechanisms that protect after vaccination. Here, we addressed whether vaccine-induced cellular immunity, rather than neutralizing antibodies alone, could mediate protection against lethal Sudan virus challenge in a mouse model. We tested the hypothesis that CD4+ T cell responses contribute directly to survival after immunization with a YF17D-based Sudan virus glycoprotein vaccine.

Material/Methods: We used a mouse model of Sudan virus infection using a chimeric vesicular stomatitis virus (VSV-SUD) lethal challenge. Mice were vaccinated with a live attenuated YF17D-based vaccine expressing Sudan virus glycoprotein, and immune responses were assessed after vaccination and challenge. We evaluated humoral and cellular responses, including antibody effector function assays and flow cytometry, to identify which immune components were associated with protection.

Results: Vaccination protected mice from lethal VSV-SUD challenge even in the absence of virus-neutralizing antibodies. Although multiple immune responses were correlated with survival (e.g. NK cell activation, cytotoxic CD8+ T cells), only proliferative antigen-specific CD4+ T cells and sustained IFN γ production were mechanistically required for protection and survival. Our experiments show that protection in this model was associated with a cellular immune signature rather than neutralizing antibody activity alone.

Discussion/Conclusion: Our findings identify CD4+ T cell-mediated immunity as a key protective mechanism in a mouse model of Sudan virus vaccination. The results suggest that immunological correlates linked to disease severity do not necessarily represent the causal effectors of protection. Overall, the work supports broader consideration of cellular immunity in the design and evaluation of Sudan virus vaccines.

CONCURRENT SESSION 8: EMERGING INFECTIONS

Wednesday 14 October 2026 • 12:20–12:35 • Gorilla 1

Characterization of the immune response to *Fusobacterium nucleatum*, an emerging pathogen associated with adverse pregnancy outcomesTracy S. LEE^{1,2}, Cody A. DESPINS¹, Petra JOZSA¹, Nicholas J.P. VIEGAS¹, Lisa DREOLINI¹, Eric YUNG¹, Scott D. BROWN¹, Robert A. HOLT^{1,3,4}¹ Department of Basic and Translational Research, BC Cancer Research Institute, Vancouver, Canada² Interdisciplinary Oncology Program, University of British Columbia, Vancouver, Canada³ Department of Medical Genetics, University of British Columbia, Vancouver, Canada⁴ Department of Molecular Biology and Biochemistry, Simon Fraser University, Burnaby, Canada

Background: *Fusobacterium nucleatum* (Fn) is a commensal oral microbe that can become pathogenic when it spreads hematogenously. Fn is implicated in a wide variety of disease settings including autoimmunity, cardiovascular disease, oncology, and maternal & fetal health. Fn infection of the fetoplacental unit is linked to adverse pregnancy outcomes (APO), including chorioamnionitis, preeclampsia, preterm birth, stillbirth, and neonatal sepsis. Placental colonization by Fn is mediated by binding of its Fap2 lectin to GalGalNAc, a maternal blood facing glycan expressed by the syncytiotrophoblast. We and others have recapitulated Fn pathology in mice, whereby intravenously-injected Fn colonizes the placenta, amniotic fluid, and fetus, leading to fetal demise. Whether a vaccine could block Fn placental colonization and thereby prevent the associated APOs needs to be tested. To inform vaccine development, we sought to explore the immune response to Fn.

Methods: We injected C57BL/6 and BALB/c mice with killed Fn, using different Fn strains, doses, and routes of administration. We isolated serum from the Fn-exposed mice and measured Fn binding antibody titers by indirect ELISA, against Fn lysates. Neutralizing antibody activity was measured by assessing inhibition of Fn-mediated hemagglutination, whereby Fn was pre-treated with serum from Fn-exposed mice before incubating with sheep red blood cells. Finally, we immunoprecipitated the antigens bound by serum antibodies from Fn-exposed mice and identified these antigens by tandem mass spectrometry.

Results: Fn exposure elicited strong humoral immunity and serum from Fn-exposed mice was able to inhibit Fn-mediated hemagglutination in vitro. Antibody titers were dose-dependent, with intravenous injection leading to higher titers than the same doses delivered intramuscularly. Interestingly, the anti-Fn antibody response was significantly dampened in pregnant mice compared to non-pregnant mice. We identified humorally immunodominant Fn proteins, the majority of which were outer membrane autotransporters, including Fap2. However, the binding and neutralizing antibodies elicited by Fn exposure were highly strain-specific.

Conclusions: Fn exposure evokes a strain-specific antibody response in mice that is dependent on dose, delivery method, and pregnancy status. Fap2, the primary adhesin that mediates placental colonization, was confirmed to be an immunodominant antigen, suggesting the potential for an adhesin-blocking vaccine targeting this and perhaps additional Fn outer membrane proteins. However, the strain specificity of the anti-Fn antibody response suggests the need for a subunit vaccine strategy such that antigens can be selected that are well represented and highly conserved across multiple Fn strains of importance. Our next step is to test the immunodominant Fn antigens as subunit vaccines in our pregnancy model to assess whether they can block Fn placental colonization and thereby prevent the associated APOs.

CONCURRENT SESSION 9: VETERINARY VACCINES

Wednesday 14 October 2026 • 11:50–12:05 • Gorilla 3

Selection and characterization of a contemporary respiratory syncytial virus subtype B strain for use in Controlled Human Infection Model (CHIM) studies

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Introduction: Human respiratory syncytial virus (RSV) is the most common cause of acute lower respiratory infections (ALRI) in children younger than 5 years of age and is a significant contributor to severe respiratory disease in older adults and immunosuppressed patients. Although three RSV vaccines (GSK: Arexvy; Pfizer: Abrysvo; Moderna: mRESVIA) have now been approved for use in older adults and some at risk groups, largely uncontrolled RSV epidemics occur annually, resulting in high levels of morbidity and mortality worldwide. The only approved monoclonal antibodies for the prophylactic prevention of RSV infection are Palivizumab (Synagis, AstraZeneca) and more recently Nirsevimab (Beyfortus, AstraZeneca & Sanofi) and Clesrovimab (Enflonsia, MSD) were approved. The development of the Controlled Human Infection Model (CHIM) for RSV has provided additional opportunities to study virus pathogenesis, associated immune responses and has enabled better testing of candidate vaccines or therapeutics. However, new contemporary RSV challenge strains are needed, especially from subtype B, to be developed for use in this model. The development of this RSV strain has been undertaken within Inno4Vac, a public-private partnership involving academic institutions, SMEs and pharma companies funded by the IMI/IHI.

Methods: A panel of contemporary RSV-A (x3) and -B (x2) clinical isolates (P1 on HEp-2 cells, November 2022) were characterized with respect to glycoprotein sequences and in vitro virus replication and cytopathic effects (CPE). A selected RSV strain was further characterized with respect to virus growth kinetics in primary cells, and thermal stability prior to generation and validation of a master virus stock (MVS) and a master virus bank (MVB) by a selected CDMO.

Results: Analysis of virus growth and CPE in vitro enabled the consortium to select a contemporary RSV-B strain (RSV-B-I54) for further characterization. Next generation sequencing (NGS) was used to determine the full genome sequence of RSV-B-I54, with phylogenetic analysis showing that this strain is a member of the B.D.E.1 clade. No differences were observed in primary human epithelial cells cultured on air-liquid interface (ALI) with respect to growth of RSV-B-I54 stocks generated on Vero or HEp-2 cells in comparison to the reference RSV-B-9671 strain (BA9 genotype). The optimal multiplicity of infection for virus growth on Vero cells was determined to be 0.001 with a time of harvesting of 5 days post-infection. Re-isolation of RSV-B-I54 from the original clinical sample was performed on Vero cells (Nuvonis Technologies) with approved reagents. The resulting passage 1 stock was used as seed virus for generation of the MVS and MVB using GMP-grade Vero cells by a selected CDMO. All quality control checks performed on the MVS (125 × 1mL vials) and MVB (750 vials × 1mL vials) were compliant with pre-specified criteria. The titer of the MVB was determined to be 106.4 TCID₅₀/mL. Analysis of sequence reads generated by NGS of the virus seed, MVS and MVB showed that the consensus virus sequence was retained upon virus passage.

Conclusions: A well characterized MVB for a contemporary RSV-B strain (B.D.E.1 genotype) with a titer of 106.4 TCID₅₀/mL is now available for CHIM studies.

CONCURRENT SESSION 9: VETERINARY VACCINES

Wednesday 14 October 2026 • 12:05–12:20 • Gorilla 3

Development of a vaccine against deadly elephant endotheliotropic herpesvirus

Tabitha E. HOORNWEG^{1,2}, Willem SCHAFTENAAR³, Victor P.M.G. RUTTEN^{2,4}, Cornelis A.M. DE HAAN¹¹ Section Virology, Division Infectious Diseases and Immunology, Department of Biomolecular Health Sciences, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands² Section Immunology, Division Infectious Diseases and Immunology, Department of Biomolecular Health Sciences, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands³ European Association of Zoos and Aquaria (EAZA) Elephant Taxon Advisory Group (TAG), Rotterdam Zoo, Rotterdam, The Netherlands⁴ Department of Veterinary Tropical Diseases, Faculty of Veterinary Science, University of Pretoria, Onderstepoort, South Africa

Introduction: Elephant endotheliotropic herpesvirus (EEHV) may cause a fatal hemorrhagic disease (EEHV-HD) particularly in young Asian elephants and represents a major threat to the survival of this endangered species. EEHV cannot be grown in cell culture, which severely hampers development of vaccines. Essentially, all adult elephants are seropositive for several EEHV (sub)species, indicating that elephants are commonly infected with these viruses. During their first years of life, young elephants are protected against EEHV-HD, but this changes upon waning of maternal antibodies. Young elephants with no or low antibody levels against the dimer formed by glycoproteins H and L (gH/gL), are susceptible to EEHV-HD, when infected for the first time with a particular (sub)species. This typically occurs when they are between 1-5 years of age. The majority of EEHV-HD cases are caused by EEHV subspecies 1A. Recently we elucidated the structure of EEHV-1A gH/gL associated with glycoprotein O (gH/gL/gO) and showed that this trimeric complex is involved in receptor binding on host cells. Given that (i) (maternal) antibody levels against gH/gL of a particular EEHV subspecies correlate with protection against disease, (ii) the gH/gL/gO complex has a conserved and essential role in herpesvirus entry, and (iii) most EEHV-HD cases are caused by EEHV-1A, we propose that the EEHV-1A gH/gL/gO complex constitutes an attractive vaccine candidate for the prevention of EEHV-HD.

Material/Methods: Recombinant soluble gH/gL/gO was produced in HEK293F cells and affinity purified from the cell culture supernatant using affinity tag purification. The recombinant protein was formulated with Montanide ISA 206 to form a water-in-oil-in-water emulsion. One vaccine dose contained 100 microgram protein in 2 ml volume. Elephants were vaccinated intramuscularly in their upper leg. Initial safety of the vaccine was tested by immunizing 6 (sub)adult Asian elephants. Subsequently, young elephants in European zoos with low antibody levels against EEHV-1A gH/gL, and thus at risk of developing EEHV-HD, were vaccinated 3-4 times. Sera were collected at different time points and analyzed for EEHV-specific antibody levels.

Results: (Sub)adult elephants immunized twice with the adjuvanted subunit vaccine exhibited minimal adverse effects, limited to transient swelling at the injection site. Similarly, limited side effects were observed upon vaccination of the young elephants at risk of developing EEHV-HD. Vaccination resulted in increased antibody levels against gH/gL/gO. Up to date, 9 young elephants have been fully vaccinated. Of these, one elephant died of EEHV-1B, indicating that protection provided by the EEHV-1A vaccine does not extend to other (sub)species as expected based on earlier serological analyses. Vaccinated elephants will be monitored for the coming years and their survival rate will be compared to that of a historical cohort of young, unvaccinated elephants.

Conclusion: We developed a gH/gL/gO subunit vaccine against EEHV1A and vaccinated young elephants at risk of developing EEHV-HD. The coming years, protective efficacy of the vaccine will be monitored, while additional at-risk elephants will be included in the efficacy study.

CONCURRENT SESSION 9: VETERINARY VACCINES*Wednesday 14 October 2026 • 12:20–12:35 • Gorilla 3***Evaluation of the protective efficacy of foot-and-mouth disease vaccines against O/CATHAY topotype virus in pigs**Yoon Hee LEE, Ji-Hyeon HWANG, Hyejin KIM, Jong-Hyeon PARK*Animal and Plant Quarantine Agency, Korea, Republic of (South Korea)*

Foot-and-mouth disease (FMD) viruses are classified into seven distinct regional pools according to their serotypes and geographic distribution patterns. The Republic of Korea (ROK) is situated in Pool 1, where serotypes O, A, and Asia1 are consistently reported in domestic livestock. Recently, the risk of incursions by the O/CATHAY topotype in Pool 1 has markedly increased, raising concerns regarding its potential introduction into the ROK. To evaluate the protective efficacy of three commercially available FMD vaccines currently deployed in the ROK against this topotype, a controlled experimental challenge was conducted using four separate groups of pigs. The vaccines tested included O1/Manisa+ O/3039, O/Primorsky, and O1/Campos. Each of the three groups received a 2 mL dose of a designated vaccine at eight and ten weeks of age, while two pigs were maintained as unvaccinated controls. At 21 days post-vaccination, all pigs were challenged with the O/HKN/5/2019 virus of the O/CATHAY topotype. The results demonstrated that although all vaccines provided protective effects, O1/Campos exhibited superior efficacy by producing the fewest clinical signs and substantially reducing viral shedding compared with unvaccinated controls. Collectively, these findings suggest that while O1/Campos could be utilized in emergency situations, the development of a vaccine specifically targeting the O/CATHAY topotype remains necessary.

PLENARY SESSION 6: CHALLENGE STUDIES

Wednesday 14 October 2026 • 15:20–15:35 • Okapi 1, 2, 3

Predicting West Nile Virus Outcomes: Insights and Limitations from Murine and Avian Models

Byron MARTINA, Sudip KUMAR DUTTA, Stephanie LIM

Artemis Bioservices, Netherlands, The

Animal models are indispensable for flavivirus research, yet their predictive value is conditional rather than absolute. The usefulness of a model depends on the biological question being addressed and the endpoint being measured. Drawing on our West Nile virus (WNV) studies, supported by complementary work on Japanese encephalitis virus (JEV), dengue virus (DENV), and Zika virus (ZIKV), this presentation examines how murine and avian models can inform risk assessment, pathogenesis research, and countermeasure development, while highlighting the limits of translation to human disease and natural transmission settings.

Comparative studies in mice and European corvids revealed host-dependent differences in WNV virulence. While all circulating lineage 1 and lineage 2 strains produced severe disease in immunocompetent mice, the FIN strain displayed an attenuated phenotype in jackdaws and carrion crows. In immunocompetent mice, all lineage 1 and lineage 2 viruses produced severe disease. Experimental infections of jackdaws and carrion crows showed that most lineage 1 strains, with the exception of FIN, and one lineage 2 strain caused systemic infection and mortality. The avian studies further demonstrated that susceptibility is both virus-strain-dependent and host-species-dependent: jackdaws developed lower viraemia and displayed lower mortality than carrion crows despite being susceptible to disease, indicating that mortality and amplification competence are distinct phenotypes. Recent detection of WNV in dead Dutch corvids reinforces the need to interpret field observations in the context of host ecology, transmission intensity, and surveillance sensitivity.

Mouse models also proved valuable for dissecting mechanisms of pathogenicity. Comparative infection studies differentiated the neuroinvasive potential of European WNV strains and identified viral determinants associated with attenuation. These findings demonstrate the strength of murine models for mechanistic analysis of neuroinvasion and brain pathology, while emphasizing that experimental disease severity does not directly predict human clinical outcomes.

The predictive value of mouse models is particularly evident in vaccine evaluation. Across recombinant envelope-domain III, virus-like-particle, influenza-vectored, and modified vaccinia Ankara vaccine platforms, neutralizing antibody responses consistently correlated with protection against lethal WNV challenge. Protective immunity extended across WNV lineages and, in some cases, provided partial protection against JEV. These studies illustrate the utility of murine challenge models for candidate ranking, proof-of-concept evaluation, and identification of immune correlates of protection. However, they cannot reliably predict human dose requirements, durability of immunity, safety, or the magnitude of clinical benefit.

Overall, animal models are most predictive when used as fit-for-purpose tools and interpreted alongside data from natural-host studies, pharmacokinetic and pharmacodynamic analyses, and field surveillance.

PLENARY SESSION 6: CHALLENGE STUDIES

Wednesday 14 October 2026 • 15:35–15:50 • Okapi 1, 2, 3

SARS-CoV-2 humoral waning kinetics are reversed by inactivated vaccine boosting, restoring functional responses, durability and breadthRafael MEDINA*Emory University, United States of America*

Xin Tong,^{1†} Benjamin Kellman,^{1†} Maria-Jose Avendano,^{2,3†} Maanasa Mendu,¹ Jeff C. Hsiao,^{1,9} Eileen Serrano,^{2,3} Tamara Garcia-Salum,^{2,3,4} Nicolas Muenza,⁵ Catalina Pardo-Roa,^{3,4,6} Mauricio Morales,² Jorge Levican,³ Erick Salinas,³ Simone Cardenas-Cáceres,⁵ Arnoldo Riquelme,⁷ Nicole D. Tischler,^{5,8} Douglas A. Lauffenburger,⁹ Galit Alter,¹ Ryan P. McNamara,^{1*} Rafael A. Medina,^{2,3,4,10*}

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SARS-CoV-2 vaccine-acquired immunity provides robust cross-variant recognition, while infection-acquired immunity can be heterogenous and shaped by disease severity. Although hybrid immunity resulting from infection followed by vaccination provides enhanced protection, it remains incompletely characterized, particularly in population immunized with inactive vaccines. We performed a comprehensive comparison of humoral immune responses induced by infection, vaccination, and hybrid immunity. We assessed antibody waning dynamics through antibody subclass, Fc receptor binding, and antibody-dependent effector functions across variants of concern (VOC). mRNA vaccination induced potent, cross-VOC Spike responses that waned faster for the antigenically distinct Omicron Spike. Hospitalized individuals developed more durable but lower-peak functional responses than mRNA vaccinees, while outpatients exhibited lower titers than hospitalized, but had slower decay than recipients of inactivated vaccines. RBD-specific antibody waning paralleled neutralizing antibody titers, while S2-directed responses tracked with antibody-dependent phagocytosis. Importantly, boosting recovered patients with inactivated vaccines restored functional responses, broadened humoral recognition, and eliminated the severity- and platform-associated differences seen during waning. This post-recovery hybrid immunity, compensates for this distinction and broadens humoral breadth, highlighting the value of boosting immunity in previously infected individuals. This study provides a rationale for the induction of protective humoral responses by inactivated SARS-CoV-2 vaccines, which were extensively used in the developing world.

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POSTER ABSTRACTS

POSTER 105

Maternal HIV Infection and Timing of Antiretroviral Therapy Shape the Placental Transfer and Functional Quality of IgG Antibodies in Newborns

Dansala WELBA^{1,2,4,5}, Yiwei JIANG^{1,2}, Shilpee SHARMA^{1,2}, Loïc DE DONCKER^{1,2}, Tessa GOETGHEBUER³, Martin Luther KOANGA MOGTOMO⁴, Arnaud MARCHANT^{1,2}

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Background: Transplacental transfer of maternal immunoglobulin G (IgG) antibodies provides critical passive immunity to newborns during the first months of life. Maternal infections, including human immunodeficiency virus (HIV), may impair the efficiency and functional quality of antibody transfer to the fetus. Infants born to HIV-infected mothers but who remain uninfected, known as HIV-exposed uninfected (HEU) infants, have been reported to present increased susceptibility to infectious diseases. Understanding how maternal HIV infection and the timing of antiretroviral therapy (ART) influence placental antibody transfer is therefore important for improving neonatal immune protection.

Methods: This study was conducted at Saint-Pierre Hospital, Brussels, Belgium. Maternal and cord blood samples were collected at delivery from three groups of mother-infant pairs: HIV-negative mothers with HIV-unexposed infants (HU), HIV-positive mothers who initiated ART before pregnancy (HIV B) with HIV-exposed uninfected infants (HEUB), and HIV-positive mothers who initiated ART during pregnancy (HIV D) with HIV-exposed uninfected infants (HEU D). Total IgG concentrations were measured using enzyme-linked immunosorbent assay (ELISA). In addition, antigen-specific IgG responses were assessed against Tetanus toxoid, Pertussis toxin, and Respiratory syncytial virus using Luminex beads to evaluate the placental transfer of antibodies targeting vaccine and respiratory pathogens. IgG subclass distribution (IgG1 and IgG3), Fc receptor-binding capacity (FcRn, FcγR2A, FcγR3A), and antibody effector functions including antibody-dependent cellular phagocytosis (ADCP) and antibody-dependent complement deposition (ADCD) were also evaluated to characterize the functional quality of transferred antibodies.

Results: Infants born to HIV-infected mothers who initiated ART during pregnancy showed reduced placental transfer efficiency of IgG compared with infants born to HIV-positive mothers who initiated ART before pregnancy and HIV-negative mothers. Alterations were observed in the transfer of IgG subclasses, particularly IgG1 and IgG3. Antibodies from HIV D also exhibited modified binding profiles to Fc receptors (FcRn, FcγR2A, FcγR3A). Functional analyses demonstrated differences in antibody-mediated immune responses, including ADCP and complement activation. Notably, mothers who initiated ART before pregnancy displayed improved antibody transfer compared with those who initiated ART during pregnancy.

Discussion: These findings suggest that maternal HIV infection and the timing of ART initiation may influence both the quantity and functional quality of antibodies transferred to the fetus. Reduced transfer efficiency observed in mothers initiating ART during pregnancy may reflect persistent immune activation, placental inflammation, or alterations in Fc receptor interactions associated with HIV infection. In contrast, earlier ART initiation may help restore maternal immune homeostasis and improve the transfer of protective antibodies. The observed differences in Fc receptor binding and antibody effector functions further indicate that maternal HIV infection may not only affect antibody levels but also their functional capacity to mediate immune protection in newborns. These mechanisms may contribute to the increased susceptibility to infections reported in HEU infants.

Conclusion: Maternal HIV infection may impair the efficiency and functional quality of IgG antibodies transferred to the fetus. Early initiation of antiretroviral therapy before pregnancy appears to improve placental antibody transfer. Optimizing maternal treatment strategies may therefore enhance passive immunity in newborns and reduce infection risk in HIV-exposed uninfected infants.

POSTER 106

Adjuvant Treatment with Recombinant BCG and Nanoparticles Potentiates the Antimycobacterial Activity of Conventional AntibioticsShamsuddeen Yusuf MAARUF¹, Neeraj DHAR²¹ School of Public Health and Vaccine and Infectious Disease Organization, University of Saskatchewan, Canada² Vaccine and Infectious Disease Organization, University of Saskatchewan, Canada

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), remains a major global health challenge, responsible for millions of deaths each year. Current TB treatment relies on prolonged antibiotic regimens, which contribute to poor adherence and the emergence of drug-resistant strains. Immunotherapeutic approaches are increasingly recognized as promising adjuncts to antibiotic therapy or as adjuvants for TB vaccination. By stimulating host immune cells, such strategies can enhance bacterial clearance, reduce relapse risk, and retain efficacy even against drug-resistant Mtb. In this project, we are developing novel recombinant *Mycobacterium bovis* BCG and nanoparticle (NP)-based delivery systems incorporating selected immunogenic antigens or host immune stimulants derived from airway pathogens. The efficacy of these constructs is being evaluated using an in vitro three-dimensional (3D) granuloma model that mimics Mtb persistence and reactivation, allowing for the ranking of candidates for future in vivo studies. We have successfully generated recombinant BCG (rBCG) strains expressing host-cell immunomodulatory molecules and encapsulated in lipid-based NP. In an in vitro trained immunity model using U937-derived macrophage-like cells, immunization with the rBCG and encapsulated NP enhanced macrophage responsiveness and potentiated the antimycobacterial activity of standard antibiotics (rifampicin) against Mtb. Preclinical evaluation in a mouse model will be done to further assess the immunogenicity and therapeutic potential of these immunotherapeutic adjuvants, focusing on their ability to modulate host immune responses and improve bacterial clearance. This multifaceted approach aims to advance next-generation immunotherapeutic strategies for TB, addressing current treatment limitations and contributing to the global effort to control this devastating disease.

POSTER 107

Structural Insights into Rotavirus Interactions with Human and Pig Receptors: Implications for Cross-species Rotavirus Vaccine Development in Africa

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Introduction/Background: Rotavirus diarrhoea significantly impacts both humans and animals worldwide, with cellular receptor interaction being a crucial step in its pathogenesis. However, the biological relevance of the variations in host receptor interaction with diverse African rotavirus strains are poorly understood. Therefore, this study was designed to investigate the molecular interactions of rotavirus glycoproteins with host cell receptors.

Material/Methods: Sequences of the viral proteins (VP4 and VP7) of the predominant human group A rotavirus (RVA) strains (G1[P8], G2[P4], G9[P6], G9[P8], G8[P6]) and a porcine strain (G4[P6]) were retrieved from the GenBank and all aligned using MEGA11 and Jalview to identify consensus sequences. The human- and pig-specific α -1,2-fucosyltransferase (FUT2), α -1,3-fucosyltransferase (FUT3), vimentin (VIM) and actin-related protein 2 (ACTR2) were subjected to ProtParam, AlphaFold3 and Swiss-Model for structural predictions. Protein-Protein docking was performed using HADDOCK2.4 and PyMOL2 was used to analyze the protein-protein interactions between docked complexes.

Results: The study found that human RVA VP4 and VP7 had molecular weights of 87.4 kDa and 37.3 kDa, while the pig strain had slightly lower values (87.2 kDa and 37.1 kDa). Although VP4 is cleaved into VP8* and VP5*, the identified host receptors in both humans and pigs preferentially bound to the VP5* subunit, with MolProbity Scores of 2.51 and 2.44, respectively. Protein-protein interaction analysis revealed that human RVA VP4 binds most efficiently to FUT3 (interface molecular weight: 13.2 kDa, explicit surface area: 12,606.45 Å²), while VP7 binds predominantly to VIM (10.7 kDa, 10,264.62 Å²). In contrast, both VP4 and VP7 of the pig strain preferentially bind to VIM, with interface molecular weights of 13.5 kDa and 11.9 kDa, and explicit surface areas of 12,829.95 Å² and 11,418.43 Å², respectively.

Discussion/Conclusion: Although our findings suggest distinct glycoprotein-receptor binding preferences between human and pig RVA strains, FUT3 and VIM were identified as the primary receptors in both species. Using predictive modelling, our study is the first to comparatively analyse the structural basis for RVA interactions with human and pig receptors; thus, providing a basis for experimental evaluation of VIM as a potential key receptor for RVA infections in African human and pig populations.

POSTER 111

Animal Human Transmission of Cowpox Virus in Indigenous Sahiwal Cattle: A One Health Outbreak Investigation from Jammu and Kashmir, India

Mandeep Singh AZAD, Rajinder BHARDWAJ, Kowardeep KOUR

Sher-E-Kashmir University Of Agricultural Sciences & Technology Of Jammu, India

Background: Cowpox virus is considered to be a re-emerging zoonotic orthopox virus pathogen and a public health threat due to increasing numbers of cases in humans and animals. The present study reports an outbreak of cow pox in resilient indigenous Sahiwal cattle breed in Jammu and Kashmir (UT). Reports of cow pox outbreak in resilient indigenous breeds and transmission to associated human handlers are rarely documented

Objective: To document the clinical presentation, epidemiological characteristics, zoonotic transmission, and welfare implications of a cowpox outbreak.

Method: An outbreak investigation was conducted at Udhampur district, involving 17 Sahiwal cattle. Clinical examination, morbidity assessment, monitoring of human handlers, supportive therapeutic interventions and biosecurity measures were implemented.

Results: In a group of 17 Sahiwal cattle, 7 lactating Sahiwal cattle and 3 calves were affected with cowpox. It was also observed that the morbidity was as high as 70% in lactating cattle, followed by suckling calves at 42.85%. No mortality was observed in the farm. Suckling calves showed lesions after 9 days of outbreak in a lactating cow. Cowpox lesions were prominent and clearly visible on the teats and udder of lactating animals, whereas lesions on the face and muzzle were seen in suckling calves. All affected Sahiwal cattle and calves were treated with Inj. Enrofloxacin @ 5mg/kg O.D. for 5 days followed by Inj. Meloxicam @ 0.5mg/kg B.I.D. for 2 days as supportive therapy. Teat dipping with betadine-glycerin two times a day was also done. Complete clinical recovery in animals was seen within 12-14 days of treatment.

Importantly, zoonotic transmission was observed in milkers and farm workers/handlers. Affected handlers and milkers in the farm mainly showed lesions on their hands and fingers in the form of papules and pustules. Human cases were managed conservatively by local doctor recommendations. The outbreak showed a clear temporal progression, where the first lesions appeared in a lactating cow, followed by clinical signs in suckling calves approximately 9 days later, and subsequently in human handlers.

It was also seen that affected Sahiwal cattle showed a transient decline in milk yield during the active lesion phase which may be due to painful teat and udder lesions that interfered with normal milking. Affected lactating Sahiwal cattle showed a 33-34% reduction in milk yield, decreasing from 9.5 L/day to 6.3 L/day during the active lesion stage. With a local milk price of ₹60/L, the estimated economic loss was approximately ₹192 per animal per day and about ₹2,300 per cow over the disease period, resulting in a total herd-level loss of nearly ₹16,000-₹17,000 during the outbreak. Milk yield gradually recovered to near-normal levels within 10-14 days following treatment and lesion healing.

Conclusion: This outbreak highlights the zoonotic potential of cowpox in organized dairy settings and underscores the need for integrated One Health surveillance, occupational safety measures, and strengthened farm biosecurity.

POSTER 114

Epidemiological Burden of Lassa Fever in Kaduna State, Nigeria, 2025: A Retrospective Analysis of Surveillance Data

Isiaq SHEHU¹, Amina SHEHU², Musa ABDULLAHI³, Amina BIRMA⁴, Jeremiah DAIKWO⁵

¹ NCDC, Nigeria

² World Health Organization, Kano State, Nigeria

³ Primary Health Care Board, Kaduna State, Nigeria

⁴ Ministry of Agriculture, Kaduna State, Nigeria

⁵ Ministry of Health, Kaduna State, Nigeria

Introduction: Lassa fever is an acute viral hemorrhagic illness caused by the Lassa virus and is endemic in several West African countries, including Nigeria. The disease is primarily transmitted to humans through contact with food or household items contaminated with urine or feces of infected rodents. Human-to-human transmission can also occur, especially in healthcare settings with inadequate infection prevention and control measures. In Nigeria, Lassa fever outbreaks occur annually, posing significant challenges to public health systems due to delayed diagnosis, limited laboratory capacity, and weak surveillance systems.

Recent years have witnessed increasing efforts to strengthen surveillance and response mechanisms through the Integrated Disease Surveillance and Response (IDSR) framework and improved laboratory diagnostic capacity coordinated by the national public health authorities. Understanding the epidemiological burden of Lassa fever at the state level is essential for strengthening early detection, response strategies, and preventive interventions.

Objectives:

1. To determine the number of suspected and confirmed Lassa fever cases reported in Kaduna State in 2025.
2. To analyze laboratory testing outcomes for suspected Lassa fever cases.
3. To estimate the proportion of confirmed cases among suspected cases.
4. To provide evidence to strengthen surveillance and response strategies for Lassa fever in Kaduna State.

Methods: Retrospective descriptive study was conducted using surveillance data collected in Kaduna State, Nigeria, for the year 2025. Data were obtained from the state disease surveillance system under the Integrated Disease Surveillance and Response (IDSR) framework. The dataset included all reported suspected Lassa fever cases recorded within the surveillance period. Variables extracted included the number of suspected cases, laboratory samples collected, and confirmed cases. Laboratory confirmation was conducted through reverse transcription polymerase chain reaction (RT-PCR) testing at designated reference laboratories. Data were analyzed using descriptive statistics. Frequencies and proportions were calculated to describe the distribution of suspected cases, laboratory samples collected, and confirmed cases.

Results: A total of 64 suspected Lassa fever cases were reported in Kaduna State during the 2025 surveillance period. Out of these, 60 laboratory samples were collected and tested for Lassa virus infection. Laboratory results confirmed 8 cases of Lassa fever, representing approximately 12.5% of the suspected cases. The remaining tested samples were negative for Lassa virus. The findings indicate that while a moderate number of suspected cases were reported, only a small proportion were confirmed through laboratory testing, highlighting the importance of laboratory diagnosis in distinguishing Lassa fever from other febrile illnesses.

Conclusion: The study highlights the presence of Lassa fever cases in Kaduna State during 2025, with a proportion of suspected cases confirmed through laboratory testing. Although the number of confirmed cases was relatively low compared with suspected cases, the findings underscore the continued public health importance of Lassa fever surveillance in the state.

Strengthening surveillance systems, improving laboratory diagnostic capacity, and enhancing community awareness are critical strategies for early detection and effective response to Lassa fever outbreaks. Continued investment in public health infrastructure and surveillance systems will support better monitoring and control of Lassa fever in Kaduna State and Nigeria at large.

POSTER 115

Epidemiological Burden of Lassa Fever in Kaduna State, Nigeria, 2025: A Retrospective Analysis of Surveillance Data

Isiaq SHEHU¹, Amina SHEHU², Dr. Jeremiah DAIKWO³, Dr. Musa ABDULLAHI⁴, Dr. Amina BIRMA⁵

¹ NCDC, Nigeria

² World Health Organization, Kano State, Nigeria

³ Ministry of Health, Kaduna State, Nigeria

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Strengthening surveillance systems, improving laboratory diagnostic capacity, and enhancing community awareness are critical strategies for early detection and effective response to Lassa fever outbreaks. Continued investment in public health infrastructure and surveillance systems will support better monitoring and control of Lassa fever in Kaduna State and Nigeria at large.

POSTER 118

Cross-Reactive SARS-CoV-2 Antibodies in Pre-Pandemic Gambian Sera Exhibit Fc-Mediated Effector Activity

Dawda JOBE¹, Ya-Jankey JAGNE¹, Natalie BARRATT², Aji-Fatou TOURAY¹, Hailey HORNSBY², Sheikh JARJU¹, Madikoi DANSO¹, Rhys WENLOCK³, David HODGSON⁴, Benjamin LINDSEY², Alansana DARBOE¹, Beate KAMPMANN⁴, Thushan de SILVA^{1,2}

See oral presentation:

Concurrent Session 3: "Bright Sparks" in Vaccinology – PhD Student Session • Monday 12 October, 15:30

POSTER 121

Evaluating Immunogenicity of Inactivated and Recombinant Foot-and-Mouth Disease Vaccines in Zambia: Implications for Control Strategies

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² Department of Reproductive health, Pan African University Institute of Life and Earth Sciences, Ibadan, Nigeria

Background: Foot-and-Mouth Disease (FMD) is endemic in Zambia, causing recurrent outbreaks that undermine livestock productivity, rural livelihoods, and regional trade. The disease contributes to significant economic losses, with sub-Saharan Africa estimated to lose over USD 1.5 billion annually due to reduced milk yields, mortality, and restrictions on exports. Vaccination remains the cornerstone of control, yet immunogenicity varies across vaccine types and circulating serotypes, particularly SAT1, SAT2, SAT3, and O. Comparative immunogenicity studies are essential to guide national vaccination policy and optimize outbreak prevention.

Objectives: This study aimed to evaluate and compare the immunogenicity of conventional inactivated polyvalent FMD vaccines with recombinant subunit formulations in cattle populations across selected provinces in Zambia. The focus was on antibody titers, duration of immunity, and cross-protection against circulating serotypes.

Methods: A controlled field study was conducted between 2023 and 2025 in Central, Southern, and Eastern provinces. A total of 480 cattle were randomly assigned to two groups: Group A received the inactivated trivalent vaccine (SAT1, SAT2, O), while Group B received a recombinant subunit vaccine targeting SAT2 and O. Serum samples were collected at baseline, 21 days, 3 months, 6 months, and 12 months post-vaccination. Neutralizing antibody titers were measured using virus neutralization tests (VNT), with protective thresholds defined as $\geq 1:45$. Booster doses were administered at 6 months. Statistical analysis was performed using ANOVA to compare mean titers between groups and Kaplan–Meier survival curves to assess duration of protective immunity.

Results: Both vaccine groups elicited measurable immune responses, but differences in magnitude and persistence were observed. Inactivated vaccines induced protective titers in 78% of cattle by day 21, yet immunity declined rapidly, with only 42% maintaining protective levels at 6 months and 15% at 12 months. Recombinant vaccines produced higher initial responses, with 85% of cattle achieving protective titers at day 21. Importantly, persistence was superior, with 68% maintaining protective levels at 6 months and 40% at 12 months. Booster administration restored protective titers above 80% in both groups, but recombinant vaccines consistently maintained higher mean titers, a difference that was statistically significant ($p < 0.05$). Cross-protection against SAT3 was limited in both groups, underscoring the need for updated polyvalent formulations. Field data also revealed that smallholder herds exhibited faster antibody decline compared to commercial farms, likely due to nutritional and management differences. Cost-effectiveness analysis suggested that recombinant vaccines, though more expensive initially, reduced outbreak frequency and long-term losses by approximately 25% compared to conventional vaccines.

Conclusion: This comparative immunogenicity study demonstrates that recombinant subunit vaccines provide more durable protection against FMD than conventional inactivated formulations in Zambia. However, gaps in cross-serotype coverage remain, particularly for SAT3. Integrating recombinant vaccines into Zambia's FMD control program, alongside improved surveillance, regional manufacturing, and tailored booster schedules, could strengthen One Health outcomes by safeguarding livestock productivity, rural livelihoods, and national food security.

POSTER 129

Seroepidemiology and serum bactericidal activity of IgG antibodies to Non Typhoidal Salmonella in healthy Children in Mukuru informal settlement in Kenya

Schola KAMWETHYA¹, Mercy NGETICH¹, Cecilia MBAE¹, Hellen DALE^{2,3}, Robert ONSARE¹, Tonney NYIRENDA⁴, Melita GORDON^{2,3}, Sam KARIUKI^{1,5,6}

See oral presentation:

Concurrent Session 3: "Bright Sparks" in Vaccinology – PhD Student Session • Monday 12 October, 15:40

POSTER 131

Charting Mucosal Immune Responses to Influenza using Human Immune-competent Organoids

Martin BEUKEMA¹, Jacqueline DE VRIES¹, Nilima DINESH KUMAR¹, Nils DOESBURG¹, Barbro MELGERT^{2,3}, Anke HUCKRIEDE¹

See oral presentation:

Plenary Session 2: Mucosal Vaccines • Monday 12 October, 14:20

POSTER 132

AI-Driven Infodemic Surveillance and Its Impact on COVID-19 Vaccine Uptake in Sub-Saharan Africa: A Multi-Country Study

Angyiba SERGE ANDIGEMA^{1,3,4}, Dimalla Paola APHRODITE OLIVE²

See oral presentation:

Concurrent Session 3: "Bright Sparks" in Vaccinology – PhD Student Session • Monday 12 October, 16:50

POSTER 133

Rebuilding Vaccine Confidence in Sub-Saharan Africa: A Multi-Country Analysis of Trust, Misinformation, and Behavioral Determinants of Vaccine Uptake

Angyiba SERGE ANDIGEMA^{1,3,4}, Dimalla Paola APHRODITE OLIVE²

¹ Department of Research, Bisons' Scholars, Douala, Cameroon

² Health and Education for African Youth Excellence, Yaounde, Cameroon

³ Department of Health and Research, Youth Health Action Network, Africa, Cameroon

⁴ Department of Research and Education, Oli Health Magazine Organization, Kigali, Rwanda

Background: Vaccine hesitancy remains a critical barrier to achieving global immunisation targets, particularly in sub-Saharan Africa, where declining confidence threatens routine and emerging vaccination programs. Recent studies highlight that trust deficits in government, science, and health systems are central drivers of hesitancy.

Methods: We conducted a secondary data analysis of 5,203 individuals across six African countries (Ghana, Kenya, Nigeria, South Africa, Tanzania, Uganda) using nationally representative survey datasets. Multivariate logistic regression models were applied to assess predictors of vaccine hesitancy across COVID-19, HPV, and polio vaccines.

Additionally, we triangulated findings with a 2024 multinational mpox vaccine survey (n = 1,832) assessing vaccination readiness using the 7Cs behavioural model.

Results:

- Overall vaccine hesitancy ranged between 18% and 42%, depending on vaccine type and country context.
- A one standard deviation increase in trust in government reduced vaccine hesitancy by ~5 percentage points ($p < 0.01$).
- Trust in societal actors and healthcare systems showed consistent protective effects across all vaccine types.
- In the mpox readiness analysis, low confidence and high exposure to misinformation significantly predicted hesitancy (adjusted OR > 1.8).
- Cross-country comparisons revealed behavioural consistency of hesitancy drivers, suggesting transferable intervention strategies.

Discussion: Our findings confirm that vaccine hesitancy in Africa is not solely driven by access issues but is deeply rooted in institutional trust and information ecosystems. The persistence of these determinants across diseases indicates a structural challenge requiring systemic intervention.

Conclusion: Strengthening vaccine confidence requires integrated trust-building strategies, including community engagement, transparent communication, and digital misinformation control.

Implications for ISV: This study provides evidence for designing context-specific yet scalable vaccine confidence interventions, particularly relevant for emerging vaccines (e.g., TB, mpox, malaria).

POSTER 134

Harnessing Systems Vaccinology and Artificial Intelligence to Predict Vaccine Uptake and Optimise Immunisation Strategies in Low-Resource Settings

Angyiba SERGE ANDIGEMA^{1,3,4}, Dimalla Paola APHRODITE OLIVE²

¹ Department of Research, Bisons' Scholars, Douala, Cameroon

² Health and Education for African Youth Excellence, Yaounde, Cameroon

³ Department of Health and Research, Youth Health Action Network, Africa, Cameroon

⁴ Department of Research and Education, Oli Health Magazine Organization, Kigali, Rwanda

Background: The convergence of systems biology, artificial intelligence (AI), and digital epidemiology is transforming vaccinology. Traditional models fail to capture the complexity of vaccine uptake behaviour, necessitating integrative approaches combining biological, behavioural, and digital data streams.

Methods: We developed a systems vaccinology framework integrating behavioural survey data (n > 17,000 across 8 African countries)

- Vaccine confidence datasets (2020–2023)
- Digital proxies of vaccine intent (search behaviour and information exposure models)

Bayesian hierarchical models and machine learning classifiers were used to:

1. Predict vaccine uptake
2. Identify high-risk hesitancy clusters
3. Model intervention impact scenarios

Results:

- Across 17,187 individuals, declines in vaccine confidence were observed post-COVID-19, with significant heterogeneity across regions.
- Machine learning models achieved >85% predictive accuracy in identifying vaccine-hesitant individuals based on behavioural and digital indicators (validated against known uptake trends).
- Individuals classified as “vaccine holdouts” showed up to 69% higher engagement with low-credibility information sources, strongly correlating with hesitancy.
- Simulation models demonstrated that targeted trust-based interventions could increase uptake by 10–18% in high-risk populations.

Discussion: Systems vaccinology enables a paradigm shift from reactive to predictive immunization strategies, allowing real-time identification of hesitancy hotspots and tailored interventions.

Conclusion: Integrating AI into vaccinology pipelines can significantly enhance precision public health, particularly in low-resource settings where efficient targeting is critical.

Implications for ISV: This work supports the development of AI-driven immunisation ecosystems, aligning with global priorities in digital health and pandemic preparedness.

POSTER 135

Machine Learning-Driven Design of Multi-Epitope Subunit Vaccines Against the Emerging Shamonda Virus: Safeguarding Ruminants and Addressing Zoonotic Potential

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Background: Since its detection, the Shamonda virus (SHAV), an emerging orthobunyavirus, has posed a significant threat to ruminant health, causing abortion, stillbirth, premature delivery, and congenital anomalies in offspring. With no licensed vaccine available and increasing evidence of zoonotic potential, there is an urgent need for rapid vaccine development under a One Health framework to prevent outbreaks in livestock and mitigate human spillover risk.

Methods: Available SHAV polyprotein sequences were retrieved from NCBI. Bioinformatics tools predicted B-cell, cytotoxic T-lymphocyte (CTL), and helper T-lymphocyte (HTL) epitopes, which were screened for antigenicity, allergenicity, toxicity, and induction of IL-4, IL-6, and IFN- γ . Selected epitopes were linked with appropriate spacers and fused to adjuvants (HMGB1, bovine β -defensin, or β -synuclein) to generate six distinct subunit vaccine constructs. Physicochemical properties, secondary and tertiary structures, refinement, and validation were assessed. Top constructs (1, 3, and 5) were docked with Toll-like receptor-3 (TLR-3); the best candidate underwent molecular dynamics simulation and in silico immune simulation.

Results: The six constructs had molecular weights of 31.19–52.26 kDa, lengths of 296–472 amino acids, aliphatic indices of 50.17–78.38, instability indices of 25.47–37.83, and GRAVY scores of –1.088 to –0.280, with solubility scores of 0.583–0.678. Construct 5 exhibited the highest TLR-3 binding affinity (docking score –310.72). Molecular dynamics confirmed complex stability, while immune simulations demonstrated robust innate and adaptive responses (elevated cytokines, B- and T-cell activation).

Conclusion: Construct 5 represents a promising, stable, and immunogenic subunit vaccine candidate against this emerging infection. It offers immediate targeted protection for ruminant livestock and supports broader One Health efforts to counter SHAV and related emerging orthobunyaviruses in animals and potentially humans.

POSTER 136

Nanoparticle-based Intranasal SARS-CoV-2 Vaccine Strategy combining TLR7/8 Agonists and Carbohydrate Targeting

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Introduction/Background: The global COVID-19 crisis prompted the rapid development of vaccines, yet current intramuscular options face challenges in preventing mucosal transmission. This study evaluates a chitosan derivative formulation, incorporating TLR agonist and the SARS-CoV-2 omicron variant antigen, for nasal immunization efficacy.

Material/Methods: Chitosan nanoparticles functionalized with carbohydrates, either loaded with the CL097 TLR7/8 agonist (CHIT-A CL NPs) or without (CHIT-A NPs), were prepared using a coacervation approach with TPP as a cross-linking agent. The resulting particles were characterized for particle size, surface charge and loading efficiency of the TLR agonist. Cellular uptake and activation/maturation markers were assessed in human monocyte-derived dendritic cells (moDCs), and the secretion of cytokines and chemokines (IP-10, RANTES, GRO- α , TNF- α , IL-12, and IL-6) was measured following nanoparticle stimulation. T cell differentiation and cytotoxic activity were evaluated in an autologous mixed lymphocyte reaction (MLR) using moDCs pre-incubated with particles and lymphocytes. Immunization studies in C57BL/6 mice included serum antibody and neutralizing activity analysis, measurement of secretory IgA in nasal washes, and evaluation of cellular immune responses in spleen and lung.

Results: The synthesized nanoparticles—CHIT NPs, CHIT-A NPs, and CHIT-A CL NPs—displayed average sizes of 395, 352, and 385 nm, respectively, and were positively charged. Additionally, the encapsulation efficacy of CL097 was 24.7 %. Concerning the NPs' effect on moDCs, results showed that chitosan-based NPs significantly increased the expression of CD80, CD86, CD40, and MHC class I and II molecules. CHIT-A CL NPs stimulated the secretion of cytokines and chemokines including IP-10, RANTES, GRO- α , TNF- α , and IL-12, and were the only formulation to induce IL-6 production, indicating strong immunostimulatory activity while confirming the nanoparticles were endotoxin-free. In the context of the MLR, an elevated expression of Tbet in CD4⁺ T cells and Granzyme B in CD8⁺ T cells was observed for cells incubated with CHIT-A CL NPs. Regarding the NP vaccine efficacy, vaccinated mice showed high serum IgG and mucosal IgA responses against SARS-CoV-2, along with potent neutralizing activity. Functionalized and TLR7/8 agonist-loaded nanoparticles showed high neutralization against the Omicron variant, with responses sustained at higher dilutions, and cross-neutralization of the ancestral strain. Immunized mice exhibited a robust cellular response, notably with CHIT-A CL NPs, characterized by an elevation in the frequency of IFN- γ ⁺ and Granzyme B⁺ CD8⁺ T cells observed in both spleen and lung cells, as well as a balanced secretion of Th1, Th2, and Th17 cytokines.

Discussion/Conclusion: This nanovaccine induced robust systemic and mucosal immune responses against SARS-CoV-2, including strong neutralizing activity and CD8⁺ T cell responses. The integration of carbohydrate targeting and TLR7/8 activation enhanced both humoral and cellular immunity, underscoring the value of rational adjuvant design for mucosal vaccines. These findings highlight the potential of this platform as a versatile intranasal vaccination strategy against current and emerging respiratory pathogens.

Acknowledgements: This work was co-funded by the European Regional Development Fund (Centro 2030, COMPETE 2030), the EU Recovery and Resilience Facility, Portuguese national funds (FCT projects LA/P/0058/2020, UID/PRR/4539/2025, UID/04539/2025, 2023.16670.ICDT), a doctoral grant (2020.10043.BD), and the 2021 Gilead GÉNESE Program (PT).

POSTER 137

The Effect of Malaria Intermittent Preventive Treatment on Vaccine Responses and SARS-CoV-2 Seroprevalence in Adolescents: Findings from a Randomised Controlled Trial

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See oral presentation:

Concurrent Session 3: "Bright Sparks" in Vaccinology – PhD Student Session • Monday 12 October, 15:50

POSTER 138

Machine Learning-Driven Design of a Multi-Epitope Subunit Vaccine Targeting Plasmodium falciparum Antigens: A Novel Strategy to Combat Vector-Borne Malaria

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Introduction: Malaria remains one of the most devastating vector-borne diseases, transmitted by Anopheles mosquitoes and disproportionately affecting children under five, pregnant women, and immunocompromised populations in tropical regions. Despite the modest efficacy of the RTS,S vaccine, there is an urgent need for next-generation candidates capable of eliciting broad, multi-stage protective immunity.

Methods: This study employed a machine learning-integrated pipeline to design a multi-epitope subunit vaccine targeting four key Plasmodium falciparum antigens: Apical Membrane Antigen 1 (AMA1), Knob-Associated Histidine-Rich Protein (KAHRP), Merozoite Surface Protein 1 (MSP1), and Sporozoite Surface Protein 2 (SSP2). Protein sequences retrieved from NCBI and UniProt were analyzed using ML-enhanced predictive models for antigenicity, epitope mapping, and immune response profiling. Cytotoxic T-lymphocyte (CTL), helper T-lymphocyte (HTL), and linear B-cell epitopes were identified and screened for antigenicity, allergenicity, and toxicity. Selected epitopes were fused using linkers and conjugated to the adjuvant to enhance immunogenicity.

Results: The final 1473-amino-acid construct demonstrated favorable physicochemical properties (molecular weight 15.21 kDa, theoretical pI 8.94, instability index 31.66, GRAVY -0.385), high stability, and non-allergenic/non-toxic profiles. Molecular docking with human TLR2 and TLR4 revealed strong binding affinities (-305.14 and -303.77 kcal/mol, respectively), while iMODS normal-mode analysis confirmed complex stability. Codon optimization for E. coli K12 yielded a CAI of 0.91 and GC content of 59.31%, with successful in silico cloning into pET-28a(+).

Conclusion: This machine learning-driven multi-epitope vaccine candidate offers a promising, safe, and broadly immunogenic platform against Plasmodium falciparum. By leveraging computational intelligence, it provides a novel strategy to combat vector-borne malaria. In vitro and in vivo validation studies are warranted to advance this candidate toward clinical development.

POSTER 139

A Platform Optimization Approach for the Human CD8-Targeted mRNA-LNP Delivery

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Introduction: Precise delivery of mRNA to certain cell populations is required for many promising in vivo gene therapy approaches, including CAR-T cell generation and genomic engineering. With the recent success of cell therapies in treating autoimmune conditions, platforms that selectively and efficiently deliver immunomodulatory mRNA to CD8⁺ T cells are of wide interest. In this study, we aimed to optimize mRNA delivery to CD8⁺ T cells using the antibody-targeted mRNA-LNP platform.

Material/Methods: Monoclonal antibodies that bind human CD8 α (RPA-T8, OKT-8) or CD8 β (S21011A, QA20A40) were conjugated to eGFP mRNA-LNPs using SATA-maleimide thioconjugation. Targeted LNPs were incubated with human PBMCs and eGFP expression was quantified by flow cytometry to determine targeting efficiency. Targeting specificity was examined across PBMC subsets, including CD4⁺ T cells, B cells, and natural killer (NK) cells.

Results: CD8-targeted LNPs selectively delivered mRNA to CD8⁺ T cells with minimal off-target expression (<10%) in other PBMCs (CD4⁺ T cell, B cell, and NK cells). Among clones tested, RPA-T8 (anti-CD8 α) demonstrated superior performance with the highest percentage of GFP-positive cells (73.2%) and Mean Fluorescence Intensity (MFI) of 2050. Following treatment with RPA-T8-targeted mRNA-LNPs, CD8⁺ populations exhibited reduced surface CD8 expression, consistent with receptor internalization.

Conclusion: We identify RPA-T8 as a promising candidate for CD8-targeted LNP-mediated mRNA delivery. Ongoing efforts include fully humanization of RPA-T8, which should reduce risk of anti-drug antibody responses upon repeated administration in humans. This platform provides a robust, customizable, and selective strategy for CD8⁺ T cell targeting, with broad future application to in vivo gene therapy.

POSTER 140

Immunoinformatics-guided Design of a Multi-Epitope mRNA Vaccine Candidate against Hantavirus for Pandemic Preparedness

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Introduction: Hantaviruses are globally distributed zoonotic RNA viruses that pose significant public health threats, particularly through Hantavirus Cardiopulmonary Syndrome (HCPS) and Hemorrhagic Fever with Renal Syndrome (HFRS), which are associated with high mortality rates. Despite ongoing efforts, no universally approved vaccine is currently available, highlighting the need for safer and more effective strategies. This study aimed to design and evaluate a multi-epitope mRNA vaccine targeting the Gn and Gc glycoproteins of hantaviruses using an immunoinformatics-driven approach.

