2021 ISV ANNUAL VIRTUAL CONGRESS

SEPTEMBER 13 - 15, 2021

Program & Abstract Book

www.isv-online.org www.isvcongress.org

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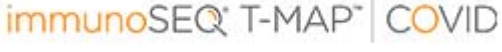

Upcoming Conference

Co-Sponsored by ISV

2021 HWASUN INTERNATIONAL VACCINE FORUM

Nov. 4(Thu) ~ 5(Fri), 2021 Hwasun Hanium Culture Sport Center | On-line Live Streaming

Korean Vaccine's Position in Pandemic World

VISIT WEBSITE FOR MORE INFO & REGISTRATION

http://www.hivf.org/main/

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Laura Palomares
Congress Co-Chair National Autonomous University of Mexico-Mexico

Guus Rimmelzwaan
Congress Co-Chair The University of Veterinary Medicine Hannover-Germany

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- Matthias Schnell, Thomas Jefferson University-USA
- Indresh Srivastava, Novavax-USA
- David Weiner, Wistar Institute, USA
- Yu-Mei Wen, Fudan University-Shanghai

*Eastern Time Zone

Day 1

ORAL PROGRAM MONDAY, SEPTEMBER 13	
0820-0830	**THEME OF THE DAY** **Guus Rimmelzwaan,** *The University of Veterinary Medicine Hannover*
0830-0930	**OPENING SESSION *LIVE*** **Session Chair and Introduction: Manon Cox**, *ISV/NextWaveBio* **Welcome: Ted Ross, President, ISV** **KEYNOTE SPEAKER 1: Mind the GAPP: A Vision for Ending Pandemics** **W. Ian Lipkin**, *Columbia University* **Q&A**
0930-1100	**PLENARY SESSION 1: NEW VACCINES ON THE HORIZON**
5 min	**Session Introduction** **Chairs: David Weiner,** *The Wistar Institute*; **Sanjay Phogat**, *GSK*
25min	**RSV Immunization Approaches for Infants and Children** **Jon Heinrichs**, *Sanofi Pasteur*
25 min	**HA Stalk and NA-Based Next Generation Influenza Virus Vaccines** **Florian Krammer**, *Icahn School of Medicine at Mount Sinai*
25 min	**Efficient Selection of Tumor Associated Neoantigens in the Design of Personalized Cancer Vaccines** **Michael Princiotta**, *EpiVax Therapeutics*
1100-1130	**QUESTION AND ANSWER SESSION ON PLENARY SESSION 1 *LIVE*** **Chairs: David Weiner,** *The Wistar Institute*; **Sanjay Phogat**, *GSK*
1130-1200	**POSTER SESSION 1**
1200-1330	**PLENARY SESSION 2: NEW DEVELOPMENTS IN TECHNOLOGY**
5 min	**Session Introduction** **Chair: Lenny Moise**, *EpiVax;* **Amy Espeseth**, *Merck*
25min	**Computational Design of Nanoparticle Vaccines for Influenza Viruses, Coronaviruses, and Beyond** **Neil King**; *University of Washington*
25 min	**Delivery of mRNA Vaccines - Current Status and Future Opportunities** **Colin Pouton**, *Monash University*
25 min	**Vaxxas' High Density Micro-Projection Array Patch (HD-MAP) – Delivering the Future of Needle-Free Vaccination** **Angus Forster**, *Vaxxas*
1330-1400	**QUESTION AND ANSWER SESSION ON PLENARY SESSION 2 *LIVE*** **Chair: Lenny Moise**, *EpiVax;* **Amy Espeseth**, *Merck*
1400-1430	**SELECT YOUR MASTERCLASS 1 – T-CELL IMMUNOLOGY** **Katherine Kedzierska**, *University of Melbourne*
1430-1500	**MEET THE FELLOWS 1** **David Weiner**, *The Wistar Institute* with **Sarah Gilbert**, *University of Oxford*
1500-1530	**SELECT YOUR MASTERCLASS 2 – INNOVATION & MANUFACTURING OF COVID VACINES** **Barry Buckland**, *BiologicB*
1530-1600	**MEET THE FELLOWS 2** **Linda Klavinskis**, *King's College London* with **Xavier Saelens**, *Ghent University*