Methods: Conserved regions of Gn and Gc glycoproteins were identified through multiple sequence alignment and used to predict cytotoxic T lymphocyte (CTL), helper T lymphocyte (HTL), and B-cell epitopes. Predicted epitopes were rigorously screened for antigenicity, allergenicity, toxicity, physicochemical properties, and homology to human proteins. Four multi-epitope constructs were generated by varying epitope arrangement (Con1 and Con2) and adjuvant type (Toll-like receptor 4 (TLR4) agonist [TLR4ag] and human β 3-defensin [β 3def]). Selected epitopes were assembled using appropriate linkers, and all constructs were evaluated by structure modelling, molecular docking with human TLR4, and immune simulations.

Results: A total of eight epitopes (one CTL, three HTL, and four B-cell epitopes) were selected for vaccine construction. Molecular docking identified TLR4ag-Con2 and β 3def-Con1 as having strong binding affinity to human TLR4, with binding energies of -17.4 kcal/mol and -17.5 kcal/mol, respectively. However, immune simulations revealed distinct immunogenic profiles among the constructs. TLR4ag-Con1, β 3def-Con1, and β 3def-Con2 elicited both cellular and humoral immune responses. In contrast, TLR4ag-Con2 was predicted to be non-immunogenic despite favourable docking results. Among the immunogenic constructs, β 3def-Con2 induced the strongest overall response, characterized by the highest IgG1 levels and enhanced IL-2 production, which drives T-cell activation, suggesting a desirable humoral response and memory potential. β 3def-Con1 also generated a robust and sustained immune response, although slightly weaker compared to β 3def-Con2. In contrast, TLR4ag-Con1 exhibited a comparatively stronger early innate but weaker adaptive immunity. Considering both structural and immunological evaluations, β 3def-Con1 was identified as the most balanced vaccine candidate.

Discussion/ Conclusion: These findings demonstrate that strong receptor binding does not necessarily translate into effective immunogenicity. Integrating structural and immunological analyses is important for the screening and prioritisation of multi-epitope mRNA vaccine candidate. Collectively, these findings highlight the value of reverse vaccinology and immunoinformatics-driven rational design in accelerating mRNA vaccine development for emerging zoonotic pathogens, enabling rapid clinical translation and strengthening global pandemic preparedness.

POSTER 142

Effectiveness of PCV10 and PCV13 against invasive pneumonia disease in vietnamese children prior to national introduction: a matched case-control study

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See oral presentation:

Concurrent Session 6: "Bright Sparks" in Vaccinology – ECR Session • Tuesday 13 October, 11:20

POSTER 143

Sequential HIV vaccination matures VRC01-class neutralizing antibodies in humans

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Introduction: Eliciting a potent and broad neutralizing antibody (bnAb) response is a major goal in HIV-1 vaccine development. However, the generation of such a bnAb response has been challenging, in part due to the scarcity of bnAb-precursor B cells. BG505 SOSIP GT1.1 gp140 (GT1.1), designed to activate VRC01-class bnAb-precursor B cells that target the conserved CD4 binding site (CD4bs) on HIV-1 Env, was shown to effectively activate these precursors in a first-in-human clinical trial (IAVI C101).

Methods: To address whether this response can be matured into a bona fide bnAb response, we immunized a subset of GT1.1 recipients (n=12) with fully glycosylated trimer BG505 SOSIP.664, adjuvanted with 3M052-AF/alum (IAVI C107/C110).

Results: Prior to the first booster immunization and 80 weeks (range: 51-114 weeks) after the final GT1.1 immunization, 11/11 (100%) participants still had VRC01-class memory B cells in circulation. Two weeks after the first BG505 SOSIP.664 boost, 9/11 (82%) of participants had increased frequencies of VRC01-class memory B cells, constituting up to 0.03% of the total memory B cell population. Individual pre-existing, GT1.1-induced VRC01-class memory B cell clones expanded by up to ten-fold after the first BG505 SOSIP.664 boost. Unsupervised high-dimensional analysis of B cell phenotypes revealed distinct resting and activated memory B cell populations after BG505 SOSIP.664 boost, where in particular the re-activated memory B cell clusters showed an increase in somatic hypermutation and BG505 SOSIP.664 probe binding. When expressed as monoclonal antibodies (mAbs), VRC01-class mAbs bound heterologous, fully glycosylated clade A, B and C trimers and a subset of them neutralized diverse circulating strains of HIV-1. X-ray crystallographic structure determination of three VRC01-class mAbs in complex with heterologous clade A Q23 gp120 revealed accommodation of the N276 glycan and show high overlap in epitope with VRC01-class bnAbs.

Conclusion: This work provides proof-of-concept in humans for reactivation and maturation of VRC01-class memory B cells that have now acquired a capacity to neutralize diverse HIV-1 strains, providing opportunities for optimization of vaccination schedules and broader implementation.

POSTER 146

Age-specific immunity gaps and residual susceptibility to measles and rubella before and after the measles-rubella supplementary immunisation campaign in South India

Ramya MADHAVAN, Akilandeswari ESWARAN, Vaishnavi GANDHI, Tintu VARGHESE, Poornima SARAVANAN, Lakshmi RAJ, Reshma RAJU, Julian Vivek LEANDER XAVIER

See oral presentation:

Concurrent Session 6: "Bright Sparks" in Vaccinology – ECR Session • Tuesday 13 October, 11:30

POSTER 147

Robust innate and adaptive immune responses to a novel PfCSP nanoparticle vaccine candidate

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Malaria, caused by Plasmodium parasites, remains a serious global health challenge with an estimated 280 million cases and 600 000 associated deaths yearly. Vaccine-induced protection correlates with antibody titres against the circumsporozoite protein (CSP) present on the surface of Plasmodium in its pre-erythrocytic stage. The approved vaccines (RTS,S and R21) incorporate the central repeat region and C-terminal motif of Plasmodium falciparum CSP (PfCSP). Though protective, the responses to the highly repetitive region are often transient. Recently, antibodies that cross-react to the PfCSP junction and repeat regions have been found to elicit a durable and protective immune response. This inspired the design of a novel vaccine immunogen incorporating the junction motif and shorter repeat construct (NANP5) displayed on a glycan engineered Helicobacter pylori apoferritin-based nanoparticle.

Cynomolgus macaques were vaccinated with two doses of the immunogen and followed over a period of one year. Macaques were divided into 4 groups (n = 4 per group), receiving 5 µg or 50 µg of the immunogen formulated with either Matrix-M or LMQ (AS01E-like adjuvant) to mimic the adjuvants in the approved R21 and RTS,S vaccines. The vaccine responses were evaluated using flow cytometry-based immunophenotyping, bulk RNA sequencing and B cell receptor (BCR) sequencing analysis of blood and bone marrow across multiple time points.

The immunogen given with either of the adjuvants exhibited a prominent innate immune activation one day after vaccination. Comparable frequencies of vaccine-specific CD4⁺ T-cell responses were detected in immunised macaques, and plasma antibody titres showed functional capacity to block sporozoite traversal of hepatocytes. Vaccine-specific memory B cells in the circulation and plasma cells in the bone marrow showed diverse BCR repertoires with preferential expansion of IGHV3-49 orthologues, lineages previously shown in humans to cross-react to junction and repeat motifs. Antibody sequences accumulated somatic hypermutation over time, indicative of a T-dependent response. Prominent sequences will be expressed as monoclonal antibodies to further test for binding specificity and capacity to block sporozoite traversal of hepatocytes.

Overall, the study shows robust CD4⁺ T cell and humoral responses to the new PfCSP immunogen with either of the two relevant adjuvants. Antibodies to both the junction and repeat motifs were induced. The data indicate that this vaccine candidate is promising and merits further preclinical and clinical evaluation.

POSTER 149

Mothers-to-child transmission of HBV infection according to preventive interventions in Southern Vietnam's Hospitals

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Introduction: The World Health Organization (WHO) recommends Tenofovir Disoproxil Fumarate (TDF) for pregnant women with hepatitis B virus (HBV) presenting with HBV DNA levels of 106 copies/ml or more to hinder mother-to-child transmission (MTCT). Moreover, it is suggested that neonates of HBV-infected mothers receive an HBV vaccine birth dose within 24 hours of birth to mitigate transmission risk.

Methods: The study included 661 HBV-infected pregnant women and 316 infants from three hospitals in Southern Vietnam between October 2019 and November 2020. Infants were classified based on their mothers' TDF prophylaxis into: I-TDF (+) group (107 infants) whose mothers received TDF; I-TDF (-) group (56 infants) whose mothers missed TDF; and I-NTDF group (153 infants) whose mothers did not necessitate TDF. Almost all infants received an HBV vaccine birth dose with HBIG administered based on parents' financial standing.

Results: MTCT was found in 2.2% of the cases. The respective MTCT rates for I-TDF (+), I-TDF (-), and I-NTDF groups were 2.8%, 5.4%, and 0.7%. Immune response rates to the HBV vaccination in the total cohort, I-TDF(+), I-TDF(-), and I-NTDF groups, were 90.3%, 91.3%, 88.9%, and 90.2%, respectively. Vaccinated infants exhibited a statistically lower risk of HBV infection post-birth (aRR=0.1, CI 95% 0.0-0.6, p=0.012).

Conclusion: TDF can equate the MTCT risk in pregnant women with HBV DNA levels of 106 copies/ml or more to those with lower levels. Early administration of the HBV vaccine post-birth also effectively curtails MTCT. Thus, expanding TDF prophylaxis and vaccine coverage is pivotal to impede MTCT.

Keywords: mother-to-child, TDF prophylaxis, HBV vaccine.

POSTER 153

Antigen composition, not T-cell functionality, limits cross-reactivity to distant Coronaviruses after bivalent SARS2 Spike vaccination

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See oral presentation:

Concurrent Session 6: "Bright Sparks" in Vaccinology – ECR Session • Tuesday 13 October, 11:40

POSTER 154

Toward Pan-T-cell Vaccines: Identification and Preclinical Evaluation of Conserved Epitope constructs across diverse viral pathogens

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The COVID19 outbreak has highlighted the importance of pandemic preparedness in preventing future global health crises caused by diverse and emerging viral pathogens. Although current vaccines have been highly effective at reducing severe disease and mortality, they primarily focus on eliciting neutralizing antibody responses against variable surface antigens, which are often susceptible to antigenic drift and immune escape. In contrast, T-cell-mediated immunity, particularly when directed against conserved regions shared across multiple strains and variants within viral families, offers the potential for broader and more durable protection.

Harnessing advances in immunoinformatics, epitope mapping, and high-dimensional immune profiling, we have identified Conserved T-cell epitope regions (CTERs) that are highly conserved within individual viral families and exhibit strong immunogenic potential and broad population coverage. Notably, we demonstrate that this approach is applicable across multiple viral families, demonstrating its generalizability for pan-T-cell vaccine design. Here, we structurally modelled CTER sequences using AlphaFold-based approaches and assembled them into multi-epitope constructs using flexible glycine-serine (GS) or glycine-proline (GP) linkers to promote proper folding and epitope accessibility. Junction analyses were performed to ensure that no de novo epitopes were generated. These optimized designs were subsequently encoded into next-generation mRNA platforms to enable in situ antigen expression following immunization. This integrated strategy allowed efficient intracellular delivery of structurally informed antigens while supporting rapid iteration of vaccine design.

We next administrated the CTER-based vaccines intramuscularly into murine models and evaluated key parameters influencing vaccine performance, including antigen composition and T cell kinetics, and assessed their impact on cross-reactive potential using a combined activation-induced marker (AIM) and intracellular cytokine (ICS) assay. We showed that CTER-based vaccines are safe and well-tolerated in murine models, and can elicit polyfunctional, Th1-biased CD4+ and CD8+ T cell responses in the spleen.

By systematically assessing how these variables shape the magnitude, quality, and durability of T-cell responses, we aim to optimize CTER-based vaccine strategies to enhance their cross-reactive potential. Together, this work establishes a rational framework for the development of next-generation pan-T-cell-focused vaccines designed to provide broad and durable protection against diverse viral pathogens.

POSTER 155

Implementation Effectiveness of a Community-Driven Vaccination Model at Boosting Immunization in Two Conflict-Affected Health Districts of Cameroon: A Quasi-Experimental Study

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See oral presentation:

Concurrent Session 6: "Bright Sparks" in Vaccinology – ECR Session • Tuesday 13 October, 11:50

POSTER 156

Immunoinformatics-Driven Design and In Silico Evaluation of Multi-Epitope mRNA Vaccine Candidates Against Ilesha Virus

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Ilesha virus (ILEV) is a mosquito-borne orthobunyavirus in the family Bunyaviridae, primarily isolated in Africa. It typically causes febrile illness with erythema, though severe cases of fatal meningoencephalitis and hemorrhagic fever have been documented. Despite its public health importance, no approved vaccine or antiviral therapy exists, creating the urgent need for rapid, cost-effective vaccine development.

In this study, an immunoinformatics-based reverse vaccinology approach was used to design two multi-epitope mRNA vaccine candidates. Protein sequences of the RNA-dependent RNA polymerase, M polyprotein, and nucleoprotein were retrieved from NCBI and screened for antigenicity. Consensus cytotoxic T-lymphocyte (CTL), helper T-lymphocyte (HTL), and linear B-cell epitopes were predicted using multiple bioinformatics tools and rigorously evaluated for antigenicity, allergenicity, toxicity, and population coverage. The nine most promising epitopes (three of each type) were assembled into two constructs, each incorporating human β -defensin 1 as adjuvant, strategic linkers (GP GPG, EAAAK, KK), MHC class I-targeting domain, tPA signal peptide, Kozak sequence, 5' and 3' UTRs, and a poly-A tail.

Both constructs (1063 and 1060 amino acids; molecular weights 118,528.86 Da and 118,084.27 Da) were predicted to be highly antigenic, stable, soluble, non-allergenic, and non-toxic. Secondary and tertiary structural modeling confirmed stable globular folds with excellent Ramachandran plot quality (>91% residues in favored regions). Molecular docking with Toll-like receptors TLR-3 and TLR-4 showed strong binding affinities (lowest energy scores of -1149.5 and -882.6, respectively), while molecular dynamics simulations verified complex stability. In silico immune simulations further demonstrated robust activation of innate and adaptive responses, including memory B- and T-cell formation.

These results indicate that the proposed mRNA vaccine candidates have strong potential to elicit protective immunity against Ilesha virus. However, in vitro and in vivo validation is essential to confirm their immunogenicity, safety, and efficacy.

POSTER 157

CO-CIRCULATION OF CHIKUNGUNYA AND ONYONG'NYONG VIRAL INFECTIONS IN UGANDA: IMPLICATIONS FOR VACCINE DEVELOPMENT

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Background: Chikungunya virus (CHIKV) and Onyong'nyong virus (ONNV) are mosquito-borne alphaviruses under the Togaviridae family, historically endemic to Africa. Both viruses cause febrile illness with debilitating joint pain, and CHIKV infections can lead to severe complications, particularly in neonates, immunocompromised individuals, and the elderly. Despite their potential public health impact, ONNV infections remain underreported due to limited surveillance and diagnostic challenges, making their epidemic potential unclear. Understanding the circulation of these viruses is crucial for guiding vaccine development and public health strategies.

Methods: We conducted sentinel hospital-based surveillance in Uganda to assess the occurrence, geographical distribution, and clinical manifestation of Chikungunya and Onyong'nyong viruses. Serological and molecular diagnostic methods were employed to detect active and recent infections. Epidemiological data were analyzed to characterize clinical manifestations and determine risk factors for severe disease.

Results: A total of 2,756 serum samples were collected from febrile patients across 63 districts in Uganda between 2018 and 2022. While no Chikungunya infection was detected by PCR, two cases tested positive for Onyong'nyong virus. Serological evidence of recent alphavirus infection was found in 8.79% of samples, with peak prevalence in 2020. Most positive cases reported fever, joint and muscle pain, and other non-specific symptoms. PRNT analysis revealed stronger neutralizing antibody responses to Onyong'nyong virus than Chikungunya virus, suggesting ongoing but under-recognized Onyong'nyong virus transmission across Uganda.

Conclusion: Our study highlights the endemic nature of CHIKV and ONNV in Uganda, emphasizing the need for improved surveillance, enhanced diagnostic capacity, and targeted public health interventions. The results will inform clinical management strategies and contribute to vaccine development efforts and outbreak preparedness.

POSTER 159

Assessing the Impact of Hepatitis B Immunization Among Children Aged 1 to 14 Years and Health Workers in Ogbomoso, Oyo State, Nigeria.

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Background: Hepatitis B Virus (HBV) infection remains a significant global health concern, despite the availability of effective vaccines since 1992. Nigeria introduced the HBV vaccine into its National Program on Immunization (NG-NPI) in 2004. However, no nationwide surveys have been conducted to assess the vaccine's impact.

Methods: This study aimed to evaluate the population impact of the HBV vaccine in Nigeria post-introduction into the NG-NPI. An age-stratified, cross-sectional study was conducted, involving 336 vaccinated children aged 1-14 years and 50 healthcare workers. Blood samples were collected and screened for various serological markers of HBV infection using ELISA techniques. Samples with evidence of infection were further analyzed using real-time PCR and whole-genome sequencing.

Results: The study found high immunity rates among vaccinated children (98.5%) and healthcare workers (100%), with anti-HBs Titre values of 10-100 IU/mL. However, a significant percentage of vaccinated children (87.0%) showed waning immunity (anti-HBs Titre less than 10 IU/mL). The prevalence of HBV infection was reduced in both populations compared to national prevalence rates (1.2% and 0.0%, respectively). Chronic carriage was observed only in participants aged 11-14 years (0.6%). No HIV antibody was detected. Genotypic analysis revealed genotype E, common in Nigeria, without notable mutations.

Conclusions: The HBV vaccine introduction into NG-NPI has been successful, significantly impacting immunity and chronic carriage. However, concerns arise from waning immunity in vaccinated children. Regular anti-HBs Titre monitoring post-vaccination is recommended to ensure sustained immunity against HBV.

POSTER 162

Improved efficacy of an influenza DNA vaccine through high-density microarray patch delivery

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Introduction/Background: Influenza is a major zoonotic threat to global public health, causing annual disease from seasonal strains and posing pandemic risks when novel viruses emerge from animal reservoirs and spread to humans. Effective pandemic preparedness relies on vaccine platforms that are easy to manufacture, adaptable, scalable, and thermostable. While DNA vaccines are a promising tool for rapid and equitable pandemic response, they have historically demonstrated poor immunogenicity when delivered intramuscularly and often require electroporation post-injection to enhance uptake and efficacy. These limitations highlight the need for improved delivery technologies that can maximise the potential of DNA vaccines while preserving their safety and distribution advantages. The Vaxxas high-density microarray patch (HD-MAP) is one such approach, consisting of a polymer based microprojection array with 5,000 microprojections per cm² that can be coated with dried vaccine formulations. HD-MAPs deliver vaccine directly to the skin, targeting antigen-presenting cells to enhance immune responses, while enabling needle-free, scalable administration without the need for trained healthcare personnel. These features make the platform well suited for rapid deployment to resource-limited settings. In this study, we developed an influenza haemagglutinin (HA)-based DNA vaccine using the 2009H1N1 pandemic strain as a model antigen and evaluated the immunogenicity and protective efficacy of HD-MAP delivery compared with intramuscular (IM) injection in mice.

Materials/Methods: An influenza HA-encoding DNA vaccine based on the A/California/01/2009 (H1N1pdm09) strain was cloned into the pVAX1 plasmid and in vitro expression was validated by immunofluorescence microscopy and flow cytometry. HD-MAPs were dry coated with plasmid DNA and assessed for coating morphology and delivery efficiency. In vivo expression kinetics were evaluated in BALB/c mice using a luciferase reporter system following HD-MAP or IM administration. Immunogenicity was assessed in C57BL/6 mice following a prime-boost regimen, with HA-specific IgG measured by ELISA. Protective efficacy was evaluated by a homologous viral challenge with A/Auckland/1/2009 (H1N1pdm09).

Results: In vivo bioluminescent imaging of a luciferase reporter construct showed that HD-MAP application produced earlier and higher transgene expression than intramuscular (IM) injection in BALB/C mice. HA expression from the DNA construct was validated on transfected cells using immunofluorescence microscopy and flow cytometry, confirming surface expression. HD-MAPs were coated with the plasmid, and scanning electron microscopy demonstrated an even coating on the microprojections with minimal bridging. Delivery efficiency analysis revealed 20% of the coated DNA was removed upon application to mouse skin. Delivery of the HA-encoding DNA vaccine to C57BL/6 mice via HD-MAP elicited robust HA-specific IgG responses. Conversely, IM administration failed to elicit detectable antibody responses. Following challenge with a homologous H1N1 virus, all mice vaccinated with the HD-MAP were protected from weight loss, while only half of those vaccinated intramuscularly reached humane endpoints.

Discussion/Conclusion: HD-MAP delivery of an influenza HA DNA vaccine significantly enhances immunogenicity and protective efficacy compared to IM injection, inducing rapid and robust antibody responses that confer complete protection in mice. These findings demonstrate that targeted skin delivery via HD-MAP can overcome key limitations of DNA vaccines, supporting its potential as a scalable, practical platform for outbreak and pandemic preparedness.

POSTER 163

Immuno-Evaluation of High-Density Microarray Patch Delivered Ebola Virus Vaccines

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Introduction: Ebola virus (EBOV) is a member of the Orthoebolavirus genus and is associated with severe disease and high mortality rates. EBOV has been responsible for multiple outbreaks of Ebola virus disease (EVD) in human populations across Central and West Africa. EVD is characterised by severe symptoms including fever, liver impairment, and haemorrhage, with mortality rates known to reach 90%. While there are two licensed EBOV vaccines based on the EBOV glycoprotein (GP), which are effective in outbreak scenarios, their regimes could be improved to increase vaccination coverage. The high-density microarray patch (HD-MAP) platform technology is a promising alternative to traditional injection-based vaccines. HD-MAPs are a polymer-based array of microscopic projections on which vaccines are dry-coated. When applied to the skin, the microprojections deliver the dried vaccine to layers of the skin rich in antigen-presenting cells, thereby enhancing immune responses. These HD-MAPs also have the potential to be stored for extended periods at elevated temperatures, removing cold chain dependency. This is critical for EBOV outbreaks that often occur in sub-Saharan regions where cold-chain storage is limited. This HD-MAP delivery of EBOV vaccines has the potential to increase vaccination ranges to protect at-risk communities.

Materials/Methods: This study evaluated a pre-fusion, trimeric EBOV GP as a vaccine candidate. The recombinant EBOV GP included a foldon trimerisation domain to promote folding to the native-like conformation with conserved epitopes recognised by neutralising antibodies. To ensure stability of the vaccine upon dry down on the HD-MAP, a high-throughput excipient screen was performed. We also investigated the HD-MAP coating morphology and delivery efficiency. We then evaluated the immunogenicity of HD-MAP-delivered EBOV GP using a prime-boost vaccination model, 21 days apart, compared with intramuscular injection, with or without the adjuvant QS-21. Samples harvested from mice following vaccination were assessed for vaccine-specific immune responses.

Results: Recombinant EBOV GP was expressed in high yields in mammalian cell lines, with high purity in the trimeric, pre-fusion conformation. Neutralising EBOV antibodies bound to recombinant EBOV GP with high affinity, confirming conserved neutralising epitopes. The high-throughput HD-MAP drying stability screen identified g-cyclodextrin as a lead excipient, with complete recovery of EBOV GP post coating to HD-MAPs and storage for 7 days at 40°C. Both HD-MAP coating morphology and delivery efficiency results were consistent with other subunit vaccines (SARS-CoV-2) delivered using the HD-MAP platform technology. The immunogenicity study showed high recombinant EBOV GP serum IgG responses following HD-MAP delivery, outperforming mice vaccinated via intramuscular injection after both dose 1 and 2, highlighting the dose-sparing and immune-enhancing potential of HD-MAP vaccine delivery.

Discussion/Conclusion: This project is the first to test an EBOV GP-based vaccine administered via HD-MAPs. Overall, our findings add to the growing evidence of the superior immune responses generated by HD-MAP delivery. We highlight the compatibility of EBOV vaccines with the HD-MAP platform technology, offering a promising alternative to current vaccine regimes with potential to increase vaccination ranges during EVD epidemics.

POSTER 165

Enhancing Aluminum Adjuvant Freezing Stability and Efficacy via Insights from Interfacial Physics and Engineering

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Introduction: Aluminum adjuvants are critical for enhancing the efficacy of inactivated and subunit vaccines; however, their stability is often compromised during freeze-thaw and lyophilization due to poorly understood freeze-induced damage mechanisms. Therefore, ensuring the stability of aluminum-based adjuvants under such conditions is essential for maintaining vaccine effectiveness.

Material/Methods: To address this challenge, we systematically investigated the physicochemical properties of aluminum adjuvants and their solvent environments. Aluminum hydroxyphosphate nanoparticles (AAHP NPs) with tunable surface charges were engineered, and their interactions with ice crystals were characterized comprehensively at the ice-particle interface. By manipulating ice-water interfacial dynamics through solute chemistry, we controlled ice microstructure to enhance freeze resistance. Molecular dynamics simulations were employed to elucidate the underlying mechanisms, and protective formulations were developed: positively charged AAHP NPs with 5% sucrose, and the addition of alkyl glycosides featuring a balanced head-tail structure. The protective effects were validated through in vivo immunogenicity assessments and colloidal stability evaluations.

Results: Surface charge was identified as a key determinant of adjuvant-ice interactions; charged AAHP NPs electrostatically repelled ice growth, which reduced mechanical stress, minimized structural damage, and significantly improved colloidal stability after reconstitution. Manipulating ice-water interfacial dynamics transformed freeze-thaw processes into a tunable design space, preserving surface chemistry, antigen-binding capacity, and immunogenicity of nanoadjuvants as confirmed in vivo. Molecular dynamics simulations revealed that ice growth was inhibited via the Gibbs-Thomson mechanism, reducing detrimental adjuvant-ice interactions. Additionally, the formulation using positively charged AAHP NPs with 5% sucrose maintained immune responses in vaccination models, while alkyl glycosides prevented aggregation and surface hydroxyl loss in aluminum oxyhydroxide nanorods during freeze-drying.

Conclusion: By bridging fundamental interfacial physics with practical vaccine adjuvant development, this study provides innovative strategies to preserve the stability and enhance the efficacy of aluminum adjuvants under low-temperature conditions.

POSTER 166

APC-Mimetic Dendritic Cell-Derived Extracellular Vesicle Nanovaccine with STING Adjuvant Induces Long-Term Th1 Immunity and Immune Memory Against Dengue Virus

Anindita SENGUPTA^{1,2}, Jayanta BHATTACHARYYA^{1,2}

See oral presentation:

Concurrent Session 3: "Bright Sparks" in Vaccinology – PhD Student Session • Monday 12 October, 16:00

POSTER 169

A Rapid Multicountry Qualitative Assessment of the Impact of 2025 U.S. Government Funding Cuts on Immunization Programs: Findings from the Democratic Republic of Congo

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The United States Agency for International Development (USAID) played a major role in supporting immunization service delivery in the Democratic Republic of Congo (DRC). But in early 2025, significant reductions to U.S. government (USG) global health funding marked a critical juncture and as a result created an urgent need to assess the impact of these sweeping cuts on immunization services delivery. This rapid qualitative case study explores how the 2025 U.S. Government funding cuts affected routine immunization in the Democratic Republic of the Congo (DRC), focusing on two provinces with different profiles, namely Kasai Oriental and Sankuru.

Using 164 participants involved in 69 face-to-face interviews and 16 focus group discussions (KIIs/FGDs) with Expanded Program on Immunization (EPI) managers, vaccinators, community health workers (CHWs or community relays), provincial/national officials, and partners, we analyzed transcripts in NVivo 15.2 with a mixed deductive/inductive codebook.

We find three pillars most affected: (1) outreach logistics (fuel/transport, per diems), (2) data/management information system, MIS (connectivity, validation meetings, paper tool stock-outs), and (3) community engagement (health area committees for health development, CODESA/ inputs and facilitation). Fixed posts generally continued, but advanced/mobile sessions declined sharply, collapsing in Sankuru, disproportionately harming zero-dose and remote populations. Cold-chain risks rose (non-functional fridges, no maintenance), and data quality degraded (completeness/timeliness down; mismatches between registers and tallies; outliers in District Health Information Software 2, DHIS2). Staff resilience persisted but motivation was fragile without incentives or supervision. Cross-program echoes in malaria/HIV/Maternal and Child Health (MCH) indicate system-wide fragility.

A time-bound bridging package, restoring data connectivity/validation, supplying paper tools, funding targeted outreach logistics, and modest CHW incentives, could rapidly stabilize core functions, while medium-term actions (micro-planning, integrated supervision) and progressive domestic financing improve sustainability. Findings reflect two provinces and rely on qualitative perception data; nonetheless, triangulated evidence suggests urgent equity risks and imminent outbreak potential especially in isolated zones.

POSTER 170

Newcastle Disease Control : Do Perception Structures Drive Vaccine Adoption among Smallholder Poultry Farmers in Tanzania?

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Newcastle disease (ND) continues to threaten smallholder poultry production and rural livelihoods in Tanzania despite the availability of effective vaccines. This study examines whether farmers' perceptions influence vaccination adoption. Exploratory factor analysis based on tetrachoric correlations identifies two latent perception structures reflecting institutional access and cultural constraints. Logistic regression results show that access to livestock officer, vaccine awareness, prior outbreak experience and education significantly affect vaccination adoption while, reliance on traditional medicine and access to agricultural employment do not. The findings suggest that improving, awareness, access to veterinary services and addressing cultural barriers are essential to enhance ND vaccine adoption and strengthen poultry-based livelihood resilience.

POSTER 172

Environmental drivers of oral typhoid vaccine responses in Uganda: dissecting rural-urban differences and the role of *Schistosoma mansoni*

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See oral presentation:

Plenary Session 2: Mucosal Vaccines • Monday 12 October, 14:35

POSTER 173

Induction of influenza-specific immunity in pigs using dissolvable microneedle patches to deliver an adenovirus-based vaccine

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See oral presentation:

Concurrent Session 3: "Bright Sparks" in Vaccinology – PhD Student Session • Monday 12 October, 16:10

POSTER 174

A Bivalent HPV11/16 L1 mRNA-LNP Vaccine Elicits Potent Neutralizing Antibody and T-cell Responses in Mice

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Introduction: Cervical cancer and genital warts, predominantly caused by human papillomavirus (HPV) infection, remains a significant global public health issue. Although existing prophylactic vaccines are highly effective, their high manufacturing costs and limited accessibility in low-resource settings underscore the need for alternative vaccine platforms. In this study, we present the development of a prototype bivalent mRNA-based HPV vaccine targeting two key HPV types: HPV16, associated with cervical cancer, and HPV11, responsible for genital warts. The vaccine design employs an optimized L1 protein as the antigen to elicit protective immunity.

Methods: Modified nucleoside mRNA constructs encoding HPV16 and HPV11 L1 were designed, synthesized, and encapsulated in lipid nanoparticles (LNPs). The mRNA was transfected into cells, and cell lysates were analyzed for virus-like particle (VLP) formation using transmission electron microscopy (TEM). Female C57BL/6 mice were immunized with two doses (5 µg) of each HPV11 and HPV16 L1 mRNA-LNP at three-week intervals and compared with a group receiving Gardasil®4 (1:20 of the human dose). Two weeks after the final immunization, spleen and serum samples were collected to evaluate humoral (binding and neutralizing antibodies) and cell-mediated (IFN-γ ELISPOT) immune responses.

Results: HPV11 and HPV16 L1 proteins self-assembled into virus-like particles (VLPs), as confirmed by TEM, with some size heterogeneity likely arising from natural protein processing. Despite this variation, both constructs demonstrated strong immunogenicity. Two weeks after the second immunization, mice vaccinated with HPV11 and HPV16 L1 mRNA-LNP formulations exhibited robust antigen-specific IgG responses. The HPV11 L1 mRNA-LNP group showed a 15-fold higher in IgG titer compared to Gardasil®4 (mid-point titer 67,000 vs 4,500, $p = 0.0079$), while HPV16 L1 mRNA-LNP induced a 2-fold higher, $p = 0.4206$. Both mRNA vaccines also elicited functional neutralizing antibodies, with HPV11 L1 mRNA-LNP generating the highest titers ~26-fold higher than Gardasil®4, (95,853 vs 3,624, $p = 0.0079$), whereas HPV16 L1 mRNA-LNP produced comparable neutralizing activity with Gardasil®4. In addition, strong cellular immune responses were observed in mRNA vaccine, as indicated by increased IFN-γ-producing T cells. The HPV16 L1 mRNA-LNP group induced the highest T-cell responses, significantly higher than those of Gardasil®4, (1,855 vs 498 sfu/106 splenocytes, $p = 0.0079$, HPV11 L1 mRNA-LNP also elicited significantly enhanced responses, (1,780 vs 71 sfu/106 splenocytes, $p = 0.0079$).

Conclusions: The bivalent HPV11/16 L1 mRNA-LNP vaccine effectively induces humoral and cellular immune responses, exceeding those observed with Gardasil®4. Notably, it enhances both neutralizing antibody production and T-cell activation. These findings support the mRNA-LNP platform as a promising, scalable, and cost-effective alternative for HPV vaccination, with potential to improve global accessibility and broaden protective immunity. Future studies will aim to expand this approach by incorporating additional HPV genotypes to further enhance vaccine coverage.

POSTER 175

A framework for risk–benefit analysis of vaccines approved through accelerated pathways

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A framework for risk–benefit analysis of vaccines approved through accelerated pathways

Authors: Bethan Cracknell Daniels, Tim Endy, Joseph Lewnard, Jose Luis Di Fabio, Oscar Cortes-Azuero, J. Gabrielle Breugelmans, Simon Cauchemez, Alexander Precioso, Albert Ko, Rebecca E. Chandler, Stephen J. Thomas, Nicole Lurie, Henrik Salje

Background: Vaccine safety is not absolute, and risks in specific populations are incompletely characterised at licensure. This challenge is amplified for new vaccines against emerging epidemic pathogens, which require innovative approaches to evaluate and deliver them quickly, including alternative regulatory pathways. For example, the chikungunya virus (CHIKV) vaccine IXCHIQ was recently licensed based on a correlate-of-protection trial in a healthy US population. However, the first mass deployment of IXCHIQ during an outbreak in La Réunion was recently suspended in those aged over 65 years following multiple severe adverse events (SAEs).

Methods: We present a generalisable pathogen- and vaccine-agnostic framework for evaluating vaccine risk–benefit profiles. We first establish a simple model to estimate the expected number of severe outcomes in vaccinated and unvaccinated populations across different epidemic scenarios, accounting for vaccine efficacy and age-related variation in disease severity and vaccine-associated SAEs, including uncertainty. From this, we derive a safety threshold—the maximum acceptable vaccine risk that still provides net benefit. We then implement this framework probabilistically using Bayesian inference to incorporate uncertainty in both disease and vaccine risk estimates, allowing us to calculate the probability that vaccination provides a net benefit for different risk groups and outcomes. We apply this model to IXCHIQ, as well as a set of endemic (SARS-CoV-2) and other epidemic (measles, Ebola) pathogens, to help guide future vaccine implementation.

Results: We show that both the underlying infection risk and the subgroup risk of severe outcomes are key to identifying settings in which vaccine benefits reliably outweigh the risks. We identify thresholds for vaccine-associated SAEs that still yield a net benefit across multiple pathogens, showing how acceptable risk thresholds for measles and SARS-CoV-2 vary over time as disease dynamics change. For CHIKV, we show that the benefits of IXCHIQ outweigh the vaccine risks among 18–64-year-olds across all epidemiological scenarios. In those aged over 65 years, we estimate a net benefit in large outbreaks, including the La Réunion outbreak, and endemic settings over ten years. There is insufficient evidence of a net benefit in smaller outbreaks or in travellers aged over 65 years. We show that, using age-specific CHIKV infection risks, we could have concluded at the end of the Phase III trial that vaccine benefits against clinical disease outweighed SAE risks in the 18–64-year age group and in >65 years at higher attack rates, despite limited safety data.

Conclusion: Prior knowledge of infection risk can guide risk–benefit assessments of new vaccines, even when risks are incompletely characterised due to the absence of large Phase III safety and efficacy trials or underrepresentation of high-risk populations. This generalisable framework can guide trial recruitment and identify specific epidemiological scenarios and subpopulations that benefit from vaccination, supporting evidence-based decision-making.

POSTER 177

A Recombinant, Non-Replicating Oral Rotavirus Vaccine Candidate for Low- and Middle-Income Countries

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Introduction: Rotavirus (RV) is the leading cause of severe diarrheal illness in children younger than 5 years worldwide, accounting for 30% to 50% of such illnesses and approximately 150,000 deaths annually. Although effective oral live-attenuated rotavirus vaccines are available, their efficacy is limited in low- and middle-income countries (LMICs) compared to high-income countries. This may be due to factors such as genetic heterogeneity, microbiome differences, environmental enteric dysfunction, which is associated with shortened villi and inflammation, nutritional status, co-administration of oral polio vaccines, and high maternal antibody titers against RV, what limits replication of the vaccine. We propose to potentially circumvent these limitations by using a clinically tested, non-replicating adenoviral platform that delivers DNA-encoded antigens together with a molecular double-stranded RNA adjuvant (rAd5-dsRNA) into target cells. The rAd5-dsRNA is room-temperature stable, orally administered, and easily delivered, making it ideal for broad and rapid distribution, particularly in resource-constrained countries.

Methods: Codon-optimized DNA sequences encoding human RV VP4 or its tryptinized version VP8*, either as intracellular or transmembrane proteins, were linked via a T2A sequence to a codon-optimized VP6 DNA sequence and inserted into the genome of a non-replicative human adenovirus type 5 under the control of a CMV promoter. The vaccines were produced in Expi293 cells. Human epithelial cell lines were infected with the vaccine constructs, stained with human neutralizing antibodies and analyzed using an Attune NxT Flow Cytometer. BALB/c mice (6-8 weeks old) were intranasally vaccinated with two doses of 1×10⁷ infectious units (IU) of the vaccines. Serum antibodies were measured by ELISA and MSD, and neutralizing antibodies were measured by FRNT assay using MA104 cells. A RV challenge study was performed at Washington University using RANKfl/fl and RANKΔIEC mice. Stool IgA and viral shedding were measured by ELISA.

Results: The RV VP4 spike protein was expressed at high levels on the surface of human epithelial cell lines while maintaining a conformation recognized by human neutralizing antibodies. Intranasally vaccinated mice developed high levels of RV-specific serum antibodies against both VP4 and VP6, and the antibodies were neutralizing in a cell-based neutralization assay. Elicited antibodies displayed cross reactivity against the most prevalent strains of RV, including WI61 (G9P[8]), DS1 (G2P[4]) and ST3 (G4P[6]) strains, that account for the most prevalent P serotypes and some of the most prevalent G serotypes of RV. Vaccinated RANKfl/fl mice developed anti-RV IgA antibodies in feces and were protected against viral shedding after challenge.

Conclusions: To our knowledge, there are no documented examples of successful utilization of non-replicating RV vaccines in humans. We have developed several promising RV vaccine candidates using a clinically tested oral vaccine platform. The recombinant non-replicating vaccine may help address the efficacy challenges associated with live-attenuated vaccines by targeting the same intestinal mucosal tissues without requiring viral replication. In addition, adenoviral vectors may bypass interference from maternal immunity to RV in infants, with the potential to reduce RV-associated mortality in LMICs.

POSTER 179

Evaluating risk communication and community engagement to support Ebola vaccine uptake during the 2025 Kasai outbreak, Democratic Republic of the Congo: a qualitative assessment

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Background: The Democratic Republic of the Congo declared its 16th Ebola outbreak in Kasai Province on September 4, 2025. Vaccination with the rVSVΔG-ZEBOV-GP (Ervebo®) Ebola vaccine began nine days later, with 47,577 doses administered over two months. Risk communication and community engagement (RCCE) activities were implemented to increase awareness, address concerns, and promote vaccine uptake in the community.

This study evaluated how RCCE activities and coordination efforts influenced community acceptance and identified barriers and facilitators to vaccination among healthcare workers (HCWs), frontline workers (FLWs), community leaders, and community members.

Method: Focus group discussions were conducted with community members (8 groups), HCWs (8 groups), and FLWs (4 groups) in purposively selected vaccination-eligible health areas. Key informant interviews were conducted with community leaders and vaccination coordinators (n=17). Audio-recorded discussions were transcribed and analyzed using combined inductive and deductive thematic coding.

Results: High perceived risk of Ebola and its fatality rate were primary facilitators of vaccine acceptance. RCCE activities including community mobilization, radio messaging, and engagement with religious leaders and traditional healers increased vaccine awareness and trust in vaccination. Vaccination of HCWs reinforced confidence by demonstrating vaccine safety. Overall vaccine confidence and uptake were perceived as high; however, concerns regarding vaccination during pregnancy were reported and then addressed through ongoing RCCE efforts.

Conclusion: The rapid deployment of Ebola vaccination following outbreak declaration, coupled with coordinated RCCE efforts may have contributed to vaccine acceptance during the Kasai outbreak. Overall, trusted communication channels for RCCE activities and visible vaccination of HCWs contributed to vaccine confidence, despite some initial concerns regarding vaccine safety during pregnancy. These findings can inform outbreak preparedness and strengthen RCCE strategies for Ebola vaccine deployment.

POSTER 180

Bridging the Mpox Vaccine Uptake Gap in Africa: Determinants of Acceptance and Hesitancy from a Systematic Review and Meta-Analysis

Charles IBENEME^{1,2}, Olaiya Paul ABIODUN¹, Glory ONYEUGO², Lilian MALIRO³, Titilola MUNKAIL², Folake Abiola ABIODUN⁴, Omogoye Tosin SAMUEL⁴

See oral presentation:

Concurrent Session 7: Vaccine Confidence • Wednesday 14 October, 11:50

POSTER 182

Intranasal SARS-CoV-2 vaccination enhances cross-reactivity in mice with pre-existing immunity

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Introduction: Mucosal immunity can reduce breakthrough infections and transmission of SARS-CoV-2. Reduced transmission rates will help to protect vulnerable and immunocompromised individuals unable to mount an effective immune response. Therefore, the development of a next generation of mucosal vaccines is necessary. However, a majority of individuals have encountered SARS-CoV-2 antigens in form of infection or vaccination multiple times, leading to a highly complex and varied immune history.

Methods: To investigate how pre-existing immunity shapes responses to mucosal vaccination, we developed three murine models reflecting distinct immunological backgrounds: intramuscular mRNA vaccination (ancestral or ancestral plus bivalent regimen), repeated prior infections (ancestral and XBB.1), and hybrid immunity induced by ancestral mRNA vaccination followed by XBB.1 breakthrough infection. Utilizing these mouse models, we evaluated antibody responses following administration of an intranasal Newcastle disease virus (NDV)-based JN.1 vaccine (NDV-HXP-S JN.1).

Results: Mucosal vaccination broadened serum neutralizing antibody responses and increased upper respiratory tract IgA titers across all immune backgrounds. Subsequently, we developed a mucosal trivalent formulation of the NDV-HXP-S vaccine that elicited broadly cross-neutralizing antibodies against a diverse panel of SARS-CoV-2 variants and conferred protection against newly emerged, unmatched variants. In mice with pre-existing immunity, intranasal boosting with the trivalent NDV-HXP-S formulation further enhanced cross-neutralizing immunity.

Discussion: Collectively, these data support intranasal vaccination independent of prior immune history and identify multivalent mucosal vaccination as a strategy capable of broadening immunity beyond prior antigenic exposure.

POSTER 183

Rotavirus Infection Among Vaccinated and Unvaccinated Children in IDP Camps: Evidence from Sentinel Molecular Surveillance in Benue State, Nigeria.

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Introduction/Background: Viral acute gastroenteritis (AGE) remains a leading cause of death among children under five years globally, with Nigeria accounting for over 20% of the disease burden. The country is implementing rotavirus vaccination in its national routine immunization which has significantly reduced the disease. However, its performance in humanitarian settings possessing various high-risk factors remains understudied and requires actions. We present the report of our sentinel molecular surveillance in internally displaced persons (IDP) camps to assess the distribution of viral AGE pathogens, generating evidence relevant to rotavirus vaccine performance, coverage and the need for expansion of access.

Material/Methods: This study was conducted from March to August 2025 in two selected IDP camps (Daudu and Ortese) in Guma Local Government Area, Benue State, Nigeria. A cumulative of 123 children under five years of age who met the inclusion criteria for AGE were enrolled. Case demographic and epidemiological data with corresponding stool samples were collected. Stool samples were tested using multiplex real-time polymerase chain reaction (RT-qPCR) at the Nigeria Centre for Disease Control and Prevention (NCDC) National Reference Laboratory, Abuja. Viral prevalence, co-infections, and distribution by vaccination status were analyzed.

Results: Overall, 59.3% (73/123) of samples tested positive for at least one viral pathogen, with females and males having 53.7% (66/123) and 46.3% (57/123) respectively. Rotavirus was the predominant pathogen 61.8% (76/123), followed by astrovirus 12.2% (15/123), norovirus genogroup I 10.6% (13/123), norovirus genogroup II 7.3% (9/123), sapovirus 6.5% (8/123), and adenovirus 4.1% (5/123). Single infections accounted for 42.3% (52/123) of cases, 17.9% (22/123) had dual infections; 1.6% (2/123) and 0.8% (1/123) of the cases had triple and quadruple viral infections. Among participants, 51.2% (63/123) had received at least one dose of rotavirus vaccine, while 48.8% (60/123) were unvaccinated or had unknown status. Among vaccinated children, 50.8% (32/63) had received three doses, 25.4% (16/63) two doses, and 23.8% (15/63) one dose.

Rotavirus was detected in 46.0% (29/63) of vaccinated children. Other viral pathogens identified among vaccinated individuals include norovirus genogroup I 14.3% (9/63), astrovirus 7.9% (5/63), norovirus genogroup II 6.3% (4/63), adenovirus 4.8% (3/63), and sapovirus 3.2% (2/63).

Discussion/Conclusion: Our findings highlight a substantial burden of viral AGE, particularly rotavirus, among children in IDP camps. The detection of rotavirus among vaccinated children underscores the need for continuous evaluation of vaccine effectiveness in this setting, including the role of dose completion, timing of vaccination, and circulating viral strains. Furthermore, inadequate vaccine coverage observed in this population points to gaps in immunization delivery in humanitarian contexts. Strengthening routine immunization, improving vaccine uptake, and integrating molecular surveillance into vaccine program evaluation are critical for optimizing the impact of rotavirus vaccination in high-risk populations.

POSTER 185

Systemic response and short-term functional changes following infection with *Necator americanus* third-stage infective larvae: Insights from a control human hookworm infection trial in Lambarene, Gabon

Therese Vanessa AMANA BOKAGNE^{1,2}, Kossiwa Clarisse KOKOU¹, Ayodele ALABI^{1,3}, Christine NDONG EMGOME¹, Edlom Pelagie TCHADIE^{1,2}, Augustin BOUEYA BOUEYA¹, Eddy MABICKA¹, Peter KREMSNER^{1,2}, Selidji T AGNANDJI^{1,4}

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POSTER 187

Enhancing the manufacturing and immunogenicity of a gamma-irradiated whole-cell pneumococcal vaccineChloe GATES¹, Eve KENNEDY¹, Timothy HIRST¹, James PATON^{1,2}, Mohammed ALSHARIFI^{1,2}, Erin BRAZEL^{1,2}¹ GPN Vaccines, Australia² Adelaide University, Australia

Background: *Streptococcus pneumoniae* is a formidable bacterial pathogen, with over 100 different serotypes identified based on their capsule structure. This antigenic diversity has complicated current capsule-based pneumococcal vaccine approaches, with their use contributing to an increase in infection by non-vaccine serotypes. Antimicrobial resistance (AMR) exacerbates this, with *S. pneumoniae* leading AMR-associated deaths in children under the age of five. This has highlighted the need for alternative cross-protective vaccines. GPN Vaccines Ltd have previously developed a whole cell pneumococcal vaccine using an unencapsulated strain (Rx1 Δ lytA Pdt Δ psaA) inactivated by gamma irradiation. We have shown that this vaccine elicits serotype-independent protective immune responses in animals (termed Gamma-PN2). However, manufacturing and downstream processing of the whole-cell vaccine indicated fragility. We hypothesised that pneumococcal autolytic enzymes may remain active during downstream processing, potentially limiting the commercial scalability of the final vaccine. Thus, we sought to develop an engineered strain to further enhance manufacturability.

Methods: We generated a derivative strain with an additional deletion of the autolysin gene lytC (Rx1 Δ lytA Pdt Δ psaA Δ lytC) (Gamma-PN3) and evaluated the impact on thermostability in different conditions pre- and post-gamma-irradiation. Following inactivation by gamma-irradiation, vaccine immunogenicity was assessed using in vitro cell lines and in vivo vaccine efficacy testing in mouse and rabbit models. Mice and rabbits were vaccinated three times intramuscularly with 50 mg and 250 mg of total protein content, respectively. Sera from animals was harvested three weeks post final vaccination and analysed for total and functional IgG responses.

Results: Gamma-PN3 maintained thermostability for prolonged periods at ambient temperature, showing limited cell lysis and sustained cellular structure. Conversely, Gamma-PN2 demonstrated 99% cell density lost within 6 hours at ambient temperature. To assess the impact of stability on immunogenicity, in vitro and in vivo models were utilised. In vitro TLR2 stimulation showed comparable levels of activation after exposure to each vaccine. Intramuscular administration of either vaccine in mice also yielded comparable IgG titres, yet Gamma-PN3-specific antibodies demonstrated improved binding to different pneumococcal serotypes and recognition of a wider array of antigens. This enhanced immunogenicity was shown to be associated with endosomal TLR9 and type I interferon activation, suggesting stability of a whole-cell vaccine directly impacts immunogenicity. Finally, vaccination with Gamma-PN3 in a rabbit model yielded functional antibody responses that showed opsonophagocytic activity against a number of pneumococcal serotypes.

Conclusions: Deletion of LytC improved vaccine thermostability, leading to the enhanced manufacturability and immunogenicity of Gamma-PN3. This study also enabled progression of this whole-cell pneumococcal vaccine to large-scale GMP manufacture and testing in first-in-human Phase I clinical trials.

POSTER 190

A Programmable mRNA-LNP Platform for Inducing Treg-Mediated Tolerance in Allergen Immunotherapy

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Introduction/Background: Pollen allergy is a leading contributor to respiratory allergic diseases, with a steadily increasing prevalence. Although allergen immunotherapy (AIT) can alter disease progression, its efficacy is limited by inefficient allergen delivery and inadequate induction of regulatory T cells (Treg). Messenger RNA (mRNA) vaccines advantages in pollen vaccines is supported by several features, including low-inflammogenic sequence design, intrinsic targeting to the liver, an organ associated with immune tolerance, and the ability to modulate the immune response through Treg proliferation and T helper type 1 (Th1) activation. However, it remains unclear whether minimally immunogenic LNP-formulated mRNA vaccines can effectively promote Treg and Th1 responses capable of counterbalancing the Th2-skewed immune response characteristic of pollen allergies.

Material/Methods: We design mRNA encoding major mugwort pollen allergen Art v 1, fused to invariant chain (mArt v 1), to enable efficient MHC II-mediated antigen presentation. This mRNA is encapsulated in PEG-lipid-based lipid nanoparticles (LNPs), and an optimized formulation (LNP-C18mann) is obtained by screening PEG-lipid hydrophobic chain lengths. LNPs were characterized by dynamic light scattering (DLS) and cryo-transmission electron microscopy (cryo-TEM). Cellular uptake and transfection were assessed using flow cytometry. In vivo biodistribution was evaluated using firefly luciferase mRNA and an IVIS imaging system. Mechanistic studies were conducted in a short-term immunization model with the evaluation with liver gene expression by qPCR. Therapeutic and prophylactic efficacy were assessed in murine pollen allergy models, including evaluation of airway hyperresponsiveness (AHR), lung histopathology (H&E and AB-PAS staining), allergen-specific serum antibody levels (IgE, IgG1, IgG2a), and flow cytometric analysis of Treg markers (CD25, FoxP3, CTLA-4, Helios) in spleen.

Results: In vitro, LNP-C18mann induced a tolerogenic phenotype in antigen-presenting cells, characterized by high MHC II expression with low CD80/CD86, along with increased IL-10 secretion. In vivo, IVIS imaging using firefly luciferase mRNA revealed that LNP-C18mann achieved efficient and liver-specific mRNA delivery. The short-term animal model exhibited that mAr-C18mann targets tolerogenic liver, modulates dendritic cell phenotype to a tolerogenic microenvironment in draining lymph nodes, and drives the systemic expansion of allergen-specific Treg in spleen. In therapeutic murine model of pollen allergy, both mAr-C18mann and a simplified two-epitope variant, mdT, encoding mRNA vaccine (mdT-C18mann), significantly reduces allergic symptoms, airway inflammation, and serum IgE levels. Notably, mAr-C18mann induces allergen-specific Treg and confers durable tolerance during pollen re-exposure.

Discussion/Conclusion: This study establishes a synergistic strategy for next-generation allergy immunotherapy by rationally integrating antigen design and delivery engineering. The mannose-decorated LNP platform, when delivering an li-chain-fused allergen mRNA, induces a potent and durable antigen-specific tolerance. Notably, the same delivery platform also demonstrates flexibility when loaded with a simplified dual-epitope mdT, which effectively suppresses key allergic manifestations. Collectively, this work provides a versatile mRNA-LNP platform and a generalizable design framework. It highlights that antigen design can be tailored to specific clinical needs, thereby significantly advancing the potential of mRNA-based vaccines for the prevention and treatment of allergic diseases.

POSTER 191

Bridging the Mpox Vaccination Continuum Gap in Africa: Determinants of Allocation, Administration, and Uptake from a Systematic Review and Meta-Analysis

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Introduction / Background: The resurgence of mpox and the declaration of a global public health emergency underscored the urgent need to strengthen vaccine deployment and uptake across Africa. While coordinated global mechanisms facilitated the delivery of millions of mpox vaccine doses to African countries, vaccination performance has remained uneven. Evidence increasingly suggests that challenges extend beyond supply constraints, reflecting broader gaps across the vaccination continuum—from dose allocation and regulatory authorization to operational deployment and community acceptance. Understanding these interconnected barriers is essential for improving outbreak vaccination strategies. This study synthesizes available evidence to quantify gaps along the mpox vaccination continuum and identify key structural, health-system, and behavioral determinants shaping vaccine utilization across African settings.

Materials / Methods: A systematic review and meta-analysis were conducted following PRISMA 2020 guidelines. Literature searches were performed across PubMed/MEDLINE, Embase, Scopus, Web of Science, Global Health, and African Index Medicus, complemented by grey literature from international public health agencies between 2016 and 2026. Studies reporting quantitative or mixed-method evidence related to mpox or outbreak vaccination allocation, administration, or uptake in African populations were included. Random-effects meta-analysis using the DerSimonian–Laird method was applied to estimate pooled vaccine utilization rates. Subgroup analyses examined variations across outbreak phases, regulatory readiness, and health-system capacity. A vaccination continuum framework was applied to map determinants influencing transitions from vaccine allocation to population uptake.

Results: A total of 120 studies met inclusion criteria, with nine studies contributing quantitative allocation-to-administration data. The pooled vaccine utilization rate was 76%, indicating a mean utilization gap of approximately 24% between allocated and administered doses. Countries with stronger regulatory readiness and established immunization infrastructure achieved significantly higher utilization (66% vs 46% in lower readiness settings). Fragile and conflict-affected contexts experienced the largest deployment gaps, ranging from 30–45%. Uptake was also influenced by outbreak dynamics, with significantly higher vaccination rates during peak transmission phases (67%) compared with early outbreak periods (49%). Determinant analysis highlighted governance capacity, cold-chain infrastructure, health workforce availability, surveillance integration, and public trust as critical drivers of vaccination performance.

Discussion / Conclusion: The findings reveal that nearly one-quarter of vaccine doses allocated during emergency responses are not translated into administered protection, exposing a critical operational gap in Africa's vaccination ecosystem. Closing this gap requires moving beyond supply-focused approaches toward integrated strategies that strengthen regulatory readiness, health-system capacity, and community trust. Embedding vaccination continuum metrics into preparedness planning and outbreak response frameworks can enhance the effectiveness of mpox vaccination campaigns and inform broader strategies for emerging infectious disease control. These insights provide actionable evidence to support more resilient and equitable vaccination systems across Africa.

POSTER 193

Operationalizing Mpox Vaccination in Africa: Progress, Challenges, and Policy Lessons from the First Year of a Coordinated Continental Response

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Introduction / Background: The 2024 resurgence of mpox driven by Clade Ib led to the declaration of both a Public Health Emergency of Continental Security and a Public Health Emergency of International Concern. Unlike previous mpox outbreaks, vaccines were mobilized rapidly, with deployment occurring within weeks of the emergency declaration. This marked the first coordinated continental vaccination response for mpox in Africa, supported by regional institutions, global partners, and national governments. While the accelerated availability of vaccines represented a major milestone, implementation across countries revealed important operational, policy, and health-system challenges. This study describes progress achieved during the first year of mpox vaccination in Africa and identifies key operational lessons for strengthening outbreak vaccination strategies.

Materials / Methods: We conducted a descriptive analysis of vaccine policy decisions, regulatory processes, allocation mechanisms, delivery data, pharmacovigilance reports, and monitoring dashboards between August 2024 and December 2025. Data sources included the Continental Incident Management Support Team (IMST), national program reports from 16 African countries, allocation records, and vaccine deployment tracking systems. Qualitative and quantitative data were synthesized to examine vaccine rollout timelines, regulatory authorization pathways, utilization patterns, and operational challenges encountered during implementation.

Results: By December 2025, more than 5 million mpox vaccine doses, including MVA-BN and LC16m8, had been shipped to 16 African countries. Fourteen countries initiated vaccination campaigns, prioritizing contacts of confirmed cases and other high-risk groups in identified hotspot areas. Regulatory harmonization through the African Vaccine Regulatory Forum (AVAREF) enabled accelerated emergency authorizations, while global prequalification mechanisms supported multilateral procurement. Gavi-supported operational financing facilitated early rollout; however, broader funding gaps affected the pace and scale of implementation in some settings. Vaccine utilization varied widely across countries (0–100%), reflecting differences in epidemiological context, concurrent outbreaks, surveillance capacity, and stigma affecting case detection and demand generation. Importantly, pharmacovigilance monitoring identified no serious vaccine-attributable safety signals during the reporting period.

Discussion / Conclusion: Africa's mpox vaccination response demonstrates significant progress in regional coordination, regulatory collaboration, and rapid vaccine access compared with previous public health emergencies. However, disparities in operational readiness, financing, and surveillance capacity highlight the need for sustained investments in preparedness. Strengthening regulatory agility, ensuring timely operational financing, enhancing surveillance systems, and supporting context-specific effectiveness research will be essential for optimizing outbreak vaccination strategies and improving preparedness for future emerging infectious disease threats.

POSTER 194

Blood-stage controlled human malaria infection (CHMI) in healthy Tanzanian adults to assess the efficacy of the malaria vaccine candidates R78C and/or RH5.1 in Matrix-M® adjuvant.

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Background: An effective vaccine against the blood-stage of *Plasmodium falciparum* (Pf) may improve protection against clinical malaria and reduce severe disease. The Pf PTRAMP-CSS-RH5-CyRPA-RIPR (PCRCR) pentameric invasion complex is the leading target for blood-stage malaria vaccines. RH5.1 – a soluble protein targeting reticulocyte-binding protein homologue 5 – and R78C – a protein comprising RIPR EGF-like domains 7-8 fused to CyRPA – are leading PCRCR-based vaccine candidates in clinical testing. RH5.1 provides partial efficacy against clinical malaria in African children when administered with Matrix-M® adjuvant; however, the efficacy of R78C, alone and combined with RH5.1, has not previously been established.

Methods: This Phase I/II open-label age de-escalation trial was conducted in Bagamoyo, Tanzania, to evaluate the safety, immunogenicity, and efficacy of RH5.1 and R78C with Matrix-M® in Tanzanian adults and children (PACTR202407803870883). Adult participants received three doses of 10µg R78C/50µg Matrix-M® (Group 1A), 10µg R78C/10µg RH5.1/50µg Matrix-M® (Group 1B) or 10µg RH5.1/50µg Matrix-M® (Group 1C) in a delayed-third-dose regimen (0-1-6 months). Two weeks after the third vaccination, twelve (12) adult vaccinees meeting eligibility criteria and an equal number of infectivity controls underwent blood-stage controlled human malaria infection (CHMI) with the Pf strain, Pf3D7. Parasitaemia was measured daily or twice daily by quantitative polymerase chain reaction (qPCR).

Results: We enrolled 24 healthy Tanzanian adult participants in the blood-stage CHMI: 12 vaccinees and 12 infectivity controls. The blood-stage CHMI was well tolerated among participants. Parasitaemia was detectable among 6 vaccinees and 9 controls with higher maximum parasitaemia seen in controls. The time to detectable parasitaemia was shorter in control participants compared to vaccinees.

Conclusion: In a blood-stage malaria challenge in adult participants from a malaria-endemic area, prior vaccination with R78C and/or RH5.1 with Matrix-M® resulted in fewer cases of detectable parasitaemia, increased the time to detectable parasitaemia, and reduced maximum parasitaemia values.

POSTER 195

Comprehensive Insights into RSV Seroprevalence, Epidemiological Characteristics, Molecular Diversity, and The Development of Human Vaccine Production Platforms in Egypt, 2020-2025Mohamed MANDOUR¹, Nourhan ASHOUR²¹ Department of Virology and Immunology, Suez Canal University, Ismailia, Egypt² Department of Botany and Microbiology, Faculty of Science, Suez Canal University, Ismailia, Egypt

Introduction/Background: Respiratory syncytial virus (RSV) is the primary cause of lower respiratory infection (LRTI) in children. Despite its significant burden, there remains limited comprehensive data regarding RSV prevalence and the genotypes circulating in Egypt, particularly Suez Canal Area. This knowledge gap underscores the critical need for detailed local studies to inform public health strategies and vaccine development. This study aimed to comprehensively assess RSV seroprevalence, epidemiological patterns, and the genetic variability, including its association with demographic and clinical factors, of its G gene and predominant genotypes in children across the Suez Canal Area (Ismailia, Suez, Port Said) from 2020 to 2025. Furthermore, outlines a path toward meeting critical private and public health needs through advanced local vaccine development.

Material/Methods: A total of 632 nasopharyngeal aspirates and serum samples were collected from children that showed respiratory manifestations suspected of being RSV. The samples were screened by real-time (rt)-PCR, conventional RT-PCR was used to analyze the positive samples to amplify and sequence the hRSVA and hRSVB G regions for phylogenetic analysis. Furthermore, a serological investigation was conducted on the serum samples, employing ELISA kits according to manufacturer protocol, to detect the presence of anti-HRSV IgG and IgM antibodies. These diagnostic findings are translated into a production framework utilizing recombinant technology and tissue culture-based platforms to develop stabilized pre-fusion F (preF) protein antigens and mRNA-based vaccines.

Results: Of the 632 children in the study (391 male, 241 female), 188 (29.74%) were found to be RSV positive by real-time PCR. Of these positive samples, only 153 (24.2%) produced amplicons by conventional PCR. RSVA was detected in 122 (79.73%), while RSVB was identified in 31 (20.27%) samples, with 71 strongly positive bands (63 hRSVA and 8 hRSVB) and 82 weakly positive (59 hRSVA and 23 hRSVB). Serological investigation revealed 11.17% and 65.42% seroprevalence for HRSV IgM and IgG, respectively. Of the 188 RSV-positive patients, 87 (46.28%) were less than 5 years old. Cough was the most common clinical sign (159/188, 84.57%), followed by rhinorrhea (133/188, 70.74%) and nasal congestion (109/188, 57.98%). RSV levels were observed to be at their peak during winter, specifically from December to March. On a phylogenetic tree, the majority of the characterized hRSVA strains (5/6;83.33%) were grouped with the ON1 genotype, while one strain (1/6;16.66%) was clustered within strains related to the N1 genotype. Sequence analysis revealed a nucleotide insertion in the strains that altered amino acid alignment, and the hRSVB strains were genetically similar to those found in Argentina, suggests specific evolutionary patterns or shared lineages. Preliminary vaccine development trial designs focus on evaluating safety and immune response in high-risk populations, specifically infants and the elderly, aiming to reduce supply chain lead times by 40% compared to imported biologicals.

Discussion/Conclusion: Further studies are required to gain a deeper understanding of RSV's molecular epidemiology, global evolutionary patterns, and the mechanisms facilitating its host adaptation. Additionally, the development of a localized RSV vaccine in Egypt represents a major step toward regional vaccine security and health equity.

POSTER 196

Towards a tetravalent mRNA-LNP vaccine candidate against dengue fever: formulation, characterization, and in vivo testing

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Introduction/Background: Dengue fever is an arthropod-borne viral disease transmitted by the dengue virus (DENV), which has four distinct serotypes (DENV1 to DENV4). It threatens nearly half of the world's population, primarily in tropical and subtropical regions¹. A tetravalent vaccine administrable to all patients regardless of age and serostatus is still crucially needed to combat the disease. mRNA-Lipid nanoparticle (mRNA-LNP) vaccine formulations, which are biocompatible and can deliver multiple RNA cargos², were investigated for this purpose.

Materials/Methods: This two-step study focuses on the formulation and characterization of a tetravalent mRNA-LNP vaccine candidate against dengue fever. Initially, a step-by-step approach, referring to the controlled addition of one DENV mRNA serotype at a time, led to a tetravalent DENV1-2-3-4 CL2 formulation (CL2m1-2-3-4). All formulations were manufactured by the ethanol injection method (EIM). Their physicochemical properties (size, polydispersity index (PDI), Zeta Potential, morphology, pH, osmolarity, and mRNA encapsulation efficiency) and biological properties (transfection efficacy) were assessed. As mRNA-LNP formulations suffer from poor shelf-life stability, all performed assays compared freeze-dried (FD) formulations to their counterparts stored as solutions, to investigate the impact of the process on their properties. In the second step, the liquid tetravalent CL2m1-2-3-4 formulation was further optimized by adjusting the initial mRNA concentration and switching to microfluidics manufacture followed by sterile filtration. Physicochemical and biological characterization (including cytotoxicity studies) was performed. Preliminary vaccine immunogenicity (humoral and cellular responses) was recently assessed in BALB/c mice.

Results: In the first step, freeze-dried formulations exhibited, in general, larger sizes and osmolarities, and lower mRNA encapsulation efficiency and transfection efficacy. In the second step, the physicochemical and biological attributes of the improved tetravalent CL2m1-2-3-4 met the targeted values. Data analysis of the humoral and cellular immunogenicity responses in mice is currently underway, and the resulting findings will be presented at the congress.

Discussion/Conclusion: In the first step, the observed increase in size post-freeze-drying is possibly due to the rearrangement of the particles and aggregation during the process. Despite following the expected linear increase, encapsulated DENV mRNA concentrations exhibit significant variability between replicates, with some values exceeding the targeted values. Possible explanations include poor reproducibility of the EIM and potential mRNA degradation by hydrolases. The latter might have caused mRNA fragments to be detected as intact mRNA strands by the Ribogreen® reagent, leading to an overestimation of the encapsulated values. An orthogonal mRNA quantitation method is being considered. The poor overall transfection efficacy is possibly due to encapsulated DENV mRNA concentrations being too low to induce transfection. Thus, only the liquid CL2m1-2-3-4 formulation was considered for step 2. Here, the observed decrease in size and PDI can be attributed to the controlled microfluidics manufacturing process and the sterile filtration step, retaining larger particles. Variability in encapsulated DENV mRNA concentrations between replicates decreased. Transfection efficacy results improved, possibly due to the increase in mRNA content. The upcoming immunogenicity data will be critical to guide future optimization strategies and define the next steps.

1. Witte, P., Dtsch Arztebl Int 121 (2024).

2. Hou, X., Nat Rev Mater 6 (2021).

POSTER 197

Consensus Native-Like Hepatitis C Virus E1E2 Engages Broadly Neutralizing Antibody Precursors

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Background: Hepatitis C virus (HCV) is a bloodborne virus that causes a slowly progressing chronic liver infection that can cause cirrhosis or liver cancer. Despite available effective antiviral therapy, HCV infection afflicts approximately 50 million people and causes around 1 million yearly new infections, which resulted in 242,000 HCV-related deaths in 2022. Therefore, an effective vaccine will likely be necessary to eliminate HCV.

The E1E2 glycoprotein on the surface of the virus is the only target for broadly neutralizing antibodies (bNABs), which recognize conserved epitopes on this unique viral fusion protein. To induce bNABs with a vaccine, it is necessary to first engage their cognate germline B cell precursors. However, most HCV immunogens are unable to activate these precursor B cells, exemplified by their inability to bind the inferred germline bNABs (igl-bNABs). Germline-targeting vaccine strategies are aimed at specifically targeting these elusive B cell precursors using tailored germline-targeting immunogens.

Methods: Here, we developed and characterized recombinant native-like soluble E1E2 (sE1E2) immunogens based on a consensus sequence of HCV (HepCon) using biochemical, structural and immunogenicity studies and identified it as a lead germline-targeting HCV vaccine candidate. We produced the constructs in HEK293F cells followed by StreptactinXT affinity purification and size exclusion chromatography. We characterized the antigenicity, glycan composition, thermostability and B cell activation of these constructs, using (gl-)bNABs targeting multiple epitopes. Additionally, we assessed the immunogenicity in rabbits and mice.

Results: The HepCon sE1E2 antigens bind to HCV bNABs and gl-bNABs targeting multiple epitopes, showcasing native-like antigenicity and glycosylation. In rabbits, single HepCon sE1E2 immunogens invoked a similar neutralizing response as a tetravalent cocktail of sE1E2s covering three genotypes. In mice, mRNA-encoded membrane-bound HepCon sE1E2 induced a potent serum-binding response. When multivalently displayed on nanoparticles, HepCon sE1E2 induced activation of B cell lines expressing different igl-bNABs as B cell receptors in vitro. Finally, we obtained the first cryo-EM structures of the 1416-01-E03 bNAB, previously isolated from an elite neutralizing HCV infected individual, and, crucially, its inferred germline progenitor in complex with HepCon sE1E2.

Conclusion: HepCon sE1E2 antigens are promising HCV vaccine candidates, especially for germline-targeting vaccination strategies.

POSTER 204

mRNA Vaccine Against Hepatitis C Virus Tailored for Liver Tissue-Resident Memory T Cells

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Adelaide University, Australia

Background: Despite the availability of effective direct-acting antivirals, hepatitis C virus (HCV) remains a major global health burden due to ongoing transmission and the absence of a prophylactic vaccine. Previous vaccine strategies have largely failed to prevent chronic infection, despite eliciting robust circulating T cell responses, suggesting that systemic immunity alone is insufficient. Increasing evidence indicates that liver tissue-resident memory T cells (TRM) play a critical role in early viral control due to their rapid effector function enabled by their strategic localisation at the primary site of infection. This study investigates whether mRNA vaccines can effectively induce liver CD8⁺ TRM and confer protective immunity against HCV.

Materials and Methods: Female BALB/c mice (6-8 weeks) were vaccinated with 5 µg lipid nanoparticle (LNP)-encapsulated pseudouridine-modified mRNA encoding HCV nonstructural protein 5B (NS5B). NS5B mRNA encapsulated in SM-102-based LNPs delivered intramuscularly (i.m.), and DLin-MC3-DMA-based LNPs delivered intravenously (i.v.), were compared across different prime-boost regimens. NS5B-specific memory CD8⁺ T cell responses in the liver and spleen were quantified using multiparametric flow cytometry and functional assays including IFN-γ ELISpot. Liver TRM were phenotypically defined as CD69⁺CD62L⁻ CD8⁺ T cells and further characterised by expression of residency-associated markers (CXCR3, CXCR6, KLRG1, PD-1, CD11a). Longitudinal analyses were performed up to 180 days post-vaccination to assess durability and half-life of these TRM. Assessment of their protective potential using a surrogate HCV challenge model is underway.

Results: mRNA vaccination induced robust NS5B-specific CD8⁺ T cell responses with establishment of bona-fide liver TRM. Notably, SM-102 LNP formulations delivered i.m. elicited significantly higher frequencies and absolute numbers of liver TRM compared to MC3-based formulations delivered i.v., suggesting that LNP composition and delivery route critically influences tissue-specific immunity. Prime-boost strategies enhanced both magnitude and durability of TRM responses.

Conclusion: This work demonstrates that mRNA-LNP vaccines can effectively generate durable, functional liver TRM when delivered i.m., which may be capable of mediating protective immunity against HCV. These findings provide a strong rationale for the design of next-generation mRNA vaccines that prioritise tissue-targeted immune responses. Induction of liver TRM represents a promising strategy to overcome historical barriers in HCV vaccine development and may have broader implications for vaccines against other viral infections.

POSTER 205

Molecular Characterization, Phylogenetic Analysis, and Local Vaccine Production Trials of *Neisseria meningitidis* Isolates in Ismailia Province, Egypt 2020-2024

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Introduction/Background: *Neisseria meningitidis* is a Gram-negative diplococcus that colonizes the nasopharynx and can cause severe invasive meningococcal disease (IMD). Despite its impact, the molecular characterization and epidemiological status of *N. meningitidis* in Egypt remain poorly understood, creating a gap in the development of targeted local immunization strategies.

Material/Methods: This study aimed to investigate the molecular epidemiology and phylogenetic relationships of *N. meningitidis* isolates recovered from patients with IMD at University hospital, General hospital, and Suez Canal Authority hospital in Ismailia Province, Egypt, between 2020 and 2024. A total of 64 clinical specimens (blood and CSF) were screened by real-time RT-PCR and confirmed by standard microbiological and molecular techniques. Antimicrobial susceptibility testing was performed alongside multilocus sequence typing (MLST) and whole-genome sequencing (WGS). Furthermore, the study explored the feasibility of using these local isolates in preliminary vaccine production trials, evaluating growth parameters using high-performance specialized media to optimize antigen yield for potential indigenous vaccine formulation.

Results: The study revealed a varied population of *N. meningitidis* isolates, with a predominance of serogroups B and C. Nineteen (29.68%) samples were positive by real-time RT-PCR, while 14 (21.87%) were confirmed by conventional PCR. MLST analysis identified multiple clonal complexes, including ST-11, ST-32, and ST-41/44, which are globally linked with outbreaks. Sequenced strains exhibited a nucleotide insertion altering amino acid alignment, while WGS analysis revealed particular virulence factors and genes that resist antibiotics, offering a high-resolution view of genetic diversity. Initial production trials demonstrated that local serogroup B and C isolates achieved stable growth and high capsular polysaccharide expression when cultivated in optimized maintenance and growth media, marking a critical step toward a locally tailored vaccine.

Discussion/Conclusion: The findings highlight the changing dynamics of meningitis in Egypt and the importance of continuous genomic surveillance. The successful preliminary trials for antigen production suggest that utilizing local strains and advanced media platforms can support Egypt's transition toward national vaccine self-sufficiency. Implementing these effective control measures is vital to preventing future outbreaks of meningococcal disease in the region.

POSTER 206

Mapping strategies and interventions to reach zero-dose and under-immunized children: A scoping review

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Background: Zero-dose (ZD) children, those who have not received a single dose of diphtheria-tetanus-pertussis vaccine, bear a disproportionate burden of vaccine-preventable disease. Despite global immunisation gains, an estimated 14.3 million children remained ZD in 2024, underscoring persistent inequities in vaccine access and delivery. We conducted a scoping review to map global evidence on interventions targeting ZD and under-immunised children under five years, with the aim of informing equity-driven policy and programme design.

Methods: We searched PubMed, Scopus, Web of Science, and EBSCOhost for peer-reviewed studies published between 2015 and 2025. Eligible studies reported interventions to reach ZD or under-immunised children under five years. Two independent reviewers extracted data using standardised forms. Interventions were analysed thematically and stratified by World Bank income classification.

Results: Of 37 included studies, the majority originated from lower-middle-income countries (64%), with 25% from low-income, 5% from upper-middle-income, and 6% from high-income countries. Eight thematic intervention areas were identified: community engagement; community and health workforce mobilisation; health systems strengthening; outreach and service delivery; technology-driven approaches; monetary incentives; integrated human-animal vaccination campaigns; and leveraging military or security forces. Mobile outreach was the most frequently reported strategy (21%), followed by engagement of religious and community leaders (18%) and community health worker involvement (12%). Intervention profiles varied by income setting, with low-income countries emphasising community-based and outreach approaches, while higher-income settings favoured technology and incentive-driven strategies. Nine studies specifically reported outcomes for true ZD children, demonstrating meaningful improvements in first-dose vaccine uptake following intervention.

Conclusions: Multi-faceted, context-adapted interventions hold significant promise for reaching the most immunisation-deprived children. Definitional inconsistency between ZD and under-immunised populations remains a critical gap, limiting cross-study comparability and programme targeting. Standardised definitions and equity-centred measurement frameworks are urgently needed. The evidence synthesised here offers actionable, income-stratified guidance for policymakers and programme planners working towards global immunisation equity.

POSTER 207

AI-Driven Design and Evaluation of a Multi-Epitope mRNA Vaccine Against Orthommarburgvirus marburgense for Emerging Filovirus Infections

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Introduction: Marburg virus disease (MVD), caused by Orthommarburgvirus marburgense, remains a high-priority emerging infectious threat with case-fatality rates reaching up to 90% and recurrent outbreaks in Africa. The absence of any licensed vaccine highlights the urgent need for safe, effective, and broad-spectrum vaccine candidates capable of eliciting robust humoral and cellular immunity.

Methodology: An AI-driven reverse-vaccinology pipeline was employed to design two multi-epitope mRNA vaccines targeting seven conserved viral proteins (VP24, VP35, VP40, VP30, envelope glycoprotein, nucleoprotein, and L RNA-dependent RNA polymerase) representative of both active and latent infection phases. Protein sequences were retrieved from NCBI. Cytotoxic T-lymphocyte (CTL) epitopes, helper T-lymphocyte (HTL) epitopes and conformational B-cell epitopes were predicted. Consensus epitopes were rigorously screened for high antigenicity, non-allergenicity, non-toxicity and conservation across strains, resulting in the selection of CTL, HTL, and B-cell epitopes. Two mRNA vaccine constructs were designed incorporating these epitopes with different immune enhancers: HBD3 (Construct 1) and PADRE (Construct 2).

Results: Both vaccine constructs exhibited favorable physicochemical properties, including molecular weights of 135–142 kDa, theoretical pI values of 9.03–9.29, instability indices below 40, negative GRAVY scores, and high predicted solubility. Secondary structure analysis revealed stable conformations dominated by α -helices (39–41%) and random coils (46–49%). Molecular docking studies demonstrated strong binding affinity of both constructs to TLR7 (docking scores ranging from –280.76 to –295.60 with confidence scores >0.93), indicating potent innate immune activation potential.

Conclusion: This study presents the first comprehensive AI-driven multi-epitope mRNA vaccine platform against Orthommarburgvirus marburgense, offering broad HLA coverage, balanced humoral and cellular immunity, and structural stability. The designed constructs (HBD3 and PADRE) show strong promise and warrant further in vitro and in vivo validation for rapid deployment against future Marburg virus disease outbreaks.

POSTER 208

Vaccine Wastage trends and reported reasons in Uganda. Analysis of Tracer Antigens

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Background: Vaccine wastage undermines the efficiency and sustainability of immunisation programmes by increasing costs, straining supply, and potentially reducing coverage. To guide performance, the World Health Organization (WHO) and Uganda established antigen-specific wastage thresholds. WHO targets are $\leq 50\%$ for BCG, $\leq 25\%$ for MR, $\leq 10\%$ for OPV, and $\leq 15\%$ for DPT, while Uganda's in-country thresholds are $\leq 70\%$, $\leq 40\%$, $\leq 15\%$, and $\leq 10\%$, respectively. However, evidence comparing observed wastage with these benchmarks over time remains limited. We described national and subnational trends for four tracer antigens to inform supply chain optimisation and forecasting.

Methods: We conducted a retrospective descriptive analysis of routine immunisation data from Uganda's District Health Information Software version 2 (DHIS2) for all 146 districts from January 2020 to December 2025. Tracer antigens included Bacille Calmette-Guérin (BCG), measles-rubella (MR), oral polio vaccine (OPV), and diphtheria-tetanus-pertussis-containing vaccine (DPT). Wastage was defined as the proportion of issued doses not administered: $[(\text{doses issued} - \text{doses administered}) / \text{doses issued}] \times 100$. Annual wastage was summarised using medians (IQR), with trends assessed using the Mann-Kendall test. Observed wastage was compared with WHO and national thresholds. All available effective vaccine management (EVM) reports ($n=3$ reports; 50 service delivery points assessed) were reviewed to identify reported reasons for wastage.

Results: Between 2020 to 2025, national median wastage rates were 40.6% (IQR 39.9–44.6) for BCG, 25.9% (IQR 17.3–30.3) for MR, 10.0% (IQR 9.4–10.7) for OPV, and 9.2% (IQR 7.7–11.5) for DPT. OPV showed a significant declining trend ($\tau b = -1.00$; $p=0.008$), from 12.8% to 8.0%; while BCG, MR ($\tau b = 0.07$; $p=1.000$ for both), and DPT ($\tau b = -0.60$; $p=0.130$), showed inter-annual variability without significant trends. Wastage was highest at lower-level facilities, with median wastages for all antigens exceeding both thresholds throughout the six-year study period. Subnational analysis revealed marked regional and district-level heterogeneity in wastage rates across all antigens. Commonly reported reasons included low session attendance (66%, 33/50), non-compliance with the multi-dose vial policy (28%, 14/50), and vaccine expiry (12%, 6/50).

Conclusions: Uganda achieved reductions in vaccine wastage for OPV generally within national targets. In contrast, BCG and MR continued to experience higher wastage, frequently exceeding both national and WHO thresholds. Strengthening adherence to the multi-dose vial policy and improving session planning at lower-level facilities could reduce preventable vaccine wastage.

POSTER 209

Establishing a blood-stage Controlled Human Malaria Infection model in healthy Tanzanian adults with varying prior exposure to *P. falciparum*

Omar HASSAN, Florence MILANDO, Latipha MOHAMED, Nassoro LILOLIMWE, Neema BALIGE, Ally OLOTU

See oral presentation:

Concurrent Session 6: "Bright Sparks" in Vaccinology – ECR Session • Tuesday 13 October, 12:00

POSTER 212

Enhancing Influenza Vaccine Responses with Synthetic TRAC478 and Saponin Based Adjuvants using Computationally Optimized H1/H3 HA antigens.

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Introduction/Background: Current seasonal influenza vaccines often elicit suboptimal immune responses due to the rapid evolutionary changes and antigenic diversity of circulating influenza viruses. Reliance on wild-type, strain-specific antigens and egg-based manufacturing practices, which can introduce egg-adaptive mutations, further limits protection against antigenically drifted viruses. Protein subunit vaccines offer a potential solution, as they can be rapidly updated in response to emerging viral threats, produced in mammalian expression systems to reduce mutation risk, shorten manufacturing timelines, and focus immune responses on immunologically relevant viral proteins. However, subunit vaccines are often poorly immunogenic when administered without adjuvants.

Materials/Methods: To address these challenges, we developed computationally optimized broadly reactive antigens (COBRAs) for influenza hemagglutinin (HA) that incorporate immunogenic epitopes from multiple recently circulating H1 and H3 strains. These COBRA antigens were expressed as recombinant HA (rHA) subunit vaccines and formulated with either a synthetic Toll-like receptor (TLR) 4 and TLR7/8 agonist emulsion (TRAC478) or a synthetic saponin adjuvant system (SAS) containing TLR4 agonists. Vaccine immunogenicity was evaluated in influenza-naïve mice and pre-immune ferrets to model both primary and recall immune responses.

Results: In these animal models, adjuvanted COBRA rHA vaccines induced higher H1- and H3-specific IgG levels, elicited protective hemagglutination inhibition (HAI) titers against a broader panel of influenza isolates, and increased the frequency of antigen-specific antibody-secreting cells compared with unadjuvanted rHA vaccines. The inclusion of TLR agonists within the TRAC478 and SAS formulations also altered antibody subclass distribution, resulting in a more balanced Th1/Th2 immune response relative to traditional oil-in-water and saponin-based adjuvants. Additionally, these formulations increased the frequency of interferon- γ (IFN- γ)-producing cells compared with unadjuvanted rHA vaccines. While the SAS formulation induced higher overall IFN- γ responses, COBRA HA antigens formulated with either adjuvant contained conserved IFN- γ -stimulating epitopes within the HA head and stem domains. These epitopes supported broader activation of CD4⁺ and CD8⁺ T cells and enhanced immune recognition of antigenically drifted influenza viruses.

Discussion/Conclusion: The induction of IFN- γ -associated cellular immunity alongside robust antibody responses may improve cross-strain protection and the durability of vaccine-induced immunity, particularly in populations with prior influenza exposure or during seasons marked by substantial antigenic mismatch. Together, these findings demonstrate that combining broadly reactive influenza antigens with modern synthetic adjuvant systems significantly enhances the magnitude and breadth of vaccine-induced immunity, representing a promising and translational strategy to improve seasonal influenza vaccines in the context of ongoing viral evolution.

POSTER 215

General and vaccine-specific health literacy for Pneumococcal and Influenza vaccine among older adults in North India

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Health literacy influences how individuals obtain, interpret, and use health information to make decisions about their care. Among older adults, inadequate health literacy has been linked to lower use of preventive services, including vaccination. In India, despite a substantial burden of pneumococcal disease and influenza and persistently low adult vaccination coverage, evidence on both general and vaccine-related health literacy remains sparse and fragmented. This study aims to estimate the prevalence of general health literacy and vaccine-related health literacy for pneumococcal and influenza vaccines among older adults in North India. A total of 910 participants aged ≥ 60 years were recruited from Chandigarh using stratified random sampling with quota-based allocation across socio-economic strata. Data were collected through face-to-face interviews. General health literacy was assessed using the HLS-EU-Q16 instrument. Vaccine-related health literacy was operationalized using contextually adapted HLS-EU-Q16 items, supplemented with questions assessing vaccine-related knowledge. Preliminary findings indicate that a considerable proportion of participants demonstrated limited general health literacy. Vaccine-related health literacy appeared comparatively lower, particularly for pneumococcal vaccination, with notable gaps in awareness, understanding of eligibility, and perceived benefits. Socio-economic differences were observed, with lower literacy levels among individuals with lower educational attainment and income. Influenza-related literacy was relatively higher than pneumococcal literacy, although overall levels remained suboptimal. These findings suggest that limited health literacy may represent an important barrier to adult vaccination in this population. Addressing gaps in both general and vaccine-related health literacy through targeted, context-specific communication strategies may support improved uptake of pneumococcal and influenza vaccines among older adults.

POSTER 216

Factors Influencing Hepatitis B Vaccine Uptake Among Senior Secondary School Students in Abuja Municipal Area Council, Federal Capital Territory, Nigeria

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Background: Hepatitis B remains a significant public health challenge in Nigeria, with adolescent vaccination rates remaining low despite its preventable nature. This study examined the determinants of hepatitis B vaccine uptake among senior secondary school students in Abuja Municipal Area Council (AMAC), Federal Capital Territory, Nigeria.

Objectives: The study aimed to determine hepatitis B vaccination status, assess risk perception, evaluate vaccine knowledge, and identify socio-demographic factors, barriers, and facilitators influencing uptake.

Methods: A cross-sectional survey was conducted among 198 senior secondary school students in AMAC. Data were collected on vaccination status, knowledge, risk perception, and socio-demographic factors, and analyzed using chi-square tests and logistic regression.

Results: Only 12.6% of students reported receiving the hepatitis B vaccine. Nearly half (46.0%) demonstrated good knowledge of the vaccine ($\geq 70\%$), while risk perception was fairly evenly distributed across low (29.3%), moderate (28.8%), and high (28.8%) categories. Chi-square analyses revealed significant associations between uptake and gender, vaccine awareness, and knowing someone with hepatitis B. Multivariate logistic regression confirmed that vaccine awareness (AOR = 3.85, $p = 0.011$), knowing a family member (AOR = 5.60, $p = 0.007$), or a friend (AOR = 4.85, $p = 0.027$) with hepatitis B substantially increased the likelihood of vaccination. The most commonly reported barriers were lack of parental permission (23.0%) and fear of side effects (21.0%), while key facilitators included parental support (26.1%) and availability of free school-based vaccinations (24.1%).

Conclusion: Low hepatitis B vaccine uptake among adolescents in AMAC underscores the need for targeted interventions, including school-based vaccination programs, parental education campaigns emphasizing vaccine safety, and community advocacy to address barriers and leverage facilitators to enhance uptake.

POSTER 218

HPV VACCINE AWARENESS, ATTITUDES, AND UPTAKE AMONG WOMEN IN ABUJA, NIGERIA: A CROSS-SECTIONAL SURVEY

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Introduction: Human Papillomavirus (HPV) is a primary cause of cervical cancer, a leading cancer-related cause of death among women in sub-Saharan Africa. Despite the proven efficacy of HPV vaccines, uptake in Nigeria remains critically low. This study investigated HPV vaccine awareness, knowledge, attitudes, uptake, and barriers among women in Abuja, Nigeria.

Methods: A cross-sectional survey was conducted among 72 women aged 19–38 years across multiple area councils in Abuja, Federal Capital Territory, Nigeria (March 12–27, 2026). A structured questionnaire assessed sociodemographic characteristics, HPV and vaccine awareness, knowledge, perceived risk, vaccination status, barriers to uptake, trust in information sources, and willingness to vaccinate.

Results: Most respondents were single (73%), educated to undergraduate or postgraduate level, and employed. Awareness of HPV and the HPV vaccine was high (84% and 80%, respectively). Healthcare providers and social media were the most cited information sources. The majority correctly identified cervical cancer as the vaccine's target condition and expressed positive attitudes toward vaccine safety and efficacy. Despite this, only approximately 17% had received the HPV vaccine (fully or partially). Among unvaccinated women, the leading barriers were not knowing where to access the vaccine (~40%), cost, and general lack of awareness. Most participants perceived themselves at low personal risk of HPV infection. Trust in government health agencies and family/friends was moderate to high. Remarkably, 94% expressed willingness to receive the vaccine if free and available, and 93% would recommend it to others. Healthcare provider recommendation was a key motivating factor. Among mothers with daughters aged 9–14 years, willingness to vaccinate was generally high.

Conclusions: A pronounced gap exists between favourable HPV vaccine attitudes and actual uptake among women in Abuja. Key drivers include inaccessibility, cost, and insufficient guidance on where to obtain the vaccine. Scaled-up free vaccination programmes, community-level vaccine availability, and targeted awareness campaigns are urgently needed to improve HPV vaccine uptake in this population.

POSTER 220

Mapping zoonotic Bat Coronaviruses with spill over risk to humans

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Introduction/Background: The past two decades have witnessed three coronavirus outbreaks originating from bats, namely, SARS-CoV, MERS-CoV, and SARS-CoV-2. Coronaviruses (CoVs) have existed since the 1960s causing mild infections, but slowly evolved to cause deadly diseases with SARS-CoV-2 alone killing > 7 million people. It is of interest to note that all three viruses causing these outbreaks emerged from bats. With over 700 bat CoV Spike proteins already identified, the next outbreak might be imminent within the next ten years. This makes studying bat CoVs capable of infecting humans vital to tackling the next outbreak. However, screening and identifying bat CoVs of concern remain a major bottleneck. This study aims to screen, express, and test bat CoVs of concern with spill-over potential to humans. This can help prepare for and avoid a future coronavirus pandemic.

Material/Methods: Over 1000 Bat CoVs were identified from NCBI repository. The bat CoVs were bioinformatically screened and the selected bat CoVs were cloned, expressed and purified from HEK cells. The expressed candidates are further biophysically characterized for binding to human receptors using isothermal titration calorimetry (ITC) and surface plasmon resonance (SPR).

Results: In our bioinformatic analysis, we identified 1087 distinct bat spike proteins. Screening revealed that about 100 of them contained distinct sequences with a high probability of a spill-over event to humans. The selected bat CoVs have been cloned into the pcDNA vector and plasmids amplified for transfection in HEK cells. As of now, 45 of the 50 clones have been successfully expressed. Using SARS-CoV RBD, the expression and binding studies have been optimized. SARS-CoV receptor binding domain (RBD) showed a yield of 2 mg per 30 mL of suspension culture. The interaction studies with human ACE2 showed binding affinity with a K_d of 65 ± 4 nM. The evaluation of the binding capacity of selected bat CoVs to human receptors is ongoing. This study can help identify the next bat CoVs of concern.

Discussion/Conclusion: This study aims to screen the bat CoVs of concern with spill-over potential. Identifying bat coronavirus strains with the potential to bind human receptors can help with early intervention and provide information for designing emergency antivirals. It can enable us to focus our efforts on interrupting the chain of transmission of screened bat CoVs. Further, it can help prevent any future pandemics caused by coronaviruses with focused early surveillance strategies.

Keywords: Bat-CoV, RBD-ACE2 interaction, Pandemic preparedness, One Health

Abbreviations: SARS: Severe acute respiratory syndrome, CoV: Coronavirus, MERS: Middle East Respiratory Syndrome, RBD: Receptor binding domain, ACE2- Angiotensin-Converting Enzyme 2 (ACE2) Receptor

POSTER 221

Full genomic characterisation of rotavirus G3P[8] strains that have become dominant in Kenya following vaccine introduction

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Background: Kenya introduced the monovalent Rotarix® (G1P[8]) rotavirus vaccine into her national immunization program in 2014 and has recently switched to the Rotavac® (G9P[11]) vaccine. There was unusual increase in detection of G3P[8] strains, coinciding temporally with the timing of Rotarix® vaccine introduction. In view of this, we sequenced and characterized the full genomes of representative post-vaccine G3P[8] strains to assess for any antigenic epitope changes that could potentially diminish the vaccine effectiveness.

Methodology: Rotavirus RNA was extracted from the G3P[8]-positive stool specimen and analyzed by polyacrylamide gel electrophoresis. Whole genome sequencing was later performed using Illumina MiSeq platform. Analyses of sequenced data was carried out using CLC Genomic Workbench v8.0.1 (CLC Bio). The 11-gene segments were aligned using ClustalW and maximum-likelihood phylogenetic trees were constructed using MEGA12. Amino acid comparisons of the VP7 and the VP4 antigenic epitopes were performed using GENETYX v11.

Results: The Kenyan post-vaccine G3P[8] strains exhibited a conserved Wa-like genome constellation with a very high intra-strain nucleotide and amino acid sequence homology. There were distinct amino acid substitutions within neutralizing epitopes of the VP7 and VP4 proteins of the Kenyan G3P[8], which could have impacted antigenicity and immune recognition of these strains.

Discussion/Conclusion: The substantial number of amino acid differences in the antigenic epitopes of VP7 and VP4 proteins between the Kenyan G3P[8] strains and those of the vaccine strains could result in reduced antibody binding and thus reduced neutralization of these Kenyan G3P[8] strains. Since the G3P[8] strains that have become dominant in Kenya are fully heterotypic as to the current rotavirus vaccine strain regarding the genotype constellation, vaccine effectiveness against these G3P[8] strains needs to be closely monitored.

POSTER 223

Safety of a bivalent Ebola virus and Sudan virus ChAdOx1 vectored vaccine in Tanzanian adults: an open-label, non-randomised phase 1 clinical trial.

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See oral presentation:

Plenary Session 5: One Health and Pandemic Preparedness • Wednesday 14 October, 09:50

POSTER 224

An Intranasal Hemagglutinin Protein Booster After Intramuscular mRNA Vaccination Enhances Mucosal Immunity and Confers Protection Against Influenza Virus in Ferrets

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See oral presentation:

Concurrent Session 6: "Bright Sparks" in Vaccinology – ECR Session • Tuesday 13 October, 12:15

POSTER 225

IMMUNOGENICITY ASSESSMENT OF PREFUSION-STABILIZED ANDES VIRUS Gn/Gc VIRUS-LIKE PARTICLES IN BALB/C MICE

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Andes virus (ANDV), a member of the genus Orthohantavirus, is a high-priority public health threat in South America, causing Hantavirus Cardiopulmonary Syndrome (HCPS) with case fatality rates reaching 40%. Unlike other hantaviruses, for ANDV exists documented evidence for human-to-human transmission, which underscores an urgent need for the development of safe and effective immunogens, as there are currently no approved vaccines available. Using our established virus-like particle (VLP) platform, this study focuses on advanced rational vaccine design. By means high-resolution bioinformatics and AI-driven structural modeling, we engineered ANDV glycoprotein (Gn/Gc) mutants specifically designed to likely remain in their prefusion conformation. This strategy aims to stabilize and expose highly neutralizing epitopes that are typically transient and lost during the post-fusion transition. We hypothesize that these stabilized mutants, when paired with an optimized adjuvant system, will elicit significantly superior neutralizing antibody titers compared to wild-type (WT) VLPs.

An immunization study was conducted using a cohort of 36 female BALB/c mice which were administered either the selected mutants or WT VLPs, both formulated with a previously selected adjuvant to maximize immune response. The experimental design consisted in an inoculation scheme of subcutaneous doses at four-week intervals and serum collection at 21 days post-final boost. Microneutralization assays for each group will be analyzed to compare neutralizing antibodies elicited by each antigen.

This research is currently in progress. While the immunizations are ongoing, we expect to finalize a comprehensive immunogenicity profile comparing neutralizing antibody responses elicited by the different immunogens before the meeting will be held. We expect to demonstrate that prefusion-stabilized spike mutants provide a more robust and potent immune response than WT spikes.

The results of this study provide critical analysis of the integration of AI-guided, structure-based design in Hantavirus vaccinology, by establishing a new immunogenicity benchmark through precise prefusion stabilization. This study defines the structural and immunological framework necessary for selecting a final candidate for subsequent efficacy trials in lethal challenge models. This work represents a significant step toward a standardized, high-potency VLP vaccine for ANDV.

POSTER 226

Assessment of ex vivo antimalarial drug susceptibility and molecular signatures in Senegal.

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Background: Over the past decades, *Plasmodium falciparum* - the major cause of malaria - has continuously developed resistance to antimalarial drugs such as chloroquine, sulfadoxine-pyrimethamine or artemisinin derivatives. Therefore, active surveillance of ex vivo susceptibility to the antimalarial drugs used as partner drugs in artemisinin-based combination therapies (the current frontline antimalarials), such as amodiaquine, lumefantrine or piperazine, is essential.

Methods: Here we evaluated the ex vivo susceptibility, expressed using the ex vivo SYBR Green, to six antimalarial drugs (amodiaquine, chloroquine, lumefantrine, mefloquine, piperazine, and quinine) of 34 *P. falciparum* isolates collected in Thiès, Senegal, in 2018. Whole genome sequencing (WGS) was used to search for mutations in *P. falciparum* genes known to be associated with drug resistance.

Results: *P. falciparum* isolates showed reduced ex vivo susceptibility only to chloroquine (16% of isolates). The most common mutations were pfcr1 K76T (21%) and pfmdr1 Y184F (53%). A significant correlation was observed between the pfcr1 76T and pfmdr1 184F mutants and the IC50 values for chloroquine. A significant decrease in ex vivo susceptibility to chloroquine and quinine associated with pfcr1 R371I was also detected ($P < 0.001$).

Conclusion: Our results suggest that the ex vivo susceptibility of *P. falciparum* isolates to amodiaquine, lumefantrine, mefloquine, piperazine and quinine remains high in Thiès. Direct ex vivo measurement of parasite drug response and sequencing of resistance mutations over time are both useful tools for monitoring parasite drug response in field samples.

Keywords: Malaria, antimalarial drugs, ex vivo SYBR™ Green.

POSTER 227

Distinct Innate and Adaptive Immune Responses by mRNA vs Protein-Based Respiratory Syncytial Virus Vaccines

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Introduction: With the approval of three vaccines against respiratory syncytial virus (RSV) based on the stabilized prefusion (preF) glycoprotein it has become possible to assess how immune responses are shaped by the different vaccine platforms. The three vaccines are an mRNA-based vaccine (mRESVIA, Moderna), as well as two protein-based vaccines, including one unadjuvanted formulation (Abrysvo, Pfizer) and an AS01E-adjuvanted formulation (Arexvy, GSK). This provided the opportunity to directly compare approved mRNA and protein-based vaccines.

Material/Methods: To perform a detailed immunological assessment, rhesus macaques were immunized with a single dose of either of the three vaccines. The animals were subsequently followed up with longitudinal blood and bone marrow samplings. Different immunological readouts including humoral responses, innate and adaptive immune cell activation, cytokine levels and RNA transcriptomics were analysed.

Results: In animals with pre-existing RSV immunity, mimicking the clinical setting, all vaccines induced high preF-specific antibody and neutralizing titers within one week. In RSV-naïve animals, antibody responses were delayed, overall lower, and the unadjuvanted protein vaccine failed to induce durable titers. In pre-immune animals all vaccines induced detectable plasmablast and plasma cell responses in blood and bone marrow, respectively. CD4 T cell responses with detectable type I cytokine production were induced at day 8 post-vaccination while induction of CD8 responses was markedly lower. Additional analysis of early timepoints post-vaccination revealed that adjuvanted protein and mRNA vaccine elicited robust innate immune activation, characterized by an increase in circulating CD14⁺CD16⁺ intermediate monocytes and plasmacytoid dendritic cells for mRNA vaccine, as well as a coordinated increase of plasma cytokine levels, including IL-1RA and IL-6. Bulk RNA sequencing revealed transcriptional profiles in animals vaccinated with mRNA and adjuvanted protein vaccines that suggest a more inflammatory signature at early timepoints.

Discussion/Conclusion: In summary, all vaccines were immunogenic and significantly increased antibody levels, however in naïve animals the unadjuvanted protein vaccine failed to elicit durable antibody responses. mRNA and adjuvanted protein vaccine in addition were able to induce a more inflammatory innate response while the unadjuvanted protein vaccine did not elicit measurable innate immune activation. This observation, together with the robust innate immune activation elicited by mRNA and adjuvanted protein vaccines, suggests that specific vaccine formulations may be particularly well suited for certain risk groups.

POSTER 232

Development of a *Chlamydia trachomatis* mucosal vaccination and challenge model in *Cavia porcellus* (guinea pig).

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Chlamydia trachomatis (Ct) is the most prevalent bacterial sexually transmitted infection worldwide and a leading cause of reproductive morbidity, including pelvic inflammatory disease and infertility. Progress toward vaccine development has been limited in part by the need for robust and translationally relevant animal models that enable evaluation of protective immunity at mucosal sites. The guinea pig model of genital tract infection provides a valuable system for studying *Chlamydia* pathogenesis and vaccine-induced protection; however, optimization of infection, quantification, and challenge parameters remains critical for consistent and interpretable outcomes.

In this study, we established and optimized a guinea pig model of Ct serovar E infection for vaccine evaluation. We optimized generation and purification of Ct stocks and optimized infection protocols, including hormonal synchronization, infectious dose, and sex-dependent variables, to achieve reproducible genital tract infection following challenge. In parallel, we refined methods for bacterial quantification, including titration optimization using immunofluorescence (IF) staining, to enable accurate assessment of infectious burden.

Using this optimized model, we evaluated adjuvanted protein vaccination via the intramuscular and mucosal routes and assessed its ability to induce systemic and mucosal immune responses. Antigen-specific antibody responses were measured in both serum and mucosal compartments to determine the extent to which immunization strategies can elicit distal mucosal immunity. Following vaccination, animals were challenged intravaginally with Ct, and protection was evaluated by measuring bacterial titers over the course of infection.

This study aims to define serum and mucosal immune correlates of protection. We correlated serum and mucosal antibody responses with post-challenge bacterial burden to identify immunological correlates of protection. Our findings demonstrate that adjuvanted vaccination via different routes can induce measurable circulating and mucosal antibody responses and that these responses are associated with reduced bacterial load following challenge in the urogenital tract.

Collectively, this work establishes a robust guinea pig model for Ct vaccination and challenge studies and provides insight into the relationship between systemic and mucosal immunity in vaccine-induced protection. These findings support the use of this model for evaluating candidate vaccines and contribute to the broader understanding of immune correlates relevant for protection against mucosal pathogens.

POSTER 233

Beyond Viral Clearance: Treg and Type 2 Immunity as Determinants of Vaccine-Mediated Lung Protection During Influenza Breakthrough Infection

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Despite available vaccines, influenza virus infections of the upper and lower respiratory tract remain a major public health burden. Limited vaccine uptake and only moderate vaccine effectiveness leave significant room for optimization. Current seasonal vaccines are trivalent (TIV) or quadrivalent (QIV) inactivated virus formulations. Due to antigenic drift, circulating viruses can escape neutralizing antibodies, requiring yearly vaccine updates. In the absence of sterilizing immunity, breakthrough infections (BTIs) can occur, which can trigger strong inflammatory responses in the respiratory tract. While essential for antiviral defense, excessive inflammation can lead to host-driven immunopathology. In severe respiratory viral disease, dysregulated type I interferon signaling promotes a cytokine storm, recruits inflammatory myeloid cells, and amplifies tissue injury through IFN- γ - and TNF- α -secreting CD8⁺ and Th1 T cells. Ultimately, disease severity reflects immune-mediated damage more than direct viral cytopathology. Yet, current vaccine evaluation focuses almost exclusively on neutralizing antibodies and effector T-cell responses, overlooking the regulatory and reparative arms of protective immunity.

This project addresses this critical gap by redefining vaccine-mediated protection as a multidimensional process integrating antiviral activity, inflammatory regulation, and maintenance of pulmonary tissue integrity. We hypothesize that effective protection during BTI requires not only robust type 1 antiviral immunity but also a balanced regulatory milieu that limits tissue damage. Specifically, vaccine-induced regulatory T cells (Tregs) and type 2 immune populations, including eosinophils, ILC2s, and alternatively activated macrophages, are proposed to act in concert to restrain immunopathology while supporting viral clearance.

Although Th2-skewed responses with eosinophilia were historically linked to vaccine-associated enhanced respiratory disease (VAERD), emerging data indicate that controlled type 2 immunity can instead promote epithelial repair and recovery upon BTI. Cytokines and mediators such as IL-4, IL-5, IL-13, amphiregulin, and TGF- β , produced by Th2 cells, ILC2s, and reparative myeloid cells, facilitate resolution of inflammation and tissue regeneration. Likewise, Tregs contribute via IL-10, TGF- β , and CTLA-4, while fostering M2 macrophage polarization, neutrophil apoptosis, and epithelial repair through amphiregulin. Notably, lung Tregs often co-express the IL-33 receptor ST2, linking them functionally to Th2 and ILC2 pathways.

Preliminary data from murine influenza and mRNA COVID-19 vaccine models support this concept: elevated pulmonary Treg frequencies, enhanced type 2 cytokine profiles, and eosinophil influx correlate with improved BTI outcomes. In vaccinated mice, Tregs preferentially accumulate in the lung following influenza challenge, coinciding with protection.

To dissect these pathways, the project comprises two work packages. First, high-dimensional flowcytometry will map type 2 and regulatory immune landscapes across respiratory and lymphoid tissues during BTI, generating a reference atlas of reparative immune states. Second, in vivo Treg and antigen presenting cell depletion models will define their causal contribution to protection and identify the antigen-presenting cell subsets licensing regulatory immunity in the lung.

Expected outcomes include a reference atlas of regulatory and reparative responses, candidate Treg biomarkers for clinical immunomonitoring, and a conceptual framework uniting antiviral defense with immune regulation. By focusing on disease tolerance and tissue protection, this work aims to pave the way for next-generation respiratory vaccines that not only prevent infection but also preserve lung health during BTI.

POSTER 234

DEVELOPMENT OF A VACCINE CANDIDATE AGAINST TUBERCULOSIS

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Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (MTB), became the leading cause of death worldwide from a single infectious agent in 2023. Although the only vaccine approved for human use is the Bacillus Calmette-Guérin vaccine, its protective capacity has been questioned as this disease continues to cause more than 10 million active cases and 1 million deaths annually. Its effectiveness varies significantly and is dependent on the population and age, developing bacterial survival and evasion capabilities to the immune system. This is represented by its persistence in the population, infecting a quarter of the world's population and being able to remain for years as asymptomatic in latent state. The 16-kDa alpha-crystallin (Acr) protein is an MTB antigen recognized in patients with active TB, important multidrug resistant strains, and expressed at high levels in the latency state, being a virulence factor necessary for colonization and evasion by the immune system. Since MTB attacks the mucous membranes of the airways, it is necessary to generate an adaptive immune response with high levels of specialized mucosal antibodies where the IgA is known to be the main mucosal resident antibody which has been reported that participates in the inhibition of bacterial adherence and the neutralization of toxins and viruses. The development of the mucosal immune response is associated with the uptake of antigens by M cells where the synthetic peptide "Co1" has been described as a ligand to the 5a receptor present on M cell, enabling the design of vehicles that promote a mucosal response. In this work, the Acr protein and Co1 peptide were expressed on the surface of the filamentous phage M13, a bacterial virus known to infect *Escherichia coli* and to replicate without triggering bacterial lysis. The recombinant bacteriophages were inoculated into C57BL/6 mice by the oral and subcutaneous routes, each route had 4 groups (control [PBS], Phage Helper [M13KO7], M13 Phage with Acr [ϕ -Acr], and M13 Phage Acr/Co1 [ϕ -Acr-Co1], n=5) The development of IgA and IgG antibodies was evaluated using One-Way and Two-Way Anova with the Tukey HSD to demonstrate significant differences. It was shown that the recombinants bacteriophages M13 acts as a vaccine carrier of the Acr protein and specifically, the Co1 peptide has a direct effect on the levels of antibodies generated. The study took place on the Recombinant Biopharmaceuticals laboratory at the Universidad de Concepción, Chile.

POSTER 238

Ethnicity shapes the antibody response to dengue virus infection in Pacific Islanders

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Introduction/Background: Primary infection by one of the four dengue virus (DENV) serotypes elicits monotypic antibodies conferring durable serotype-specific protection. Yet, secondary heterologous exposure triggers antibody-dependent enhancement (ADE), increasing the risk of severe disease. While ethnicity shapes interindividual differences in susceptibility to severe dengue, how ethnic background modulates monotypic immunity remains to be explored, especially among highly exposed Pacific Islanders.

Material/Methods: We built a cohort of 177 healthy individuals from New Caledonia with documented monotypic DENV-1 immunity from distinct ethnic backgrounds, including historically highly exposed Pacific Islanders (Polynesian and Melanesian) communities. We deployed a systems serology approach combining multiplex microsphere-based serological assays, focus reduction neutralization tests (FRNT), and functional assays to quantify inter-population differences in antibody specificity, cross-neutralizing breadth, and Fc-mediated effector functions.

Results: While serotype-specific neutralizing titers were comparable across ethnic groups, microsphere-based assays revealed broader cross-reactivity to envelope proteins from heterologous DENV serotypes among Pacific Islanders compared with Europeans. Antigenic mapping showed that Pacific Islanders also deployed expanded cross-neutralization profiles to heterologous serotypes relative to Europeans.

Discussion/Conclusion: These findings highlight population-specific differences in the functional architecture of monotypic DENV immunity. By defining protective antibody signatures across ethnic groups, this work holds translational potential for adapted prevention and targeted clinical management in exposed populations, while informing the rational design of next-generation vaccines and monoclonal antibody therapeutics.

POSTER 239

Insect-cell based nanoparticle vaccine platform to combat zoonotic arthropod-borne viruses

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Background: Novel vaccine platforms are urgently needed to produce efficacious, safe, low cost, and rapidly adaptable ('plug-and-play') vaccines to face the threat of zoonotic viral diseases in livestock. Protein nanoparticle vaccines are generally considered an optimal vaccine format because of their high efficacy and intrinsic safety. In this project, OneHealth vaccines were developed by implementing a two-component nanoparticle vaccine platform.

Materials/Methods: This technology involves expression of viral antigens in Sf9 insect cells using the well-established baculovirus expression system, combined with antigen presentation on AP205 bacteriophage capsid nanoparticles, which are produced in *E. coli* and are self-adjuvanting.

Results: Stable glycoprotein antigens of the zoonotic arthropod-borne viruses Japanese Encephalitis Virus (JEV; flavivirus) and Getah virus (GETV; alphavirus) were engineered using a rational design pipeline involving AI tools. Multiple viral glycoprotein designs (JEV and GETV subunits, AI-stabilized JEV dimers, secreted GETV spikes) were efficiently expressed in Sf9 insect cells to mimic their native conformation. The viral antigens were then purified and coupled onto AP205 nanoparticles to generate novel vaccine candidates.

Conclusion: The GETV and JEV vaccines were subsequently evaluated in vaccination-challenge studies in transgenic ifnar^{-/-} and wildtype C57/BL6 mouse models to assess the feasibility and efficacy of this novel vaccine platform. We will present details on the vaccine design, manufacture of the vaccine candidates and outcomes of the pre-clinical trials. We conclude that stabilization of viral glycoproteins is a promising strategy to induce an effective neutralizing immune response that can protect against viraemia and disease.

POSTER 240

Vacuum Foam Drying Stabilises Newcastle Disease Virus Vaccines

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Live attenuated vaccines are highly effective but remain critically dependent on uninterrupted cold chain systems due to their inherent heat sensitivity, limiting deployment in resource constrained and field settings. To address this challenge, we evaluate the effect of vacuum foam drying (VFD) on the thermostability of a live attenuated Newcastle Disease Virus (NDV) vaccine and investigate the underlying mechanisms of thermal protection.

NDV was subjected to controlled heat exposure, and the effects on viral infectivity, morphology, and the activity of key surface glycoproteins, hemagglutinin neuraminidase (HN) and fusion (F), were assessed. Heat stress induced a time and temperature dependent decline in viral infectivity with and progressive disruption of virion structure. HA, neuraminidase, and fusion assays demonstrated heat induced loss of HN and F activity, identifying these glycoproteins as primary sites of thermal inactivation. Given their central role in viral attachment, membrane fusion, and host cell entry, impairment of these proteins directly compromises viral infectivity.

In contrast, NDV subjected to vacuum foam drying (VFD) exhibited markedly improved resistance to thermal degradation. VFD treated virus retained higher infectivity and preserved both virion structural integrity and glycoprotein activity under comparable heat exposure conditions. Notably, HN and F activity were substantially maintained following thermal challenge, consistent with sustained fusion capacity. These findings indicate that VFD mitigates heat induced conformational and structural damage to critical viral components.

Overall, this study identifies NDV surface glycoproteins as key thermal damage sites and demonstrates that vacuum foam drying preserves their functional integrity, thereby enhancing vaccine thermostability. This work highlights VFD as a promising processing strategy to reduce cold chain dependence and improve the accessibility of live attenuated vaccines in low resource settings.

POSTER 242

PapMV Nanoparticle: A New Generation of TLR7/8 Agonists

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Introduction: Toll-like receptor (TLR) 7/8 agonists, such as imidazoquinoline derivatives (IMDs), hold great potential as immune modulators that enhance innate antiviral and anticancer immunity. However, achieving strong efficacy while minimizing toxic side effects remains a major challenge. To date, only imiquimod (IMQ) has received FDA approval, and its use is limited to topical applications (e.g., the treatment of warts and basal cell skin cancers). We therefore developed a new generation of TLR7/8 agonists based on the Papaya mosaic virus nanoparticle (PapMV nano). IMDs and PapMV nano both activate innate immunity and have demonstrated antiviral and anticancer activities, but they differ in composition, structure, and mechanisms of action. In this study, we compared cell responses to these two classes of agonists and investigated whether PapMV nano, like IMDs, can induce antiviral immunity against respiratory viral infections.

Methods: Human monocyte-derived macrophages (hMDMs) were exposed to PapMV nano or three IMDs. We assessed: (1) cell motility by live-cell tracking, (2) metabolism by measuring extracellular acidification rate (ECAR) and oxygen consumption rate (OCR), and (3) apoptosis induction using the FITC Annexin V Apoptosis Detection Kit with 7-AAD. To assess in vivo antiviral activity, female K18-hACE2 mice received two intranasal administrations of PapMV nano or formulation buffer, spaced 7 days apart. Three days after the final dose, mice were challenged with SARS-CoV-2, and lungs were collected 3 days post-infection to quantify viral load and IL-6 levels.

Results: Our data show that, in hMDMs, PapMV nano enhanced cell motility and mitochondrial respiration while reducing glycolysis. In contrast, IMDs did not affect cell motility or mitochondrial respiration but significantly increased glycolysis. Notably, PapMV nano was also the only agonist that did not induce apoptosis in hMDMs. In vivo, intranasal PapMV nano administered 3 days before SARS-CoV-2 infection significantly reduced lung viral load and IL-6 levels compared with formulation buffer controls, suggesting that PapMV nano effectively mitigates infection.

Conclusion: Although both classes of molecules target the same TLR7/8 receptors, we demonstrated that they elicit distinct cellular responses. Interestingly, both are capable of promoting antiviral immunity. Finally, these results reveal the superior safety profile of PapMV nano compared with IMDs and underscore the potential of this technology for preventing respiratory viral disease.

POSTER 246

Adjuvants are Central for the Immunogenicity of Bacterial Subunit Vaccines

POSTER 248

Broad mucosal adjuvant profiling in mice identifies c-di-GMP as a promising mucosal adjuvant for protein based vaccines, exemplified by SARS-CoV-2 antigens

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Background: Next-generation SARS-CoV-2 vaccines must elicit strong mucosal immunity to block infection and transmission, yet protein-based intranasal vaccines require potent mucosal adjuvants to overcome rapid clearance and limited antigen uptake in the respiratory tract. Building on a protein-based vaccine comprising Omicron BA.4/5 RBD fused to an IgG2A Fc domain (RBDmFc) and nucleocapsid (N) protein, we systematically evaluated innate immune agonists to identify optimal adjuvants for enhancing humoral, mucosal, and cellular immunity.

Materials & Methods: Female BALB/c mice received an intramuscular prime followed by two intranasal boosts with RBDmFc and N antigens formulated with one of twelve adjuvants or combinations, including MPLA, ODN2395, imiquimod, CL429, branched polyethyleneimine (BPEI), and c-di-GMP. Serum and bronchoalveolar lavage samples were analyzed for antigen-specific IgG, IgG subclasses, and IgA by ELISA. Neutralizing activity was assessed using an ACE2-RBD inhibition assay. Splenocyte cytokine secretion (IFN- γ , IL-2, TNF) was quantified by FluoroSpot.

Results: Among all tested formulations, c-di-GMP elicited the strongest immune responses. It induced significantly higher systemic IgG titers to both RBD and N, robust mucosal IgA and IgG responses, and potent T-cell immunity characterized by elevated IFN- γ and IL-2 secretion. c-di-GMP also promoted dual- and polycytokine-secreting T cells and generated a more balanced IgG1/IgG2A profile compared with other adjuvants. While several formulations showed moderate enhancement when combined with BPEI, none matched the magnitude or consistency of responses induced by c-di-GMP alone.

Discussion/Conclusions: This comprehensive adjuvant screen identifies c-di-GMP as a highly effective mucosal adjuvant for protein-based SARS-CoV-2 vaccines, outperforming TLR-based and combination adjuvants across systemic, mucosal, and cellular readouts. Incorporating c-di-GMP into intranasal vaccine platforms may substantially improve the breadth, durability, and functional quality of immunity against SARS-CoV-2 and emerging variants.

POSTER 251

Genotyping of Varicella-Zoster Virus in China and the Impact of Different Site Mutations on Vaccine Efficacy

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Background: Shingles is caused by the reactivation of Varicella-Zoster Virus (VZV) that persists latently in the dorsal root ganglia of the spinal cord or the sensory ganglia of cranial nerves. Mutations at key sites in its genome may impair the protective efficacy of existing vaccines. This study aimed to clarify the epidemiological genotypic characteristics of circulating VZV in China, screen mutation sites that may impair vaccine protection efficacy, and further analyze the effects of these mutations on clinical symptoms and immunogenicity in patients with herpes zoster.

Methods: We collected all subjects who developed herpes zoster (HZ) and their lesion samples from a completed phase III clinical trial of a live attenuated herpes zoster vaccine. Whole-genome sequencing (WGS) was performed on the wild-type VZV strains isolated from the lesion specimens of these HZ cases and the vOka-BK vaccine strain (also known as Baiken) produced by Changchun BCBT Biotechnology Co., Ltd. The primary objective of this study is to evaluate the impact of mutations at different sites in the wild-type strains on the protective efficacy of the vaccine.

Findings: 24949 participants (12474 in vaccine group, 12475 in placebo group) were evaluated. During 1 year follow-up period after vaccination, herpes zoster was confirmed in 66 vaccine recipients and in 155 placebo recipients. Whole-genome sequencing (WGS) of skin lesion samples from these confirmed cases revealed that Clade 2 is the predominant circulating genotype of VZV in China. Comparative analysis was performed between these clinical isolates and the vOka-BK vaccine strain using WGS data, with a specific focus on 73 open reading frames (ORFs) of VZV. Ultimately, nonsynonymous mutations in ORF66 were identified as factors influencing vaccine efficacy. In the absence of ORF66 mutations, the vaccine effectiveness was 64.77% (95% CI: 50.69-74.83). However, mutations at this locus led to a reduction in vaccine effectiveness of 39.31% (95% CI: -338.95-55.78). We compared pain scores and pain duration between patients with ORF66 mutations and those without ORF66 mutations. The results showed that patients carrying ORF66 mutations had slightly higher pain scores and longer pain duration than non-mutated counterparts, with no statistically significant differences. In contrast, the predicted immunogenicity scores and antigen-specific T-cell responses determined by the ELISPOT assay were significantly lower in the ORF66 mutation group relative to the non-mutation group ($P < 0.05$).

Interpretation: Genomic comparison with the vOka-BK vaccine strain revealed that ORF66 mutations attenuate vaccine immunogenicity and further induce viral immune evasion. Additionally, ORF66 mutations may enhance the virulence of VZV, leading to exacerbated clinical symptoms.

POSTER 252

Long-Term Immune Persistence of a Recombinant gE-Fc Fusion Protein Subunit Vaccine Against Herpes Zoster in Adults ≥ 50 Years of Age

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Background: LZ901 is a novel recombinant herpes zoster vaccine based on a CHO cell-derived VZV glycoprotein E (gE)-Fc fusion protein. This study evaluated the persistence of humoral and cellular immune responses induced by LZ901 compared with the licensed HZ/su vaccine in adults aged ≥ 50 years.

Methods: This observational follow-up study was conducted within a randomized, active-controlled clinical trial. Participants received two doses of either LZ901 or HZ/su and were evaluated 1 year after full vaccination. Anti-gE antibody concentrations were measured by ELISA, and gE-specific CD4⁺ and CD8⁺ T-cell responses were assessed by intracellular cytokine staining and flow cytometry. The primary outcome was the proportion of participants with polyfunctional gE-specific T-cell responses expressing ≥ 2 cytokines.

Results: Both vaccines induced persistent humoral and cellular immune responses at 1 year. HZ/su elicited significantly higher anti-gE antibody levels than LZ901 at both 30 days and 1 year post-vaccination (all $p < 0.0001$), with higher seroconversion rates (91.3% vs 69.2%). However, antibody waning kinetics were comparable between groups. In contrast, LZ901 induced stronger cellular immune responses, particularly higher frequencies of cytokine-producing and polyfunctional CD8⁺ T cells. Cellular immunity was maintained across all age groups, including older adults.

Conclusions: Both LZ901 and HZ/su induced durable immune responses in adults aged ≥ 50 years. Although HZ/su generated stronger humoral immunity, LZ901 demonstrated enhanced cellular immune responses, especially in the CD8⁺ T-cell compartment, supporting its potential as a promising herpes zoster vaccine candidate.

POSTER 254

Nasal Microbiota Composition and Its Association with Mucosal Immune Responses to Intranasal Live Attenuated Influenza Vaccine in Children and AdolescentsTongtong YAN*Nanjing Medical University, China, People's Republic of*

Background: Influenza is an important respiratory disease, with children being particularly susceptible. Intranasal live attenuated influenza vaccine (LAIV) can mimic natural infection and induce mucosal and systemic immune responses. As the nasal microbiota may influence mucosal immunity, this study aimed to characterize the nasal microbiota in children and adolescents aged 6–17 years, assess its changes after LAIV administration, and explore its association with LAIV-induced mucosal immune responses.

Methods: This study was based on a single-center, randomized, open-label phase IV clinical trial of intranasal live attenuated influenza vaccine (LAIV) in Jiangsu Province (NCT06609811). A total of 200 healthy children and adolescents aged 6–17 years were randomly assigned to immediate- or delayed-vaccination groups. Participants received one dose of intranasal LAIV on day 0 or day 28, respectively. Nasal swabs and nasal mucus samples were collected before and after vaccination. Vaccine strain-specific secretory IgA (sIgA) was measured by ELISA, and nasal microbiota was characterized by high-throughput 16S rRNA sequencing.

Results: A total of 183 participants, including 93 in the immediate-vaccination group and 90 in the delayed-vaccination group, were included in the analysis. At 28 days after intranasal live attenuated influenza vaccine (LAIV) administration, strain-specific sIgA levels against all influenza subtypes were significantly increased ($P < 0.001$). The immune response rates to any vaccine strain, A/H1N1, A/H3N2, and B/Victoria were 60.1%, 45.4%, 45.9%, and 43.7%, respectively. Males and participants with normal body mass index (BMI) showed better responses to any vaccine strain than females and those who were overweight or obese ($P < 0.05$).

Based on the two pre-vaccination time points, 309 and 276 long-term nasal colonizers were identified in the immediate- and delayed-vaccination groups, respectively, with 212 shared taxa. Fourteen core nasal colonizers were identified, mainly including *Dolosigranulum pigrum*, *Corynebacterium propinquum*, *Sphingomonas pituitosa*, *Moraxella nonliquefaciens*, and *Staphylococcus aureus*. Age significantly affected the community structure of long-term nasal colonizers ($R^2 = 3.3\%$, $P = 0.001$), while no significant baseline differences were observed between vaccination groups ($P > 0.05$, $\text{Padj} > 0.05$).

At 28 days post-vaccination, the immediate-vaccination group showed significantly decreased relative abundance and colonization rate of *Haemophilus influenzae* ($\text{Padj} < 0.001$), decreased colonization rate of *Corynebacterium fastidiosum* ($\text{Padj} = 0.042$), and increased relative abundance of *Staphylococcus aureus* ($\text{Padj} < 0.05$). No significant differences in core nasal colonizers were observed between responders and non-responders ($\text{Padj} > 0.05$).

Conclusion: LAIV showed good mucosal immunogenicity in children and adolescents aged 6–17 years, with immune responses influenced by sex and BMI. A relatively stable core nasal microbiota was identified, and age was a major factor shaping its community composition. LAIV did not significantly alter the overall structure of long-term nasal colonizers, although it was associated with changes in specific taxa, including reduced *Haemophilus influenzae* and increased *Staphylococcus aureus*. No significant association was observed between core nasal microbiota and LAIV-induced mucosal immune responses, but differences in dominant commensal and opportunistic taxa between responders and non-responders suggest a potential role of nasal microbiota in modulating vaccine responses.

POSTER 255

HPV16-L1 VLPs as a highly-adaptable nanoparticle carrier platform to improve the antibody response towards low immunogenic HIV-Env and Peptide Epitopes

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Displaying low-immunogenic antigens on nanoparticles has been shown to effectively enhance cognate B cell activation and increase antibody responses against these antigens. Building on the successful use of human papilloma virus (HPV) virus-like particles (VLPs) as vaccine antigens for preventing cervical cancer, we aim to leverage the high immunogenicity of these nanoparticles to enhance the humoral immune response against low-immunogenic antigens. To achieve this, we developed click-chemistry-ready HPV16 L1 capsid protein VLPs that allow for interchangeable display of various azide-labeled antigens on the VLP surface:

L1 proteins were produced using a bacterial expression system and assembled into HPV16-L1 VLPs in vitro. The crude VLPs were subsequently functionalized with Dibenzocyclooctyne (DBCO) followed by size exclusion chromatography to remove residual functionalization reagents and malformed particles, yielding high-purity, click chemistry-ready HPV16-L1 VLPs. As proof-of-concept antigens, we used azide-labeled peptides (Pep) and azide-labeled Human Immunodeficiency Virus (HIV) envelope protein (Env), which were both orthogonally conjugated to the VLP surface via copper-free click chemistry. Unconjugated peptides were removed by ultrafiltration, and unconjugated Env was removed by size exclusion chromatography.

To evaluate the immunogenicity of the L1-Env and L1-Pep conjugates, mice were vaccinated intramuscularly in weeks 0 and 4 with either the conjugates or a control consisting of unconjugated VLPs mixed with the unconjugated antigen at the same dosage. All immunizations were performed without adjuvants. Blood was drawn in weeks 3 and 6. The L1-, Env-, or Pep-specific immune responses were subsequently analyzed by serum ELISA.

The L1-Pep conjugates induced a significantly higher peptide-specific immune response than the control group that received the equivalent dose of unconjugated Peptides and L1. Both groups induced a similar L1-specific antibody response.

Concurrently the L1-Env conjugates induced a significantly higher Env-specific antibody response than the unconjugated control group. However, the control group elicited higher L1-specific antibody levels than L1-Env at the same dose, indicating that conjugated Env trimers may partially shield L1 epitopes.

These results establish proof-of-concept that click chemistry-ready L1 VLPs can serve as an attractive nanoparticle platform for enhancing the antibody response to low-immunogenic antigens. The displayed peptides and Env can easily be interchanged with different antigens, making L1-VLPs a highly adaptable vaccine platform for inducing a potent immune response against present and emerging pathogens.

POSTER 256

Recombinant live attenuated mumps vaccine of genotype F induces immune responses against epidemic strains: preclinical studies and first-in-human trial

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Introduction/Background: Despite widespread administration of live attenuated genotype A mumps vaccines, mumps still imposes a severe public health burden worldwide. Ongoing sporadic global outbreaks are mainly attributed to antigenic mismatch between vaccine strains and prevailing circulating strains (F and G genotypes), as well as progressive waning of vaccine-elicited immunity. Vaccination with genotype A vaccines induces insufficient neutralizing antibodies against heterologous epidemic strains. This study aimed to develop an updated mumps vaccine to resolve such unmet clinical needs.

Materials/Methods: We developed a recombinant live attenuated mumps vaccine (rMuV) of genotype F by deleting the SH gene. Preclinical evaluation included neurovirulence testing in neonatal rats and rhesus monkeys, and immunogenicity assessment in guinea pigs and mice using microneutralization assays against genotypes A and F. We then conducted a phase 1, first-in-human, randomized, double-blind, dose-escalation, placebo-controlled trial (ChiCTR2300073206) in Songzi City, Hubei, China. A total of 388 healthy participants aged 6-59 years were randomized (3:1:1) to receive one of three rMuV doses (3.1, 4.8, 5.6 lg CCID₅₀/mL), a licensed genotype A mumps vaccine (positive control), or placebo. Safety was assessed over 30 days post-vaccination; immunogenicity endpoints included seroconversion rates and geometric mean titers of neutralizing antibodies against MuV genotypes F and A at days 14 and 30.

Results: Preclinically, rMuV elicited significantly higher neutralizing antibody titers against genotype F compared those elicited against reference strains (S79 and Jeryl Lynn), with robust cross-neutralization against genotype A. No neurovirulence was observed in either neonatal rat or rhesus monkey models. In the clinical trial, adverse reactions were reported in 9.0-22.1% of rMuV recipients across dose groups, comparable to the positive control (11.7%) and placebo (10.3%) groups, with no serious vaccine-related adverse events recorded. At day 30, seroconversion rates against genotype F were 64.1% in the middle-dose group and 60.3% in the high-dose group, both significantly higher than those in the positive control (41.6%) and placebo (7.7%) ($P < 0.001$).

Discussion/Conclusion: rMuV demonstrates a favorable safety profile and superior immunogenicity against epidemic genotype F, accompanied by robust cross-protection against genotype A. This vaccine effectively overcomes the antigenic mismatch defect of existing commercial mumps vaccines, and the overall findings support further development of rMuV as a promising next-generation mumps vaccine candidate.

POSTER 257

Ionizable lipid selection and α -GalCer co-formulation cooperatively modulate delivery, innate immune activation, and T-Cell responses of mRNA-LNP Vaccines

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Messenger RNA (mRNA) vaccines have emerged as versatile platform for infectious disease prevention, cancer immunotherapy, protein replacement, and gene therapy applications. Their rapid scalability and clinical efficacy during the COVID-19 pandemic highlighted the transformative potential of mRNA-based technologies (Chaudhary et al., 2021). Despite these advances, the mechanisms governing the balance between mRNA-LNP immunogenicity, reactogenicity, and delivery efficiency are incompletely understood. Innate immune activation induced by both the mRNA and the lipid nanoparticle (LNP) carrier contributes substantially to vaccine efficacy by promoting antigen-presenting cell (APC) maturation and adaptive immune responses (Verbeke et al., 2022).

The incorporation of adjuvants into LNP formulations offers represents a promising strategy to enhance vaccine potency, precision and broaden immune responses. By incorporating immune-stimulating molecules directly into the same nanoparticle that delivers the antigen or nucleic acid payload, both components reach antigen presenting cells in a coordinated manner (Xie et al., 2023). This co-delivery can strengthen innate immune activation at the site of antigen expression and reduce the required dose of both antigen and adjuvant. Additionally, embedding adjuvants within LNPs can minimize systemic exposure—potentially improving safety—and enables fine control over release kinetics and immunological signaling.

In this study, we investigated the impact of the glycolipid adjuvant α -galactosylceramide (α -GalCer) when co-formulated with two ionizable lipids: C12-200 and S-Ac7-DOG. C12-200 has previously been shown to possess strong pro-inflammatory properties (Meulewaeter et al., 2024), whereas S-Ac7-DOG, an in-house developed ionizable lipid, was designed to reduce reactogenicity while maintaining immunogenicity comparable to MC3 (De Lombaerde et al., 2024).

Following in vitro transfection of human peripheral blood mononuclear cells (PBMCs), all formulations demonstrated comparable levels of uptake and mRNA expression for all formulations across different APCs, except for B cells where S-Ac7-DOG mediated substantially higher transfection levels than C12-200.

Subsequently, in vivo biodistribution and transfection efficiency were evaluated after intramuscular injection in C57B6/6 mice. In vivo imaging demonstrated predominant localization of all formulations at the injection site 4 and 24 hours post administration. Nevertheless, C12-200 formulations exhibited broader systemic biodistribution and overall higher uptake and stronger luciferase expression compared to S-Ac7-DOG formulations, which was likely related to differences in chemical stability.

Similar trends were observed at cellular levels, where the incorporation of the adjuvant further enhanced uptakes and expression. Moreover, analysis of CD86 expression across different APC subsets systemically revealed innate immune activation driven by both the ionizable lipid and the adjuvant. C12-200 elicited higher levels of maturation than S-Ac7-DOG, while the inclusion of α -GalCer further enhanced APC activation, indicative of a synergistic effect between the ionizable lipid and adjuvant.

Finally, immunogenicity results using a prime-boost regimen of mRNA-LNP encoding OVA demonstrated higher numbers of antigen-specific T cells for C12-200. Co-formulation with α -GalCer increased the frequency of tissue-resident memory precursor T cells, indicating improved long-term immunity.

Together, these findings demonstrate that both choice of ionizable lipid and adjuvant integration critically influence the balance between delivery efficiency, innate immune activation, and adaptive immune responses. This work contributes to the rational design of next-generation mRNA-LNP vaccines with optimized safety and immunogenicity profiles.

POSTER 259

Intranasal protein-based COVID-19 vaccine induces superior mucosal and cellular immunity compared to mRNA vaccination

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Background: To effectively prevent respiratory diseases like COVID-19, vaccines must activate mucosal immune responses. However, all current COVID-19 vaccines are administered intramuscularly, which, while effective at generating high levels of antibodies against systemic viral infections, does not efficiently induce mucosal immunity. In contrast, mucosal administration can promote both local and systemic immune responses, offering broader and potentially more durable protection. An intranasally administered protein-based coronavirus vaccine combined with appropriate adjuvant to enhance both humoral and cellular immunity, could address the limitation of current vaccines.

Materials and Methods: 6-8 weeks old female BALB/c mice were immunized with either protein-based or mRNA vaccine formulations. Mice were immunized two or three times with three-week intervals. Systemic IgG responses were quantified by ELISA from serum samples collected throughout the study and mucosal IgA/IgG from bronchoalveolar lavage samples collected upon termination. The neutralization ability of the antibodies was determined from termination serum. Cellular immune responses (IFN- γ , TNF, IL-2) were assessed from isolated splenocytes using antigen-specific stimulation followed by FluoroSpot assay.

Results: The recombinant protein-based vaccine comprising RBDmFc and nucleoprotein formulated with c-di-GMP induced superior mucosal and cellular immune responses compared to the commercial mRNA vaccine Comirnaty. In addition, the vaccine elicited strong systemic humoral responses, with neutralizing antibody levels that were comparable to those induced by the mRNA vaccine.

Conclusions: These findings highlight the potential of intranasal protein-based vaccines to induce robust mucosal, cellular, and humoral immune responses. Future work will focus on extending this platform to multivalent vaccine formulation targeting both corona and influenza viruses to achieve broad immunity.

POSTER 262

Quantitative virus infectivity titration and dose response analyses using cell-culture based methods and python code assisted data analysis

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Introduction: Enteroviruses cause large impact on public health worldwide. Therefore, methods to reliably and quickly identify virus infections and screen treatments or preventatives against them are needed. Although, traditional techniques such as plaque assays remain as golden standard, they are labor-intensive, time-consuming, and limited in scalability. This study aimed to develop faster, quantitative, and less labor-intensive cell-based assays for measuring infective virus titers, neutralizing antibodies, and antiviral efficacy, supported by automated data analysis using Python scripts.

Materials and Methods: Cell-based microtiter plate assays were developed using green monkey kidney cells and coxsackievirus B1. Infective virus titers were determined from virus and tissue samples using endpoint dilution assay (TCID₅₀) in 96-well plates. Cell viability was quantified via fluorescence- and absorbance-based methods. Dose-response analyses (IC₅₀, EC₅₀, CC₅₀) were conducted by incubating serial dilutions of serum samples or antiviral compounds with cells, followed by viral challenge. Data processing, normalization, four-parameter logistic curve fitting, and statistical analyses were performed using custom Python scripts and compared with commercial software.

Results: The developed assays enabled quantification of infective virus titers and dose-response within 72 hours. Fluorescence- and absorbance-based TCID₅₀ measurements yielded comparable results, demonstrating reliability across detection methods. Python-based analysis produced IC₅₀, EC₅₀, and CC₅₀ values consistent with commercial software outputs, while successfully processing datasets where commercial software failed. The scripts additionally generated accurate statistical outcomes and graphical outputs, supporting the efficient large-scale screening and reducing manual data handling.

Conclusion: The study presents fast, flexible, and scalable cell-based assays combined with Python-assisted data analysis for quantifying viral infectivity and evaluating antiviral responses. The developed scripts automate data organization and analysis, reducing reliance on commercial software while also providing a valuable tool for assay optimization and validation processes. Although optimization might be required for different viruses and laboratory conditions, the methods and tools provide a robust platform for viral diagnostics, therapeutic screening, and vaccine evaluation, with potential applications across a wide range of cell culture-adapted viruses.

POSTER 263

Live attenuated pertussis vaccine carrying Mtb Ag85A boosts Mycobacterium bovis BCG cellular immune response in mice

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The use of live attenuated bacterial vectors has emerged in the last decades as a tool for vaccine delivery. Bacterial cells can be engineered to express recombinant heterologous antigens, allowing the induction of a broad range of immune responses, including local mucosal and systemic humoral and/or cell-mediated responses. In this work we have investigated the use of a highly attenuated *Bordetella pertussis* vaccine strain as a live vehicle for the expression of *Mycobacterium tuberculosis* Ag85A through the auto-transporter SphB1 secretion machinery. Ag85A was fused to the passenger domain of SphB1 using an expression cassette containing the pertactin secretion signal and promoter regions. The chimeric protein was successfully produced and secreted into the extracellular medium. Nasal administration of the live recombinant *B. pertussis* strain to mice together with *Mycobacterium bovis* BCG or as a heterologous booster after BCG vaccination triggered long-lasting specific systemic cell-mediated response against Ag85A. While BCG alone induced IFN- γ responses in both spleen and lungs, but no IL-17 responses, recombinant *B. pertussis* induced IL-17 responses and low IFN- γ responses in spleen and lungs. Co-administration of both resulted in combined IFN- γ and IL-17 responses, which lasted for at least up to 8 months post-vaccination, while cellular immunity induced by either vaccine alone had waned at 8 months. These findings suggest that recombinant attenuated *B. pertussis* carrying Mtb Ag85A combined with BCG could be a promising mucosal vaccine to induce sustained immunity against tuberculosis.

POSTER 265

Exploiting hyaluronan as a natural and effective immunological adjuvant for protein/peptide-based vaccines against HER2-expressing breast cancer

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Background: HER2-expressing breast cancers account for approximately 20% of all breast cancer cases and are typically associated with aggressive clinical behaviour and poor prognosis. In this context, anti-HER2 vaccines may present a promising alternative or complementary therapeutic strategy, with the potential to target early disease stages, prevent metastasis, and improve long-term patient outcomes overcoming high cost, toxicity risk and emergence of resistance associated to current clinical therapies. However, cancer vaccines face the dual challenge of breaking immune tolerance to self-antigens and inducing durable memory, with protein/peptide platforms, though safe and easily produced, still requiring strong adjuvants. In this context, hyaluronan (HA), a biocompatible glycosaminoglycan, has recently gained attention for its immunomodulatory properties: indeed, HA fragments of approximately 200 kDa have demonstrated intrinsic adjuvant capabilities when covalently conjugated to protein antigens eliciting robust, durable immune responses.

Material and Methods: Two main mouse models were used: Balb/c mice, administered with syngeneic tumoral rHER2/neu-positive cells according to preventive or therapeutic setting, and Balb/NeuT mice that spontaneously develop rHER2/neu-expressing carcinomas, used as pre-cancerous model. In preventive and pre-cancerous settings, both models received either rHER2/HA bioconjugates or rHER2 protein formulated with aluminium hydroxide, and were, for effectiveness assessment, respectively challenged on day 30 or monitored in spontaneous tumour development. In therapeutic settings, mice were injected with tumour cells 12 days before the first dose. In vitro assays comprised IgG subclasses and cytokine profile characterization. Functional responses were evaluated via 51Cr-release in complement/antibody-dependent cytotoxicity, as well as inhibition of cell growth quantification and mediation of antibody-dependent cellular phagocytosis. Additionally, in vivo depletion of B and T cells was conducted to define the role of different immune subsets in tumour control. According to structural HER2 analysis, multiple cross-species immunogenic HER2-conserved peptides were identified, then conjugated to HA for immunogenicity testing.

Results: HA-conjugated vaccines elicited strong and durable immune responses across all experimental settings, exhibiting mainly a Th1-polarized response. Antigen-specific antibodies remained functional up to one-year post-vaccination, showing remarkable results in inducing antigen-specific anti-tumoral effector functions. In the preventive model, HA-based protein vaccines conferred 100% survival, while in the therapeutic setting, partial tumour regression was observed in 2 out of 12 mice. Notably, it effectively broke tolerance to the rHER2/neu antigen and significantly delayed tumour onset in pre-cancerous model. Furthermore, in vivo depletion studies confirmed the involvement of both B and T lymphocytes in the antitumor response. Preliminary data from HER2-peptide-based vaccines identified three immunogenic candidates, currently investigated as in combinatorial formulations.

Conclusion: HA-based vaccines represent a promising strategy for inducing robust, long-lasting immune responses using low antigen doses, particularly in contexts where conventional vaccines may be less effective as low responding patients, or for relapse prevention.

POSTER 268

Antiviral T Cell-Targeted Immunotherapy Alleviates Long COVID Symptoms in a Mouse Model of Human Disease

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Introduction: Long COVID (LC) affects over 400 million people globally, yet no approved treatments exist. Persistent SARS-CoV-2 reservoirs and dysfunctional antiviral T cells are thought to drive LC pathology, suggesting that functional T cell responses and the reduction of these virus reservoirs could reverse LC disease.

Results: We previously demonstrated that (1) three highly conserved SARS-CoV-2 proteins, NSP-2, NSP-14, and Nucleoprotein, are preferentially targeted by functional CD4⁺ and CD8⁺ T cells in unvaccinated asymptomatic COVID-19 patients, and (2) immunization with these antigens confers durable, strain-independent, T cell-mediated protection in animal models. Therefore, NSP-2, NSP-14, and Nucleoprotein represent high-priority immunological targets that could drive an immunotherapy strategy to restore antiviral T cell function, eliminate multi-organ viral reservoirs, and reverse LC disease manifestations. We found that, compared with COVID-19 convalescent controls, patients with LC had increased numbers of exhausted antigen-specific CD4⁺ and CD8⁺ T cells, together with reduced numbers of antigen-specific cytotoxic and effector T cells. These data are consistent with the hypothesis that dysfunctional antiviral T cells are a causative factor of LC disease and could be used as a biomarker to definitively identify LC patients. Next, we developed a humanized triple-transgenic mouse model of LC that recapitulates the characteristics of disease in humans. Treatment of LC mice with an mRNA/LNP-based immunotherapy encoding NSP-2, NSP-14, and Nucleoprotein resulted in significant frequencies of functional tissue-resident antiviral CD4⁺ and CD8⁺ TRM cells, decreased tissue virus levels across multiple organs, and reversal of behavioral, cognitive, and memory deficits.

Discussion: These findings demonstrate that T cell-targeted antiviral immunotherapy is a potential strategy to eliminate the root cause of LC and reverse its pathogenic sequelae.

POSTER 270

Glucan-EV Platform for HBV Vaccination

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Introduction: Hepatitis B (HBV) requires effective therapeutic vaccines to overcome global health burdens. Glucan particles (GPs) are versatile delivery platforms for targeted antigen encapsulation, while extracellular vesicles (EVs) from *Giardia lamblia* possess proinflammatory properties, suggesting potential as vaccine adjuvants. This study evaluated a subcutaneously administered GP-encapsulated vaccine incorporating EVs to enhance HBV-specific immune responses.

Methods: GPs were derived from *Saccharomyces cerevisiae*, and EVs were isolated via differential ultracentrifugation. EVs were encapsulated into GPs through passive loading and freeze-drying (GPs(EVs)). Cellular uptake, ROS production, and cytokine/chemokine profiles (ELISA) were assessed in human moDCs and macrophages. C57BL/6 mice received two subcutaneous doses of GPs(HBcAg+EVs) at two-week intervals. Immune responses were analysed through IgG titration, flow cytometry of splenocytes, and IFN- γ levels in liver interstitial fluid.

Results: GPs (~5 μ m) were efficiently internalised by moDCs and macrophages, inducing ROS and increasing IL-12, CXCL10, and CXCL1 levels. In vivo, GPs(HBcAg+EVs) demonstrated superior immunogenicity, eliciting higher antigen-specific IgG and promoting CD4⁺ T-cell migration. Splenocyte analysis showed a robust Th1-skewed response, marked by increased IFN- γ , TNF- α , IL-12, IL-18, and IL-27. The inclusion of EVs significantly promoted Th1 polarisation while limiting Th2/Th17 responses, crucial for HBV clearance.

Conclusion: These findings highlight the potential of GPs as delivery platforms and *Giardia*-derived EVs as potent Th1-promoting adjuvants. This vaccine design shows promising efficacy in modulating cellular immunity for Hepatitis B therapy.

POSTER 271

Generation of High-Yield H5N1 and H5N2 Vaccine Strains against Highly Pathogenic Clade 2.3.4.4b H5N1 Avian Influenza VirusesSun-Min AHN¹, Kang-Seuk CHOI³, Hyuk-Joon KWON^{1,2}¹ Laboratory of Poultry Medicine, Department of Farm Animal Medicine, College of Veterinary Medicine and BK21 PLUS for Veterinary Science, Seoul National University, Seoul 08826, Republic of Korea² Geniner Inc³ Laboratory of Avian Diseases, College of Veterinary Medicine, Seoul National University, Seoul 08826, Republic of Korea

The repeated global outbreaks of clade 2.3.4.4b highly pathogenic H5N1 avian influenza virus (AIV) continue to pose a significant threat to the poultry industry and public health, underscoring the need for vaccine strains with improved productivity and efficacy under diverse field conditions. Conventional PR8-based vaccine strains, derived via reverse genetics, are reassortant viruses retaining mammalian-adaptive mutations such as the PB2 E627K substitution. Consequently, they often exhibit suboptimal growth in embryonated chicken eggs. Here, we describe the development of high-yield recombinant vaccine strains that are non-pathogenic in mammals, achieved through the incorporation of avian-origin PB2 genes and targeted mutations that preserve antigenicity. In this study, viral titers of a clade 2.3.4.4b H5N1 vaccine strain were further enhanced by introducing a novel mutation in the matrix 1 (M1) gene. In parallel, we generated optimized H5N2 vaccine strains designed to confer cross-protection against both H5N1 and H9N2 AIVs. To enable the differentiation of infected from vaccinated animals (DIVA), these strains were engineered with balanced hemagglutinin (HA) and neuraminidase (NA) activities, alongside a stabilized HA conformation. Consistent with the established correlation between antigen yield and vaccine efficacy, these optimized strains demonstrate strong potential for further clinical evaluation. Moreover, leveraging recent advances in inactivated whole-virion mucosal vaccines, these strains support combined immunization strategies, such as mucosal priming followed by intramuscular boosting, to maximize protective immunity in poultry.

POSTER 273

Systems Serology Reveals Age-Associated Immune Signatures Following Typhoid Conjugate Vaccination in an Endemic Setting

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Background: Typhoid conjugate vaccines (TCVs) are increasingly recommended for deployment in endemic regions, particularly among young children. Despite their growing use, the qualitative characteristics of the antibody responses elicited by TCVs, as well as the influence of age and immunological background on these responses, remain incompletely characterized.

Methods: A systems serology approach was utilized to comprehensively profile the biophysical and functional characteristics of antibody responses elicited by the Vi-DT and Vi-PS vaccines in a phase 1 clinical trial. Study participants were stratified by age group (children vs. adults) and baseline anti-Vi IgG serostatus (seronegative vs. seropositive). Multivariate analyses were performed to delineate immune signatures associated with vaccine formulation, age, and immunological status at baseline.

Results: Vi-DT induced significantly greater magnitude and functional quality of antibody responses than Vi-PS across all subgroups analyzed. Among recipients of Vi-DT, distinct immunological profiles were observed according to age and baseline serostatus. In children and seronegative individuals, antibody responses were predominantly characterized by IgG3, enhanced antibody-dependent cellular phagocytosis (ADCP), antibody-dependent neutrophil phagocytosis (ADNP), and antibody-dependent complement deposition (ADCD), immune features associated with early innate immune activation. By contrast, in adults and seropositive individuals, the response was enriched for IgG2, IgG4, IgA2, and Fc α receptor binding, indicative of a more antigen-experienced (memory) immune profile. Notably, booster administration of Vi-DT in children further augmented qualitative aspects of the humoral response, with marked increases in Fc γ receptor binding capacity and ADNP activity. Collectively, these data delineate the pivotal role of Fc-mediated antibody functions in the immunoprotection conferred by Vi-DT, particularly within pediatric and other immunologically vulnerable populations.

Conclusion: Vi-DT vaccination elicits robust and qualitatively distinct antibody responses regardless of immunological background, characterized by features indicative of both systemic and mucosal immune activation. These findings offer important immunological insights into the superior efficacy of Vi-DT, especially among young or immunologically naïve individuals, and support the potential benefit of booster dosing strategies to further enhance functional antibody responses.

POSTER 275

Pneumococcal and Influenza Vaccine Hesitancy Among Older Indian adultsManjeet KAUR, Madhu GUPTA, Vikas SURI, Kapil GOEL, Shankar PRINJA*Post Graduate Institute of Medical Education and Research, India*

Introduction: Immunization against pneumococcal disease and influenza is critical to reducing morbidity and mortality among older adults; however, uptake remains suboptimal in resource-limited settings. Understanding the psychological and socio-demographic drivers behind vaccine acceptance is essential for designing effective public health interventions to increase the uptake. This study was conducted to assess pneumococcal and influenza vaccine hesitancy (VH) among older adults (≥ 60 years) in North India.

Methods: A cross-sectional study was conducted among 910 older adults (≥ 60 years) in Chandigarh, Union Territory. Socioeconomic status (SES) was documented using the Modified Kuppuswamy Scale (2025). Pneumococcal and Influenza VH was evaluated across five psychological domains, including Confidence, Complacency, Constraints, Calculation, and Collective Responsibility, using validated 5C VH scale (Cronbach's alpha 0.94-0.97), utilizing median scores and Interquartile Ranges (IQR). Each domain comprised 3 items on a 7-point Likert scale (1=strongly disagree to 7=strongly agree), with domain scores ranging from 3 to 21. Higher scores for Complacency, Constraints, and Calculation indicate greater hesitancy, whereas higher scores for Confidence and Collective Responsibility indicate lesser hesitancy. Multivariate linear regression models evaluated independent predictors of domain-specific hesitancy.

Results: The cohort was predominantly aged 60–69 years (61.8%), mean age 68.2 ± 7.1 years, and 50.8% were male. While socioeconomically diverse, 82.1% reported a monthly income of $\leq$ USD 105.3/month, and 81.9% completely lacked health insurance coverage. For both vaccines, the Calculation domain (weighing risks vs. benefits) showed the highest overall baseline median score (Median = 13) and widest variability. Conversely, Collective Responsibility yielded the lowest baseline medians (~ 11 to 12.5). Low SES participants exhibited a significantly wider spread (IQR 9–13) in Complacency and Constraints compared to high SES peers ($p < 0.001$). For influenza vaccine, the Confidence domain showed no statistically significant difference across socioeconomic tiers ($p = 0.329$), meaning trust in the vaccine itself is relatively uniform. However, Complacency, Constraints, and Calculation differed significantly by SES ($p < 0.001$).

General health literacy showed no meaningful association with hesitancy domains. In contrast, specific Pneumococcal Vaccine Literacy strongly predicted higher scores, notably in Confidence (beta = 2.02, $p < 0.001$) and Calculation (beta = 1.91, $p < 0.001$). Similarly, "Excellent" Influenza Vaccine Literacy was an extraordinary predictor of Complacency (beta = 5.64, $p < 0.001$). Possession of health insurance significantly predicted higher pneumococcal hesitancy scores across Complacency (beta = 1.26), Constraints (beta = 1.09), and Calculation (beta = 1.42). For influenza, older age (≥ 70 years) was associated with higher Confidence (beta = 0.77, $p = 0.02$), while male gender was associated with significantly reduced Constraints (beta = -0.80) and Calculation (beta = -0.91). Willingness to get influenza vaccine was negatively associated with constraints ($\beta = -0.87$) and calculation ($\beta = -1.38$).

Conclusions: Among North Indian older adults, the calculation domain was the most important driver of VH. Pneumococcal vaccine literacy emerged as the strongest predictor of VH across all five domains, while influenza vaccine literacy most prominently affected complacency. Health insurance coverage was a significant driver of VH for both vaccines. Targeted interventions aimed at improving pneumococcal and influenza vaccine-specific literacy may effectively reduce domain-specific hesitancy.

POSTER 277

mRNA-based WNV E-protein vaccine candidates with mutations in the fusion loop elicit less cross-reactive antibodies and protect mice from infection

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Introduction: West Nile virus (WNV) is a mosquito-borne zoonotic Orthoflavivirus that usually causes mild infections in humans, but in some cases can also cause severe neurological symptoms. The number of reported cases in Europe has risen steadily in recent years. A vaccine to protect humans against WNV infections is currently not available.

Protection against Orthoflavivirus-induced disease is provided by neutralizing antibodies, predominantly targeting the envelope protein (E). Thus, the E protein is the central vaccine antigen in flavivirus research. The fusion loop (FL) domain within the E protein is highly conserved and can elicit cross-reactive antibodies that can enhance infections with related flaviviruses, a phenomenon called antibody dependent enhancement of infection (ADE). ADE in Orthoflavivirus infections is most notably observed in sequential infections with different dengue serotypes. By introducing point mutations in the FL we recently demonstrated, that vaccination with recombinantly expressed WNV FL-mutants elicits less cross-reactive antibodies. We now demonstrate that this strategy can be successfully transferred to an mRNA-based vaccine approach. This contributes to improved vaccine safety, particularly in regions with multiple co-circulating Orthoflaviviruses.

Materials/Methods: Four mRNA candidates (E Ecto WT, E Ecto mutant, VLP WT, VLP mutant) were developed, with the latter two containing four point mutations in or near the fusion loop (FL) domain., followed by assessing protein expression after transfection into 293T cells and Western Blot analysis using a WNV-specific antibody. To further investigate immunogenicity and protective efficacy against infection, WNV mRNA was encapsulated into lipid nano particles and intramuscularly administered in a prime-boost-boost regimen into BALB/c mice (n=18). Immune response after vaccination was assessed by analyzing binding and neutralizing antibodies. Cross-reactivity was analyzed by ELISA on heterologous Flaviviruses followed by measuring in-vitro ADE in a subset of animals (n=6) using K562 cells. Protection of vaccinated animals (n=12) was investigated by challenge-infection with active WNV and monitoring the animals for three weeks. Viral load in brain and spleen of challenged animals was determined by qRT PCR.

Results: All vaccine candidates were well tolerated and induced WNV-specific binding and neutralizing antibodies. Although the WT versions elicited significantly higher titers, better protection (100 % survival vs. 91.7 % for VLP mutant), and markedly lower viral loads in tissues, they also induced strong cross-reactive antibodies against ZIKV, DENV-2, TBEV, and USUV, and promoted antibody-dependent enhancement (ADE) in vitro, whereas the FL-mutant vaccines largely abrogated these effects. Notably, despite lower antibody responses, the E Ecto mutant group showed the highest WNV-specific IFN- γ -producing T-cell responses.

Conclusion: The study demonstrates that fusion-loop-mutated mRNA-LNPs induce robust T-cell responses and avoid ADE in vitro, while protecting against lethal West Nile virus challenge. It represents a promising strategy in the development of Orthoflavivirus vaccines with reduced cross reactivity and a higher safety profile.

POSTER 280

Non waning immunity elicited by a herpesvirus vaccine vector in xenotropic latency

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Introduction: Durable vaccine-induced immunity remains a central challenge for respiratory viruses such as SARS-CoV-2 or respiratory syncytial virus (RSV). Cytomegaloviruses are uniquely capable of establishing lifelong immunity, but their strict species specificity has restricted their vaccine vector potential to animal models. We have considered a disruptive vaccine innovation based on xenotropic latency of murine cytomegalovirus (MCMV) in species-discordant hosts. The vector that is restricted by the non-natural host environment retains key immunological properties relevant for durable vaccination. This concept may enable a new class of vaccine vectors that combine strong immunogenicity, persistence-associated immune stimulation, and an improved safety profile.

Material & Methods: MCMV-based vaccine candidates encoding respiratory viral antigens were generated and evaluated in preclinical species-discordant settings. Recombinant MCMV vaccines were tested in mice and hamsters after single-dose immunization. Immunogenicity was assessed by antigen-specific binding assays, neutralization assays, and cellular immune readouts. Tolerability and protection-relevant immune signatures were monitored longitudinally and challenge studies were conducted in immunized hamsters.

Results: Our SARS-CoV-2 prototype provided proof-of-concept that MCMV can function as a potent vaccine vector in species-discordant hosts, inducing neutralizing antibody responses ten times more durable than conventional vaccines, robust cellular immunity, and long-lasting protection in preclinical models. These findings support xenotropic latency as a central mechanistic and translational principle of the platform. Building on this, MCMV-based vaccine candidates encoding respiratory viral antigens induced antigen-specific immune responses in naïve animals after a single administration. Importantly, in hamsters, this single-dose response was observed under conditions where a high dose of a clinically approved vaccine did not induce comparable measurable responses, highlighting a potential advantage of the MCMV-based approach.

Conclusion: These findings position xenotropic latency as a disruptive vaccine-vector concept and support MCMV as a promising platform for durable vaccination. The combination of MCMV vector biology with BIBAX antigen engineering could enable single-dose, long-lasting, vaccines. Beyond the scientific rationale, this program is being advanced with a clear translational strategy toward product development and spin-off formation, aiming to move durable vaccine technologies from academic discovery into clinical and industrial development.

POSTER 283

Stable CHO pools as a platform for rapid vaccine antigen manufacturing

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Stable CHO cell clones are commonly used to manufacture therapeutic recombinant proteins but require months to develop and characterize. Faster alternatives such as non-clonal stable CHO pools have historically been limited by lower productivity and regulatory restrictions. However, recent improvements have made stable pools a practical option for rapidly producing drug material for toxicology studies and early clinical trials, especially during urgent situations like pandemics. In this study, we compared trimeric SARS-CoV-2 spike protein produced from CHO pools and clones. Biophysical and biochemical analyses showed similar product quality, and pools achieved sufficient productivity for vaccine candidate production. We also show high productivity of other spikes derived from various coronaviruses as well as HA and NA antigens from avian flu virus H5N1. These findings suggest an opportunity for regulatory flexibility to allow early clinical trial materials to be produced from CHO pools to enable faster and more cost-effective vaccine development, particularly to address a pandemic or emerging epidemic.

POSTER 284

Host Receptor Evasion via Rational Design of Coronavirus Vaccines and Beyond

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Background: A potential drawback of many vaccines is that their antigens can be masked by ubiquitously expressed host receptors, with negative effects on the quality of the immune response against such vaccine antigens and the risk of side effects. Our solution is to eliminate the receptor binding while maintaining binding sites for neutralizing antibodies, a novel design strategy called BIBAX (Body-inert B cell Activating VaCCine).

Objectives: Here, we aim to generate BIBAX prototypes for MERS-CoV spike by i) abrogating receptor binding while ii) maintaining epitopes important for binding of neutralizing antibodies.

Methods: We adopted Deep Mutational Scanning (DMS) of the MERS-CoV receptor binding domain (RBD) to profile which mutations increase or decrease binding to its receptor DPP4. In addition, we applied in silico ranking of MERS-CoV spike mutants. Single amino acid exchange mutants from both approaches were validated to obtain BIBAX candidates. We selected rabbits as an in vivo model for evaluating immune responses upon MERS-CoV immunization.

Results: Both the DMS and in silico screen provided MERS-CoV RBD variants with abrogated receptor-binding. Since many abrogating variants from the in silico screen had complete retention of neutralizing antibody binding, we selected one such variant as our BIBAX prototype for rabbit immunization. Our MERS-CoV BIBAX improved neutralizing antibody titers 2-fold following spike prime spike and RBD boost compared to wildtype. Surprisingly, antibody titers against the N-terminal domain were higher for BIBAX immunized rabbits following spike prime and boost.

Conclusions: Since rabbits show lower MERS RBD-DPP4 affinity and thus model epitope masking conservatively, we speculate that the moderate effects observed may translate into greater benefits in humans vaccinated with a MERS-CoV BIBAX candidate.

Outlook: In the future, the BIBAX design strategy may be applied more broadly to vaccine antigens against pathogens in which receptor abundance and epitope masking are critical determinants of immune efficacy. The safety benefit from eliminating receptor-interactions fits particularly well with vaccines that establish an antigen depot, such as MCMV vectored vaccines.

POSTER 289

Novel dengue virus non-structural protein vaccine that can prevent disease exacerbation caused by existing vaccines

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See oral presentation:

Concurrent Session 5: Vaccines for Vector-borne Diseases • Tuesday 13 October, 12:40

POSTER 291

Conjugation of polyethylene glycol to whole inactivated influenza virions enhances the hemagglutinin specific humoral response and protection from infection

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Introduction: Whole inactivated virions were used as influenza vaccines (WIV) prior to the development of the current detergent-split, inactivated vaccines. WIVs were replaced because of their greater reactogenicity despite generally better immunogenicity. Prolonging antigen exposure in vivo has recently been identified as a promising strategy to enhance immunogenicity. Slowing antigen release also has the potential to reduce reactogenicity.

Methods: To extend the period of antigen exposure, we conjugated different sized methyl-polyethylene glycol-succinimidyl esters to b-propionolactone-inactivated WIV (A/California/07/2009 (H1N1)) at various concentrations (WIV-PEG). PEG conjugation is a known method to enhance protein stability and retention in vivo. A PEG specific enzyme-linked immunosorbent assay (ELISA) demonstrated successful conjugation and 'optimal' PEGylation density was determined by partial loss of hemagglutination activity. To evaluate these vaccine constructs, female BALB/c mice (6-8 weeks old) were vaccinated intramuscularly with two doses (3 µg/dose) of WIV or WIV-PEG, 21 days apart. A candidate vaccine was identified by measuring serum antibody responses and lung viral load post-infection.

Results: WIV-PEG vaccinated mice generated significantly higher antigen-specific serum IgG titers (~4 fold after prime, ~2 fold after boost) and hemagglutination inhibition (HAI) titers (~2 fold) compared to WIV vaccinated mice after both priming and boosting doses. Although all vaccinated mice were protected from sublethal challenge, vaccination with WIV-PEG significantly decreased lung viral loads in both one and two dose vaccination schedules. These benefits are likely driven by prolonged delivery of antigen to the draining lymph nodes. Current studies are focused on understanding the mechanism(s) that underlie the increased immune response and improved protection. Although there were no obvious differences in weight loss or behaviour between groups, the murine model is an insensitive tool for predicting adverse events for influenza vaccines.

Conclusion: In summary, PEGylation of WIVs may be a simple but effective mechanism to enhance vaccine-induced immune responses and protection. In addition to these immunological benefits, the PEGylated WIV vaccine may reduce adverse events associated with WIV vaccines, although this will need to be evaluated clinically.

POSTER 292

Towards a Next-Generation Leptospirosis Vaccine: Tailoring Immune Responses with LigA and LigB Liposomal PlatformsHenrique PIRES¹, Aline TEIXEIRA², Wagner QUINTILLIO³, Ana Lúcia NASCIMENTO⁴¹ Laboratório de Desenvolvimento de Vacinas, Instituto Butantan, São Paulo, SP, Brasil.² Laboratório de Desenvolvimento de Vacinas, Instituto Butantan, São Paulo, SP, Brasil.³ Laboratório de Biotecnologia Viral, Instituto Butantan, São Paulo, São Paulo, SP, Brasil.⁴ Laboratório de Desenvolvimento de Vacinas, Instituto Butantan, São Paulo, SP, Brasil.

Background: Leptospirosis is an emerging zoonotic disease caused by pathogenic *Leptospira* that affects approximately 1 million people every year. Human vaccines are licensed in some countries but they have some drawbacks as they fail to induce a broad and persistent immune response. Several leptospiral recombinant proteins have already been tested but, they induce partial protective immune response, and they do not promote bacteria clearance from target organs. Thus, the search for new vaccine delivery systems linked with nanobiotechnology is an interesting approach to improve the protective efficiency of recombinant proteins. In this context, liposomes emerge as an innovative method to their versatility and plasticity. Objectives: This project aims to encapsulate the immunogenic domains of LigA and LigB proteins from *L. interrogans* in liposomes.

Methods: The coding sequences (CDS) of the immunogenic domains from LigA (625-1224) and LigB (131-645) were amplified by PCR, cloned into the pET-28a vector, expressed in *E. coli*, and purified by affinity chromatography. A screening with different lipids (DOTAP, DOPE, Egg PC, DSPC, DOPC and CHO) in different ratio and methods (microfluidic and lipid film method) was performed to verify the stability of nanosystem. The two formulations that presented better stability during 30 days were selected for the subsequent tests. Mice were immunized intramuscularly with formulations adsorbed or not with aluminum hydroxide in 15-day intervals and serum was collected for IgG/IgG subtypes titration. Splenocytes were collected for cytokines and lymphoproliferation assays. Mice were immunized intramuscularly with liposomal formulations incorporating 18:1 Liss Rhod PE in their membranes, and monitored for 2 days to assess the local retention of the nanostructures.

Results: In this study, the CDS of LigA and LigB immunogenic domains were successfully cloned, expressed, and purified to be evaluated within two optimized liposomal nanocarriers (DOPC:CHO and EggPC:DOPE:CHO:DOTAP). Both formulations demonstrated exceptional technical performance, exhibiting robust 30-day stability and high encapsulation efficiency. In vivo immunological profiling revealed that both systems elicited high antibody titers and successfully induced a comprehensive panel of key cytokines, including IL-4, IFN- γ , IL-12, IL-17A, and TNF- α . Crucially, the platforms allowed for precise, antigen-specific immunomodulation: LigA-liposomes (LipoA) triggered a balanced Th1/Th2 immune response accompanied by an exceptionally high lymphoproliferation rate, whereas LigB-liposomes (LipoB) effectively polarized the immune system toward a Th2-biased response with low cellular activation. Furthermore, both formulations established a potent 2-day depot effect at the injection site, ensuring sustained antigen retention and prolonged immune presentation.

Conclusion: The formulation of LigA and LigB into liposomes successfully bridges the gap between recombinant protein safety and high immunogenicity. The sustained antigen release at the injection site promoted distinct immune signatures, with LipoA driving a robust, broad-spectrum Th1/Th2/Th17 response and lymphoproliferative response. These nanovaccines represent a major step forward in designing protective immunization against *Leptospira* infection.

POSTER 293

Optimization of Emerging Bundibugyo Ebola Virus Glycoprotein Antigens Using Immunoinformatics-Guided Vaccine Design

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Introduction/Background: The glycoprotein (GP) antigen is the primary target for Ebola virus vaccine development. Analysis of newly emerging Ebola outbreak strains using the iVAX Toolkit revealed markedly reduced T-cell epitope content compared with established vaccine antigens, indicating that vaccines developed with this antigen would be less antigenic than expected. The objective of this study was to assess whether computational antigen optimization could improve vaccine efficacy. We hypothesized that low T-cell epitope density may limit vaccine-induced seroconversion, antibody affinity, and vaccine efficacy and that rational antigen redesign could enhance protective responses.

Materials and Methods: Ebola virus GP sequences from Sudan, Zaire, and Bundibugyo strains were analyzed using the iVAX Toolkit, including EpiMatrix for HLA-DR-restricted T-cell epitope prediction and JanusMatrix for conservation of the T cell epitopes in the GP antigen with the human proteome. Immunogenicity scores were compared with benchmark vaccine antigens and previously studied pathogens. Published data from malaria RTS,S circumsporozoite protein (CSP) and H7N9 influenza hemagglutinin (HA) vaccine investigations were reviewed to evaluate relationships between predicted epitope content and observed vaccine performance. Potential optimization strategies involving incorporation of conserved T-cell epitopes were assessed based on prior antigen-engineering studies. (Methods details are in De Groot et al. 2020).

Results: EpiMatrix analysis demonstrated low predicted immunogenicity for all evaluated Ebola GP antigens. Scores were -2.15 for Sudan Ebola GP, -10.30 for Zaire Ebola GP, and -26.98 for Bundibugyo Ebola GP, placing these antigens below the median immunogenicity score for random proteins (in the negative range of the Immunogenicity Scale) and substantially below effective vaccine antigens such as hepatitis B surface antigen (+80) and influenza hemagglutinin (+20) (Liu et al., 2015; Khan et al. 2020). The Bundibugyo GP score approached values associated with poorly immunogenic antigens, including malaria CSP (-30). Prior studies demonstrated that low EpiMatrix scores accurately predicted poor vaccine performance, including low seroconversion rates observed with H7N9 influenza vaccines.

Discussion/Conclusion: Improvement of Bundibugyo GP antigenicity is possible. In previous studies, computational optimization of H7N9 HA (Jang et al. 2020) through introduction of conserved CD4+ T-cell epitopes resulted in enhanced memory T-cell responses, increased follicular helper T-cell activation, improved antibody responses, and greater protection against lethal viral challenge (in HLA transgenic mice).

Emerging Ebola virus GP antigens, particularly the Bundibugyo variant, exhibit exceptionally low predicted T-cell epitope content, suggesting potential limitations in vaccine immunogenicity, durability, and cross-protective efficacy if used without modification. Evidence from prior malaria and influenza vaccine studies supports the association between low epitope density and reduced vaccine performance. Immunoinformatics-guided antigen optimization using the iVAX Toolkit, including EpiMatrix and EpiCC analyses, may provide a rapid strategy to enhance Ebola vaccine efficacy while preserving antigen structure. Follow-on preclinical evaluation of optimized GP constructs is warranted to support accelerated vaccine development during emerging outbreaks.

POSTER 295

Identifying and Engineering ZIKV E Protein Residues Responsible for DENV Cross-Reactivity to Create an Immunogen that Diminishes Anti-DENV Immune ResponseChristina GO*Integral Molecular*

Development of ZIKV vaccines is complicated by high homology between ZIKV and DENV envelope (E) proteins, resulting in immunological cross-reactivity that can exacerbate disease via antibody-dependent enhancement (ADE). We tested previously epitope-mapped anti-DENV MAbs for cross-reactivity with ZIKV E protein, identifying 70 MAbs of which 66 had epitopes that included at least 1 of 7 E protein residues, establishing these 7 conserved residues as determinants of DENV-ZIKV cross-reactivity. We engineered a ZIKV E protein variant ("ZIKVm10") mutated at these and other residues. ZIKVm10 had reduced cross-reactivity with DENV MAbs and incorporation into subviral particles for mouse immunizations resulted in a reduced induction of anti-DENV antibodies. Passive serum transfer from ZIKVm10-immunized mice conferred near-complete protection against lethal ZIKV challenge and reduced ADE for DENV infection in vitro, providing a pathway for improved ZIKV vaccine design. ADE and neutralization assays in this study were enabled by flavivirus reporter virus particles (RVPs) we have developed for vaccine development and other research. RVPs are produced by expressing in trans CprME and a full-length replicon with the structural genes replaced by a luciferase or GFP reporter gene. RVPs are antigenically similar to live virus, but perform only one round of infectivity, detected by optical readout. RVPs are effective models for DENV1-4, Zika, yellow fever, and West Nile viruses, and have been produced for specific virus variants. RVPs demonstrate reproducible neutralization titer data (NT50) across different production lots, infection volumes, and laboratories, and are stable in long-term storage. Multiple publications show good correlations between NT50 titers obtained using RVPs and live viruses. DENV and ZIKV RVPs have been used in vaccine studies to determine neutralization titers of animal and human sera following immunizations. Extensive characterization has demonstrated that RVPs are safe and convenient reagents for infectivity, neutralization, and ADE studies, including high-throughput analyses.

POSTER 297

Discrete Event and Dynamic Modelling as a Gateway towards the Necessary and Sufficient Conditions of Pandemic Preparedness

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Background: Covid-19 has brought multiple learnings, which should enhance preparedness and response. Recent outbreaks have shown that preparedness is not a free gift for fast and effective response. For infectious diseases, effective and efficient vaccination is yet the best road ahead as it avoids costly therapeutic, health, social and economic burdens. However, there are necessary and sufficient conditions to take into consideration while modelling supports preparedness and response.

Methods: Landmarked by the 100 days mission of CEPI, many private, public and academic organizations prepare for response during non-pandemic times. Keeping facilities, people and procedures warm, reaction times should be minimized within reasonable constraints. Modelling allows consistent decision support through scenario analysis, pointing to bottlenecks, disruptions, reaction time, throughput volumes, scaling, utilization etc.

Results: Taking off with the necessary condition: without vaccine availability, preventive and reactive vaccination are a mirage.

Vaccine manufacturing systems constitute a complex interplay of multiple factors, ultimately boiling down to outputs, for instance throughput volumes or time to first dose, relevant in routine, outbreak and pandemic situations. A digital twin of the manufacturing eco-system is highly valuable, allowing off-line simulation and scenario analysis.

Constructed using a discrete-event simulation methodology, models enable manufacturers and policy makers to quantify the impact of disruptions, uncertainty and bottlenecks to be able to assess mitigation strategies (<https://doi.org/10.48550/arXiv.2602.08988>). Through stakeholders engagement, models embed production processes, QA/QC and raw materials.

A high merit lies in the analysis of event- and decision-based scenarios, such as facility shutdowns, workforce reductions, raw material shortages, infrastructure failures, extended procurement lead times, and increased QA/QC capacity, among others. Upfront bottleneck detection and subsequent debottlenecking resolution(s) are key for resilience. These models, are of interest for policy makers (HERA, ZEPAL, CEPI, WHO, ...), research institutes and manufacturers, who need to collaborate to obtain the best pandemic preparedness and response.

Having a vaccine available is only part of the story: it enters a complex health system in an emergency situation. Sufficiency conditions have to be fulfilled: regulatory protocols and harmonization, distribution, uptake, market efficiency, administration, among others. Special attention is needed to social context, communication and policy execution as it impacts public understanding, acceptance, hesitancy and resistance. Systems thinking, with embedded stakeholder engagement, is needed here. Finally, in some situations, the system that contains the root cause of the emergency can also be modelled and interactively linked with the preparedness and response models. A good example is the emergence of new variants, which dynamically impacts the effectivity of the respective preparedness and response efforts.

Both qualitative (containing stakeholder analysis, system mapping, causal loop diagramming, ...) and quantitative models (system dynamics) are at stake here (<https://doi.org/10.1080/20476965.2021.199230>). Together with discrete event models, they form a consistent knowledge/data base for impactful decision making. On top, scenario analysis with these dynamic models are extremely well suited for future oriented response.

Conclusion: This approach is applied to vaccines, therapeutics and diagnostics but it can be applied to any (non-)emergency response action (non-medical products and services, general emergency responses) towards natural and human-made disasters

POSTER 298

A Universal Genome Backbone for Rapid Generation of Safe and Immunogenic Recombinant Infectious Bronchitis Virus VaccinesSeung-Min HONG¹, Hyuk-Joon KWON^{1,2,3}¹ Geniner Co., Ltd., 1 Gwanak-ro, Gwanak-gu, Seoul 08826, Korea, Republic of (South Korea)² bLaboratory of Poultry Production Medicine, Seoul National University, 1 Gwanak-ro, Gwanak-gu, Seoul 08826, Korea³ Research Institute for Veterinary Science, College of Veterinary Medicine, Seoul National University, 1 Gwanak-ro, Gwanak-gu, Seoul 08826

Introduction: The global co-circulation of genetically diverse infectious bronchitis virus (IBV) genotypes has increased the demand for vaccine strains that closely match field viruses. In particular, GI-19 (QX-like) and the rapidly expanding GI-23 genotype exhibit substantial genetic diversity, with S1 amino acid identities ranging from approximately 84–97% among circulating strains. Antigenic mismatch between vaccine and field strains can reduce vaccine efficacy and may contribute to the emergence of novel variants through continued viral circulation and recombination. Therefore, a platform capable of rapidly generating safe and effective vaccine strains that closely resemble currently circulating field viruses is highly desirable. Previously, we developed an embryo- and cold-adapted GI-19 (KM91-like) strain, designated caKII, and established a reverse genetics system using this strain as a vaccine backbone. The present study evaluated whether the caKII genome backbone could serve as a universal platform for generating diverse recombinant IBV vaccine strains while retaining favorable biological characteristics.

Methods: The attenuated caKII strain was originally generated through serial embryo passage and cold adaptation and was selected as a vaccine backbone because of its high replication efficiency, safety, and immunogenicity. A CPER (Circular Polymerase Extension Reaction)-based reverse genetics platform was established using the complete caKII genome. Spike genes from three Korean GI-19 QX-like sub-genotypes (III, IV, and V), one GI-15 genotype strain, and three GI-23 strains originating from Brazil, Egypt, and the Middle East (IBV/GI23/Brazil/2022/VarML1, EGYPT-PG181, and IS/1494/06) were individually introduced into the caKII backbone to generate chimeric recombinant viruses. Virus recovery and growth characteristics were evaluated in embryonated chicken eggs. Safety was assessed by monitoring viral clearance and histopathological lesions, and protective efficacy was evaluated using previously established challenge models.

Results: All targeted recombinant viruses were successfully rescued using the CPER-based platform. Recombinant vaccine strains representing multiple geographically and genetically distinct IBV lineages were generated efficiently. Regardless of spike gene origin, all recombinant viruses exhibited growth characteristics comparable to the parental caKII strain, reaching titers exceeding 108.0EID50/mL in embryonated eggs. In safety evaluations, the recombinant viruses demonstrated rapid viral clearance and did not induce significant histopathological lesions. Furthermore, they elicited robust protective immunity against homologous challenge viruses. These results indicate that the attenuated caKII genome backbone maintains its desirable phenotypic properties, including high productivity, safety, and immunogenicity, even after replacement with highly divergent spike genes from different IBV genotypes.

Discussion: Effective control of IBV requires vaccine strains that closely match circulating field viruses in each region. The caKII-based reverse genetics platform provides a practical strategy for rapidly updating vaccine strains by replacing only the spike gene while preserving a well-characterized, safe, and highly productive genome backbone. The ability of the caKII backbone to retain its favorable biological characteristics across diverse recombinant viruses suggests that it can serve as a versatile platform for generating customized vaccines against newly emerging IBV variants. This approach may facilitate faster vaccine deployment, improve field protection, and contribute to sustainable control of infectious bronchitis in poultry production systems worldwide.

POSTER 299

Gardasil-9 Benchmarks for mRNA HPV Vaccine Evaluation: Type-Specific Responses and Predicted L1 Structural FeaturesTimothy AN¹, Hyogyong HWANG², Jeong-in KIM², Eun-hye SEO³, Pil-gu PARK⁴, Kee-jong HONG^{1,2,3}¹ Department of Bio-Medical Sciences, Gachon University, Republic of Korea² Lee Gil Ya Cancer and Diabetes Institute, Gachon University, Republic of Korea³ Department of Microbiology, Gachon University, Republic of Korea⁴ Department of Life Science, Gachon University, Republic of Korea

Background: Licensed virus-like particle (VLP)-based human papillomavirus (HPV) vaccines, such as Gardasil-9, provide highly effective protection against major disease-associated HPV types. However, HPV comprises a large number of genotypes, and current prophylactic vaccines cover only selected high-risk or clinically prioritized types. mRNA vaccines may provide a flexible platform for rapid development of HPV vaccines against additional target types, but standardized criteria for evaluating mRNA HPV vaccine candidates remain insufficiently defined. Because protective immunity against HPV largely depends on neutralizing antibodies that recognize properly presented L1 conformational epitopes, antigen structure may also be an important consideration for mRNA vaccine design. This study aimed to establish a Gardasil-9-based immune benchmarking framework for mRNA HPV vaccines and to explore whether predicted L1 structural features may help interpret type-specific differences in vaccine responses.

Material/Methods: HPV virus-like particles and luciferase-expressing pseudoviruses were generated for VLP-based ELISA and pseudovirus-based neutralization assays. Gardasil-9 and NIBSC international standard serum were used to support benchmark-based quantification of vaccine-induced antibody responses. Binding antibody responses were expressed as arbitrary units per milliliter (AU/mL), and neutralizing antibody responses were evaluated using 293TT cell-based pseudovirus neutralization assays and expressed as neutralizing titers. Protective efficacy was assessed using a Depo-Provera-treated mouse pseudovirus challenge model followed by IVIS imaging. mRNA vaccines encoding HPV16 and HPV18 L1 antigens were synthesized and evaluated for antigen expression, binding antibody responses, neutralizing activity, and protection. AlphaFold-based structural modeling was used to compare predicted monomeric and pentameric L1 models of HPV16 and HPV18. Model confidence and predicted aligned error patterns were examined to assess differences in predicted structural reliability and inter-chain organization.

Results: The Gardasil-9-based framework enabled integrated evaluation of binding antibody responses, neutralizing activity, and in vivo protection. Under the same experimental framework, HPV16 L1 mRNA induced higher binding antibody responses, neutralizing activity, and protection in the pseudovirus challenge model, whereas HPV18 L1 mRNA showed limited immunogenicity and protective efficacy. AlphaFold-based modeling suggested differences in model confidence and predicted aligned error patterns between HPV16 and HPV18 L1 pentamer models, indicating that predicted structural reliability may differ between the two antigens. These observations suggest that predicted L1 structural features may help interpret type-specific differences in antigenicity and protective immune responses. Based on this hypothesis, chimeric or substitution-based L1 antigens incorporating HPV18 epitope-containing regions into an HPV16-based backbone are being generated for further evaluation.

Conclusion: This study establishes a Gardasil-9-based immune benchmarking approach for mRNA HPV vaccine evaluation and identifies type-specific differences between HPV16 and HPV18 L1 mRNA vaccine responses. The findings further suggest that AI-assisted structural modeling may provide useful information for interpreting antigen performance and prioritizing candidates for experimental validation. Integrating immune benchmarks with predicted antigen structural features may support rational assessment and future development of next-generation mRNA HPV vaccines.

POSTER 300

Establishment of a Pseudovirus System for Nipah Virus Research

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Background: Nipah virus is a highly pathogenic henipavirus associated with severe human disease and high case-fatality rates. Research using authentic Nipah virus requires maximum biocontainment, limiting the accessibility of vaccine and antibody evaluation. Pseudovirus-based systems provide a biosafe alternative for studying viral entry and measuring neutralizing antibody responses. This study aimed to establish a vesicular stomatitis virus delta-G luciferase reporter-based Nipah virus pseudovirus platform for use in vaccine candidate and therapeutic antibody evaluation.

Materials/Methods: Nipah virus pseudoviruses were generated using a VSV-ΔG-Luc reporter system complemented with Nipah virus F and G glycoproteins in a mammalian producer-cell platform. Pseudovirus-containing supernatants were harvested, clarified, and concentrated for downstream assays. Infectivity was evaluated using a luciferase reporter assay in susceptible target cells. To assess functional applicability, neutralization assays were performed using Nipah virus-specific antisera, and reporter activity was compared with appropriate negative and virus-only controls.

Results: VSV-based Nipah virus pseudoviruses were successfully generated and produced measurable luciferase reporter signals in target cells, indicating functional glycoprotein-mediated entry. The reporter-based infectivity assay provided a quantifiable readout suitable for evaluating pseudovirus infection. In neutralization assays, Nipah virus-specific antisera markedly reduced reporter activity compared with control conditions, demonstrating that the system can detect antibody-mediated inhibition of pseudovirus entry.

Discussion: These findings support the feasibility of a VSV-based Nipah virus pseudovirus platform as a biosafe and practical surrogate system for Nipah virus vaccine research. By enabling reporter-based infectivity and neutralization assays under lower-containment conditions, this platform may facilitate the screening of vaccine candidates and therapeutic antibodies against Nipah virus. Further optimization and standardization of assay performance will support its broader application in emerging infection preparedness and vaccine evaluation.

POSTER 302

A Flagellin-Adjuvanted DC-Targeting Mucosal Vaccine Confers Effective Protection Against *Streptococcus pneumoniae* via Coordinated Th17 and Antibody Responses

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Current PCV pneumococcal vaccines are highly effective against vaccine-included serotypes. However, their protective efficacy remains limited by serotype-restricted coverage, serotype replacement, and poor protection at the portal of entry. Th-17 mediated neutrophil responses at respiratory mucosae was proved to be a requisite for the prevention of initial stage of pneumococcal infection. There exists the need for alternative mucosal vaccine strategies capable of inducing protective antibody responses in both mucosal and systemic compartments together with Th17 immunity that supporting neutrophil recruitment and bacterial clearance.

Herein, we developed a mucosal vaccine platform comprising a DC-targeting peptide promoting efficient antigen delivery to dendritic cells and mucosal adjuvant flagellin along with pneumococcal protein antigen PspA. Our results showed that mucosal vaccination selectively increased conventional dendritic cell populations in cervical lymph nodes, suggesting enhanced antigen presentation and T-cell priming at mucosal-draining sites. This response was accompanied by the induction of Th1- and Th17-type immunity against the pneumococcal antigen. The vaccine elicited robust mucosal and systemic protective antibody responses, including secretory IgA and circulating IgG. Together, these coordinated humoral and cellular immune responses were associated with effective protection against live pneumococcal challenge. These findings suggest that our protein-based mucosal vaccine platform should serve a promising strategy to overcome the limitations of current serotype-restricted PCV pneumococcal vaccines by inducing balanced antibody and T-cell immunity in both mucosal and systemic compartments.

POSTER 305

A flagellin-IL-15 fusion adjuvant for enhanced mucosal immunity against influenza

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Influenza remains a major global public health threat. Conventional parenteral influenza vaccines primarily induce systemic IgG responses but often provide limited immune protection at the respiratory mucosa. Thus, there is an urgent need to develop mucosal vaccine strategies that elicit local protective immunity and enhance overall protection against influenza infection. Flagellin activates Toll-like receptor 5-dependent innate immune pathways, whereas interleukin-15 (IL-15) supports natural killer cells and memory CD8⁺ T cells. Here, we developed Sushi-IL-15-FlaB (SIB), a recombinant fusion adjuvant that physically integrates the IL-15/IL-15R α Sushi complex with *Vibrio vulnificus* FlaB. Intranasal co-administration of SIB with H1N1 influenza antigen enhanced both systemic and mucosal immune responses in BALB/c and C57BL/6 mice. SIB-adjuvanted intranasal vaccination promoted T follicular helper cell responses and expanded germinal center B cells in the cervical lymph nodes. It also induced durable antigen-specific immune responses across mouse strains, including increased antigen-specific plasma cells and memory B cells, as well as antigen-specific cytokine production (IL-4, IFN- γ , and IL-17A). These immune responses were associated with reduced pulmonary viral RNA burden and robust protection against lethal influenza challenge. Furthermore, in BALB/c mice, vaccine-induced protection was abolished by CD4⁺ T cell depletion but was less affected by CD8⁺ T cell depletion. In contrast, in C57BL/6 mice, depletion of either CD4⁺ or CD8⁺ T cells partially impaired vaccine-mediated protection, as reflected by increased body-weight loss after viral challenge. NK cells also contributed to early-phase protection.

POSTER 308

Systematic Screening of Genome-Wide Deletion-Tolerant Regions in Chikungunya Virus for the Design of Novel Live-Attenuated Vaccines

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Introduction: The Chikungunya virus (CHIKV) is a single-stranded positive-sense RNA virus transmitted by mosquitoes. When it infects humans, it causes symptoms such as fever, rash, chronic joint pain and in severe cases, encephalitis. Climate change has led to the global expansion of epidemic areas, highlighting the importance of vaccination against CHIKV. Aiming to develop new live-attenuated CHIKV vaccines, we first established a novel method to comprehensively identify positions within the viral genome where deletion mutations can be introduced. Then, we constructed strains with different mutations and characterized them in vitro and in vivo.

Methods: Using the MuA transposon system, we introduced 3-base-pair deletions ($\Delta 3$) at random positions within the plasmid containing the CHIKV SL1131 strain's genome, without shifting the reading frames. We transfected the plasmid library into cells of different species to generate virus libraries. Viral RNAs isolated from these libraries were analyzed by next-generation sequencing (NGS) to determine the location and frequency of the $\Delta 3$. Using this information, we constructed clones containing specific deletions via reverse-genetics and evaluated their virulence and immunogenicity in mice.

Results: The NGS analysis revealed that $\Delta 3$ were enriched within specific regions of the viral genome, suggesting that these hot-spots possess mutational tolerance. Furthermore, analysis of the virus libraries after 5 passages in mammalian and mosquito cell-lines led to the discovery of distinct regions that could be important for viral replication in a host-cell-specific manner. Thirteen clones containing individual $\Delta 3$ were constructed and infectious clones were successfully amplified to perform in vivo immunogenicity and pathogenicity experiments. Our results indicated that some clones showed attenuated phenotypes but elicited neutralizing antibodies.

Conclusion: We established a method to determine sites permissive for $\Delta 3$ mutations in the CHIKV genome, some of which led to attenuated phenotypes. This approach proved to be suitable for screening promising mutations for viral vectors and provides a platform for the development of live attenuated vaccines for various viruses.

POSTER 309

Intramuscular delivery of LNP-formulated trans-amplifying RNA for versatile and efficacious vaccination at nanogram doses

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Introduction/Background: Trans-amplifying RNA (taRNA) is a split-vector system consisting of non-replicating messenger RNA (mRNA) encoding an alphaviral replicase and an antigen-encoding transreplicon (TR). Previous studies with non-formulated, intradermally-injected taRNA demonstrated protective immunity at low TR doses due to TR amplification by replicase. Based on these encouraging data, we set out to mechanistically characterize and functionally validate the taRNA platform for intramuscular vaccination using taRNA formulated within lipid nanoparticles.

Material/Methods: To establish taRNA as an RNA-based modality for intramuscular immunization by formulating it within lipid nanoparticles we investigated its mechanism of action by elucidating its in vivo biodistribution via quantification of luciferase signals and immunohistochemistry in various organs and evaluated its potential for repeated vaccination by immunogenicity and challenge studies in mice.

Results: In mice, biodistribution studies showed that TR-encoded luciferase expression is focused on the injection site and its draining lymph nodes. Immunohistochemistry further showed that TR was mainly expressed in macrophages and dendritic cells in the subcapsular sinus of lymph nodes draining the injection site. Prime-boost immunization with nanogram doses of replicase-encoding mRNA (REPL) and TR encoding the model antigen influenza hemagglutinin (HA) resulted in TR dose-dependent antigen-specific antibody and T-cell responses. Doses in the nanogram range protected mice from lethal influenza virus infection. We furthermore demonstrated the feasibility of sequential vaccinations with taRNA, despite induction of T-cell responses against replicase.

Discussion/Conclusion: Together, these data support the potential for taRNA as a versatile and dose-efficient platform for infectious disease vaccines. LNP-formulated taRNA delivered IM can induce protective immune responses at very low antigen-encoding TR doses and can be applied in subsequent vaccination regimens, warranting further preclinical optimization to assess its clinical applicability.

POSTER 310

Neutrophils are the dominant early responders to a potent liposomal vaccine adjuvant

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See oral presentation:

Concurrent Session 1: Adjuvants • Monday 12 October, 16:50

POSTER 311

Antibody reactions against influenza in cynomolgus macaques remain stable over time with increased avidity and somatic hypermutation

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The antibody response formed after a first exposure to influenza is thought to have a major impact on the response to subsequent exposures. However, it is not completely understood how long such initial responses persist in the absence of any new stimulation. In humans, such studies are hampered by the complex exposure history in adults and studies in children that have undergone a first infection are very few and only followed for a relative short time.

Here, we studied the longevity of the antibody and B cell response against the haemagglutinin (HA) protein in adult macaques after a single exposure to pandemic H1N1 virus. The macaques were infected with Influenza A/Mexico/InDRE4487/2009 and followed over a four-year period. Using haemagglutinin-specific (HA) protein probes we analysed antibody responses in serum as well as HA specific B-cells in the PBMC fraction and analysed the B cell receptor heavy chain sequences of these cells at day 56 and four years after infection.

Antibody binding as well as virus neutralization titres in serum remained stable from day 56 to four years after infection. Antibody binding strength, as detected by high urea ELISA, even increased. In contrast, the frequency of HA-specific B-cells was decreased significantly over time. These remaining B-cells showed however significantly higher SHM levels attesting to an ongoing process of affinity maturation. Binding specificities of these B-cells to the HA-head and HA-stem domain were unaltered four years after infection, as shown both by FACS analysis using these antigens and by testing the specificity of monoclonal antibodies generated from these B-cells.

Based on these results, we conclude that a single infection with influenza can elicit long-term antibody responses, that will mature over time, despite lack of re-exposures. Not only the first exposure itself, but also the subsequent further maturation may affect future responses and affect optimization of vaccine strategies.

POSTER 314

Safety, Reactogenicity and Immunogenicity of a Launch-iT Rabies Vaccine: A Randomized, Double-Blind, Placebo-Controlled, Dose-Escalation Phase 1 Study in Healthy Adults

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See oral presentation:

Plenary Session 3: Vaccine Technology • Tuesday 13 October, 10:15

POSTER 315

RSV Burden in Hospitalized Palestinian Children: A Pre-Immunization Burden Baseline to Support RSV Vaccination Program Introduction in an LMIC Setting

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Introduction/Background: Respiratory Syncytial Virus (RSV) is the leading cause of acute lower respiratory tract infection in infants and young children, a pathogen that disproportionately affects low- and middle-income countries (LMICs), where 97% of attributable deaths occur. Nirsevimab and maternal RSVpreF vaccination are safe, and efficient early infancy RSV prevention strategies. However, implementation of vaccination programs requires local burden data. The West Bank, Palestinian Territories, an LMIC, has no published pre-immunization baseline of RSV hospitalization burden, leaving policymakers without the evidence necessary to model the population-level impact of introducing RSV prophylaxis.

Material/Methods: We conducted a single-center retrospective cohort study of laboratory-confirmed RSV admissions at Caritas Baby Hospital, West Bank, the primary tertiary pediatric referral center in the region, between June 2021 and July 2025. The primary cohort comprised 2,306 community-acquired admissions in children aged 0–60 months. Fifty-nine clinical, sociodemographic, and resource-utilization variables were analyzed. Severe clinical course was defined as a composite of ICU admission, mechanical ventilation, in-hospital mortality, or length of stay exceeding 6 days. Multivariable logistic regression identified independent predictors of severe course.

Results: Over four RSV seasons, 86.9% of total admissions were infants younger than 12 months; the 1–<3 month age group alone accounted for 37.2% of hospitalizations and 41.4% of cumulative direct costs (total: 1,900,000 EUR). Admissions displayed seasonality, with 85.2% occurring between October and February. Severe course occurred in a total of 22.8% of admissions, ICU admission occurred in 7.8%, with admissions from October 2023 onward carrying a higher odds of severe course (aOR 1.28, 95% CI 1.02–1.61). Independent predictors of severe course also included age 0–<1 month (aOR 10.28, 95% CI 6.00–17.62), age 1–<3 months (aOR 4.41, 2.77–7.04), premature birth (aOR 2.01, 1.51–2.67), co-infection (aOR 2.41, 1.81–3.21), and pneumonia (aOR 5.77, 3.99–8.35).

Discussion/Conclusion: This study establishes the first pre-immunization burden baseline for RSV in the region, demonstrating that RSV burden is concentrated in the youngest infants, accompanied by substantial critical care use, and direct hospital spending, and follows a predictable October to February seasonality, with increasing rates of severe clinical course coinciding regional conflict-driven health system strain. These findings support prioritization of RSV immunization strategies, enable the construction of a population impact model for RSV vaccine introduction in Palestinian Territories by applying published vaccine real-world effectiveness, and contribute LMIC-specific evidence to the global evidence base on the population-level benefits of RSV immunization programs.

POSTER 316

ArboSero: a High-Throughput and Validated Arbovirus Serology Platform

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Arthropod-borne viruses (arboviruses) pose a rapidly expanding global health threat. Currently, more than half of the world population is at risk of dengue virus infection, while recent outbreaks of chikungunya virus and Oropouche virus across Latin America further emphasize the increasing burden of arboviral infections. Climate change, urbanization, and increased global mobility are driving the expansion of arthropod vectors (mosquitoes, ticks, and midges) and the viruses they transmit into tropical as well as more temperate regions.

Despite a growing threat, diagnostic capacities remain underdeveloped and not adequately prepared to meet growing needs. Current approaches are constrained by a limited specificity (e.g., flavivirus cross-reactivity in ELISA), a narrow diagnostic window (e.g., difficulty to pick up short-lived viremia by PCR), and poor scalability. The classical plaque reduction neutralization test (PRNT) is the gold standard for arboviral serology, but inherently remains constrained by a low throughput and labor-intensive workflows, high biocontainment requirements, and finally operator-dependent data interpretation. Consequently, both high-income countries as well as low- and middle-income countries (LMICs) remain insufficiently prepared for future outbreaks, while valuable immunological information from clinical trials and serosurveys remains largely underexploited.

To address this gap, we developed ArboSero, a high-throughput arbovirus serodiagnostics platform centered around a fluorescence-based microneutralization assay (SNT-FLUO). SNT-FLUO matches the sensitivity and specificity of PRNT while requiring minimal sample volumes (μL serum volumes) and enabling rapid turnaround (3-5 instead of 7-10 days), scalability (several hundred assays a day), automation, and cost efficiency. The assay has been validated against ISO15189-accredited PRNT and allows the integration of single-round infectious particles (SRIPs), enabling BSL-2 compatibility for pathogens that normally require high BSL-3 containment. We further demonstrated (i) multiplexing of arboviruses using distinct fluorescent reporters (e.g., differential diagnosis for JEV, YFV, and DENV2), as well as (ii) proof-of-concept for functional assay integration (e.g., antibody-dependent enhancement), thereby increasing the analytical depth of the platform. Current efforts focus on validating a comprehensive DENV program covering all four serotypes and multiple genotypes in SRIP format.

ArboSero aims to provide scalable, high-quality arbovirus diagnostics translatable to vaccine and antiviral development, surveillance, and outbreak response without compromising gold-standard sensitivity or specificity. Together with the VirusBank Platform, ArboSero is working towards ISO accreditation by 2027/2028 to further support this vision. By bridging the gap between diagnostic innovation and implementation, ArboSero addresses an urgent unmet need and has the potential to serve as a reference platform for arbovirus serology, to support R&D and public health in both high-income and resource-limited settings.

POSTER 317

A deep dive into safety: 2.5 year follow up of chikungunya virus (CHIKV) virus-like particle (VLP) vaccine

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Bavarian Nordic

The CHIKV VLP vaccine, licensed in the US, EU/EEA, and UK for the prevention of chikungunya disease in individuals aged 12 years and older, starts eliciting high titers of neutralizing antibodies at seroprotective levels as early as 1 week postvaccination. Here we report clinical safety data up to 2.5 years postvaccination. The initial CHIKV VLP safety population included 3141 vaccinated and 675 placebo participants across 5 clinical trials, who were followed for 6 months: 217 adolescents (12-17 years), 2738 adults (18-65 years), and 186 older adults (>65 years) received a single dose of CHIKV VLP vaccine. An ongoing 5-year follow up trial (n=711) is evaluating long-term immunogenicity and safety. In the initial safety population, the most frequently reported solicited adverse events (AEs) in individuals 12-64 years were injection site pain (24%), fatigue (20%), headache (18%), and myalgia (18%), and in individuals ≥65 years were injection site pain (5%), myalgia (6%), and fatigue (6%). Most solicited AEs were grade 1 or 2 in severity and lasted a single day. Older adults were the least likely to report AEs (solicited 11%, unsolicited 14%). Serious AEs (SAEs), all unrelated to treatment, occurred in 1.0% of vaccine and 0.6% of placebo participants. AEs of special interest (AESI: new onset or worsening arthralgia that was medically attended) occurred in 6 participants in the vaccine group; 3 (0.1%) were deemed treatment-related; all were nonserious and grade 1 or 2 in severity. No neurological or cardiac safety signals were observed; there were 4 unrelated grade ≥3 neurological AEs (all had relevant medical history) and no grade ≥3 cardiac AEs. Three unrelated deaths occurred during the trials. In the follow up trial, through 2.5 years postvaccination, there were 7 SAEs (all in 18-65 year-olds and all unrelated), no AESI, no neurological or cardiac AEs, and no deaths. CHIKV VLP is a virus-like particle vaccine, as such it cannot replicate or cause infection/ disease and can be used for a broad range of people. The safety data 2.5 years postvaccination shows a continued favorable safety profile with no observed safety signals, including in older adults.

POSTER 318

Selective Induction of Antibody Responses Reveals Antibody-Mediated Tumor Control in a Melanoma Model

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Introduction/Background: The development of cancer vaccines has largely focused on the identification and targeting of tumor antigens, including neoantigens and tumor-specific antigens. Despite this antigen-centric approach, clinical efficacy remains limited. One potential explanation is that vaccine design often does not distinguish between the different types of immune effector mechanisms that are required, such as antibody-mediated versus T cell-mediated cytotoxicity, which may differ substantially in their capacity to control tumor growth. This study aimed to evaluate the contribution of antibody-mediated vaccine responses to tumor control in the absence of a cellular immune response.

Materials/Methods: C57BL/6 mice were vaccinated in a prophylactic setting on days 0 and 14 with a yellow fever 17D-based vaccine encoding a 25 amino acid epitope derived from the extracellular loop of human CD20 (hCD20), which induces antibody responses without eliciting antigen-specific T cell immunity.

To enable selective targeting, a B16 melanoma cell line stably expressing hCD20 was generated using a lentiviral transduction system, allowing antibody-specific recognition of tumor cells. Vaccinated (n=6) and sham-vaccinated (n=8) mice were subsequently challenged with these B16-hCD20 tumor cells on day 28.

Tumor progression was monitored longitudinally using bioluminescent imaging and caliper measurements, enabling quantitative assessment of tumor growth kinetics, and survival was recorded.

Results: Vaccination induced a focussed anti-hCD20 IgG response which was associated with improved survival, with 66% of vaccinated mice remaining alive at 21 days post-challenge, whereas all sham-vaccinated animals reached a humane endpoint within the same timeframe.

Consistent with this survival benefit, vaccinated mice exhibited delayed tumor progression compared to controls, as assessed by both bioluminescent imaging and physical tumor measurements. These observations indicate that antibody-mediated responses exert a measurable and sustained effect on tumor outgrowth in this synthetic model.

Discussion/Conclusion: These findings demonstrate that antibody responses, in the absence of antigen-specific T cell immunity, can mediate measurable tumor control in vivo. By experimentally separating the type of effective immune response induced by vaccination, this study provides direct evidence of the functional contribution humoral immunity may have on anti-tumor activity.

Building on this, the system provides an opportunity to investigate how antibody-mediated tumor cell killing shapes downstream anti-tumor immune responses. Particularly, it enables interrogation of processes such as immunogenic cell death and subsequent antigen spreading, which are thought to be critical determinants of durable and broad anti-tumor immunity. By enabling the study of these processes in a setting where the initiating immune effector mechanism is defined, this approach may help to clarify how distinct immune responses influence the quality and persistence of tumor control.

POSTER 319

Comparative Fc functions, immunoglobulin type signatures, B-cell responses, and neutralisation after Omicron XBB-adapted PHH-1V81 and BNT162b2 COVID-19 boosters

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Introduction/Background: Immune-evasive SARS-CoV-2 variants have spurred Omicron-adapted COVID-19 booster development, including the adjuvanted Omicron XBB.1.16 receptor-binding domain (RBD) protein vaccine PHH-1V81 (HIPRA). While serum neutralisation remains the standard readout of vaccine-induced antibody immunity, Fc-dependent effector functions mediated by cytophilic IgG subclasses and mucosal immunity by IgA may be important against SARS-CoV-2 variants that evade neutralising antibodies. However, the determinants and functions of PHH-1V81-elicited antibodies remain incompletely characterised.

High-affinity protective antibodies are induced by memory B cells (MBCs) that rapidly proliferate upon antigen reencounter and differentiate into antibody-secreting cells. The increased stability and cross-variant breadth of the MBC repertoire, compared to serum antibodies, make MBCs a key target for characterising vaccine-elicited responses.

This study compared the antibody and B-cell immunogenicity of PHH-1V81 with that of mRNA-based XBB.1.5-adapted BNT162b2 (Pfizer/BioNTech), when administered as boosters to adult volunteers with established hybrid immunity, and characterised antibody types/subtypes, specificities, functions, and MBC phenotypes.

Material/Methods: This study included subjects from the HIPRA-HH-14 clinical trial (NCT06181292). Adults aged ≥ 18 years were included in November 2023 at ten clinical sites in Spain, and study visits were finalised in June 2024. Participants had previously received a primary series of two doses and ≥ 1 booster dose of an EU-approved mRNA vaccine, with the last dose administered ≥ 6 months before inclusion, and tested SARS-CoV-2-negative at day 0 (D0). Participants randomly received a single intramuscular dose of PHH-1V81 (N = 404 for antibody outcomes; N = 27 for B cell outcomes) or BNT162b2 XBB.1.5 (N = 191 and N = 13, respectively). Blood samples were collected pre-booster (D0), on day 14 (D14), and at month 3 (M3) after booster, while peripheral blood mononuclear cells (PBMCs) and paired sera were obtained at D0 and D14.

Levels of IgM, IgA, IgG subclasses 1-4, and C1q- and FcγR-binding antibodies (IA, IIA, IIB, and IIIA) were measured using multiplexed antigen-coupled microspheres (nucleocapsid (N), spike (S), and RBD of ancestral WH1 and vaccine-target XBB variants). Total IgG were measured by electrochemiluminescence immunoassay. Immunophenotyping of lymphocyte populations was performed on PBMC samples with recombinant RBD antigens. Neutralisation titres were assessed using a pseudovirus-based neutralisation assay expressing S protein.

Results: Compared to homologous boosting, PHH-1V81 induced higher and more durable RBD-specific IgA through M3, alongside stronger RBD-specific IgG1-4 and C1q/FcγR-binding antibodies. BNT162b2 increased S-specific IgG, particularly IgG3, and S-directed functional antibodies. Both boosters elicited a cytophilic-to-non-cytophilic response shift post-D14. PHH-1V81 sustained Omicron cross-recognition, reducing ancestral variant immune imprinting, and predicted lower breakthrough risk via IgG1, XBB neutralisation, and C1q binding, with FcγR binding showing a similar protective trend. Both vaccines significantly increased ancestral-reactive B

cells cross-recognising the vaccine homologous variant. Notably, PHH-1V81-induced XBB.1.16 cross-reactive B cells were associated with neutralising responses.

Discussion/Conclusion: Overall, PHH-1V81 induced a robust, RBD-centred protective functional antibody profile and B-cell response, in contrast to BNT162b2. Although the smaller sample size of BNT162b2 arm could limit some analyses, the protection and neutralisation correlation results reinforce the potential of PHH-1V81 as a strong booster candidate against emerging SARS-CoV-2 variants.

POSTER 320

Lipid Nanoparticles Incorporating Pathogen Recognition Receptor Agonists Shape Distinct Immunological Patterns and Enhanced Vaccine Responses.

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Lipid nanoparticles (LNPs) function not only as delivery vehicles for mRNA but also as potent vaccine adjuvants. The combination of adjuvants in vaccines has been used frequently to enhance the immune-activating function of vaccine adjuvants. We utilized systems serology to screen a range of adjuvants to identify candidates that synergize with LNPs. Herein, we determined that a TLR7/8 agonist (TLR7/8a) adjuvant incorporating LNPs exhibited a unique IgG subclass profile, with increased Fc Receptor binding and enhanced germinal center responses. In an influenza study using a new LNP formulation, the incorporation of TLR7/8a similarly improved the humoral response, with increased potency and breadth. Cellular immunity against influenza was also enhanced in the LNP group incorporating the adjuvant, with increased Th1 responses. The accessibility of the lipid adjuvants used in this study and the scalability of LNPs offer great promise for the applicability of combination adjuvant LNPs in future mRNA vaccines.

POSTER 322

Identifying CD4+ T cell Epitopes in Poliovirus Uncovers Epitopes in the Nonstructural Domain

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Enteroviruses are a pervasive group of RNA viruses associated with human diseases in the Picornaviridae family. The polyprotein is composed of 11 proteins: 4 structural proteins (VP1-4) and 7 nonstructural proteins (P2A, P2B, P2C, P3A, Vp1, P3C, Rdrp). Annually, Enteroviruses cause a wide range of diseases affecting approximately 40 million people in the United States and leading to many hospitalizations. Poliovirus, the causative agent of poliomyelitis, is the only member with FDA-approved vaccines in the US. Its near eradication is attributed to two vaccines: Oral Poliovirus Vaccine (OPV) and Inactivated Poliovirus Vaccine (IPV). Despite contributing to herd immunity, OPV was discontinued due to the increased risk of vaccine-associated paralytic poliovirus. Previous literature establishes the role of T-cells in Poliovirus infection outcomes, but little is known about the specific antigens involved in shaping the different immune response between OPV and IPV-vaccinated individuals. Further concerns associated with non-poliovirus Enteroviruses have prompted examination into how Poliovirus vaccines could offer broader Enterovirus protection.

The study's main focus is to identify Poliovirus epitopes. 30 donors were recruited from San Diego and PBMCs were isolated from their blood donations. Poliovirus vaccination is required in the United States; thus, we selected Poliovirus Type 1 Mahoney as the prototype for Enteroviruses and synthesized peptides, fifteen amino acids in length overlapping by 10 residues, spanning the entire proteome. Two separate megapools (MPs), Structural (S) and Nonstructural (NS) were made. The MPs were used to stimulate PBMCs for in vitro expansion of memory antigen-specific T-cells. The immunoprofile was characterized using Intracellular Cytokine Staining (ICS) flow cytometry and FluoroSPOT assays to define the epitopes that drive T-cell response by measuring cytokines and total IFN γ signal, respectively. Additionally, we analyzed conservation across the Picornaviridae family.

Overall, we identified 149 epitopes between both S (62 epitopes) and NS (87 epitopes) proteins. Of the proteins tested, epitopes from VP2, P2C and Rdrp were the most immunodominant, with VP2 having the highest frequency of responders at 62.95%. Stratifying the data by vaccine type presented no differences in CD4+ T-cell MP response.

Comparisons showed immunogenicity was not necessarily correlated to protein size: VP2 and Rdrp are positively correlated, but proteins like VP1 or VP3 had weak immunogenicity despite their size. Juxtaposing the magnitude of response with median conservation, there are regions that are both immunodominant and highly conserved within the Enterovirus genus, particularly non-Polio Enterovirus C. This suggests that these segments are biologically essential for the virus and have the potential to induce T-cell responses able to recognize other Enteroviruses.

Our study decodes the immunogenic epitopes of Poliovirus recognized by CD4+ T-cells across the full polyprotein and investigates if specific antigens promote differences in OPV and IPV mechanisms and efficacy. Both currently available vaccine formulations for Poliovirus allow for recognition of the capsid shell, meaning any protective neutralizing antibodies are generally mapped to the VP1-3 proteins. By building a robust Poliovirus T-cell epitope library, we can guide future Poliovirus studies and unravel the underestimated contribution of Poliovirus T-cell cross-reactivity in building comprehensive immunity applicable to Enteroviruses.

POSTER 323

Anti-HIV ADCC and ADCP Functions Mediated by Monoclonal Antibodies

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Background: Human antibodies provide important immunity against HIV infection and function through two distinct functional domains: the antigen-binding fragment (Fab), which mediates viral neutralization, and the crystallizable fragment (Fc), which recruits immune effector mechanisms. Broadly neutralizing antibodies (bNAbs) that act through Fab-mediated neutralization have been well characterized using robust high-throughput assays. In contrast, antibodies that mediate antiviral activity through Fc-dependent effector functions remain less well understood due to the limited availability of sensitive, specific, and reproducible assays. This study aimed to optimize HIV antibody Fc functional assays by evaluating multiple effector cell platforms and by developing mechanism-of-action (MOA)-based surrogate assays to improve the detection and quantification of Fc-mediated antiviral activity.

Methods: An Fc effector functional assay consists of three key components: HIV-infected target cells, monoclonal antibodies (mAbs), and effector cells. Target cells were MT4-CCR5 Tat-responsive GFP-Luc cells, a highly HIV-susceptible human T-cell line engineered to express GFP and luciferase reporters. To directly measure Fc-mediated antiviral activity, MT4-CCR5_GFP-Luc cells were infected with HIV-1(Yu2) for 3 days, resulting in at least a tenfold increase in luciferase relative light units (RLUs). For each experiment, infected target cells were incubated with serial dilutions of mAbs to form antibody-target complexes. Subsequently, effector cells were added at target-to-effector ratios of 1:5 or 1:10 and incubated overnight to allow antibody-dependent cellular cytotoxicity (ADCC) or antibody-dependent cellular phagocytosis (ADCP) to occur. Fc effector activity was quantified by measuring reductions in luciferase RLUs, reflecting the elimination of HIV-infected target cells. To improve assay sensitivity and reproducibility, we also evaluated MOA-based surrogate assays that measure Fc receptor (FcγR) activation rather than direct target-cell elimination. These assays detect enhanced FcγR clustering and downstream signaling through activation of the nuclear factor of activated T cells (NFAT) pathway. HIV-infected MT4-CCR5_GFP cells lacking the luciferase reporter were used as target cells, while NFAT-responsive effector cell lines served as reporters. Fc activity was quantified by measuring increases in effector-cell luciferase RLUs following FcγR engagement.

Results: Individual mAbs generally produced modest Fc-mediated activity, with approximately 10% target-cell elimination observed in ADCC and ADCP assays. In contrast, antibody pools generated stronger responses, achieving approximately 30% ADCC activity. Moreover, afucosylated human IgG1 mAbs demonstrated stronger binding to CD16 (FcγRIIIa) compared with their fucosylated counterparts. Consistent with this enhanced receptor engagement, afucosylated antibodies exhibited superior ADCC and ADCP activity across multiple assay platforms. Both ADCC and ADCP responses were highly dependent on the functional state of effector cells, including their cytotoxic and phagocytic capacities.

Conclusion: The development and optimization of sensitive Fc effector functional assays will facilitate the identification of human antibodies capable of mediating broad and potent antiviral activity against HIV. Improved characterization of Fc-dependent mechanisms may accelerate the development of antibody-based strategies for HIV prevention and therapy.

POSTER 324

Anti-HTLV-1 neutralizing antibody induction by immunization with mRNA-LNP expressing modified Env antigens

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Introduction/Background: Development of an effective HTLV-1 vaccine is in demand for global HTLV-1 control. We have recently shown that macaques inducing anti-HTLV-1 neutralizing antibodies (NAbs) by immunization with a Sendai virus vector expressing an HTLV-1 Env antigen are protected from an HTLV-1 challenge, indicating the rationale for strategies aimed at efficient anti-HTLV-1 NAb induction in prophylactic HTLV-1 vaccine development (Mol Ther, 32:2328-2339, 2024). In the present study, we examined the immunogenicity of mRNA-LNPs expressing modified Env antigens in mice to develop a prophylactic HTLV-1 vaccine efficiently inducing NAbs.

Material/Methods: mRNA-LNPs encoding SU-TM (full-length HTLV-1 Env), SU monomer (Env surface gp46 subunit), SU trimer (a trimerized SU), and a membrane-anchored HTLV-1 Env extracellular domain were prepared (by Moderna, Inc.). Induction of anti-HTLV-1 Env antibodies and NAbs in mice after immunization with these mRNA-LNPs was examined.

Results: Western blot analyses showed that SU-TM expression is poor whereas other modified antigens are efficiently expressed by mRNA. Intramuscular immunization of mice with these mRNA-LNPs induced detectable NAbs. mRNA-LNPs encoding SU trimer induced higher levels of NAbs and those encoding a membrane-anchored Env extracellular domain induced the highest.

Discussion/Conclusion: Our results indicate that membrane-anchored, modified Env antigens can be a promising immunogen candidate for mRNA-LNP vaccine platform against HTLV-1 infection.

POSTER 327

A simplified and sensitive assay for tracking virus-specific T cell responses in the nasal cavity during SARS-CoV-2 human challenge studies

Previtha Dawn SAKTHI VALE, Natalene Hui Shan YUEN, Joey Ming Er LIM, Adeline CHIA, Huiwen ZHENG, Yirong DAI, Anthony Tanoto TAN, Antonio BERTOLETTI, Nina LE BERT

See oral presentation:

Concurrent Session 3: "Bright Sparks" in Vaccinology – PhD Student Session • Monday 12 October, 16:40

POSTER 328

Development of a Complement-Dependent mRNA vaccine candidate for Gonorrhoea for LMICs enabled by AI-powered antigen selection

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Introduction: With the rise in gonorrhoea infections and antimicrobial resistance, vaccine development is crucial to curb the spread of the disease. Untreated gonorrhoea can cause severe reproductive health issues and has a significant impact on increasing the risk of acquiring other sexually transmitted infections such as HIV/AIDS, which is very pertinent in low- and middle-income countries (LMICs), especially in Southern Africa. Leveraging the mRNA technology platform developed at Afrigen Biologics and Evaxion's proprietary artificial intelligence (AI) driven antigen discovery platform, the objective is to develop a cost-effective, accessible and broadly protective mRNA vaccine against *Neisseria gonorrhoeae* for LMICs.

Initial immunogenicity studies showcased the efficacy and significant in vivo protection conferred by a fusion protein combining two highly ranked antigens from Evaxion's AI antigen discovery platform. The protective effect was complement-dependent, requiring C9, further validating serum bactericidal activity (SBA) as a functional readout for pre-clinical optimisation and as a potential clinical correlate of protection. An mRNA construct was then designed to code for the fusion protein, and immunogenicity data indicated comparable antibody titres and in vivo protection to the recombinant protein. Further optimisation of the mRNA construct was conducted by testing out 6 alternate 5' UTRs to improve on the mRNA yield, integrity, as well as protein expression and immunogenicity. Outcomes from the comparison showed that 3 out of the 6 UTRs tested were comparable or better than the original UTR, with one, GNR-010, generating functional serum IgGs that showed SBA against 3 different *N. gonorrhoeae* strains. GNR-010 was selected for further immunogenicity testing in a mouse challenge study with the University of Massachusetts. The mRNA to be tested was produced using the Quantoom Biosciences Ntensify® system, with initial testing in the mano small-scale system and then scaled to the micro system to generate enough mRNA material to be formulated at a 100 mL scale using the KNAUER NanoScaler system to produce mRNA-lipid nanoparticles (LNPs). This material was placed on stability to generate data to support the shelf-life of the mRNA-LNP drug product and the mRNA drug substance.

Methods: The fusion mRNA construct was manufactured using the Ntensify® Micro system at a 20 mL scale to generate the mRNA and formulated at a 100 mL scale to generate the mRNA-LNPs. The mRNA and mRNA-LNPs were placed on stability to determine shelf life at -20 °C and -80 °C.

Results: Preliminary indicators are that the mRNA and mRNA-LNPs are stable for up to 6 months at both -20 °C and -80 °C, with further testing of the mRNA at 9 and 12 months at -80 °C and the mRNA-LNPs at 9 and 12 months for both the -20 °C and -80 °C temperatures. This is in line with previous data generated using the same lipids, but with different mRNA constructs.

Discussion: Formulation optimisation for improved thermostability and dose-sparing is underway to support clinical translation and scalable manufacturing in LMICs via the WHO/MPP mRNA technology transfer partner network. This work exemplifies a novel, AI-driven, and globally accessible approach to combat antibiotic-resistant *N. gonorrhoeae*.

POSTER 329

Divergent innate and humoral immune responses to 4CMenB vaccination in transgender individuals receiving gender-affirming hormone therapy

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See oral presentation:

Concurrent Session 6: "Bright Sparks" in Vaccinology – ECR Session • Tuesday 13 October, 12:30

POSTER 330

Cross-protection against Bundibugyo virus by Ebola and Sudan vaccines

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Introduction/Background: Orthoebolaviruses continue to cause recurrent outbreaks in Central Africa, yet available countermeasures remain largely species-specific and no licensed vaccine or therapy exists for Bundibugyo virus, the virus driving the ongoing outbreak in the Democratic Republic of Congo. Here we assessed whether monovalent vaccines developed against Ebola virus, Sudan virus, or Bundibugyo virus could confer cross-protection across these related orthoebolaviruses. We hypothesize that existing GP-based vaccine candidates could provide heterologous protection through cross-reactive humoral and cellular immunity, even when neutralizing antibodies are limited.

Material/Methods: We used a mouse challenge platform based on Ifnar and Ifnar/Fcgr1 mice, together with recombinant vesicular stomatitis virus surrogates expressing EBOV, SUDV, or BDBV glycoproteins. Mice were vaccinated with yellow fever 17D-vectored monovalent vaccine candidates expressing the glycoproteins of BDBV, EBOV, or SUDV, then challenged one month later with the relevant surrogate viruses. We assessed survival, body weight, disease scores, tissue viral loads, binding antibody titers, neutralization, Fc receptor dependence, FluoroSpot and intracellular cytokine T-cell responses, and T-cell depletion experiments.

Results: The BDBV vaccine candidate YF-BDB protected mice from homologous BDBV surrogate challenge, preventing systemic viral dissemination and improving survival. Unexpectedly, YF-EBO and YF-SUD also protected against BDBV surrogate challenge, while YF-BDB and YF-EBO gave only partial protection against SUDV surrogate challenge. Serology showed broadly comparable cross-reactive binding antibody titers across vaccine groups, but neutralization and especially cross-neutralization were limited, implying that non-neutralizing mechanisms were important. Fc receptor deficiency reduced YF-BDB cross-protection against EBOV surrogate challenge, whereas YF-SUD retained broad protection. T-cell analyses identified CD4 T cells as the main driver of the broad cross-protective phenotype.

Discussion/Conclusion: Here we show that cross-protective immunity among orthoebolavirus vaccines is asymmetric across EBOV, SUDV, and BDBV. In this model, SUDV GP-based vaccination appeared to elicit the broadest and most resilient protection, suggesting it may be a useful template for broader orthoebolavirus vaccine design. Our findings also argue that binding antibodies alone are insufficient to predict protection, and that CD4 T-cell responses are central to broad cross-protection. Overall, our results support considering SUDV-based vaccines as potentially versatile tools for outbreak preparedness, while also suggesting that EBOV-based vaccines may offer some protection against BDBV.

POSTER 333

From Outbreak to Vaccination in Days: Operational Lessons from Rapid Marburg Vaccine Trial Activation in Rwanda and Ethiopia

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Introduction / Background: Public health emergencies involving hemorrhagic fever viruses require clinical trial activation at unprecedented speeds. The 2024 Marburg virus outbreak in Rwanda and the 2025 outbreak in Ethiopia presented rare and urgent opportunities to deploy investigational vaccines under emergency conditions. Conventional clinical trial activation timelines—typically measured in months—are incompatible with outbreak response needs, within a broader One Health context requiring coordinated health system responses.

This abstract describes the operational framework and multistakeholder coordination that enabled the activation of Marburg vaccine trials in two African countries within days of outbreak notification and presents comparative lessons from both settings.

Materials / Methods: We describe a retrospective comparative analysis of two emergency vaccine trial activations — Rwanda (September–October 2024) and Ethiopia (November–December 2025) — both conducted in response to Marburg virus disease outbreaks. Both activations received ethics approval through their respective institutional and national review bodies: the Rwanda National Ethics Committee (RNEC) in Rwanda, and the AHRI/ALERT Ethics Review Committee (AAERC) in Ethiopia, both of which have established mechanisms for expedited review. Key operational variables examined included: regulatory submission and approval timelines, protocol and informed consent adaptation processes, vaccine cold-chain and logistics management, and contract execution between funder (CEPI), CRO (IQVIA), developer (Sabin Vaccine Institute), and local implementing partners. Activation time was defined as the interval from initial CEPI contact following outbreak confirmation, to first participant vaccination in each country. Milestone data were prospectively recorded during each deployment.

Results: In Rwanda, first participant vaccination was achieved 8.5 days following outbreak notification — from Friday 27 September 2024 to Sunday 6 October 2024 at 12:30pm. Key milestones included protocol and informed consent adaptation by Day 4, concurrent regulatory approval (Rwanda FDA and RNEC) by Day 6, and vaccine labelling/shipment, site activation and vaccination by Day 8.5.

In Ethiopia, first participant vaccination was achieved 18 days following outbreak notification — from Thursday 20 November 2025 to Monday 8 December 2025. Protocol adaptation and regulatory submission to Ethiopia FDA and AAERC were completed by Day 7, with regulatory approval and vaccine labelling on Day 8, vaccine arrival on Day 14, and first participant vaccinated on Day 18. Across both deployments, full regulatory compliance and participant safety oversight were maintained throughout.

Discussion / Conclusion: These deployments demonstrate that rapid clinical trial activation can be achieved without compromising regulatory rigor or participant safety.

Achieving first participant vaccination within 8.5 and 18 days respectively of outbreak notification — while maintaining full regulatory compliance — highlights the critical role of pre-established operational infrastructure, regulatory relationships, and multistakeholder coordination are established ahead of an emergency.

The difference in timelines between Rwanda and Ethiopia underscore the impact of site readiness, regulatory familiarity, and logistical complexity on activation timelines and is itself instructive. Together, these case studies provide a scalable and replicable model for rapid vaccine trial activation, with important implications for future outbreak preparedness efforts across sponsors, clinical research organizations, and National Health in Authorities in Africa and beyond.

POSTER 335

Intramuscular mRNA delivery via glycodendron-functionalized lipid nanoparticles limits hepatic off-targeting and enhances immune responses

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Introduction/Background: Lipid nanoparticles (LNPs) for intramuscular mRNA delivery often show off-target transfection in the liver, limiting the efficacy of the mRNA cargo. Antigen-presenting cells (APCs) drive adaptive immune responses and express C-type lectin receptors that recognize carbohydrates. Therefore, incorporating carbohydrate-conjugated phospholipids (hereafter referred to as glycodendrons) into LNPs may enable active APC targeting, enhance immunogenicity, and reduce hepatic off-targeting. Here, we aimed to develop an APC-targeted LNP formulation for intramuscular mRNA delivery based on three glycodendron candidates previously identified by in vitro screening.

Materials/Methods: Glycodendron-functionalized LNPs were characterized in vitro and investigated for their biodistribution in vivo in mice using luciferase-encoding nucleoside-modified mRNA (modRNA). Tissue samples from numerous organs were analyzed for luciferase activity and mRNA abundance. Furthermore, the immunogenicity of a modRNA-encoded bacterial antigen delivered by functionalized LNPs was assessed in a murine prime/boost immunization model.

Results: In vitro characterization showed that LNPs functionalized with 2% lipid-conjugated glycodendrons had favorable particle sizes and low polydispersity indices (PDIs). The three glycodendrons exhibited specificity for at least one of the target receptors -CD206, CD209, or CD301 - in various primary cells and cell lines. In mice, a biodistribution study revealed that luciferase expression was concentrated at the injection site, whereas liver expression was detected only with the non-functionalized control LNP. This finding was supported by reduced luciferase protein and mRNA abundance in liver tissue from mice injected with glycol-targeted LNPs. Ligand-functionalized particles were well tolerated in a prime/boost immunogenicity study while inducing enhanced T-cell responses compared to the non-functionalized control LNPs. IgG antibody responses and germinal center B-cell responses were stronger following immunization with a trivalent galactose-containing ligand (TrisDendroGal) than with the other glycodendrons or the non-functionalized LNPs.

Discussion/Conclusion: Together, these data suggest that glycodendron-functionalized LNPs enable efficient intramuscular mRNA delivery while reducing liver off-target transfection. Cellular and humoral immune responses against a bacterial antigen were enhanced specifically when modRNA was delivered via TrisDendroGal-functionalized LNPs. Active targeting of APCs remains to be elucidated through immunohistochemical analyses of embedded tissues.

POSTER 336

In vivo antigen expression and immunogenicity of multiple adenoviral vectors after intranasal administration

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Introduction/Background: A ChAdOx1-vectored SARS-CoV-2 vaccine failed to induce consistent mucosal and systemic antibody responses when administered intranasally (IN) in a Phase I clinical trial (NCT04816019). This contrasted with favourable clinical results obtained with IN SAd36 and inhaled HAdV-C5 products (NCT05522335 and NCT04552366). Multiple factors differed between these trials but one possible explanation is varying immunogenicity of adenovirus serotypes after mucosal administration. To our knowledge this has never been investigated by head-to-head comparison of multiple adenovirus types, either clinically or pre-clinically. The limited number of adenovirus vaccine types in clinical development has been selected largely on the basis of historical studies of immunogenicity after intramuscular administration.

Materials/Methods: We are developing a growing panel of vectorised adenoviruses, each E1- and E3-deleted and carrying HAdV-C5 E4orf6 to facilitate manufacturing. At the time of writing this includes eight adenoviruses from five species (A-E). Administration of a 1:1 mix of viral vectors containing full length SARS-CoV-2 spike and a luciferase reporter gene facilitates tracking of transgene expression and both antibody and T-cell immunogenicity.

Results: We have validated this platform by detecting systemic and mucosal humoral and cellular immune responses in mice following IN administration of ChAdOx1, ChAdOx2, and Ad5. Work to fully characterise the panel's immunogenicity after IN administration is ongoing. We intend to perform similar comparisons after inhaled and oral administration, and in human ex vivo mucosal cultures.

Conclusion: The panel of vectors will be a valuable tool, enabling rational selection from a broad panel of optimal adenovirus types for use by a variety of mucosal administration routes.

POSTER 338

 α -GalCer-based liposome adjuvant enhances Protective Mucosal and Systemic Immunity in mice

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Introduction: Intranasal vaccination has the potential to induce long-lasting protective airway immunity based on neutralizing secretory IgA (SIgA) and tissue-resident memory lymphocytes. However, developing efficient intranasal vaccine strategies remains challenging due to antigen delivery and airway immune tolerance. Here, we evaluated an α -Galactosylceramide (α -GalCer)-based liposome as an intranasal adjuvant for enhancing the immunogenicity and efficacy of an Influenza A Hemagglutinin (HA)-based vaccine formulation in mice.

Material/Method: The vaccine formulation was prepared by combining an α -GalCer-based liposome with Influenza virus A (A/California/04/2009, H1N1) HA antigen. Naïve mice were immunized intranasally with three doses. Two weeks following the final dose, mucosal and systemic antibody and cellular responses were quantified by ELISA and ELISpot, respectively. In addition, tissue-resident memory responses were analyzed by spectral flow cytometry. To evaluate the protective vaccine effect, mice were challenged with Influenza virus A California and body weights, viral loads and lung damage were assessed.

Results: We observed that the intranasal vaccine formulation including α -GalCer-based liposome induced the strongest HA-specific IgA and SIgA responses in Bronchoalveolar lavages compared to HA alone or adjuvanted HA. Furthermore, this formulation induced lung tissue-resident memory T cells along with secretion of IFN- γ responses by lung lymphocytes upon re-stimulation. At systemic level, robust functional HA-specific IgG responses were detected after immunization with α -GalCer-based liposome vaccine formulation. Interestingly, we found immunity response shifted toward a Th2 phenotype with this formulation. Finally, the intranasal α -GalCer-based liposome vaccine formulation was the most efficient to protect mice from viral challenge by mitigating body weight loss and lowering viral loads in the respiratory tract.

Discussion/Conclusion: We demonstrated that an Influenza vaccine formulation composed of α -GalCer-based liposome conferred protective local immunity. We will further evaluate its universal potential against heterologous Influenza A strains and dissect the mechanisms of the action of this adjuvant.

POSTER 339

Dendritic cells and fibroblasts are the main targets for the live-attenuated Yellow Fever virus vaccine in the dermis of mice

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Introduction: The live-attenuated yellow fever 17D (YF17D) vaccine induces long-lasting protective immunity in over 99% of vaccinees. However, the mechanisms underlying this robust immune response, particularly the cellular targets of early viral replication, remain poorly understood. Identifying the initial infected cell populations and tracking early viral spread is critical to understanding how protective immunity is initiated. Given the immunological richness of the skin and the potential of intradermal vaccination as a dose-sparing strategy, we investigated the cellular tropism and replication dynamics of YF17D following intradermal administration.

Materials & Methods: Using luminescent and fluorescent reporter YF17D viruses, we tracked viral replication and cellular targeting in AG129 mice using a combination of in vivo imaging (IVIS) and multi-color flow cytometry. Intradermal vaccination was performed, and skin and draining lymph nodes were analyzed over time. Infected cell populations were identified using immunological and imaging approaches. Additionally, laser poration was employed to assess the impact of delivery depth on vaccine efficacy.

Results: YF17D replication was detected in the skin, predominantly in dermal fibroblasts and classical dendritic cells (cDCs), both known for their strong T-cell priming capacity. Despite substantial recruitment to the dermis, monocyte-derived dendritic cells showed limited infection in draining lymph nodes. Viral replication remained pronounced in the skin and was sustained over time. By day 1 post-vaccination, the virus was detectable in draining lymph nodes, where replication was transient yet persisted for at least 3 days. Importantly, these dynamics were associated with robust induction of YF17D-specific antibodies and polyfunctional T-cell responses. Effective immunization required delivery to a minimum depth of 100 µm within the dermis.

Conclusion: Our findings demonstrate that early YF17D replication occurs primarily locally in dermal fibroblasts and cDCs, highlighting their key role in initiating adaptive immune responses. The prolonged replication in the skin and subsequent lymph node involvement underpin the strong immunogenicity of the vaccine. These insights improve understanding of vaccine pharmacokinetics and YF17D-induced immunity in general yet also support the optimization of intradermal vaccination strategies, with implications for dose-sparing approaches and the development of vaccines against other flaviviruses.

POSTER 340

Decoding epitope immunodominance in viral antigens using cryoEM and machine learning

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Viral surface glycoproteins, such as the HIV envelope protein (Env), present numerous antibody (Ab) epitopes, yet immune responses consistently focus on only a subset, a phenomenon known as immunodominance. Although structural studies have provided insights into Env antigenicity, our understanding of the molecular features that govern efficient Ab engagement remains incomplete, thereby limiting the predictive and rational design of vaccines. Here, we characterized the structural determinants of epitope immunodominance in HIV Env by integrating high-resolution cryoEM-based polyclonal epitope mapping (cryoEMP) across different clades with quantitative analyses of epitope topology, accessibility, and physicochemical properties. More than 70 new structures were resolved to assemble a library of >100 Env-antibody complexes. These data informed the development of a surface-centric, machine-learning model to predict relative Antigen Surface Immunodominance (ASI model). Comparison of ASI-predicted epitope sites with the specificities of Env-induced antibodies showed that the model accurately identifies immunodominant regions and highlights the structural features driving immune bias. Notably, immunogens redesigned based on model predictions successfully redirected Ab responses toward a normally subdominant epitope, demonstrating the potential of strategies coupling targeted assembly of focused structural libraries with machine learning to uncover complex molecular patterns and enable design of more effective vaccine antigens.

POSTER 341

Development of a novel mRNA-LNP optimized for RSV PreF expression

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Background: Respiratory syncytial virus (RSV) is a ubiquitous respiratory pathogen which typically causes self-limiting illness. However, immunologically naïve infants and other high-risk populations, such as the elderly and immunocompromised, may progress to lower respiratory tract infections. The incidence of severe disease is highest in low- and middle-income countries (LMICs) where approved vaccines and therapeutics are largely inaccessible. An affordable mRNA-lipid nanoparticle (LNP) vaccine could ameliorate the disease burden, particularly in vulnerable infants where the incidence of hospitalisation and death is highest. In order to address this unmet need Afrigen Biologics is developing an affordable mRNA-LNP vaccine, for maternal immunization and active immunization of high-risk groups, that will be manufactured in LMICs through the network of partners established under the mRNA technology transfer hub.

Methods: Afrigen is developing a novel mRNA-LNP vaccine that is distinguished from approved modalities through optimisation of the mRNA cassette and PreF antigen. The programme commenced with the design and testing of a series of mRNA constructs comprising different 5' UTRs with a model PreF antigen. This was followed by the evaluation of different 3' UTRs with a model 5' UTR and the original antigen. Finally, lead 5' and 3' UTRs were evaluated in combination with a new PreF antigen sequence. Initial screening was based on mRNA yield and physicochemical properties, as determined by an established suite of tests. Protein expression validation of 5' and 3' UTRs was based on western blotting of transfected HEK293T cell lysate, whereas combinations of 5'/3' UTRs were assessed by measuring cell-surface RSV F expression, using a flow cytometry binding assay, following treatment of Expi293F cells with mRNA-LNPs. All UTR permutations were benchmarked against controls comprising the respective Spikevax®-derived 5' and 3' UTRs.

Results: The first phase of screening identified four 5' UTRs yielding promising mRNA critical quality attributes including IVT yield, capping efficiency, mRNA size, integrity, dsRNA content and expression in vitro. Screening of 3' UTRs similarly enabled the identification of promising leads for further development. The evaluation of 5'/3' UTR combinations resulted in the identification of 4 pairs that improved expression of RSV F compared to the benchmark comparator. These UTRs are currently being incorporated into a series of novel mRNAs incorporating different PreF antigen sequences.

Conclusion: An optimised mRNA cassette was developed potentiating improved RSV PreF antigen expression in vitro. Vaccination studies are planned to evaluate the concordance of in vitro expression with immunogenicity in mice. Future work will evaluate the immunogenicity of different PreF antigens with the down selected UTRs.

POSTER 342

Investigating an anti-membrane protein antibody with cross-Sarbecovirus reactivity

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The ongoing evolution of SARS-CoV-2 has diminished the effectiveness of many antibody responses elicited by vaccination and prior infection, largely due to extensive mutation in the spike protein, underscoring the need to target more conserved viral antigens. The coronavirus membrane (M) protein, the most abundant structural component of the virion, plays a central role in virus assembly and membrane curvature and is highly conserved across coronaviruses. The SARS-CoV-2 M protein comprises a short 19-amino-acid N-terminal ectodomain (M19), three transmembrane helices, and a larger cytoplasmic domain. Here, we present the first epitope characterization of a monoclonal antibody, SARS7, that binds the M19 ectodomain and exhibits broad reactivity across the Sarbecovirus subgenus. Using cryo-EM, we resolved a high-resolution structure of SARS7 in complex with M embedded in lipid nanodiscs, demonstrating that SARS7 recognizes a conformational epitope spanning the M homodimer. We observed broad reactivity of SARS7 across SARS-CoV-1, SARS-CoV-2, BatCoV RaTG13, and BatCoV RsYN04, indicating that this epitope is conserved across sarbecoviruses. Alanine scanning identified key binding residues, which were consistent with the cryo-EM epitope mapping. These findings expand current understanding of M-targeting antibodies and establish a structural basis for cross-sarbecovirus recognition of a conserved, non-spike antigen.

POSTER 344

MucorVax: A viral vector based vaccine for mucormycosis

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Introduction: Mucormycosis is an Invasive Fungal Disease (IFD) caused by spores of the order Mucorales. People with uncontrolled diabetes, hematological malignancies and immune suppression are at risk for contracting mucormycosis. Considering the increasing incidence and limited treatment options, preventive strategies are urgently needed. Recent studies identified proteins present on the surface of Mucorales spores known as Coth proteins as crucial virulence factors. Coth proteins are conserved across the different genera and their removal reduced mortality in an animal model of mucormycosis. Leveraging this discovery, we developed a vaccine candidate expressing a conserved Coth3 epitope from *Rhizopus arrhizus*, the most common cause of mucormycosis, using our yellow fever (YF17D)-based vaccine platform to generate prophylactic antibodies capable of protecting against mucormycosis.

Materials & Methods: The vaccine candidate (YF-Coth3) was designed to generate virus-like particles (VLPs) displaying a dense array of a 16 amino-acid Coth3 epitope following viral transduction. Antigenicity was confirmed by confocal microscopy of YF-Coth3 transfected and infected Vero-E6 and BHK-21J cells. Immunogenicity of the vaccine candidate was assessed in IFNAR^{-/-} mice in a two-dose regimen spaced 21 days apart. Immunogenicity of YF-Coth3 as well as, native spore recognition via flow cytometry, and macrophage-mediated phagocytosis with RAW cells were evaluated using serum samples. Immunosuppression (cyclophosphamide, 200 mg/kg i.p.) and DKA (streptozotocin, 190 mg/kg i.p.) models were used to assess the effect of risk-factors on vaccine immunogenicity. Finally, vaccine efficacy was tested in challenge models of pulmonary mucormycosis.

Results: YF-Coth3 generated Coth3-expressing VLPs following transduction of Vero-E6 and BHK-21J cells in vitro. Vaccination induced Coth3-specific IgM and IgG antibodies in mice, with class switching toward IgG after the second dose. Vaccine induced antibodies recognized native spores, cross-reacted with other Mucorales genera (*Lichtheimia*, *Mucor*, etc.), and increased macrophage-mediated phagocytosis of fungal spores. Immunosuppression and DKA did not significantly impair the vaccine-induced antibody response. Preliminary results from challenge studies show a reduction in fungal burden (in CFUs) in vaccinated animals as compared to the sham vaccinated animals.

Conclusion: We developed a YF17D-vectored Coth3 vaccine candidate that produces Coth3-expressing VLPs and elicits functional anti-Coth3 antibodies with cross-reactivity against other spores from multiple Mucorales genera. Immunization with YF-Coth3 reduces pulmonary fungal burden in infected animals compared to their sham vaccinated controls. Together, these findings highlight the potential of our approach to confer broad antifungal protection, supporting its further development and evaluation toward clinical benefit in advanced animal models.

POSTER 346

Safety assessment of YF17D vaccination during late pregnancy in a Syrian hamster model

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Introduction: Viral infections during pregnancy can cause miscarriage, preterm birth, intrauterine growth restriction, and congenital abnormalities through fetal infection or placental damage. Although contraindicated in pregnancy, live vaccines may be administered during outbreaks when pathogen risk outweighs vaccination risks. Yellow fever virus (YFV), a mosquito-borne Orthoflavivirus causing severe disease with a mortality approaching 40%, exemplifies this dilemma. With only a live vaccine available (YF17D), pregnant women in endemic regions remain inadequately protected. Evidence for YF17D safety during pregnancy is scarce, particularly regarding placental mechanisms limiting fetal exposure. We hypothesize that type III interferons (IFN- λ), key innate antiviral mediators, protect the maternal-fetal interface, as observed for teratogenic Zika virus from the same Orthoflavivirus group. This study aims to: (1) evaluate YF17D safety during late pregnancy, and (2) investigate how IFN- λ signaling may restrict vertical transmission of vaccine virus using a Syrian hamster model.

Methods: Female Syrian hamsters (wild-type or IFNLR1^{-/-}) were vaccinated on embryonic day 10.5 with 10⁴ PFU of YF17D. At E15.5, maternal blood, placental, and fetal tissues were collected and analyzed for viral RNA, cytokine expression, antibody responses, and histopathology. Comparisons between genotypes assessed the role of type III interferon (IFN) signaling in controlling YF17D dissemination and immune responses.

Results: YF17D vaccination did not adversely affect pregnancy outcomes in wild-type hamsters. Maternal body weight gain, litter sizes, fetal weights, and placental weights were comparable between mock- and YF17D-vaccinated dams. Viral RNA was only sporadically detected, i.e., in one spleen sample out of 3 dams. Similarly, IFNLR1^{-/-} dams showed no gestational effects or detectable systemic viral loads.

Placental viral loads were detected in 5 out of 34 (14.7%) of wild-type and in 5 out of 27 (18.5%) of IFNLR1^{-/-} placentas. Notably, there was no evidence of vertical transmission, as no viral RNA was detected in fetal liver tissues. Nevertheless, YF17D vaccination induced significant upregulation of type I and type II IFN-stimulated genes (ISGs) in wild-type placentas, exemplified by increased MX2 ($p < 0.001$) and IP10 ($p < 0.001$) expression. While baseline type I interferon levels were elevated in IFNLR1^{-/-} dams, YF17D vaccination decreased IP10 expression ($p = 0.0159$), while MX2 remained upregulated ($p < 0.0001$), indicating intact type I IFN signaling independent of IFN- λ .

Both wild-type and IFNLR1^{-/-} dams seroconverted to anti-NS1 IgG within five days post-vaccination, with antibody titers further increasing by 21 days post vaccination as expected for efficient YF17D immunization. Additionally, robust anti-NS1 IgG antibodies were also detected in weanlings, indicating successful maternal-fetal antibody transfer.

Discussion/Conclusion: YF17D vaccination is well tolerated during late gestation, with no adverse fetal or maternal effects in hamsters. YF17D replication in the placenta remains limited and efficiently controlled by an antiviral type I IFN response, whereby protection from vertical transmission and adverse pregnancy outcomes may not depend on additional IFN- λ signaling. Importantly, maternal vaccination induced protective IgG antibodies that were transferred to offspring, providing immunity during immunological immaturity. These findings support the safety and immunological benefits of maternal YF17D immunization during pregnancy, with implications for protecting pregnant women during yellow fever outbreaks.

POSTER 348

Immunogenicity and Stability Assessment of Soluble Monomeric and Tetrameric Nipah Virus G Glycoprotein Vaccine Candidates

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Introduction: Nipah virus (NiV) is a highly pathogenic, negative-sense single-stranded RNA virus that belongs to the Paramyxoviridae family. These viruses are zoonotic in nature, associated with high mortality rates, for which no licensed vaccine is currently available. It has six structural proteins, two of which are surface proteins (Glycoprotein and Fusion protein) that are responsible for binding to the host receptors ephrin-B2 and ephrin-B3 on epithelial cells, making it an attractive target for a vaccine.

Material and Methods: In this study, we have designed and produced two soluble forms of the NiV-G glycoprotein: a monomeric variant (NiV-G-Mr) and a tetrameric variant (NiV-G-Tr). Both variants were expressed transiently in a mammalian expression system and compared their biophysical properties, stability, and in vivo immunogenicity. By evaluating both the monomeric and tetrameric forms, we aimed to assess how structural configuration influences antigenicity and immunogenic potential. The purified proteins were subjected to biochemical and biophysical characterization to assess their structural integrity and stability. Immunogenicity was evaluated in BALB/c mice over a period of up to six months. Humoral immune responses were analyzed by measuring total IgG titers and antibody isotype profiles. Functional neutralization capacity was assessed using pseudovirus-based neutralization assays due to restricted access to BSL-4 facilities required for live virus studies.

Result: Both constructs demonstrated proper expression, structural integrity, and stability. Immunization with G-Mr and G-Tr elicited strong humoral immune responses, as evidenced by high IgG titers and distinct antibody isotype profiles. Importantly, sera from immunized mice effectively inhibited pseudovirus entry, indicating the induction of neutralizing antibodies.

Discussion: Our study strengthens and expands upon this body of evidence by demonstrating that even a soluble monomeric form of the G glycoprotein (G-Mr) without multivalent display can induce robust and long-lasting antibody responses, including functional neutralization, when formulated with an appropriate adjuvant. At the same time, the tetrameric construct (NiV-G-Tr) enhances structural fidelity and modestly improves immunogenicity, highlighting its promise for future optimization. Importantly, this work provides a direct comparative Congress framework for understanding how antigen architecture influences immune outcomes.

POSTER 350

Maximizing mucosal memory: Systemic prime-mucosal boost vaccination provides long-term protection against SARS-CoV-2

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Introduction: While the important role of mucosal immunity in controlling viral respiratory infection has been highlighted in recent year, efficient mucosal vaccines providing durable protection in humans are still lacking. During the SARS-CoV-2 pandemic, hybrid immunity established by intramuscular vaccination followed by a natural infection with SARS-CoV-2 conferred superior protection against re-infections with newly emerging variants compared to repeated mRNA vaccinations. To mimic this situation, many studies utilized a systemic prime and mucosal boost vaccination regimen to induce systemic and mucosal immune responses. However, data on long-term effects of this vaccination schedule remain strongly limited.

Material/Methods: In this study, the longevity of vaccine-induced immunity was analysed in a systemic mRNA prime-mucosal adenoviral vector boost model and directly compared to two intramuscular vaccinations with a licensed SARS-CoV-2 mRNA vaccine. To this end, C57BL/6JRj mice were intramuscularly primed with Comirnaty® followed by an intranasal boost with a spike-encoding recombinant adenoviral vector (Ad5-S) or a second intramuscular shot of Comirnaty®. Sera, bronchoalveolar lavage (BAL), lungs, bone marrow, and spleens were analysed for up to 18 months after the boost. Additionally, mice were challenged with different SARS-CoV-2 variants three to 12 months after the boost.

Results: In our comprehensive longitudinal study, the heterologous RNA/Ad5 vaccination regimen were highly immunogenic and protective immune response could be detected for up to 18 months post boost. This covers the implementation of a stable systemic immune response consisting of CD8+ central memory T cells, serum IgG antibodies, and long-lived plasma cells in the bone marrow. The persistence of these systemic responses was comparable to the one observed in mice having received two consecutive intramuscular mRNA vaccinations. Most important, robust and long-lived CD8+ tissue-resident memory T cells and secretory IgA antibodies are induced only by the RNA/Ad5 vaccination regimen. In addition, RNA/Ad5-immunized mice display local memory B cells, plasma cells, and Th17 cells in the lung. As late as one year after vaccination, these RNA/Ad5 treated mice showed superior protection against homologous and heterologous challenges compared to RNA/RNA-immunized mice. This effect can be further enhanced by the delivery of a variant-adapted antigen in the mucosal vaccine.

Discussion/Conclusion: In conclusion, the combined systemic and mucosal vaccination approach presents provides long-term immunity at the viral entry side which could not be achieved by repeated mRNA vaccination. Our study broadens the understanding of mucosal vaccination strategies, which will be important for the design of future vaccines for better containment of current and new emerging respiratory viruses.

POSTER 352

Development and Characterization of a Soluble Trimeric H5N1 Hemagglutinin with Balanced Immunogenicity

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Introduction: The ongoing spread of highly pathogenic avian influenza H5N1 clade 2.3.4.4b in birds, with repeated spillover into mammalian hosts, continues to raise concerns for pandemic preparedness. This also underlines the need for vaccine antigens that can be produced quickly and at scale. Hemagglutinin is the major target of neutralizing antibodies against influenza A viruses and remains a preferred antigen for subunit vaccine development. One practical challenge is to produce HA in a scalable system without losing the native-like trimeric structure that is important for antigenicity. In this work, we evaluated a soluble trimeric HA antigen based on H5N1 A/Wyoming/01/2025 genotype D1.1, representing a currently circulating H5N1 strain.

Methods: The H5N1 HA-trimer was designed with a C-terminal foldon domain to support trimer formation. It was first expressed transiently in Expi293F cells to obtain protein rapidly and then moved into a stable CHO-K1 expression system to assess its suitability for manufacturing. Purified HA-trimer was analysed by size-exclusion chromatography, dynamic light scattering, and circular dichroism to examine its size distribution, solution behaviour, and secondary structure. Mouse immunogenicity studies were performed using HA-trimer with or without adjuvant. Antibody responses were measured by HA-specific ELISA, hemagglutination inhibition, and virus neutralization assays. Cellular responses were assessed by ELISpot and flow cytometry of T- and B-cell subsets. Protective efficacy is being evaluated in a reassortant H5N1 challenge model using survival, clinical score, lung viral load, and histopathology.

Results: The purified HA-trimer showed good biophysical behaviour, with a largely monodisperse profile and acceptable thermal tolerance. Circular dichroism showed a mixture of antiparallel β -sheets and α -helices, which is consistent with a folded HA protein and supports a native-like conformation. These results suggest that the protein assembled as a trimer and retained important conformational features. In vitro functional assays confirmed receptor-binding activity and expected HA function, indicating that the recombinant antigen preserved key structural and antigenic properties after expression and purification. In mice, the soluble HA-trimer induced clear HA-specific antibody responses. Both IgG1 and IgG2b subclasses were detected, suggesting that the response was not strongly skewed to either a Th2- or Th1-type profile, but showed a relatively balanced pattern.

Conclusion: Overall, the soluble H5N1 HA-trimer appears to be a useful vaccine antigen for further development. The construct retained native-like structural features, showed acceptable stability and solution behaviour, and could be produced through a CHO-K1 stable expression platform, which is relevant for scalable cGMP manufacturing. The antigen also induced HA-specific antibodies, including both IgG1 and IgG2b responses, consistent with a mixed Th1/Th2-type humoral profile. Ongoing mouse immunogenicity and H5N1 challenge studies will help define the neutralizing activity, breadth of response, and level of protection, and will support further dose and adjuvant selection.

POSTER 353

A multiplex method for high-throughput quantification of conjugated saccharide in glycoconjugate vaccines

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Glycoconjugate vaccines rely on the accurate quantification of its active ingredient, also called conjugated saccharides (CS), which is usually estimated from the indirect measurement of total and free (unconjugated) saccharide to ensure product quality and efficacy. Conventional methods like HPAEC-PAD often require harsh and time-consuming sample pre-treatment, especially in multivalent formulations. In this study, we introduce a tetraplex sandwich immunoassay based on Luminex technology, capable of directly and simultaneously quantifying the conjugate saccharide in MenACWY vaccine without pre-treatments (e.g., hydrolysis, solid-phase extraction, and ultrafiltration steps). The new assay exhibits robust specificity, sensitivity, linearity, precision, and accuracy across a broad concentration range, and effectively discriminates conjugated saccharides from free saccharides and carrier protein. Stability studies under both accelerated and long-term conditions confirm the method's suitability as a stability-indicating assay. This high-throughput, multiplex platform offers a robust and efficient alternative to traditional physico-chemical approaches, streamlining analytical workflows for increasingly complex glycoconjugate vaccines.

1. Santostefano G. et al. Anal. Chem (2025)
2. Santostefano G. et al. Anal Bioanal Chem (2025)

POSTER 354

R21/Matrix-M Vaccination Alters the Acquisition of Blood-Stage Malaria Antibody Responses in Young Children in Burkina Faso: Four Year Follow-Up of a Phase II Trial

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Rationale: Since 2024, two pre-erythrocytic malaria vaccines for *P. falciparum* (RTS,S/AS01E and R21/Matrix-M) have been recommended for use in medium to high malaria transmission areas for children under 5 years. Here, using serological markers of malaria exposure, we investigate how R21/Matrix-M vaccination influences the acquisition of blood-stage antibody responses and how these responses are shaped by subsequent malaria infections. This will contribute to our understanding of these antigens as markers of malaria exposure, with implications for understanding how vaccine-derived protection influences the development of naturally acquired immunity.

Methods: Serum samples from 450 5-17-month-olds enrolled in a Phase II R21/Matrix-M trial in Burkina Faso were investigated using a multiplex serology panel of 30 *P. falciparum*-associated antigens. Using samples collected over four years following a primary three-dose vaccination series and up to three annual booster doses, we assessed longitudinal acquisition of malaria-specific IgG responses. We fit a linear mixed effects model to analyse trends in responses, adjusting for age and sex, and variation between vaccination groups (R21-vaccinated and control-vaccinated). To better characterise these blood stage markers as markers of exposure, Spearman's rank correlations were performed between IgG responses and cumulative clinical malaria incidence prior to sample collection. Correlation analysis was performed separately for unvaccinated and vaccinated participants.

Results: In the year following R21/Matrix-M vaccination, IgG responses to blood-stage malaria markers were lower compared with control vaccination, with responses to PfAMA1 ($p < 0.001$), GLURP2 ($p < 0.05$), PfGARP Ag2 ($p < 0.05$) and Etramp4 Ag2 ($p < 0.05$) remaining significantly different over the four years of follow up. The magnitude of this difference did not vary according to the number of booster doses received, and remained significant when adjusting for age and sex. R21 vaccination was also associated with unexpectedly elevated responses to the blood-stage marker MSP5, suggesting a potential off-target effect. In the R21-vaccinated group, there were significant positive correlations between cumulative malaria incidence and responses to PfAMA1 and PfGARP Ag2, among others, supporting their potential utility as markers of exposure to clinical malaria.

Conclusions: R21 vaccination significantly influences the acquisition of IgG responses to blood-stage malaria antigens, while the number of booster doses appears not to affect this acquisition over time. There is also evidence for off-target blood stage responses which may reflect cross-reactivity with blood stage malaria antigens, warranting further investigation as a contributory mechanism of R21-mediated protection. The significant correlations observed here suggest that markers such as PfAMA1 could be useful markers of exposure in infants, but do not provide sufficient insight as to their protective capacity. These findings highlight the need for continued investigation of immune responses following R21 implementation to better understand how vaccine-induced protection interacts with the development of blood-stage immunity as vaccine efficacy wanes.

POSTER 355

Novel mucosal infection model for Coxsackie B viruses for evaluating mucosal vaccine efficacy

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Background: Enteroviruses, including Coxsackie B viruses, are common human viruses that infect through faecal-oral- and respiratory routes. There are no vaccines or therapeutics available against CVBs, even though they are responsible for a tremendous disease burden including common colds, myocarditis, aseptic meningitis and strongly linked to type 1 diabetes development. Despite enteroviruses are naturally infecting via mucosa, most experimental mouse infection models predominantly use intraperitoneal administration to initiate infection. In this study, we established a novel mucosal mouse infection model for CVBs, which enables us to evaluate the efficacy of our mucosal vaccines in challenge studies that better resemble human infection.

Material/Methods: The study was conducted in Tampere University in Virology and Vaccine Immunology research group. Several administration routes were tested to find the best route for mucosal infection. Successful infection required creation of mouse-adapted CVB strain, which was produced by serial passaging. The adapted virus was then propagated in GMK cells and concentrated with ultracentrifugation. In the optimized infection model, female Balb/c mice were infected with adapted virus intranasally, their wellbeing and weight were checked daily, and the mice were terminated 3 days after the infection. Infection in mice were confirmed from weight loss, visual changes in behaviour and tissues, histology, and Tissue Culture Infectious Dose 50 method (TCID₅₀). Non-infected mice were included as negative controls.

Challenge studies were conducted to evaluate whether our mucosal vaccine protects against mucosal infection. In the challenge study, mice were vaccinated twice intranasally within 2 weeks interval before a challenge with our novel infection model. Titres of infective virus in organs were detected with Tissue Culture Infectious Dose 50 method. Infection was also determined by the weight loss after infection and wellbeing of the mice. Neutralizing antibody levels were measured with microneutralization assay. Control mice did not receive any vaccine and were expected to show signs of infection.

Results: We were able to establish a mucosal mouse infection model for CVB after serial passaging in mice. Our mucosal model consistently shows weight loss and infective virus in pancreas, lungs or small intestine. Our challenge studies with intranasally administrated CVB1-VLP vaccines show protection after mucosal infection, as the signs of infection are significantly reduced after vaccinations.

Discussion: Our established novel infection model enables efficacy evaluation of mucosal vaccines and antivirals against viruses that spread through faecal-oral route. The infection model is optimized for adult mice which enables conduction of different vaccination strategies prior to the challenge. Our infection model resembles human infection, which may enhance our vaccine's performance in later clinical studies.

POSTER 356

AI-Based Engineering of Viral Fusion Glycoproteins Improves Developability and Enables Multivalent Respiratory Vaccines

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Background: Viral fusion glycoproteins are attractive vaccine targets because they contain the epitopes recognized by the most potent neutralizing antibodies. However, these proteins are inherently metastable and prone to transitioning from their prefusion to postfusion conformation, often resulting in poor expression, reduced stability, and manufacturing challenges. Most vaccine designs rely on heterologous trimerization domains to enforce correct oligomerization, which induce off-target immune responses and complicate the design of multivalent vaccine formulations.

Methods: We developed an in-house AI-based protein engineering approach that identifies amino acid substitutions predicted to stabilize prefusion conformations by optimizing complex structural interaction networks, thus enabling stable trimer formation without the need for exogenous trimerization domains. To assess the broad applicability of this approach, the platform was applied to fusion proteins from multiple clinically relevant respiratory viruses, including respiratory syncytial virus (RSV), human metapneumovirus (HMPV), parainfluenzavirus (PIV), influenza viruses, and coronaviruses. Predicted substitutions were combined and introduced into recombinant antigens, which were subsequently evaluated using biochemical, biophysical, structural, and immunological assays.

Results: Across all targets tested, AI-guided stabilization improved key developability characteristics, including expression, conformational stability, and thermal resilience, while preserving critical neutralization-sensitive epitopes. Structural studies demonstrated that stabilization frequently resulted from strengthening interaction networks that restrict conformational transitions associated with membrane fusion. Importantly, improved antigen properties translated into enhanced immunogenicity in vivo, demonstrating that the engineered antigens retained their biological relevance while offering substantial manufacturing and stability advantages.

Conclusion: These findings demonstrate that AI-enabled protein engineering provides a broadly applicable framework for optimizing viral fusion glycoproteins across diverse respiratory virus families. By simultaneously improving expression, stability, manufacturability, immunogenicity, and by removing the need for heterologous trimerization domains, this approach addresses several critical challenges in vaccine development and supports the development of next-generation multivalent respiratory vaccines that combine multiple antigens into a single product while maintaining favorable developability characteristics.

POSTER 357

Assessment of Humoral Immune Response in Naturally Infected EBV Individuals

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Introduction/Background: Epstein-Barr virus (EBV) infects over 90% of adults worldwide and establishes lifelong latency in memory B cells. Beyond infectious mononucleosis (IM), EBV is causally linked to multiple sclerosis (MS) and several malignancies. A comprehensive understanding of naturally elicited humoral immune responses in seropositive individuals is essential to better understand disease pathogenesis and immune control mechanisms. The objective was to characterize the breadth, magnitude, and quality of humoral immune responses against EBV glycoproteins in naturally infected individuals.

Material/Methods: EBV-seropositive and seronegative donors were recruited from the French Blood Bank (EFS). Humoral responses were evaluated by ELISA, seroneutralization in B cells and epithelial cells, memory B cell FluoroSpot analysis, and glycoprotein-specific antibody immunodepletion assays.

Results: Broadly detectable binding and neutralizing antibody responses were observed against all four major glycoproteins (gB, gH/gL, gp42, gp350/220). Notably, the antigen-specificity proportions differed between the long-lived plasma cell-derived circulating antibody compartment and circulating memory B cells: gp350/220 was dominant among circulating antibodies but poorly represented in memory B cells, whereas gH/gL showed the opposite pattern. Sequential immunodepletion of glycoprotein-specific antibodies cumulatively abolished B cell neutralization, confirming the non-redundant contribution of each glycoprotein to overall seroneutralization.

Discussion/Conclusion: Humoral profiling of naturally infected EBV individuals reveals broadly distributed immunity against all major glycoproteins, with compartment-specific differences in glycoprotein immunodominance between circulating antibodies and memory B cells. These findings provide a detailed immunological blueprint.

POSTER 358

Humoral Correlates of Risk for SARS-CoV-2 Breakthrough Infection Following mRNA Vaccination

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has repeatedly demonstrated an ability to mutate and generate variants of concern which can effectively evade pre-existing immunity and are also frequently more infective than their predecessors. Although COVID-19 vaccines have been highly effective, the durability and breadth of protection against emerging variants remain limited. While neutralizing antibodies are an established correlate of protection, their predictive value declines as immunity wanes and viral evolution progresses. These limitations highlight the need to identify additional humoral immune mechanisms associated with protection. We therefore sought to define humoral correlates of breakthrough infection risk following mRNA vaccination using a systems serology approach.

Methods: We conducted a case-control study comparing Fc biophysical and functional features after BNT162b2 vaccination in SARS-CoV-2 breakthrough cases with individuals who were not infected within a six-month timeframe. ~260 baseline seronegative participants from the UK SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) cohort study of healthcare workers were included, 71 becoming cases and 188 controls. Humoral features were measured 14 days and 90 days following the administration of the second vaccine dose in the primary series to identify antibody features associated with PCR-confirmed breakthrough infections that occurred during the Alpha (B.1.1.7) and Delta (B.1.617.2) waves in the United Kingdom. Antibody isotype/subclass and Fc receptor binding profiles were measured against a panel of ten SARS-CoV-2 spike antigens spanning ancestral USA-WA1/2020 through the Omicron JN.1 variant. Fc-mediated effector functions, including antibody-dependent monocyte and neutrophil phagocytosis, NK cell activation/cytotoxicity, and complement deposition, were assessed against two spike antigens. Multivariate Random Forest analysis was used to identify immune correlates associated with breakthrough infection risk.

Results: Distinct Fc receptor binding patterns were associated with breakthrough infection risk following BNT162b2 vaccination. At 14 days after the second dose, the FcγR3-F158-to-total IgG ratio emerged as the strongest correlate of infection status, with lower ratios associated with protection from infection. By 90 days post-vaccination, similar associations were observed for additional Fcγ receptors and for the FcαR-to-IgA1 ratio. FcγR-to-IgG ratios demonstrated consistent associations across SARS-CoV-2 variants, whereas FcαR-to-IgA1 associations were limited to WA1/2020 and Beta (B.1.351). These Fc features were significantly more informative predictors of infection status than clinical or demographic variables.

Discussion: The association between FcγR3A-F158 binding and breakthrough infection risk may reflect underlying FCGR3A allelic variation. The FcγR3A-F158 allotype binds IgG1 and IgG3 with lower affinity than FcγR3A-V158 and has been linked to increased susceptibility to infection and reduced responses to ADCC-mediated immunotherapies. These observations suggest that breakthrough infections may be enriched among individuals carrying the FCGR3A-F158/F158 genotype, a hypothesis that warrants investigation through receptor genotyping. The FcαR-to-IgA1 association may reflect the dual signaling capacity of FcαR. Unlike FcγR3A, FcαR can mediate either activating or inhibitory signals depending on receptor cross-linking. Because serum IgA decays more rapidly than IgG, spike-specific IgA is expected to be substantially reduced by 90 days after vaccination. We hypothesize that low-valency FcαR engagement under these conditions favors inhibitory signaling, suppressing Fcγ receptor-mediated effector functions and contributing to increased susceptibility to breakthrough infection.

POSTER 359

In situ cancer immunotherapy with modified MVdeltaC measles virus induces potent RIG-I-dependent tumor clearance and immune memory

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See oral presentation:

Concurrent Session 4: Immunotherapies • Tuesday 13 October, 12:10

POSTER 360

Cross-protection of wildtype and vaccine-derived chikungunya virus antibodies against chikungunya and Mayaro viruses in mice

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Background: In 2023, the live attenuated vaccine IXCHIQ (VLA1553), was approved against chikungunya virus (CHIKV), a re-emerging arthritogenic alphavirus. Almost all studies characterizing the vaccine-protective efficacy have focused on short-term responses, primarily evaluating sera collected within months of vaccination through in vitro neutralization assays. Consequently, there is no in vivo data evaluating protection at low concentrations of CHIKV-specific antibodies, which are essential to mimic long-term immunity. This is true for both vaccination and natural infection, particularly regarding cross-protection against diverse CHIKV genotypes and related co-circulating alphaviruses such as Mayaro virus (MAYV). Moreover, whether sub-optimal antibody levels could predispose to antibody-dependent enhancement (ADE) remains poorly characterized.

Methods: We investigated antibody-mediated cross-protection and ADE following vaccination or natural infection. Transiently immunocompromised mice were passively immunized with multiple doses of immune sera from either vaccinated or naturally infected mice. One day later, the protective efficacy against infection with two different CHIKV lineages (East-Central-South African and West-African) or MAYV was evaluated. Protection was assessed primarily based on blood viral loads at three days post-infection, specifically by estimating serum antibody inhibitory concentrations (IC) leading to a reduction in viral loads of 90, 99, and 99.9%, but also based on clinical criteria for disease.

Discussion: Both vaccine-induced and natural immunity conferred robust protection against both CHIKV genotypes, even at antibody concentrations nearing ELISA detection limits. In contrast, protection against MAYV required 20- to 100-fold higher antibody titers. No evidence of ADE was detected regardless of the antibody concentration or the origin of the immunity.

These findings support the long-lasting, pan-genotypic efficacy of the vaccine strain against CHIKV. While cross-protection against MAYV is less robust, it suggests a potential to prevent MAYV-associated disease in regions where both viruses co-circulate. Importantly, no ADE was observed, even at low antibody concentrations.

POSTER 362

Characterization of the antibody-antigen binding aimed to develop an in vitro potency assay for a Group A Streptococcus vaccine

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Growing ethical concerns about animal testing and the widespread adoption of the 3Rs (Replacement, Reduction, Refinement) have increased the need for validated in vitro assays that reliably demonstrate product potency and quality in pharmaceutical research. In this context, antibody-based immunoassays offer the possibility of correlating an antigen's in vitro potency with its in vivo immunogenicity. Developing a fit-for-purpose in vitro potency assay (IVRP) therefore requires detailed characterization of antibody binding sites and their interactions with vaccine antigens under reference and subpotent conditions.

This project combines development of an IVRP for a Streptococcus A vaccine with the structural characterization and epitope mapping of antibody-antigen interactions. Specific mouse monoclonal antibodies (mAbs) were preselected to identify and quantify the three recombinant proteins in our candidate vaccine (SLO, SpyCEP, and SpyAD) directly in the final formulation. Antigens and corresponding antibodies were expressed, and multiple structural techniques were applied to characterize complexes and define epitopes, including HDX-MS, X-ray crystallography, and cryo-EM. Fab fragments of each selected antibody were produced to facilitate the performance of such structural methods.

Furthermore, binding affinity and stability assessments were conducted using competitive ELISA (cELISA) and bio-layer interferometry (BLI) on antigens at reference conditions and after thermal stress to evaluate mAb suitability for monitoring vaccine stability. Antigen-specific functional assays were also performed to measure the inhibitory potential of the mAbs.

Together, the structural, binding affinity, and functional data will support the development and refinement of the IVRP, validating its use as a reliable tool to determine Streptococcus A vaccine potency.

POSTER 363

Preliminary Development and Evaluation of a Monovalent Clostridium septicum Vaccine with Potential for Multivalent Application

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Livestock diseases caused by clostridial species remain a major threat to agricultural productivity and food security, owing to their high morbidity and mortality in affected animals. These challenges underscore the importance of effective prophylactic measures. Multivalent vaccines are widely regarded as a primary strategy for managing and controlling clostridial infections; however, their success depends on reliable antigen production and formulation processes that ensure both safety and immunogenicity. Developing scalable approaches for antigen generation and vaccine design is therefore critical to advancing sustainable livestock health strategies. Clostridium septicum culture conditions were optimized at laboratory scale to enhance extracellular toxin production, followed by scale-up in a bioreactor for antigen generation. A monovalent C. septicum vaccine was formulated and is undergoing evaluation in experimental models. Three different adjuvant systems are being explored to assess their potential influence on safety and immune responses in animals. Scale-up of the optimised fermentation process yielded a highly potent C. septicum antigen suitable for vaccine formulation. The monovalent vaccines proved to be safe and elicited appreciable immune responses. Adjuvant comparisons demonstrated differences that warrant further investigation. This study outlines a scalable biotechnology process for antigen production and vaccine formulation, with promising early implications of safety and immunogenicity. Importantly, the antigen production process developed here could be adapted for inclusion in future multivalent clostridial vaccines, thereby enhancing livestock protection and contributing to improved animal health, food security, and alignment with the One Health strategy.

POSTER 364

REAL-WORLD EVIDENCE SUMMARY OF MVA-BN MPOX VACCINE IN POPULATIONS DISPROPORTIONATELY AFFECTED BY MPOX

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Background: Mpox outbreaks in the US and Europe since 2022 have disproportionately affected men who have sex with men and people living with HIV. MVA-BN is a non-replicating third-generation orthopoxvirus vaccine developed with an improved safety profile compared with older smallpox vaccines. Randomized controlled trials for mpox prevention are difficult to conduct because of ethical and epidemiologic constraints, making real-world evidence essential for evaluating vaccine performance.

Methods: We reviewed 12 real-world evidence studies and systematic reviews from Israel, the United States, the United Kingdom, Canada, Spain, and Germany published between 2022 and 2025. Outcomes included vaccine effectiveness after one and two doses, effectiveness by route of administration, outcomes among people living with HIV, breakthrough infection, hospitalization, and disease severity.

Findings:

Across settings, MVA-BN was consistently associated with reduced mpox risk and favorable clinical outcomes. Single-dose vaccine effectiveness ranged from 58% to 86%, while two-dose effectiveness ranged from 75% to 88%. Protection was observed across subcutaneous and intradermal administration routes and in studies including people living with HIV. Breakthrough infections among fully vaccinated individuals were uncommon and generally milder than infections in unvaccinated individuals. Studies also reported lower hospitalization and disease severity among vaccinated people, including among people living with HIV.

Discussion: Because correlates of protection for mpox remain undefined and case numbers are often limited, real-world evidence provides a pragmatic and ethically appropriate framework for assessing vaccine benefit. These findings are particularly relevant for public health, as mpox prevention strategies must address communities disproportionately affected by the outbreak, including those facing stigma and barriers to timely vaccination.

Conclusion: Published real-world evidence supports MVA-BN as an effective tool for reducing mpox infection and severe outcomes in populations most affected by recent outbreaks. Public health programs should prioritize equitable vaccine access, two-dose series completion, community-centered outreach, and continued real-world monitoring to guide mpox preparedness and response.

POSTER 365

From Antibody Measurement to Protection: In Vivo Evaluation of Serological Reference Materials Across High-Priority Pathogens

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Introduction/Background: Globally available high order serological calibrants, such as International Standards (ISs) and reference reagents have enabled harmonised assessment of antibody binding and neutralisation assays across laboratories and over time, improving comparability between studies. At the Medicines and Healthcare products Regulatory Agency (MHRA), such materials are developed to support vaccine evaluation, focusing on standardising antibody measurements and identifying immune correlates of protection. We have developed a pipeline for the development and characterisation of such materials that includes material sourcing, safety screening, in vitro and in vivo characterisation. In vitro assays evaluate antibody reactivity while animal models assess whether these responses confer functional protection, to increase the utility of materials by providing a correlate of protection. Here, we have applied this framework to assess and demonstrate the in vivo protective potential of candidate reference materials against high-priority pathogens, including viruses such as Marburg virus and Chikungunya virus (CHIKV) and the bacteria *Coxiella burnetii* (Q fever).

Materials/Methods: To conduct these studies, mice or cynomolgous macaques were passively administered candidate ISs either neat or serially diluted and subsequently challenged with the respective pathogens. The serological ISs utilised in this pipeline were Marburg virus (NIBSC: 23/146), Q fever (NIBSC: 21/304) or CHIKV IS (PEI: 1502/19). Disease progression was monitored post-challenge in the in vivo models and pathogen dissemination at the end of the studies was characterised.

Results: For Marburg virus the IS demonstrated limited neutralising activity in vitro against two variants (Popp and Angola). Furthermore, the Marburg IS showed no protective effect in vivo, suggesting that antibody binding alone may not correlate with protection for this pathogen. For Q fever, contrasting results were observed, in vitro analyses showed that the IS had no significant effect on bacterial uptake or growth. However, in vivo mice studies demonstrated that IS administration prior to bacterial challenge reduced disease severity and bacterial burden. Interestingly, differences between male and female animals highlighted the importance of biological variability in assessing immune responses. The CHIKV IS has previously demonstrated neutralisation activity against various CHIKV lineages. In vivo, the IS demonstrated a titratable protection against CHIKV LR2006-IOL in macaques. Moreover, the IS demonstrated a suppression of fever and reduction in RNAemia and infected tissue. Furthermore, this study deduced a serological correlate of protection of 10 International Units/mL.

Discussion/Conclusion: Overall, these findings demonstrate that while ISs are essential for measuring immune responses their correlate to protection is pathogen-specific and cannot be assumed. The integration of in vitro and in vivo approaches is therefore critical. This work provides a foundation for supporting preparedness against emerging infectious diseases thereby improving vaccine development.

POSTER 366

Intensification Strategies for Influenza A Virus Production in Suspension MDCK Cells

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Introduction / Background: Modern vaccine manufacturing processes rely on flexible, robust, and scalable production platforms. While batch production using suspension MDCK cell culture represents a viable alternative to traditional egg-based manufacturing for influenza vaccines, further process intensification can enhance productivity, reduce timelines, and improve immunogenicity. This study investigates strategies for intensified influenza A virus (IAV) production, combining high cell density (HCD) cultivation with continuous virus harvesting, and seed train optimization.

Material/Methods: Monoclonal suspension MDCK cells were cultivated in 4Cell® MDCK CD Medium (Sartorius, Germany) in a 3 L stirred-tank bioreactor operated in perfusion mode. A tangential flow depth filtration (TFDF) system (Repligen, USA) was used for cell retention to expand cells to HCD. Following, the media was fully exchanged with a trypsin-containing medium and cells were infected with IAV to initiate the production phase. Over the next 3.5 days, progeny virus was continuously harvested through the TFDF filter.

To further advance the upstream process, seed train intensification approaches were investigated. N-1 perfusion cultivation was implemented to achieve HCD inocula, and HCD cryopreservation was evaluated for direct bioreactor inoculation, with the aim of reducing the number of preculture expansion steps. These strategies were benchmarked against conventional seed train expansion workflows.

Results: For the intensified IAV production process in perfusion mode, monoclonal suspension MDCK were infected at about 20×10^6 cells/mL. Unlike conventional hollow fiber membranes, which often result in virus accumulation within the bioreactor, progeny virus was continuously harvested over three days using the TFDF module. This resulted in a cumulative hemagglutination titer of $4.05 \log_{10}(\text{HAU}/100 \mu\text{L})$. Compared to batch operation, this process achieved a threefold increase in cell-specific virus yield and a tenfold increase in space-time yield, while maintaining comparable volumetric productivity.

For seed train intensification, N-1 perfusion cultures using an ATF2-module (alternating tangential flow filtration) reached up to 63.9×10^6 cells/mL. Cells harvested at different concentrations were used to inoculate shake flasks for batch IAV production. In addition, HCD cryovials containing up to 4.7×10^8 cells were generated and successfully applied for direct inoculation of a production bioreactor. Both intensification strategies reduced overall production timelines without negatively impacting viral titers.

Discussion/Conclusion: This study highlights the potential of using suspension MDCK cells for intensified IAV production. IAV yields and productivity could be significantly improved with the implementation of TFDF-based perfusion. Moreover, the evaluation of perfusion-based N-1 seed train intensification and HCD cryopreservation reduced steps of manual labor and process timelines while preserving virus titers. These strategies represent promising tools for improving efficiency, flexibility, and sustainability in upstream virus production processes.

POSTER 368

Evaluation of an Anti-Yersinia pestis Serological Reference Material in an in vivo plague model

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Introduction/Background: The development of physical serological reference materials is critical for improving the comparability and interpretation of vaccine immunogenicity data for high-consequence pathogens such as Yersinia pestis (causative agent of plague) and a lack of harmonised reagents limits cross-study comparisons. To address this gap, a candidate serological reference material was developed and its capacity to protect in vivo was evaluated in a mouse model of bubonic plague.

Materials/Methods: The candidate material was prepared by pooling convalescent serum from individuals with a known previous infection of Y.pestis. The material was solvent detergent extracted and filtered prior to freeze-drying and was designated Anti-Yersinia pestis serum (human) (NIBSC cat no: 25/276). The pooled reference material and individual donations were evaluated for binding to Y.pestis antigens F1 and V by Simple Western. The reference material capacity to protect when administered i.p., either neat or at dilutions (1 in 4, 1 in 16) prior to challenge with Y.pestis (150 CFU, Strain C092) and the outcome was monitored by survival, clinical signs and weight loss.

Results: Administration of the candidate reference material conferred a measurable level of protection compared with the control group, with increased survival and reduced disease severity observed in treated animals. These findings indicate that the material contains functional antibody activity capable of mediating protection in vivo.

Discussion/Conclusions: These findings support the potential use of this candidate serological reference material to support assay harmonisation and standardisation efforts for plague vaccine evaluation. The in vivo protection afforded by the material represents a key step towards establishing a correlate of protection. The reference material can support accelerating vaccine development and regulatory decision-making for rare but high-consequence Y.pestis infections where traditional efficacy studies may not be feasible.

POSTER 369

Characterization of the immune response to Fusobacterium nucleatum, an emerging pathogen associated with adverse pregnancy outcomes

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See oral presentation:

Concurrent Session 8: Emerging Infections • Wednesday 14 October, 12:20

POSTER 370

Neutralisation is a poor predictor of protection by Epstein Barr Virus vaccines: antibodies to glycoprotein B are predominantly non-neutralising but achieve disproportionately robust protection of humanised mice

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Background: There is increasing interest in EBV vaccine development for prevention of infectious mononucleosis, multiple sclerosis and cancers. Vaccines based upon the antigens gp350 and gH/gL/gp42 have entered clinical trials. No candidate in clinical trials includes the fusion protein glycoprotein B (gB), largely because it is perceived to be a relatively poor inducer of neutralising antibody. Recent results of a Phase III trial of a human cytomegalovirus vaccine have cast doubt on the relationship between in vitro antibody neutralisation of herpesviruses and in vivo protection against infection.

Methods: We made EBV immunogens by display of the candidate antigens gp350, gH/gL and gB on hepatitis B surface antigen (HBsAg) virus-like particles using the SpyCatcher – SpyTag system. We assessed their immunogenicity in mice using neutralisation assays on Raji B cells and HEK293T epithelial cells, and assessed the protective effect of vaccine-induced antibody by passive transfer followed by EBV challenge in humanised NSG mice. We also produced a simian adenovirus (ChAdOx1) expressing full length gB and identified 39 novel anti-gB monoclonal antibodies (mAbs) by screening single plasma cells from immunised mice using a Berkeley Lights Beacon instrument.

Results: We found protective capability of IgG induced by the VLP-based candidate vaccines was poorly predicted by in vitro neutralisation. Anti-gHgL was neutralising and protective, anti-gp350 was strongly neutralising but poorly protective, while gB was essentially non-neutralising yet protective (on Raji cells, median NT50s 8, 63, <1 respectively; median splenic viral qPCR undetectable, 1260 units/spleen, undetectable respectively, vs median 2×10⁵ units/spleen in naives; gB recipients vs naives p=0.004, Kruskal-Wallis & Dunn's post-test).

The 39 murine anti-gB mAbs predominantly recognised post-fusion and cell-associated gB similarly, despite being raised by immunisation with viral vector expressing full-length cell-associated gB. By cryo-EM of mAb:gB complexes, we identified neutralising antibodies targeting multiple domains, but non-neutralising antibodies to domain IV dominated the response.

Fc-dependent mechanisms may explain protection despite weak neutralisation, but their effectiveness against EBV is poorly understood, and it is not fully known which effector mechanisms are active in NSG mice. Certain mechanisms are likely to be ineffective, including complement downstream of C5. We found C1q present at physiological levels in the challenged NSG mice, but observed no enhancement by C1q of neutralisation by either polyclonal or monoclonal anti-gB antibodies. It therefore appears possible that anti-gB is mediating protection in this model by an Fc-receptor-dependent mechanism.

Conclusion: Reliance on neutralisation data to select EBV antigens for clinical trials appears unwise. Clinical evaluation of gB vaccines is worthwhile, as is additional investigation of Fc-dependent mechanisms of anti-gB, such as ADCP and ADCC. We are preparing for clinical trial of the HBsAg-VLP-based vaccine candidates and will briefly discuss these plans.

POSTER 371

Antigenic landscape of a highly mutated SARS-CoV-2 Spike in ongoing viral evolution

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Introduction: The ongoing emergence of SARS-CoV-2 variants in an increasingly immune-experienced population is largely enabled by the plasticity of the Spike protein, which lies at the frontline of host immune pressure. Here we use BA.2.87.1, a variant heavily mutated in the N-terminal domain (NTD) in Spike, as a model system to interrogate how extensive remodeling of this domain reshapes the structural, functional, and antigenic properties of the SARS-CoV-2 Spike protein.

Material/Methods: We integrated pseudoviruses assays, high-resolution cryo-electron microscopy, surface plasmon resonance and negative-stain electron-microscopy-based polyclonal epitope mapping (nsEMPEM), to characterize this variant functionally and immunologically.

Results: We found that even large deletions in the NTD do not substantially disrupt overall Spike structure or pseudovirus infectivity. However, our structural and binding analyses revealed that the NTD exhibits increased flexibility and that interaction with a heme-metabolite, contributing to assembly of an immunodominant epitope, is lost. These conformational effects, coupled with 33 NTD mutations, compromised the ability of human convalescent antibodies to engage this domain, contributing to their reduced neutralizing capacity. Consequently, BA.2.87.1-like variants may escape recognition by the pre-existing NTD-targeting antibodies, potentially reducing protection.

Conclusion: Together, our results highlight the intrinsic adaptability of the Spike beyond the receptor-binding domain, with important implications for immune escape during viral evolution.

POSTER 372

Development of a WHO International Standard for anti-Sudan Virus Antibodies

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Sudan virus (SUDV) causes Sudan virus disease (SVD), a severe illness with a case fatality rate of up to 71%. Compared to the closely related Ebola virus, there is currently no licensed vaccine against SUDV, however multiple candidates have entered clinical trials, and several serological assays have been developed. To increase comparability of results generated by these assays, an International Standard (IS) is required. The IS represents the highest order of reference material for biological substances and established by the WHO Expert Committee on Biological Standardization (ECBS). Calibration of serological assays against the IS allows reporting of sample potencies in IU/mL therefore facilitating data comparison between laboratories and defining a correlate of protection. To develop the first WHO IS for anti-SUDV antibodies, sera from 28 survivors of the 2000 or 2012 outbreaks of SVD in Uganda were characterised for binding and neutralising activities, in parallel at the MHRA Science Campus and Battelle. The candidate IS was prepared by pooling 14 individual sera with the highest antibody binding and neutralising activities, formulated and lyophilised to increase stability. To assess the suitability of the candidate IS for anti-SUDV antibodies in serological assays, a multi-centre collaborative study was launched. Results of the collaborative study showed increased harmonisation of sample binding and neutralising antibody quantification when potencies were expressed relative to the candidate IS. Comparable harmonisation was also observed when sample potencies were reported relative to a preparation composed of anti-SUDV GP monoclonal antibodies spiked in negative human serum, suggesting that such material could serve as a suitable calibrant for future reference standard production. The first WHO International Standard for Sudan virus antibodies is now available to order for use in binding assays (NIBSC code: 24/124_BA) and for neutralisation assays (NIBSC code: 24/124_NT).

This effort was funded by the National Institutes of Health, National Institutes of Allergy and Infectious Diseases under contract HHSN272201800013I / 75N93023F00001.

POSTER 375

Optimization and immune evaluation in C57BL/6 mice of multivalent filoviral nanoparticle-based vaccine candidates

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Introduction/Background: The Filoviridae family includes highly pathogenic viruses responsible for severe hemorrhagic fever outbreaks with high case-fatality rates. The most relevant human-infecting filoviruses are Orthoebolavirus zairense (EBOV), Orthoebolavirus sudanense (SUDV), Orthoebolavirus bundibugyoense (BDBV), and Orthomarburburgvirus marburgense (MARV). As these viruses co-exist in several African regions, broadly protective vaccination strategies are urgently needed. We hypothesized that a multivalent nanoparticle-based vaccine platform displaying glycoproteins (GPs) from multiple filoviruses could induce broad cross-reactive immune responses and serve as foundation for pan-filoviral vaccine development.

Material/Methods: Multivalent vaccine candidates displaying GPs from EBOV, SUDV, BDBV, and MARV were developed using two nanoparticle platforms: (i) mosaic filovirus-like particles (mFLPs) generated by co-expression of EBOV VP40 and NP proteins and (ii) SpyTag–SpyCatcher003-mi3 nanoparticles displaying either full-length stabilized GPs (4F) or mucin-like domain-deleted GPs (4FΔ). For mFLP generation, the transmembrane domain and cytoplasmic tail of SUDV, BDBV, and MARV GPs were replaced by those of EBOV to facilitate incorporation into the particle scaffold. Nanoparticles were characterized by biochemical analyses and electron microscopy. Female C57BL/6J mice (n=5/group) were immunized orally or intramuscularly with mosaic vaccine candidates, with or without AddaVax adjuvant. Humoral and cellular immune responses were evaluated using serum, mucosal, spleen, and lymph node samples. Neutralizing activity was assessed using an extensive panel of filovirus pseudovirus neutralization assays.

Results: All nanoparticle platforms successfully displayed the intended antigens and formed structurally intact particles. Vaccination induced robust anti-filoviral antibody responses, particularly in adjuvanted groups. Higher IgG titers were observed against EBOV, SUDV, and BDBV GPs than against MARV GP. Anti-NP IgG responses were also detected in adjuvanted and orally immunized groups. Neutralization assays demonstrated broad pseudovirus-neutralizing activity for all adjuvanted mosaic candidates against Orthoebolavirus, although neutralization against MARV was generally lower across groups.

Discussion/Conclusion: These findings demonstrate the feasibility of multivalent nanoparticle-based vaccine platforms for the development of next-generation pan-filoviral vaccines. Mosaic FLP and SpyCatcher nanoparticles elicited broad humoral responses and neutralizing antibodies against multiple filovirus species, supporting their further evaluation as broadly protective filoviral vaccine candidates.

POSTER 378

ANTIGEN OPTIMIZATION BOOSTS RIFT VALLEY FEVER MRNA VACCINE IMMUNOGENICITY IN MICE

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Rift Valley fever (RVF) poses a substantial socio-economic burden, largely driven by livestock losses and human mortality. In September–October 2025, Senegal and Mauritania experienced a major RVF outbreak. Although the disease is endemic to sub-Saharan Africa, outbreaks have also occurred in the Arabian Peninsula. Due to its outbreak potential and public health impact, Rift Valley fever virus (RVFV) has been designated a priority pathogen by the World Health Organization (WHO) and the Coalition for Epidemic Preparedness Innovations (CEPI). Currently, no licensed human vaccine exists for RVF. Despite significant advances on several RVF vaccine platforms, the mRNA platform remains critical for rapid and adaptable outbreak response.

Materials and Methods: A previously developed RVF mRNA vaccine candidate encoding the RVFV glycoprotein (GP) gene, formulated with the patented ionizable lipid SM-102, was evaluated in preclinical immunogenicity studies using BALB/c mice. A pseudovirus-based neutralization assay (PBNA), utilising a modified vesicular stomatitis virus (VSV) lacking the VSV-G gene and carrying a luciferase reporter, was established using a Kenyan RVFV reference GP sequence (46A-66). Optimizing the PBNA to match the mRNA sequence involved replacing the Kenyan sequence with the previous mRNA vaccine sequence. The effects of sequence variation on pseudovirus infectivity and GP protein expression were investigated.

Based on the findings from the PBNA optimisation, a revised mRNA construct was designed and assessed for binding and neutralizing antibody responses. Structural modelling and comparative analysis of GP spikes encoded by the previous and revised mRNA vaccine sequences were performed to evaluate potential structural impacts of sequence variation. In addition, the revised mRNA drug substance was reformulated using a freedom-to-operate (FTO) ionizable lipid, followed by the reassessment of antibody titres.

Results: While the previous mRNA vaccine candidate elicited robust humoral and cellular immune responses in mice, following a two-dose vaccination regimen, pseudoviruses generated using the previously vaccine-matched GP sequence exhibited markedly reduced infectivity compared with pseudoviruses generated using the Kenyan GP sequence. Reduced GP expression, following transfection of cells with a DNA plasmid encoding the vaccine-matched GP sequence, suggested that sequence-specific features adversely affected GP expression and pseudovirus production.

Structural modelling showed no detectable global conformational differences between the previous and revised mRNA vaccine GP structures, suggesting that functional differences are likely due to localized sequence effects rather than major structural changes. The revised mRNA sequence demonstrated significantly increased pseudovirus-neutralizing responses compared to the previous RVF mRNA construct, formulated using the same ionizable lipid SM-102 ($p \leq 0.01$). Formulation of the revised mRNA construct with the FTO lipid resulted in comparable immunogenicity following a single prime immunization at both low (0,1 µg) and high (1,0 µg) doses.

Conclusion: Optimizing the target antigen enhanced the overall performance of the RVF mRNA vaccine candidate by a marked improvement in immunogenicity in BALB/c mice. The FTO lipid demonstrated comparable performance to SM-102, supporting its suitability as an alternative ionizable lipid in LNP formulations. Preliminary studies showed robust stability of the revised RVF mRNA vaccine construct formulated with the FTO lipid at both -20°C and -80°C .

POSTER 379

Exploration of RNA-based vaccine strategies to induce a potent mucosal immune response against an acute infection HIV-1 Envelope

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Introduction: Developing an effective HIV-1 vaccine remains challenging due to the unique characteristics of the HIV envelope glycoprotein (Env) and the virus's ability to establish early reservoirs, which implies that the virus must be rapidly neutralized at the site of entry. The mRNA vaccine platform has recently shown great promise against HIV-1. However, its ability to induce mucosal protection remains weak. The aim of this study is to identify strategies to induce a potent mucosal immune response against HIV-1 Env. To do so, we developed a novel HIV-1 Env antigen based on an acute HIV-1 infection isolate, PHI133. Using our antigen, we tested the impact of various mRNA vaccine design strategies on both systemic and mucosal immune responses.

Material/Methods: We generated a stabilized single-chain-trimer (SCT) antigen based on the Env isolate PHI133 and analyzed, evaluated its structure by negative-stain electron microscopy (NS-EM). Next, we compared antigenicity profiles of our antigen when expressed as a soluble protein (gp140) or expressed on the cell surface (gp151), using enzyme-linked immunosorbent assay (ELISA) and flow-cytometry, respectively, testing a selection of known anti-Env antibodies. Then, an in vivo immunization mice experiment with different mRNA vaccine candidates was conducted, including a gp151 candidate, as well as an engineered virus-like particle (eVLP) forming variant. In addition, we also tested gp151 candidates with recently discovered TENT4-recruiting 3'UTRs that showed enhanced antigen expression in vitro. Throughout the experiment, we collected the animals' sera and vaginal washes to measure mucosal and systemic antibody levels by ELISA. Finally, we performed a preliminary in vivo test trans-amplifying RNA (taRNA) based vaccines for use against HIV-1.

Results: The NS-EM analysis shows the presence of mainly intact Env trimers, confirming that our design successfully stabilizes the Env trimer. Antigenicity profiles show distinct differences, with the gp151 design having an overall better binding profile, indicating improved antigen stability. The in vivo results demonstrate that an eVLP design, where the antigen is able to bud from the cell surface, showed a delay in systemic IgG kinetics response and induced lower IgA levels compared to the gp151 groups. Our 3'UTR candidates did not show drastic improvements in vaccine efficacy compared to our control 3'UTR. Finally, the preliminary in vivo experiment shows taRNA induces equally high systemic and significantly higher mucosal IgA responses compared to the mRNA control group.

Discussion: Here, we show the successful development of a novel HIV-1 Env immunogen based on an acute infection isolate. Our in vitro and in vivo tests overall suggest that a membrane-anchored gp151 immunogen design helps not only to improve antigen stability and conformation, but also outperforms our eVLP forming mRNA candidate in vivo. We also observed that the 3'UTRs that we tested did have a lower impact on overall vaccine immunogenicity than the antigen design itself. Finally, our preliminary tests using taRNA indicate that this platform may be advantageous for inducing mucosal IgA responses and will be further investigated in the future.

POSTER 381

Design, Development and Characterisation of Multivalent mRNA-LNP Vaccine Candidates for Mpox

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See oral presentation:

Plenary Session 5: One Health and Pandemic Preparedness • Wednesday 14 October, 10:20

POSTER 382

CIDR: a global reagents resource supporting vaccine development and epidemic preparedness

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A key component of effective pandemic preparedness is the cost-effective and timely access to characterised research reagents, which accelerates the development of vaccines, diagnostics and therapeutics against emerging infectious diseases. To meet this need, the Medicines and Healthcare products Regulatory Agency (MHRA) has recently launched a new reagent portfolio, the Centre for Infectious Disease Reagents (CIDR). CIDR builds upon the Centre for AIDS Reagents (CFAR), an ISO 9001 accredited repository which has supplied the scientific community with high quality reagents for the past 37 years.

The scope of CIDR is guided by priority pathogen lists from UK Vaccine Network, CEPI and WHO, and focuses on emerging viruses including Lassa, Nipah, Marburg, Ebola, Hantavirus, Chikungunya and Oropouche, while being reactive to potential new viral threats. To develop CIDR, we are actively engaging with the scientific community to anticipate reagent need, encouraging leading scientists to deposit materials to our repository, commissioning reagents as well as generating and characterising new reagents in-house.

Our catalogue is expanding and currently includes peptides, proteins, antibodies, clinical samples and adjuvants. To further support preparedness and increase research capacity, we are also producing a panel of Vesicular Stomatitis Virus (VSV) based pseudotyped viruses. These innovative tools enable evaluation of neutralising activity elicited by new vaccine candidates and can be handled safely at containment level 2.

CIDR is responding to recent outbreaks caused by Oropouche, Hanta and Bundibugyo virus. For Oropouche, CIDR can provide a variety of reagents including nanobodies, pseudotyped virus, glycoprotein and nucleoprotein antigens. With respect to Hantavirus, pseudotyped virus and the nucleoprotein will soon be available for request from the repository. In responding to the recent Bundibugyo outbreak, we will be producing pseudotyped viruses to aid vaccine development. For all three viruses, we are in the process of sourcing serum samples from convalescent patients.

Materials are made available for research use to institutions worldwide and prioritized to Low and Middle-Income Countries (LMICs) which can benefit from free of charge access. Transfers of materials are formalised by a Material Transfer Agreement which protects the depositor IP and states the conditions of use.

Scientists who would like to share reagents with the wider research community are invited to contact CIDR at cidr@mhra.gov.uk

POSTER 384

DNA delivery of plasmid-encoded incretin mimetics supports extended weight and blood glucose control in mouse models and enhances vaccine efficacy

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Introduction: Obesity and obesity-associated diabetes affect millions of patients worldwide. Incretin mimetic drugs such as glucose like peptide-1 (GLP-1) and glucose-dependent insulintropic peptide (GIP) analogs have revolutionized diabetes and obesity treatment. Importantly, in the clinic the use of these drugs is associated with improved inflammatory disease and some cancer outcomes. However, challenges with protein production and patient adherence remain.

Methods: We developed plasmid-encoded long-acting incretin analogues (pLincretins) by fusion of native and novel incretin molecules to IgG heavy chains. These molecules expressed in wild-type mice for over 70 days. Next, we evaluated their metabolic efficacy in mouse models of diet-induced obesity (DIO).

Results: pGLP1-mFc and pGIP-mFc were detectable in mouse sera for four weeks. Treated mice exhibited significant weight loss, increased glucose tolerance, and decreased food intake compared to controls. Lipidomic analysis of serum identified differentially represented lipid species between naïve animals and those treated with plasmid-encoded incretins. Further, we generated a novel incretin analog using a synthetic consensus (pSynCretin) design approach. pSynCretin supported extended weight and glucose control in vivo. To investigate the effect of incretin treatment on vaccine-induced immunity and protection we pre-treated DIO mice with pGLP1-mFc and immunized them with DNA plasmids encoding Influenza A H5N1 hemagglutinin (pCamb) or SARS-CoV-2 spike (pS). In the context of influenza immunogenicity, pretreatment with pGL1-mFc was associated with trends toward increased IFN γ secretion from CD8 $^{+}$ T cells by ICS and ELISpot. Strikingly, in the context of SARS-CoV-2 immunization and challenge, pretreatment with pGL1-mFc was associated with decreased clinical scores post-infection.

Conclusion: These studies demonstrate that DNA-delivered incretin therapy can support weight and blood glucose control following a single in vivo administration and support the translation of nucleic acid approaches for incretin mimetic delivery.

POSTER 385

synDNA vaccines targeting HPV16 and HPV18 E1/E2 proteins generate strong immune responses in animal models

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Background: Human Papilloma Virus (HPV) infection is responsible for ~4.5% of global cancers including cervical, anal, penile, head and neck, vulvar and vaginal cancers. The HPV16 and HPV18 strains are the major drivers of oncogenesis, although other strains are also implicated. Therapeutic vaccines against HPV generally target the E6 and E7 proteins which are important oncogenic drivers and have demonstrated promising results in early stage clinical trials for clearance of Cervical Intraepithelial Neoplasia, cervical cancer, anal cancers and head and neck cancer. Besides E6 and E7, HPV E1 and E2 proteins can also be useful additional antigens for therapeutic vaccines. E1 and E2 are typically expressed in earlier stages of disease, but newer studies show that they can also be expressed via episomal viral DNA in up to 70% of HPV cancers. In this study, we describe the design and development of synDNA vaccines targeting the E1 and E2 proteins of HPV16 and HPV18.

Methods: We used a global panel of HPV16 and HPV18 strains to design synthetic consensus sequences for HPV16 and HPV18 E1/E2 proteins. These sequences were RNA and codon optimized for enhanced expression and cloned into a high expression vector. The E1 and E2 proteins were separated by furin cleavage site and an IgE leader sequence was added to the N terminus to improve antigen presentation. Mice were immunized with the plasmids and immune responses analyzed via ELISPOTs and flow cytometry.

Results: The consensus sequence we designed had >95% homology with each individual strain. Both HPV16-E1/E2 and HPV18-E1/E2 vaccines demonstrated strong T cell responses evidenced by IFN γ ELISPOTs. We observed strong polyfunctional T cell responses as we observed induction of IFN γ , TNF α and IL2 from CD8+ and CD4+ T cells. Using mixed peptide pool experiments, we were able to identify the most immunogenic peptides in C57bl6 mice, and these cross referenced strongly with 8-mer peptides predicted to be immunogenic by netMHC in silico methods. To improve clinical translatability, we co-delivered HPV16-E1/E2 with clinically tested HPV16-E6/E7 vaccine and observed a trend towards higher immune responses against all four proteins when vaccines were co-delivered.

Conclusions: Our data suggests that vaccines targeting consensus sequences from a global panel of HPV16-E1/E2 and HPV18-E1/2 proteins are expressed in vitro. In C57Bl6 mice, both constructs drove strong, polyfunctional T cell response from both CD4+ and CD8+ T cell subsets. We also observed potential synergistic effect of co-delivering HPV16-E1/2 vaccine with the clinically tested HPV16-E6/E7 vaccine suggesting that co-delivery would allow us to target additional viral antigens making it more difficult for the virus to escape the immune attack. Further development of these vaccines for therapy of HPV associated cancers is warranted.

POSTER 387

IRES-Launched RNA Replicons Enable Versatile and Efficient Gene Expression

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Introduction/Background: Self-amplifying RNA (saRNA) represents a major advancement in vaccine development; its ability to autonomously replicate inside host cells significantly lowers the required therapeutic dose. Traditionally derived from alphaviruses, standard saRNA systems employ a bicistronic architecture: the replicase occupies the first open reading frame (ORF), followed by a subgenomic promoter, and the gene of interest (GOI) as the second ORF. Initiation of this replication cascade requires cap-dependent translation of the replicase, which demands complex and costly in vitro capping during manufacturing. Furthermore, this setup creates a distinct disadvantage compared to non-replicating mRNA: while non-replicating platforms benefit from advanced cap analogs throughout their entire lifespan, only the primary, in vitro synthesized saRNA transcripts utilize these analogs. All subsequent copies are capped inside the cell by the viral replicase itself, using its own methyltransferase (MTase) and guanylyltransferase (GTase) activities. Finally, because the expression of both the replicase and the GOI remains strictly cap-controlled, the entire system relies heavily on the host cell's canonical translation initiation factors, leaving it subject to standard cellular translation regulations and restrictions.

Material/Methods: To remove the constraints imposed by cap-dependent translation of the replicase, we engineered a novel RNA replicon with replicase translation independent of the 5'-terminal cap. Using Venezuelan Equine Encephalitis virus (VEEV) based saRNA, we placed the replicase under the control of an internal ribosome entry site (IRES). Thereby the initiation of translation depends on the molecular properties of the respective IRES to direct the ribosome to the translational start site.

Results: This IRES-launched replicon achieved expression levels comparable to standard 5'-capped saRNA in human primary fibroblasts. Advantageously, this architecture facilitated the insertion of a second gene of interest (GOI) upstream of the IRES, which is translated via a 5' cap added intracellularly by the replicase. The expression level of this upstream gene was intermediate, falling between that of standard mRNA and subgenomic RNA-mediated expression. Through subsequent optimization of the 5' promoter elements, we engineered IRES-launched replicons that outperformed wild-type Venezuelan equine encephalitis virus (VEEV) vectors. This enhancement was particularly pronounced for the gene upstream of the IRES, which is translated directly from the genomic replicon RNA template. Additionally, we explored the co-delivery of viral immune evasion genes, specifically Vaccinia virus E3 and Toscana virus NSs, to suppress cell-autonomous innate immunity. This strategy successfully mitigated the host antiviral response, yielding up to a seven-fold increase in replicon expression and highlighting the utility of immune evasion factors in optimizing RNA platforms.

Discussion/Conclusion: In conclusion, IRES-launched RNA replicons offer significant advantages over traditional platforms, enabling the use of uncapped synthetic saRNA without compromising its activity. By eliminating the need for in vitro capping, this approach streamlines the manufacturing process and substantially reduces production costs. Furthermore, this modular design allows for the independent co-expression of two therapeutic genes at distinct levels within transfected cells, offering a versatile tool for vaccine development and therapeutic applications.

POSTER 388

Evaluation of the Safety and Efficacy of a Reduced Dose of the Neethling Lumpy Skin Disease Vaccine for Cattle: A strategy for development of multivalent vaccine candidatesSbahle NDLOVU^{1,2}, Ntombikayise NKOMO¹, Thandeka KHOZA¹, Nobalanda MOKOENA^{2,3}¹ Onderstepoort Biological Products, 100, Old, Soutpan Road, Onderstepoort, 0110, Pretoria, South Africa² Department of Biochemistry, School of Life Sciences, University of KwaZulu-Natal (Pietermaritzburg Campus), Scottsville 3209, KwaZulu-Natal, South Africa³ Department of Biotechnology and Food Technology, Faculty of Science, University of Johannesburg, Doornfontein Campus, 2050, South Africa

Introduction: Lumpy Skin Disease is a contagious and notifiable disease of cattle that affects animals of all ages and is characterised by high morbidity and low mortality, resulting in significant economic losses to the livestock industry. The disease is endemic in many parts of Africa and has spread across Europe and Asia, posing a significant threat to cattle production and trade. Annual vaccination remains the primary and most effective control method for disease prevention. The Neethling strain vaccine manufactured by Onderstepoort Biological Products (OBP) has been successfully used for prophylactic immunisation against LSD and has played a critical role in controlling disease outbreaks in endemic and affected regions. Despite the successful use of LSD vaccines in controlling disease outbreaks, concerns have been reported regarding vaccine-associated adverse reactions. Furthermore, there is increasing interest in vaccine dose reduction and developing combination products that can provide protection against multiple diseases while reducing the number of vaccinations administered. Herein, we evaluate the safety and efficacy of a reduced dose of the Neethling Lumpy Skin Disease vaccine as a potential approach to minimise adverse reactions, optimise vaccine use, and support the future development of multivalent vaccine formulations.

Methods: To evaluate safety and efficacy, calves of ages 6 to 12 months with no previous exposure to Lumpy Skin Disease Virus (LSDV) were randomly assigned to three treatment groups. The first group was vaccinated subcutaneously with the recommended 2 mL dose of the Neethling LSD vaccine, while the second group received a reduced 1 mL dose. The third group served as a placebo and was injected with the vaccine diluent. Vaccine safety was evaluated by monitoring morning and afternoon rectal temperatures, recording and measuring local and systemic clinical reactions following vaccination. Animals in all groups were challenged with the virulent LSDV strain to evaluate vaccine efficacy and monitored until day 28 post challenge. Blood samples were collected every 7 days for serological analysis using ELISA and SNT methods. The presence of viremia was assessed through qPCR on whole blood samples collected on days 0, 2, 5, 7, 10, 12, and 14 post vaccination and challenge.

Results: Both the recommended and reduced vaccine doses were safe and induced a humoral immune response, with neutralising antibodies detected in all vaccinated animals. No post-vaccination temperature reactions were observed in any of the treatment groups. Upon challenge, all vaccinated animals were protected against clinical disease, with minor lesions observed, whereas animals in the placebo group developed enlarged lesions at the site of injection. Furthermore, animals in the placebo group were characterised by other clinical signs such as nasal discharge, enlarged lymph node, and multiple skin lesions, which are typical of LSD.

Conclusion: The Neethling LSD vaccine was safe when administered at both the recommended and reduced doses, with comparable protective efficacy supporting use of 1 ml dose in the development of multivalent vaccine candidates.

POSTER 389

Plasmid-encoded native and novel incretin mimetics enhance vaccine induced BАРF1 immunity against Epstein-Barr-virus associated carcinomas in immunocompromised mice

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Introduction/Background: The global prevalence of obesity with the convergence of aging represents a significant public health concern compounded by an increased susceptibility to severe viral infections, and diminished vaccine efficacy driven by immune dysfunction. Both phenotypes impose a hyper-inflammatory and hyper-regulatory immune state. Further, obesity accelerates biological aging and exacerbates age-related comorbidities. Alone, obesity is responsible for up to 20% of all cancers. Epstein-Barr Virus (EBV) BamHI-A rightward frame 1 (BARF1) is highly expressed in EBV-associated gastric carcinoma (EBVaGC). Obese patients have a 21% increased risk of gastric carcinoma. We previously demonstrated that plasmid DNA encoding BARF1 (pBARF1) can elicit robust CD8⁺ T cell responses capable of controlling syngeneic MC38 tumors expressing BARF1 as a model for EBVaGC. Incretin mimetics, including glucagon-like peptide-1 (GLP-1) reduce systemic inflammation and have been linked to reduced cancer risk, suggesting they may improve immunity in aged or obese populations.

Material/Methods: We generated plasmid-encoded long-acting incretins (pLincetins) by fusing dipeptidyl peptidase IV-resistant GLP-1 and GIP analogues with IgG Fc components. Plasmids were delivered to diet-induced obese mice (DIO) using a clinically validated electroporation (EP) device, driving sustained expression, supporting durable reductions in body weight, food intake and blood glucose.

Results: Importantly, when DIO mice were pretreated with pLincetins, vaccine-induced protection against SARS-CoV-2 was significantly improved. When we compared tumor control in aged versus young mice, MC38 tumors grew more quickly in aged animals. Subsequently, aged mice were pretreated with pLincetins and later immunized with pBARF1. BARF1-specific CD8⁺ T-cell responses and tumor control were evaluated by interferon-γ ELISpot, and multiparameter flow cytometry, and we observed an incretin-associated increase in anti-BARF1 immunity.

Discussion/Conclusion: Given these preliminary data we have confidence that by leveraging this technology, DNA-launched incretin mimetics, with their durability, safety, and translational feasibility, will positively impact vaccine-induced immunity in vivo for high-risk populations.

POSTER 390

Uncovering the receptor-mediated mechanism of the molecular adjuvant adenosine deaminase

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Introduction/Background: Molecular adjuvants are widely used to enhance vaccine-induced immunity, yet the mechanisms underlying many of these molecules remain poorly defined in plasmid-encoded delivery contexts. Adenosine deaminase-1 (ADA) is a highly conserved immunoregulatory protein with both catalytic and extraenzymatic functions, including interactions with CD26/Dipeptidyl Peptidase IV (DPP4) and the adenosine receptors A1, A2A, A2B, A3. We hypothesize that ADA adjuvanticity is mediated through receptor engagement and independent of enzymatic activity.

Materials/Methods: To test this, a panel of ADA variants was generated to decouple enzymatic function and individual receptor interactions, including catalytically-inactive mutants and constructs with selective disruption or retention of specific receptor-binding interfaces. Complementary literature describing A2A receptor signaling in adenosine-mediated immune regulation across dendritic cells, macrophages, and lymphocytes was used to inform receptor prioritization. ADA mutants targeting the A2A binding interface were engineered, including combination mutant schemes to further characterize receptor-specific contributions. Transgenic mouse models with selective receptor knock-in/knockout were used in combination with the mutant ADA panel to assess receptor dependence in vivo.

Results: Here, the catalytically-deficient mutant (E217D) retained adjuvanticity, as evidenced by antigen-specific IFN γ ⁺ CD8⁺ T cell responses and antibody titers in murine immunization models.

The Q142R variant, located within the structurally defined ADA-CD26 binding interface where residue 142 is a primary determinant of species-specific interaction, was associated with enhanced immune responses in vivo relative to wild-type ADA, as reflected by antigen-specific IFN γ ⁺ CD8⁺ T cell responses and antibody titers.

Discussion/Conclusion: Using site-directed mutagenesis, structural characterization, in vitro functional assays, and transgenic murine models, this work elucidates receptor-level mechanisms underlying ADA-mediated molecular adjuvanticity. The catalytically deficient ADA mutant (E217D) retains enhancement of immune responses in DNA-encoded vaccine contexts, while the CD26/DPP4 interface mutant Q142R is associated with enhanced immune responses in vivo relative to wild-type ADA, supporting a model in which receptor engagement contributes to adjuvant activity.

Ongoing work aims to define receptor-specific contributions using targeted interface mutants and transgenic receptor knock-in/knockout models, with a focus on A2A-associated signaling across antigen-presenting and lymphoid compartments.

Resolving the molecular mechanism of gene-encoded adjuvants is critical for clinical translation. This work supports a model in which ADA functions as a molecular bridge promoting interactions between CD26/DPP4 on T lymphocytes and adenosine receptor signaling pathways on antigen-presenting cells.

POSTER 391

Primary Healthcare Surveillance and Vaccination Challenges During the 2025 Meningococcal Serogroup C Outbreak Response in Sokoto State, Northern Nigeria

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See oral presentation:

Concurrent Session 2: Vaccine Regulatory Science and Policy • Monday 12 October, 16:20

POSTER 392

A Plant-Based MS2 Virus-Like Particle Platform for Rapid Production of mRNA Vaccines Against Emerging Infectious DiseasesWaranyoo PHOOLCHAROEN*Chulalongkorn University, Thailand*

Messenger RNA (mRNA) vaccines have emerged as a powerful platform for infectious disease prevention; however, alternative delivery systems that improve stability, simplify manufacturing, and reduce production costs remain highly desirable. Bacteriophage MS2 virus-like particles (VLPs) are capable of self-assembly and selective encapsidation of heterologous mRNA through pac-site-mediated packaging, providing a promising platform for mRNA delivery. In this study, we developed a plant-based MS2 VLP platform in *Nicotiana benthamiana* for the production of mRNA-loaded VLP vaccines. MS2 coat protein and antigen-encoding mRNAs containing MS2 packaging signals were co-expressed in plants to generate VLPs encapsidating either the receptor-binding domain (RBD) mRNA of SARS-CoV-2 or hemagglutinin (HA) mRNA of influenza virus. Purified VLPs were characterized and subsequently evaluated in a mouse immunization model. Successful assembly of MS2 VLPs and encapsidation of both RBD and HA mRNAs were confirmed following purification. Immunization of mice with the purified VLP-mRNA formulations induced antigen-specific immune responses against both SARS-CoV-2 and influenza antigens, demonstrating the biological functionality of the encapsidated mRNA and the immunogenic potential of the platform. These findings establish *N. benthamiana* as an effective production host for MS2 VLP-based mRNA vaccines and provide the first evidence that plant-produced MS2 VLPs encapsidating vaccine mRNA can induce antigen-specific immune responses in vivo. This work highlights the potential of plant molecular farming as a scalable, rapid, and cost-effective manufacturing strategy for next-generation VLP-based mRNA vaccines targeting emerging and re-emerging infectious diseases.

POSTER 396

Selective control of B cell activation for focused antibody responses

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Introduction/Background: Antibodies provide immune protection by binding to a specific location, or epitope, on a pathogen. However, not all antibodies are equally protective. While targeting certain epitopes can enable virus neutralisation or confer protection across variants, other epitopes may be highly variable, inaccessible, or elicit antibodies that are ineffective or even harmful. Therefore, immunofocusing, the ability to focus immune responses towards desired epitopes, is a major goal in modern vaccine design. Achieving such programmability could enable life-saving vaccines against major pathogenic threats, such as HIV, Dengue virus, or the continually evolving influenza virus. Here, we present the Duality Vaccination strategy, which enables controlled activation of B cells targeting either desired or undesired antigens or epitopes.

Material/Methods: In our Duality vaccine system, an immune-activating stimulus is NOT-gated by the down-regulation of a response subset. This inhibition is achieved by coupling the undesired antigen or epitope to a B-cell inhibitory receptor binder. We assembled our vaccine components using SpyTag/SpyCatcher protein conjugation, SpyMask bispecific assembly and the modular mi3 virus-like-particle. C57BL/6 mice were immunised in prime-boost regimens, and serum antibody titers were analysed by Enzyme-Linked Immunosorbent Assay (ELISA).

Results: We demonstrate that bridging B-cell receptor (BCR) to CD22, but not FcγRII specifically reduces activation of unwanted responses, even in the presence of adjuvant. We find that valency and linker length are key, while spatial and temporal separation of activating and inhibitory components hinders effectiveness.

Discussion: The Duality Vaccination logic gate enables antibody response focusing, with broad potential applications in rational vaccine design.

POSTER 397

Rational Genetic Design of a Safe and Efficacious delta LprG-Rv1410-DevB Live Attenuated Mtb Vaccine

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The majority of the world's population has received intradermal BCG vaccination. Live attenuated vaccines (LAV) offer unique advantages over other vaccine modalities including immune presentation of the entire mycobacterial proteome in conjunction with highly immunogenic mycobacterial lipids many of which are known potent adjuvants. We previously showed that an operonic knock-out of Mycobacterium tuberculosis (Mtb) LprG-Rv1410 was safe and efficacious in mice when used as a LAV. To meet the WHO recommendations for Mtb LAV, we used a transposon mutagenesis synthetic lethality screen to prioritize further genetic modifications to enhance safety of the delta LprG LAV. We screened a panel of modified delta LprG LAV and demonstrate efficacy of a triple knock-out (TKO) of delta LprG-Rv1410c-delta DevB against high virulence Erdman Mtb challenge in both resistant (C57BL/6) and susceptible (C3HeB/FeJ) mouse models. The modified delta LprG TKO LAV is genetically stable based on reversion and mutation rate assays and was safe in immune deficient SCID mice out to 185 days. Delta LprG TKO LAV significantly induced tissue resident memory CD4+ and CD8+ T lymphocytes in the lung following subcutaneous administration which correlates with reduced bacterial burden in both mouse models. The combination of enhanced genetic stability, demonstrable safety in immunocompromised hosts, and robust tissue-resident memory induction positions delta LprG TKO as a viable LAV platform for TB prevention.

POSTER 398

From Forest to Vaccine: An Integrated Platform for Sustainable Production of Quillaja Saponin Adjuvants

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Background: Quillaja-derived saponins are among the most widely used immunostimulatory components in modern vaccine adjuvants. QS-21 is incorporated into AS01-based adjuvant systems used in licensed vaccines against herpes zoster, respiratory syncytial virus, and malaria, while related Quillaja saponin fractions are key components of Matrix-M-based formulations. The expanding use of saponin-containing adjuvants highlights the importance of sustainable, scalable, and reliable production systems capable of supporting global vaccine development.

Methods: We describe an integrated production platform encompassing sustainable biomass sourcing, raw material selection, extraction, purification, analytical characterization, and GMP manufacturing of Quillaja-derived vaccine adjuvant saponins. The platform combines forestry stewardship, chromatographic purification technologies, advanced analytical characterization, and quality management systems to support the production of highly purified QS-21 and related saponin fractions.

Results: Quillaja biomass contains a diverse family of triterpenic saponins, including QS-7, QS-17, QS-18, QS-21, and additional adjuvant-active fractions. Through integrated control of the production chain, from biomass sourcing to final product release, consistent manufacture of vaccine-grade saponins can be achieved. Sustainable forestry practices, selective biomass management, clonal propagation programs, and plantation technologies provide a framework for long-term supply while supporting environmental stewardship and product traceability. The platform supports production of purified saponin fractions currently utilized in licensed and investigational vaccine adjuvant systems.

Conclusions: Naturally sourced Quillaja saponins remain a critical resource for vaccine adjuvant development. Current bark-based production technologies provide the most favorable balance of product quality, manufacturing scalability, sustainability, and cost-effectiveness compared with alternative emerging production approaches. Integrated management of the entire production chain, from forest to final pharmaceutical ingredient, supports reliable long-term availability of Quillaja-derived adjuvants for current and future vaccine programs.

POSTER 399

Evaluating the protection and cross-protection of recombinant vesicular stomatitis virus-vectored orthoebolavirus vaccines in ferrets

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Orthoebolaviruses, including Ebola virus (EBOV), Sudan virus (SUDV), and Bundibugyo virus (BDBV), cause sporadic outbreaks of severe disease in humans and pose significant public health threats. Indeed, BDBV re-emerged in the Democratic Republic of the Congo (DRC) in May 2026, and, as of June 2026, has already infected over 1200 people, with cases exported to Uganda and France. Although experimental vaccines for orthoebolaviruses have been developed, only vaccines against EBOV have been approved for use in humans. Among these, the recombinant vesicular stomatitis virus (VSV)-based EBOV vaccine is among the most promising and effective. This vaccine, referred to as rVSV-EBOV or by its tradename Ervebo, is a live, replication competent VSV in which the endogenous glycoprotein has been replaced with the EBOV glycoprotein (GP). Analogous vaccines have also been developed for SUDV and BDBV—referred to as rVSV-SUDV and rVSV-BDBV, respectively—but they have not yet been clinically approved. Given the limited antigenic cross-reactivity among different orthoebolavirus GPs, we sought to evaluate the cross-protective potential of different VSV-vectored vaccines against virus challenge in ferrets, which are highly susceptible to wild-type orthoebolaviruses and recapitulate all key features of disease observed in humans and nonhuman primates. Initially, ferrets were vaccinated with rVSV-EBOV or rVSV-SUDV and subsequently challenged with either the homologous or heterologous virus. In general, vaccination was well tolerated, elicited strong humoral immune responses, and provided protection against homologous challenge. That is, animals vaccinated with rVSV-EBOV and challenged with EBOV demonstrated 100% survival with no signs of disease, as did animals vaccinated with rVSV-SUDV and challenged with SUDV. However, in contrast to our previous findings in guinea pigs, but consistent with prior NHP studies, neither vaccine conferred cross-protection against heterologous challenge, with all rVSV-EBOV-vaccinated and SUDV-challenged animals as well as all rVSV-SUDV-vaccinated and EBOV-challenged animals developing severe disease and succumbing at the same time as the unvaccinated control ferrets. Interestingly, animals vaccinated with rVSV-EBOV, but not those vaccinated with rVSV-SUDV, exhibited an IgG response that was moderately cross-reactive with BDBV GP, suggesting the potential for cross-protection against this virus. In a follow up ferret study, we are currently evaluating whether vaccination with rVSV-EBOV (prime or prime/boost) will offer meaningful cross-protection against BDBV challenge, a phenomenon that could have important implications in the response to the ongoing outbreak of BDBV in the DRC. Overall, this study not only demonstrates the value of the ferret model for evaluating vaccine efficacy against orthoebolaviruses, but it also highlights important observations regarding vaccine cross-protection that may inform the public health response to outbreaks caused by these viruses, including BDBV.

POSTER 400

Probing the repertoire of serum antibodies with random peptides: discovery of diagnostic markers.

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Introduction: Serum consists of vast collections of antibodies, products of differentiated B-cells. The spectrum of antibody specificities is dynamic and varies with age, physiology, and exposure to pathological insults. The complete repertoire of antibody specificities in blood, the IgOme, is therefore an extraordinarily rich source of information – a molecular record of previous encounters as well as a status report of current immune activity. The ability to profile antibody specificities of polyclonal serum at high resolution promises to produce diagnostic markers as well as insights for improved vaccine design and health management. Here we describe the use of combinatorial phage displayed random peptides as probes to profile the IgOme. Implementation of computational pipelines combined with machine learning have proven effective for identifying and using disease defining peptide-markers.

Results and Discussion: Over the course of the last 20 years, we have analysed monoclonal antibodies and polyclonal sera representing a diversity of human infectious viruses such as HIV, HCV, influenza, SARS and MERS Coronaviruses and Dengue virus. The objective has been to identify correlates of the humoral response towards these viral infections. We have recently published a study analysing the antibody response towards H3N2 influenza infection of ferrets [1]. Sera taken from infected ferrets compared to serum samples of naïve non-infected ferrets, led to the identification of peptide motifs that can be associated with the antibody response to flu infection. The motifs proved discriminatory of the biological condition of interest, i.e., infected vs non-infected animals. Furthermore, the motifs proved useful as predictors of the infectious status.

The potential use of phage displayed peptides in analysing disease defining sera will be further discussed.

References:

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Acknowledgement: This work was funded by the Israel Science Foundation, Sanofi and the Bill and Melinda Gates Foundation (INV-004951).

POSTER 401

DNA-launched orthoflavivirus replicons expressing HCV NS3/4A induce cellular and humoral immune responses in mice

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Introduction/Background: Hepatitis C virus (HCV) remains a major global health challenge despite the availability of direct-acting antivirals, highlighting the need for effective vaccines capable of inducing robust cellular immunity. The aim of this study was to develop and evaluate DNA-launched orthoflavivirus replicons as vaccine vectors for delivery of the HCV NS3/4A-based antigen C2.2.

Materials/Methods: Replicons derived from tick-borne encephalitis virus (TBEV), Langat virus (LGTV), Kunjin virus (KUNV), and West Nile virus (WNV) were engineered to express the HCV NS3/4A-based antigen C2.2. Antigen expression was characterized in vitro, and immunogenicity was evaluated in C57BL/6J and BALB/c mice by analysis of HCV NS3-specific cellular immune responses, CD8⁺ T-cell responses, cytokine production, and antigen- and vector-specific antibody responses.

Results: Replicon-based constructs induced HCV NS3-specific cellular immune responses, including IFN- γ and IL-2 secretion, and generated antigen-specific CD8⁺ T-cell responses. KUNV- and WNV-based replicons supported efficient antigen expression and induced polyfunctional CD8⁺ T cells co-expressing IFN- γ , TNF- α , and CD107a. Replication-competent replicons preferentially induced IL-2-producing T cells, consistent with an immune profile associated with memory precursor differentiation, whereas replication-deficient constructs predominantly generated IFN- γ -secreting effector responses. KUNV-based replicons also induced HCV NS3-specific antibody responses and significantly higher WNV NS1-specific antibody levels than replication-deficient controls, supporting active replicon expression and replication in vivo.

Discussion/Conclusion: These findings demonstrate that DNA-launched orthoflavivirus replicons can efficiently deliver HCV antigens and induce both cellular and humoral immune responses in mice. The results support further evaluation of KUNV- and WNV-based replicons as vaccine platforms for HCV and other viral infections.

POSTER 403

Immunopectidomics-identified and mRNA-encoded *Mycobacterium tuberculosis* antigens elicit functional human T cells with antimycobacterial activity

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Introduction: Tuberculosis (TB), caused by the intracellular pathogen *Mycobacterium tuberculosis* (Mtb), remains a leading cause of infectious mortality worldwide, underscoring the urgent need for more effective vaccines. The only licensed TB-vaccine, Bacille Calmette-Guérin (BCG), protects against severe childhood disease but provides inconsistent protection against pulmonary TB in adults. Within the EU-consortium Baxerna, we previously identified novel Mtb-vaccine antigens by immunopectidomics, demonstrating protection against an Mtb-challenge in mice following vaccination with mRNA-lipid nanoparticles. Here, we evaluated whether these Mtb-antigens also elicit functional human T-cell responses, a critical step toward clinical translation.

Materials and Methods: mRNA encoding PPE3, PPE20, EsxK, TB8.4 and Rv2264c, flanked by lysosomal trafficking domains, was in vitro transcribed from the pLMCT plasmid. Differentiation of monocytes to dendritic cells (DCs) was induced. Immature DCs were electroporated with mRNA encoding PPE3 and PPE20, or PPE3, PPE20, EsxK, TB8.4 and Rv2264c. These DCs were used to activate autologous T cells, quantified by interferon- γ (IFN- γ) ELISpot. The functional activity of T cells, IFN- γ and/or tumor necrosis factor- α (TNF- α) was evaluated in co-culture with dsRed BCG-infected macrophages using real-time microscopy and flow cytometry to quantify dsRed signals. Cell phenotype and viability were analyzed by flow cytometry.

Results: Monocyte-derived DCs were efficiently electroporated with mRNA encoding the Mtb-antigens PPE3 and PPE20, or PPE3, PPE20, EsxK, TB8.4 and Rv2264c. These DCs were co-cultured with autologous T cells, demonstrating induction of antigen-specific, IFN- γ -producing T cells against all antigens, accompanied by a reduced CD4/CD8 ratio, indicative of preferential CD8⁺ T-cell expansion. Importantly, activated T cells significantly reduced the intracellular mycobacterial burden in dsRed BCG-infected macrophages. This antimycobacterial activity correlated with CD8⁺ T-cell frequencies. Recombinant IFN- γ only partially reproduced this effect, indicating that T cell-mediated mycobacterial control extends beyond classical IFN- γ -driven macrophage activation. Studies investigating the contribution of TNF- α and autophagy are ongoing.

Conclusion: These findings provide the functional validation of immunopectidomics-identified Mtb-antigens in human T cells, bridge preclinical antigen discovery with human immunogenicity, and support the clinical development of an mRNA-based TB-vaccine.

POSTER 404

Pre-clinical assessment of mRNA vaccines against mumps virus

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Paramyxoviruses are unique among viruses that use class I fusogens in that two distinct glycoproteins engage the receptor and facilitate virus-to-cell fusion. Whilst some paramyxoviruses have exquisite species specificity and bind proteinaceous receptors, rubulaviruses utilize widely expressed and broadly conserved sugar molecules. Mumps virus (MuV) is the prototype rubulavirus and is a highly transmissible ($R_0 = 4-7$) respiratory pathogen. Despite widespread vaccination with the measles, mumps and rubella vaccine, MuV still causes sporadic outbreaks in vaccinees due to waning immunity. There is likely a need for a third vaccination in adolescents. We rescued a recombinant (r) MuV based on a circulating MuV clinical isolate that expresses EGFP. This permits MuV to be tracked in vitro and in vivo. To understand MuV antigenicity we generated a panel of monoclonal antibodies from protein or mRNA immunized animals. These were used to isolate a panel of MuV escape mutants. Generation of a low-resolution cryo-electron tomography structure of the MuV fusion (F)/hemagglutinin-neuraminidase (HN) complex on the surface of the virion was used to map the antigenic sites bound by the antibodies. We established a small animal model for MuV respiratory infection and confirmed productive infection in the lungs by isolating MuV from bronchial alveolar cells. Lipid nanoparticle (LNP) encapsidated mRNAs encoding stabilized F or HN glycoproteins were characterized in vitro and in vivo. Both mice and cotton rats elicited robust anti-MuV neutralizing responses from single and co-administered candidate vaccines. After a prime/boost vaccination schedule, cotton rats were challenged intranasally with MuV. Immunized animals showed limited viral replication and significantly reduced viral titers compared to sham-vaccinated controls. Overall mRNA/LNPs can elicit robust immunogenic responses against MuV and may represent means to decrease the likelihood of mumps outbreaks.

POSTER 406

The potential of mRNA-LNPs for tolerogenic vaccination

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Background/Aim: Although the potency of mRNA-LNP vaccines has been extensively demonstrated by the recent COVID-19 pandemic, the underlying mechanism of their immunogenicity remains a topic of debate. Both mRNA and lipid fraction have been linked to immunostimulation, either through directly activating Toll-Like Receptors (TLRs), or indirectly through endosomal escape. In addition, byproducts of mRNA synthesis, like dsRNA, can act as a strong triggers for anti-viral immune cascades. Through dissecting the self-adjuvant effect of the different components of this vaccination platform and reducing their contribution to overall immunogenicity we aim to explore the potential of mRNA-LNPs for the generation of tolerant vaccines.

Methods: mRNA was synthesized using multiple in vitro production protocols, generating mRNA with different levels of dsRNA contaminants, subsequently incorporated into LNP formulations. These formulations were used to transfect NFkB and interferon response gene (ISG) reporter cell lines to assess the effect of mRNA byproducts on innate immune activation. In addition, labeled mRNA-LNPs containing different levels of mRNA purity were injected intravenously in mice and tested for their ability to induce either immunogenic or homeostatic dendritic cell maturation in vivo.

Results: Process optimization of in vitro transcription of mRNA led to a reduction in dsRNA in the final product. Reduced dsRNA levels corresponded to lower activation of both NFkB and interferon type I response in cells transfected with mRNA-LNPs, a difference that was no longer observed in a dsRNA-receptor MDA5 knockout cell line. When injecting mice intravenously with LNPs containing cargo with various levels of mRNA purity, standard mRNA-LNP formulations led to immunogenic maturation of dendritic cells whilst empty LNPs induce a more homeostatic, or tolerant maturation profile. When low-dsRNA containing mRNA cargo LNPs were injected, dendritic cells displayed a reduced immunogenic and increased tolerogenic maturation profile compared to standard mRNA formulations. These results show that optimizing LNP cargo can reduce the immunogenicity of LNPs and steer the immune system towards a more tolerant response.

POSTER 408

Beyond iNKT Activation: α -GalCer-adjuvanted mRNA-LNP Vaccines Elicit Broader Unconventional T-Cell Responses

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Messenger RNA–lipid nanoparticle (mRNA-LNP) vaccines have emerged as transformative platforms for infectious-disease prevention and cancer immunotherapy. However, strategies that broaden their cellular immunogenicity without compromising tolerability remain needed. We developed mRNA-Galsomes, an mRNA-LNP platform incorporating α -galactosylceramide (α -GalCer), a potent glycolipid agonist presented by CD1d to invariant natural killer T (iNKT) cells (Verbeke et al., 2019; Meulewaeter et al., 2024). We hypothesized that α -GalCer-mediated iNKT-cell activation could extend to other unconventional T-cell populations through bystander mechanisms, particularly $\gamma\delta$ T cells and mucosal-associated invariant T (MAIT) cells.

To investigate this, ovalbumin-encoding mRNA-LNPs were prepared using three ionizable lipids: C12-200, a benchmark lipid with efficient mRNA delivery and strong immunostimulatory activity; SM-102, the clinically validated ionizable lipid used in Moderna's Spikevax vaccine; and S-Ac7-DOG, a biodegradable biscarbamate lipid developed for efficient delivery with reduced reactogenicity. Each formulation was prepared with or without α -GalCer. Physicochemical characterization demonstrated comparable particle properties, high mRNA encapsulation efficiency and stability across the formulations. C57BL/6 mice (n = 4 per group) were immunized intramuscularly, and splenic iNKT, $\gamma\delta$ T and MAIT-cell responses were assessed 12 hours after priming using multiparameter flow cytometry.

α -GalCer incorporation induced robust iNKT-cell activation across all three LNP formulations, confirming effective glycolipid presentation. Importantly, this response extended beyond iNKT cells and was accompanied by activation of $\gamma\delta$ T and MAIT cells. The magnitude of this broader response was strongly dependent on the ionizable lipid. C12-200 mRNA-Galsomes induced the most pronounced $\gamma\delta$ T- and MAIT-cell activation, characterized by increased CD69 expression and enhanced IFN- γ and IL-17A production. Unexpectedly, C12-200 mRNA-LNPs without α -GalCer also activated iNKT, $\gamma\delta$ T and MAIT cells—an effect not observed with SM-102 or S-Ac7-DOG. This observation is consistent with previous evidence that selected ionizable-lipid amine headgroups can interact with CD1d and TLR4, although the involvement of these receptors was not directly investigated in the present study (Chaudhary et al., 2024).

Together, these findings demonstrate that α -GalCer-adjuvanted mRNA-LNP vaccines engage a broader unconventional T-cell network extending beyond directly activated iNKT cells. Moreover, the α -GalCer-independent activity of C12-200 reveals that ionizable lipids are not immunologically inert delivery components but active determinants of unconventional T-cell responses. These results identify both α -GalCer incorporation and ionizable-lipid selection as important design parameters for mRNA-LNP vaccines intended to generate rapid and broadly coordinated cellular immunity.

POSTER 409

Liver Immunity-Guided Discovery of Capsule-Permeable Protein Antigens Against Bacterial Sepsis

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Encapsulated bacteria are the major causes of septic infections in humans and domestic animals. Capsular polysaccharide vaccines in *Streptococcus pneumoniae*, *Haemophilus influenzae* and *N. meningitidis* have significantly reduced the global burden of invasive bacterial diseases. However, these vaccines suffer from narrow coverage and high production costs. Moreover, the diseases caused by some encapsulated bacteria are not effectively controlled by polysaccharide-based vaccines, such as serotype-3 *S. pneumoniae*, group B *N. meningitidis* and *Streptococcus pyogenes*. Due to the shielding effect of the polysaccharide capsules, the proteins predicted to be surface exposed by bioinformatic analysis often fail to be effective vaccine antigens. Based on our recent discovery of the liver-based vaccine protection mechanisms (Wang et al., 2023, Science Translational Medicine, PMID: 38117903), we have developed the Liver-based Vaccine Antigen Capture (L-VAC) platform to identify capsule-permeable proteins of encapsulated bacteria. This system combines the antibody-mediated in vitro screening for capsule-targetable proteins with the in vivo bacterial clearance visualization in the livers of mice. Applying L-VAC to *S. pneumoniae* identified multiple capsule-permeable proteins that induce rapid hepatic clearance of blood-borne bacteria. Immunization with these proteins, especially in a multivalent formulation, conferred broad cross-serotype protection. Spatial analyses revealed that protein-bound antibodies facilitate complement deposition at or near the capsular surface, enabling effective immune recognition despite capsule shielding. These findings establish L-VAC as an effective approach for identifying protective protein antigens capable of overcoming capsule barriers, offering a promising strategy to develop broadly protective vaccines against multidrug-resistant encapsulated pathogens.

POSTER 411

Safety and Immunogenicity of a Novel Trivalent Virus-Like Particle Poliovirus Vaccine (VPV): A Phase 1, Randomized, Observer-Blind Trial

Jinbo GOU, Qiaoling YAN

See oral presentation:

Plenary Session 1: Population Impact of Vaccination • Monday 12 October, 11:40

POSTER 413

NEXTGENVACC: ADVANCING EARLY CAREER ENGAGEMENT IN VACCINOLOGY

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The Next Generation of Vaccinologists (NextGenVacc; NGV) is a strategic initiative developed within the International Society for Vaccines (ISV) to promote the academic and professional visibility of early career researchers (ECRs), including doctoral candidates and postdoctoral fellows, in the global field of vaccinology.

Through a series of monthly webinars, participants disseminate original research to a global audience, engage with senior experts who share diverse career trajectories, and gain insights from industry leaders representing biotechnology and pharmaceutical sectors. The program maintains a robust collaboration with the ISV Mentorship Committee, fostering structured support for career development and long-term professional growth.

Prospective contributors and community members are invited to connect with the NextGenVacc committee during the ISV Congress to explore opportunities for involvement, join the community, or present their research at one of the upcoming webinars. Visit the NextGenVacc committee stand at the ISV congress and become part of the future of vaccinology.

POSTER 415

Design and evaluation of a poly-epitope based vaccine for the induction of influenza A virus cross-reactive CD8⁺ T cell responses

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The availability of influenza vaccines that can induce broadly protective immune responses is highly desirable and could also mitigate the impact of future influenza pandemics. Ideally, these vaccines also induce virus-specific CD8⁺ T cells, which have been identified as an independent correlate of protection. In the present study, we explored the use of an artificial immunogen that comprises of twenty highly conserved influenza virus CD8⁺ T cell epitopes with an HLA coverage of 99.5% of the world population. The highly attenuated viral vector Modified Vaccinia virus Ankara (MVA)¹ and mRNA formulated in lipid nanoparticles (LNP) were used to deliver the artificial poly-epitope sequence and by using T cell lines raised against individual epitopes, we confirmed that the epitopes were liberated from the artificial immunogen. Stimulation of peripheral blood mononuclear cells of HLA-typed blood donors with the rMVA1 or mRNA encoding the polyepitope sequence, resulted in the activation of influenza virus-specific T cell responses. Furthermore, immunization of humanized HLA-A2.1-/HLA-DR1-transgenic H-2 class I-/class II-knockout mice (HLA-A*02:01) with rMVA-PE induced influenza virus-specific CD8⁺ T cell responses¹. Thus, the poly-epitope sequence proved to be immunogenic both in vitro and in vivo and constitutes a promising vaccine candidate for the induction of cross-reactive CD8⁺ T cell responses that could afford protection against antigenically distinct seasonal and pandemic influenza A viruses.

¹ Dam S, Tscherne A, Engels L, Sutter G, Osterhaus ADME and Rimmelzwaan GF. Design and evaluation of a poly-epitope based vaccine for the induction of influenza A virus cross-reactive CD8⁺ T cell responses. *Scientific Reports* 15(1):10586. doi: 10.1038/s41598-025-95479-9 (2025)

POSTER 417

A Randomized Dose-Escalation Phase I Clinical Trial of a Nucleoprotein-Based Genetic Vaccine Against Crimean-Congo Hemorrhagic Fever

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Crimean-Congo haemorrhagic fever virus (CCHFV) is an emerging tick-borne virus transmitted primarily by Hyalomma ticks, whose geographic distribution is expanding. CCHFV infection is associated with high case-fatality rates, and there are currently no widely approved vaccines available globally. CCHFV is included on the World Health Organization (WHO) R&D Blueprint list of priority pathogens, underscoring its epidemic potential and the urgent need for effective countermeasures. We were the first to demonstrate that a genetic DNA vaccine (CCHF-N-pVAX1) expressing the nucleoprotein (N) of CCHFV can confer robust protection against lethal disease in mice and attenuate clinical symptoms in non-human primates, providing a compelling proof-of-concept for a broadly applicable and previously underexplored vaccine strategy through activation of N-specific T cells and antibodies. Here, the CCHF-N-pVAX1 vaccine was tested in a phase I clinical trial with 15 healthy volunteers (HVs) divided 5 per group in three dose groups (0.45 mg, 0.90 mg, and 1.80 mg). The participants received vaccinations at weeks 0, 4, and 12 by intramuscular (i.m.) injection using in vivo electroporation (EP; IGEA Medical), followed by 3 months of follow-up. All patients experienced temporary pain in close proximity to the vaccination/EP procedure. The vaccine was safe, and no serious adverse event (SAE) occurred. 139 other Adverse Events (AEs) occurred; 69 reactogenicity and 70 other. The AEs were mostly of mild grade (n=123); 10 AEs were of moderate intensity, and 6 AEs were of severe intensity (diarrhea (n = 1), headache (n = 1), and fatigue (n = 4)). Most AEs (114/139) were likely or possibly related to the vaccine/EP. The vaccine was safe, with mostly mild grade adverse events (AE: n=113), 3 AE of moderate intensity, and 2 AE of severe intensity (diarrhea and fatigue), likely or possibly related to the vaccine/EP. No severe AE occurred. Antibodies and T cells appeared after the 2nd dose and peaked after the 3rd dose. The T cell responses were maintained throughout the 3-month follow-up. Strong T cell responses to recombinant N protein (CD4+), but not to peptides (CD4+/CD8+), correlated with the anti-N antibody responses (p<0.05, Mann Whitney). In conclusion, we show for the first time that a genetic N-based vaccine against CCHF is safe and immunogenic in humans, inducing strong T- and B-cell responses in most vaccine recipients, and show potential to confer protection against severe disease.

POSTER 419

Inducing mucosal immunity through intranasal delivery of *Neisseria meningitidis*-derived Outer Membrane Vesicles (Nm OMV): evidence from pre clinical studies to clinical translation.

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AdJane BV, Netherlands, The

Mucosal immunity represents the first defence barrier against most viral and bacterial respiratory pathogens. Strong mucosal immunity can block infection or reduce pathogen replication and shedding, playing pivotal roles in preventing disease and transmission. The majority of licensed vaccines are delivered intramuscularly and, while capable of eliciting robust systemic immune responses, their induced immunity at the respiratory mucosa is typically modest. Hence, although highly protective against severe disease, these vaccines often fail to efficiently prevent infection and community spread.

Vaccines delivered via the nasal route induce both systemic and local mucosal immune responses. Our *Neisseria meningitidis* (Nm)-derived Outer Membrane Vesicles (OMVs) have been engineered to improve manufacturability, reduce reactogenicity and strain-specific immune-interference, while preserving their immunostimulatory properties. These characteristics make Nm-OMVs an attractive vaccine platform for both intramuscular and intranasal delivery. Here, we summarize preclinical and clinical findings from studies assessing the intranasal delivery of a SARS-CoV-2 spike antigen in combination with Nm-OMVs.

To compare intranasal versus intramuscular delivery, BALB/c mice and Syrian hamsters were vaccinated (days 0, 21) with a stabilized prefusion SARS-CoV-2 spike either mixed with OMVs or linked to these vesicles through the LPS-binding peptide mCRAMP (mC). At day 41, hamsters were challenged with live SARS-CoV-2. The subsequent Phase 1, randomized, double-blind, placebo- and OMV-controlled study, assessed safety, tolerability and immunogenicity of intranasal OMVs mixed with the stabilized spike (location: Australia). Healthy subjects aged 18–55 years, SARS-CoV-2 seropositive due to prior vaccination or natural infection (n=40), were randomized into two cohorts receiving a low-dose (140 µg OMV/70 µg Spike) or a high-dose (280 µg OMV/140 µg Spike) at days 1 and 22. Humoral systemic immunogenicity was assessed measuring SARS-CoV-2 neutralizing antibodies, IgG and IgA while mucosal immunogenicity was determined by quantifying IgA levels in nasal washes.

In mice and hamsters, only the intranasal vaccination was capable of eliciting robust levels of spike-specific IgG and IgA in the nose and lungs, while serum neutralizing antibodies were induced by both intramuscular and intranasal delivery. The highest level of protection against viral challenge was observed in hamsters vaccinated intranasally with the OMV-mC-Spike vaccine, as scored by prevention of weight loss and viral replication, correlating with absence of lung lesions. In humans, the OMV-Spike vaccine was safe and well tolerated without serious adverse events. Most of the adverse events were mild and transient with no apparent differences across cohorts and control groups. The OMV-Spike vaccine induced a dose-dependent increase in systemic and mucosal immune responses, with the high-dose group presenting a rise in serum neutralizing antibodies. Statistically significant increases in serum IgG and, importantly, nasal IgA titers were observed.

Taken together, these preclinical and clinical studies support intranasal delivery of vaccines based on the Nm-OMV platform either as a stand-alone or as a complementary intervention in prime-boost modalities to augment mucosal immunity at infection's sites. Further clinical assessments are warranted to establish broader application of this vaccination platform, including for pandemic preparedness and for enhancing the effectiveness of current seasonal vaccinations.

POSTER 422

Improved thermostability and accessibility of mRNA vaccines via Microarray-Patch

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mRNA vaccines can play an important role in rapid response to pandemics and other disease outbreaks. Rapid and equitable access to mRNA vaccines is essential to reduce morbidity and mortality, especially in underserved or hard-to-reach communities, and to reduce the global spread and impact of disease. Cold chain requirements and the need for skilled administration are significant factors in this accessibility divide. Vaxxas has developed a high-density microarray patch (HD-MAP) that delivers vaccine into the upper skin layers. The HD-MAP associated vaccine formulation and manufacturing technology that has been proven in Phase 1 studies to effectively deliver and generate comparable immune responses against IM to a variety of vaccine types at reduced doses (e.g., seasonal influenza, measles rubella, subunit proteins). HD-MAPs have successfully been stored at temperatures up to 40°C for extended periods of time – in some cases, over a year. This eliminates or reduces the need for cold chain in shipping and storage, reducing the cost and complexity of providing vaccines.

Here, we will share new data demonstrating significantly improved thermostability of mRNA encapsulated in LNP formulations akin to those used in the Moderna and Pfizer commercial vaccines, stable for ≥12 months at 2-8°C and 3 months at 40°C and 75%RH. The approach to screening, dispensing, and drying formulations will be described, along with methods used to assess quality and integrity of mRNA LNPs. We will also share preclinical data demonstrating in vitro protein expression, in vivo uptake, immune responses to different HD-MAP delivered mRNA antigen, including responses to long-term stored HD-MAPs. Based on these foundational data, an mRNA vaccine candidate has been proposed to advance into a Phase 1 clinical program.

This platform approach can be applied to other antigens and LNP formulations, supporting CEPI's "100 days" target and general mRNA vaccine development.

POSTER 423

A multivalent DNA vaccine induces mucosal immune protection from Valley Fever, an inhaled fungal disease that is rapidly spreading due to climate change

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Introduction: Fungal infections are rapidly spreading due to climate change, but no fungal vaccine is approved for humans. *Coccidioides* causes Valley Fever, a chronic fungal lung infection that can be life-threatening. Climate change is creating favorable conditions for its rapid spread in the soils of North and South America. T cell responses, including IFN- γ and Th17 responses, play a key role in controlling fungal infections, and a vaccine that can localize these responses in the lung will provide superior protection by providing a first line of defense against the inhaled conidia. Nucleic acid vaccines, including DNA and RNA vaccines, induce robust T cell responses that can protect from fungal infections. When delivered by gene gun with potent genetic adjuvants into the epidermis, nucleic acid vaccines also induce robust mucosal immune responses. However, the antigens needed for an effective Valley Fever vaccine are not known. Here, we employed DNA vaccines to screen *Coccidioides* virulence factors as novel vaccine immunogens and investigated their immunogenicity and efficacy when used alone or in combination in a mouse *Coccidioides* challenge model. From these studies, we designed a unique multi-antigen vaccine for Valley Fever and investigated its immunogenicity and protective efficacy in mice and a preclinical nonhuman primate (NHP) model.

Methods: We used DNA vaccines expressing single or multiple *Coccidioides* virulence factors to first identify candidate vaccine immunogens that are immunogenic and contribute to protection in mice. The DNA vaccines were co-formulated with genetic adjuvants to increase mucosal, Th1 and Th17 immune responses and delivered into the skin of mice by gene gun. Immune responses were measured two weeks after a second dose and mice were challenged with high doses of *C. Posadasii* Silveira. Immunogens that afforded significant protection from mortality or morbidity were then combined into a single multivalent vaccine that was evaluated for immunogenicity and protective efficacy in mice and a preclinical NHP model.

Results: We identified three immunogens that each induced antibody and T cell responses and afforded some degree of protection from challenge. When co-delivered, these immunogens were highly synergistic, inducing stronger immune responses together and unprecedented complete protection from fungal dissemination following a high-dose challenge that was superior to a live attenuated vaccine. Protection correlated with robust mucosal immune responses localized in the lung, T cell depletion abrogated protection and passive immunization protected 50% of mice indicating a role for both mucosal antibody and T cell responses. VF-1 also induced strikingly robust mucosal and systemic antibody and T cell responses NHPs, on par with NHPs naturally exposed and immune to subsequent infections. The vaccinated NHPs are now undergoing experimental challenge with *Coccidioides*.

Conclusions: These results show that a Valley Fever vaccine that induces mucosal immune responses and targets different stages of the fungal life cycle affords robust protection, providing strong evidence that nucleic acid vaccines offer a pathway toward development of effective vaccines against fungal diseases. The preclinical nonhuman primate model that closely models human disease will provide a valuable insight into the potential for this vaccine to protect humans.

POSTER 424

Novel modified carboxyvinyl polymer (nmCVP) demonstrates strong protective and therapeutic effects against HBV and the influenza virus when administered intranasally

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Objective: Intranasal vaccines are capable of eliciting both mucosal and systemic immune responses by delivering antigens directly to the nasal mucosa. Carboxyvinyl polymer (CVP) plays an essential role in enhancing the efficacy of intranasal vaccines as an excipient in mucosal delivery formulations. Although CVP-based formulations have shown promising results in clinical and preclinical studies against various pathogens, including hepatitis B virus (HBV), influenza, and SARS-CoV-2, further enhancement of immunogenicity is still needed. It has been documented that the antibody-inducing capacity of intranasal immunization with recombinant adenovirus is augmented under hyperosmotic conditions created by glycerol or similar agents. Conversely, it has also been reported that the immune response is not significantly improved by the antigen alone, even in hyperosmotic environments.

We report that intranasal immunization with antigen and modified CVP under hyperosmotic conditions enhances humoral, mucosal, and cellular immune responses.

Methods: We formulated novel modified carboxyvinyl polymer solutions (nmCVP) with varying viscosities and osmolarities, subsequently mixing them with viral antigens, specifically the influenza virus HA antigen, the HBs-Lh antigen (a hybrid HBs-L protein from two distinct genotypes C and D), and the HBc antigen. We then assessed the capacity of these formulations to elicit humoral, mucosal, and cellular immune responses following intranasal administration in mice. Additionally, infection protection assays were performed using strains identical to the HA antigen (homo strains) and strains isolated 10–25 years prior (hetero strains) to evaluate the cross-protective efficacy across different strains.

Results: A comparison of the immune-inducing capabilities of each CVP-HA revealed a novel modified CVP composition that elicited antibody titers more than 100-fold higher. Moreover, when assessing protective effects against IAV/IBV for both homologous and heterologous strains, robust protection was observed even against epidemic strains from over a decade ago, achieving 100% survival against lethal infection in mice. Mice were immunized intranasally with HBs-Lh antigen and HBc antigen, to which nmCVP had been added. Compared to the existing CVP group, the nmCVP group exhibited antibody titers more than 10 times higher against HBs-Lh antigen and HBc antigen. Additionally, the modified CVP elicited a more potent cellular immune response against HBV relative to the conventional CVP. Furthermore, we are advancing therapeutic evaluations through intranasal immunization in mice with persistent HBV infection.

Discussion and Conclusion: The intranasal vaccine using nmCVP demonstrated protective and eliminatory effects not only against acute infectious diseases such as influenza but also against chronic infectious diseases such as hepatitis B. The modified CVP, with altered compositional elements, demonstrated considerably improved humoral, mucosal, and cellular immune responses in comparison to the existing CVP. As the modified CVP elicits a robust immune response without the necessity of an adjuvant, it presents a higher level of safety and provides a nasal vaccine with enhanced immunogenicity.

POSTER 425

A Murine Cytomegalovirus Vaccine Vector Elicits Antigen-Specific B-Cell and Antibody Recall Responses in Human Tonsil Assembloids

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Introduction/Background: Tonsil assembloids have recently been adopted as an ex vivo platform to investigate human B-lymphocyte function and responses to vaccine formulations, addressing a key limitation of animal models, which predict human humoral responses only imperfectly. This technology allows antigen-specific recall responses to candidate vaccines to be measured in a human immune setting before clinical trials. We have developed a viral vaccine vector based on mouse cytomegalovirus (MCMV) and previously demonstrated its immunogenicity, efficacy, and safety in murine and xenotropic models. Hamsters immunized with an MCMV expressing the SARS-CoV-2 spike antigen (MCMVS) mounted lasting neutralizing antibody titers and were robustly protected against viral challenge. Whether MCMV vectors elicit comparable responses in human tissue remained untested.

Material/Methods: We therefore adapted the human tonsil assembloid platform to evaluate the immunogenicity of MCMV-based vaccines directly in human tissue. Assembloids were generated from tonsil tissue of adult donors and stimulated with graded doses of either MCMVS or one of six MCMV vectors expressing stabilized and codon-optimized variants of the RSV F protein (MCMVF). Antigen-specific antibody responses were monitored by ELISA over 8 days. To benchmark the vector against a licensed human RSV vaccine, parallel assembloids were stimulated with Abrysvo. At the final time point, cells were harvested and analyzed by antigen-specific B-cell ImmunoSpot. Since the assembloids were derived from donors with pre-existing exposure to these antigens, our design reads out a recall response, the setting most relevant to booster vaccination in humans. In parallel, the same six MCMVF constructs were assessed for immunogenicity in mice, allowing a direct comparison of the assembloid readout with in vivo responses.

Results: MCMVS and most MCMVF constructs induced antigen-specific antibody responses that increased over the 8-day culture, showing that the MCMV vector can express antigens in human tissue and drive humoral responses against two unrelated heterologous antigens. MCMVF stimulation generated detectable F-specific antibody-secreting cells in five out of six tested constructs, and this pattern reflected the in vivo immunogenicity of the MCMVF constructs in mice. Spot-forming unit numbers correlated with the magnitude of the F-specific antibody response measured by ELISA, linking vector-induced B-cell activation directly to antibody output. Notably, antibody responses induced by the immunogenic MCMVF constructs were similar or up to threefold higher than those induced by Abrysvo. This was also reflected in mice, where MCMVF constructs outperformed Abrysvo.

Discussion/Conclusion: Together, these findings show that MCMV-based vaccine vectors express antigens in human immune tissue and elicit antigen-specific B-cell and antibody responses. Assembloid responses mirrored murine immunogenicity, including the one construct that failed in both systems, indicating that the platform can identify non-immunogenic candidates in human tissue. Hence, the human tonsil assembloid platform provides a translational bridge between animal studies and clinical trials, and yields data that support the further development of MCMV vectors toward clinical application.

POSTER 426

Epidermal delivery of a universal Influenza A DNA Vaccine induces Broad Protection in Mice and Nonhuman Primates via induction of Systemic and Mucosal Immune Responses

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Introduction: We designed a universal influenza (UFlu) DNA vaccine to protect from annual influenza and future influenza variants and pandemic potential. The vaccine encodes the long alpha helix (LAH) within HA stem and conserved M2e consensus sequences from human, swine and avian strains to elicit broad protective antibody and nucleoprotein to induce T cell responses and two genetic adjuvants encoding IL-12 to enhance T cell responses and the heat labile enterotoxin from E. Coli (LT) to increase mucosal immune responses. To maximize immunogenicity, we administer the DNA vaccine into the highly immunocompetent epidermis using a gene gun that we previously showed this induces robust systemic and mucosal immune responses using very low doses of DNA (< 20 micrograms/dose).

Methods: To investigate immunogenicity and efficacy, we compared a UFluA DNA vaccine biased toward Group 1 consensus sequences (G1 UFluA) to a dual UFluA DNA vaccine consisting of two plasmids, one biased toward Group 1 and the other toward Group 2 sequences (G1 + G2 UFluA). The DNA vaccines were delivered via gene gun into the epidermis of the skin of mice and nonhuman primates (NHPs) and antibody and T cell responses by ELISA, IFN-g ELISPOT and intracellular cytokine staining (ICS) in the blood and lung. Mice were challenged with a panel of Group 1 and 2 influenza strains including avian strains. NHPs were sequentially challenged first with an H3N2 virus followed by an H1N1 strain 6 months later.

Results: In mice, the G1 biased UFluA DNA vaccine induced broad antibody responses against both G1 and G2 viruses and induced significantly higher antibody against the G1 strains than the combined G1+G2 UFluA DNA vaccine. Surprisingly, the G1-based UFluA DNA vaccine also induced strong antibody responses against G2 strains that was comparable to levels induced by the G1+G2 UFluA DNA vaccine. Both vaccine compositions induced robust NP-specific T cell responses and protection from a broad range of representative G1 and G2 influenza viruses in mice including avian strains. In NHPs, the combined G1+G2 UFluA DNA vaccine induced broad HA antibody against representative G1 and G2 strains, robust M2e-specific serum antibody and mucosal and systemic NP-specific T cell responses in the lungs. The macaques were protected from clinical disease after challenge with an H3N2 strain (A/Texas/71/2017) that is moderately virulent in macaques and a pandemic H1N1 strain (A/California/04/2009) that is highly virulent in macaques. Peak viral loads in bronchoalveolar lavages at 3 days post-challenge were 2-3 Logs lower than in control macaques challenged with the same viruses. The vaccinated animals also exhibited accelerated viral clearance that correlated with the frequency of mucosal NP-specific T cell responses in the lung.

Conclusions: UFluA is being advanced to phase I human trials using a clinical gene gun with innovations that increase penetration and distribution of the DNA/gold particles, local gene/antigen expression and immunogenicity and can deliver either DNA or RNA vaccines. Together, these studies support clinical development of a GG-delivered universal influenza DNA vaccine. Additional information on the clinical device and development will be presented.

POSTER 427

Safety and Immunogenicity of the Co-administration of PHH-1V and an Adjuvanted Quadrivalent Influenza Vaccine in Adults ≥ 65 Years: A Randomized, Double-Blind Phase II Clinical Trial

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Introduction/Background: Older adults remain at high risk of severe COVID-19 and influenza due to immunosenescence and comorbidities. Seasonal coadministration of both vaccines may improve coverage, but evidence on safety and immunogenicity remains limited for specific vaccine platforms and combinations, particularly those involving adjuvanted protein-based COVID-19 vaccines. This study evaluated whether coadministration of an adjuvanted recombinant SARS-CoV-2 protein vaccine (PHH-1V) with an adjuvanted quadrivalent influenza vaccine impacts safety or immunogenicity compared with separate administration.

Material/Methods: A randomized, double-blind, multicenter phase II trial including adults aged ≥ 65 years previously vaccinated against COVID-19 was performed. Participants were randomized (1:1:1) to receive influenza vaccine plus placebo, PHH-1V plus placebo, or coadministration of both vaccines with injections administered simultaneously into opposite arms. Solicited adverse events (AEs) were recorded for 7 days; unsolicited AEs, serious AEs, and adverse events of special interest were monitored throughout the study.

Immunogenicity was assessed at baseline and Day 28. SARS-CoV-2 binding antibodies were measured using electrochemiluminescence immunoassay, and influenza antibody responses were evaluated by haemagglutination inhibition assay. Geometric mean titers (GMTs) and fold rises were compared between groups.

Results: A total of 278 participants received at least one study dose. Baseline characteristics were balanced across groups (mean age 75.2 years). Approximately half of participants reported ≥ 1 solicited AE, with similar rates across groups. Most reactions were mild and transient, primarily local pain and tenderness. No serious adverse events or vaccine-related severe events were reported. Reactogenicity in the coadministration group met the predefined non-inferiority criterion.

For SARS-CoV-2, PHH-1V induced robust antibody responses both alone and when coadministered, with comparable geometric mean fold rises (3.55–3.62, respectively) and no statistically significant differences between groups (GMT ratio 0.81; 95% CI 0.62–1.06, p-value=0.1268).

For influenza, immune responses against all evaluated strains (A/H1, A/H3, B/Yamagata, B/Victoria) were similar between coadministration and influenza-alone groups. Overall, antibody responses observed following coadministration were comparable to those seen with separate administration of each vaccine.

Discussion/Conclusion: Coadministration of an adjuvanted SARS-CoV-2 protein vaccine with an adjuvanted influenza vaccine in adults ≥ 65 years demonstrated an acceptable safety profile and elicited antibody responses that were generally comparable to those observed following separate administration. No increase in reactogenicity was observed with coadministration.

These findings support the feasibility of coadministration strategies to optimize vaccination campaigns, simplifying schedules while maintaining vaccine performance.

POSTER 428

Gravimetric Evaluation of Syringe and VAX-ID Dead Volume and Its Impact on Dose-Sparing Intradermal Rabies Vaccination

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Introduction/Background: Intradermal (ID) vaccination offers dose sparing potential, reducing vaccine requirements up to one-fifth or even 1/10th of the standard intramuscular dose. While ID is recommended to expand access to rabies vaccines in LMICs—where costs and shortages are common—conventional techniques like the Mantoux method lack reproducibility and ease of use. VAX-ID is a novel ID injection adaptor designed for standardized, user-friendly delivery using a microneedle to minimize pain. To optimize dose-sparing advantages, VAX-ID was designed to have a low dead volume—the residual liquid remaining after full ejection—to limit vaccine loss. This study aims to evaluate the dead volume of syringes used with VAX-ID to quantify actual liquid losses.

Material/Methods: Dead volume was measured in fifty 1mL Tuberculin HENKE-JECT; green and fifty Eco LDS; white syringes. The sample size was determined based on dead volume measurements of VAX-ID published previously.

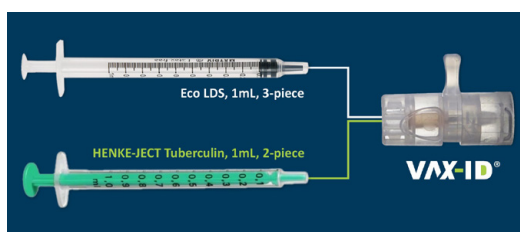
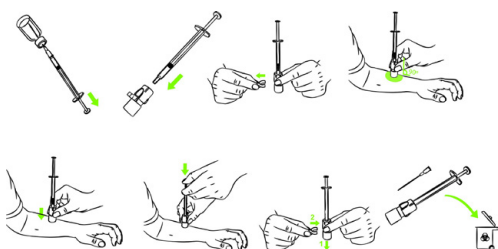
The dead volume was determined using the Gravimetric method described in ISO7886-1 Annex C:

1. Weigh the syringe empty ('empty')
2. Fill the syringe with 0.1 mL water (density 1g/mL at room temperature) based on the volume marks on the syringe
3. Weigh filled syringe ('Drawn')
4. Eject the complete volume of the fluid
5. Weigh the syringe again ('Residual ')
 - 'Liquid' = 'Drawn' - 'Empty'
 - 'Ejected' = 'Drawn' - 'Residual'
 - 'Dead volume' = 'Residual' - 'Empty'

Results: Fifty Tuberculin (green) syringes and fifty Eco LDS (white) syringes were evaluated using the ISO7886-1 gravimetric method. The mean liquid volume drawn was $121\mu\text{L} \pm 4.56\mu\text{L}$ for the Tuberculin syringe and $110\mu\text{L} \pm 3.45\mu\text{L}$ for the Eco LDS syringe. Mean ejected volumes were $98\mu\text{L} \pm 5.30\mu\text{L}$ and $101\mu\text{L} \pm 3.13\mu\text{L}$, respectively. The calculated dead volume was significantly lower for the Eco LDS syringe than for the Tuberculin syringe, measuring $9\mu\text{L} \pm 1.17\mu\text{L}$ versus $23\mu\text{L} \pm 2.42\mu\text{L}$, respectively.

Discussion/Conclusion: Using a gravimetric method, this study quantified and compared the dead volume of a conventional Tuberculin syringe and an Eco LDS syringe. The Tuberculin syringe demonstrated a substantially higher dead volume than the Eco LDS syringe (23 μ L vs 9 μ L), confirming the advantage of low-dead-space designs in minimizing product loss. Despite this difference, both syringes accurately delivered the target 0.1mL dose (mean ejection volumes of 98 μ L for Tuberculin and 101 μ L for Eco LDS), indicating that dead volume is accounted for in syringe calibration.

Comparison with published data indicates t VAX-ID 32G contributes approximately 14 μ L of additional dead volume. These findings clarify liquid losses within VAX-ID and inform the selection of optimal syringe-device combinations for dose-sparing rabies vaccination. Notably, in-house testing by a UK-based travel clinic confirmed that VAX-ID used for a 0.1mL Verorab rabies vaccination was effective and highly user-friendly.



POSTER 429

Determinants of *Mycobacterium tuberculosis* survival in hosts with vaccine-induced immunity

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Mycobacterium tuberculosis (Mtb) remains the leading cause of death from a bacterial pathogen, in part because neither natural nor vaccine-induced immunity confer sterilizing protection despite inducing a robust and durable immune response. The mechanisms by which Mtb persists under the memory immune response are unknown, a major barrier to the development of improved vaccines and therapeutics. Using a genome-wide bacterial forward genetics approach, transposon sequencing (TnSeq), we identified a unique functional genetic signature of Mtb survival in hosts with immune memory to mycobacteria. Canonical Mtb virulence systems and targets of TB vaccines currently in development, including the Esx-1 system, become less essential, while new genetic dependencies emerge. Notably, key features of this genetic signature are conserved across distinct TB-immune states, including vaccination with Bacille Calmette-Guerin (BCG) and natural immunity conferred by prior Mtb infection. We hypothesize that this distinct bacterial genetic signature reflects an altered cellular milieu experienced by Mtb in the post-immune environment. We are now mapping the cellular microenvironments encountered by Mtb in the immune host using spatial transcriptomics and bacterial response using RNAScope. This work may identify new bacterial targets for vaccines and therapeutics aimed at the persistent Mtb population that survives the host adaptive immune response.

POSTER 430

Growth Beyond Technical Expertise: Building a Global Vaccinology Community Through the ISV Mentoring Program

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Mentorship is widely regarded as an important component of scientific career development, yet opportunities for structured mentoring remain limited across much of the global vaccinology community. Career pathways in vaccinology are increasingly diverse, spanning academia, industry, public health, regulatory science, and biotechnology, making it difficult for early-career professionals to navigate available options and establish networks beyond their immediate field.

To address this need, the International Society for Vaccines (ISV) launched a mentorship program to connect early-career vaccinologists with experienced professionals from across the global vaccine ecosystem. The 2026 program included 11 mentor-mentee pairs spanning multiple countries, disciplines, and career sectors. Participants were matched based on career interests, expertise, and development goals, and were supported through structured mentoring activities and ongoing engagement with the ISV Mentorship Committee.

While scientific and career guidance were important elements of the mentoring relationships, participant feedback consistently highlighted benefits extending beyond technical expertise. Mentors and mentees reported growth in leadership, communication, teamwork, networking, stakeholder engagement, industry partnership, and confidence in pitching and storytelling. Many participants also valued the opportunity to gain perspectives from sectors outside their own and to build meaningful international professional relationships.

Mentorship provides value far beyond traditional career advice. By creating connections across disciplines, sectors, and geographic regions, the ISV Mentorship Program has helped foster a more connected vaccinology community while supporting the development of future leaders. Equally importantly, the program has demonstrated that mentoring is not a one-way transfer of knowledge, but a mutually beneficial relationship that promotes learning and professional growth for mentors and mentees alike.

Contact us via email Mentorship@isv-online.org for general information and EOI for the 2027 Mentoring Program.

POSTER 431

A plug-and-play baculovirus system for multigene expression of avian influenza proteins that form virus-like particles

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Introduction: The baculovirus expression system is a well-established platform to produce recombinant proteins for vaccine use. Cloning a gene into a transfer plasmid remains a bottleneck in terms of time and labour, especially for high-throughput processing involving multiple gene targets. We have developed a plug-and-play system using linearised baculovirus (flashBAC) DNA with gene(s) of interest flanked by 100 bp of sequence to facilitate gene transfer by homologous recombination. We have used this system to produce an influenza H5N1 VLP by triple expression of HA5, NA1 and the matrix proteins as well as triple expression of three reporter genes eGFP, mCherry and baculovirus p10.

Materials/Methods: The plug and play utilises a synthetic or PCR-generated gene fragment introduced at the 3' and 5' ends of the gene(s) to be inserted in the virus genome at the polh locus, removing the need for cloning. Recombinant viruses are prepared by cotransfection of insect cells with linear virus DNA and the gene fragment and then amplified to high titres for expression studies in SfC1B5,a rhabdovirus-free Sf cell line.

Results: Use of 100 bp flanking sequences with linearised virus DNA enhanced homologous recombination efficiency, which enabled a 40% reduction in time to generate sufficient P0 virus for downstream applications. This approach supported introduction of a triple gene cassette, enabling multi-gene expression. This was initially evaluated with baculoviruses expressing eGFP, mCherry, and baculovirus P10 proteins and more recently by triple expression of avian influenza (subtype H5N1) haemagglutinin, neuraminidase (NA) and matrix proteins. Tagging of the NA protein with a c-tag enabled purification of H5N1 virus-like particles (VLPs) using C-tagXL affinity chromatography. Transmission electron microscopy demonstrated the presence of influenza VLPs with the expected size and structure.

Conclusion: We have developed and validated a rapid plug-and-play approach to producing multiprotein VLPs in the baculovirus system that could have applications in both veterinary and human vaccine development.

POSTER 433

A multivalent DNA vaccine against *Mycobacterium tuberculosis* improves and expands Esx-specific cellular immunity in BCG-primed NHPsEM PARZYCH¹, M. VIERBOOM², E. GARY¹, T. SMITH³, L. HUMEAU³, F. VERRECK², DB WIENER¹¹ The Wistar Institute, United States of America² Biomedical Primate Research Centre, Rijswijk, South Holland, Netherlands³ Inovio Pharmaceuticals, Plymouth Meeting, PA, USA

The Bacillus Calmette-Guerin (BCG) vaccine is highly effective against active *Mycobacterium tuberculosis* (Mtb) disease in infants and young children. As this protection wanes over time, individuals become vulnerable to symptomatic disease progression and transmission. The development of next-generation vaccines to replace or supplement BCG is urgently needed. We previously utilized our synthetic DNA platform to screen 23 potential targets encoded across four multivalent constructs. All vaccines induced significant antigen-specific, polyfunctional T cell responses in small animals which correlated with degree of protection following a low dose Mtb challenge. Boosting of BCG-primed mice with the leading vaccine, pESX, resulted in the significant and prolonged suppression of lung bacterial burden relative to immunization with BCG alone. Based on these promising data, the pESX vaccine—which encodes a total of nine antigens, four of which are not represented in BCG—was selected for further evaluation in large animal models. To this end, BCG-primed NHPs (rhesus macaques) were boosted with pESX using various immunization regimens. Cellular immunity was assessed at 2 weeks and 8 weeks post-vaccination to determine the peak magnitude and durability of antigen-specific responses. At the 2-week timepoint, pESX-boosted NHP exhibited enhanced BCG-primed responses against shared antigens found in both BCG and pESX compared to BCG-only control animals. Importantly, >90% of pESX-boosted NHPs also mounted novel cellular responses against antigens only found in the pESX vaccine. The vast majority of pESX-boosted NHPs maintained these responses at 8 weeks post-boost. Together these data demonstrate that pESX is not only immunogenic in large animals, but simultaneously enhances BCG-primed responses while inducing de novo responses against antigens unique to Mtb. This validates our BCG-prime/ DNA-boost approach as a strategy to expand the magnitude and breadth of Mtb-specific immunity in BCG-primed systems.



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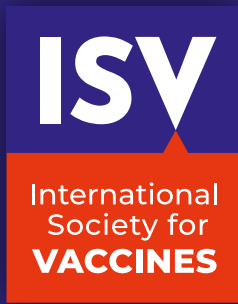
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YANG	Tzu-ping	Institute for Information Industry
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ZHOU	Xuefei	XZ GMP Consulting
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