Day 2

ORAL PROGRAM TUESDAY, SEPTEMBER 14	
0820-0830	**THEME OF THE DAY** **Laura Palomares,** *National Autonomous University of Mexico*
0830-0910	**KEYNOTE SPEAKER 2**: **Vaccine Diplomacy in a Time of Antiscience** **Peter Hotez**, *National School of Tropical Medicine*
0910-1030	**PLENARY SESSION 3: VACCINE MANUFACTURING & QUALITY CONTROL**
5 min	**Session Introduction** **Chair: Linda Lua**, *Queensland University*; **Indresh Srivastava**, *Novavax*
25min	**Leveraging Vaccine Manufacturing and Quality Control Platforms for New Modalities, MassBiologics Experience** **Mireli Fino**, *MassBiologics*
25 min	**Vaccine Production in Emerging Economies, Challenges and Opportunities** **Sergio Valentinotti**, *Liomont* and **Esteben Corley**, *mAbxience*
12 min	**ORAL ABSTRACT 1** **DNA Delivery of Immune-Focused SARS-CoV-2 Nanoparticle Vaccines Drives Rapid and Potent Immunogenicity and Achieves Single-Dose Protection** **Kevin Liaw**, *The Wistar Institute*
12 min	**ORAL ABSTRACT 2** **An mRNA vaccine against SARS-CoV-2: Polyethylene Glycol-free, liposome-based vaccine candidate EG-COVID induces high levels of virus neutralizing antibodies** **H. Christian Hong**, *EyeGene INC.*
1030-1100	**QUESTION AND ANSWER SESSION ON PLENARY SESSION 3 *LIVE*** **Chair: Linda Lua**, *Queensland University*; **Indresh Srivastava**, *Novavax*
1100-1145	**MEET THE FELLOWS 3 – EVERYTHING ABOUT ISV** **Moderator: Manon Cox,** *ISV/NextWaveBio* **Ted Ross,** *ISV/University of Georgia*; **Denise Doolan,** *ISV/James Cook University*; **Shan Lu,** *ISV/UMMS*
1145-1230	**POSTER SESSION 2**
1230-1400	**PLENARY SESSION 4: REGULATION IN TIMES OF PANDEMICS & VACCINE HESITANCY + ORAL ABSTRACT SELECTIONS**
5 min	**Session Introduction** **Chair: Laura Palomares**, *National Autonomous University of Mexico*; **Lars Frelin** *Karolinska Institutet*
25min	**Global Regulation in Challenging Times: Pandemics and Health Urgency of Innovation** **Rogerio Gaspar**, *WHO*
12 min	**ORAL ABSTRACT 3** **Perception of Vaccination of Filipino Mothers in the NCR Area Post-Dengvaxia** **Naomi Pompa**, *University of Santo Tomas*
12 min	**ORAL ABSTRACT 4** **High Throughput Biosensor Technology to Establish Dosing Frequency and Concentration for an mRNA-LNP Genital Herpes Vaccine** **Lauren Hook**, *University of Pennsylvania*
12 min	**ORAL ABSTRACT 5** **T Cell Epitope Content Comparison (EpiCC) Analysis Between PCV2 Vaccines and Field Strains** **Andres Gutierrez**, *EpiVax*

12 min	**ORAL ABSTRACT 6** **Improved Protection Against Multidrug Pseudomonas Aeruginosa Following Administration of an Fc Engineered DNA-encoded Monoclonal Antibody (DMAb) with Enhanced Complement Activity** **Jihae Choi**, *The Wistar Institute*
1400-1430	**QUESTION AND ANSWER SESSION ON PLENARY SESSION 4 *LIVE*** **Chair: Laura Palomares**, *National Autonomous University of Mexico*; **Lars Frelin** *Karolinska Institutet*
1500-1530	**MEET THE FELLOWS 4** **Margaret Liu**, *ProTherImmune* with **Gary Kobinger**, *Laval University*
1530-1600	**SELECT YOUR MASTERCLASS 3 – VACCINE CHARACTERIZATION AND ANALYTICS** **Indresh Srivastava**, *Novavax*
1600-1700	**ISV ANNUAL GENERAL MEETING *LIVE***

Day 3

ORAL PROGRAM WEDNESDAY, SEPTEMBER 15	
0820-0830	**THEME OF THE DAY** **Manon Cox,** *ISV/NextWaveBio*
0830-0910	**KEYNOTE SPEAKER 3: Preparing for the Next Pandemic in a One Health Approach** **Albert Osterhaus**, *The University of Veterinary Medicine Hannover*
0910-1030	**PLENARY SESSION 5: ONE WORLD; ONE HEALTH VETERINARY VACCINES**
5 min	**Session Introduction** **Chair: Alejandro Gil**, *Sinergium*; **Randy Albrecht,** *Icahn School of Medicine at Mount Sinai*
25min	**The Research and Development of Veterinary Vaccines from a Biodefense and One Health Perspective** **Cyril Gay**, *USDA ARS*
25 min	**Next Generation Vaccine Platform: Polymersomes as Stable Nanocarriers for a Highly Immunogenic and Durable SARS-CoV-2 Spike Protein Subunit Vaccine** **Madhavan Nallani,** *ACM Biolabs*
25 min	**Innovation in Veterinary Vaccines: Our Experience in the Development of a Targeted Vaccine for BVDV and Virus Like Particles for FMDV** **Andres Wigdorovitz,** *INTA -CONICET- Bioinnovo SA*
1030-1100	**QUESTION AND ANSWER SESSION ON PLENARY SESSION 5 *LIVE*** **Chair: Alejandro Gil**, *Sinergium*; **Randy Albrecht,** *Icahn School of Medicine at Mount Sinai*
1100-1130	**SELECT YOUR MASTERCLASS 4 – THE CONCEPTS OF GCP** **Janet Rose Rea,** *AVM Biotechnology*
1200-1230	**MEET THE FELLOWS 5** **Annie De Groot,** *EpiVax* with **Tonya Villafana** *AstraZeneca*
1230-1330	**PLENARY SESSION 6: GLOBAL HEALTH AND VACCINE DEVELOPMENT**
5 min	**Session Introduction** **Chair: Linda Klavinskis** *King's College London*; **Nathalie Garcon,** *BioAster*
25min	**Challenges in Establishing Vaccine Manufacturing from a Research Set Up** **Subhash Kapre,** *Inventprise*
25 min	**Correlates of Protection for COVID-19: What We've Learned So Far** **Peter Dull,** *Bill & Melinda Gates Foundation*
1330-1400	**QUESTION AND ANSWER SESSION ON PLENARY SESSION 6 *LIVE*** **Chair: Linda Klavinskis** *King's College London;* **Nathalie Garcon,** *BioAster*
1400-1415	**CLOSING SESSION & 2022 ISV Congress** **Chair: Manon Cox,** *ISV/NextWaveBio* **Closing Remark: Denise Doolan, ISV President for Next Term** **2022 ISV Congress: Joon Rhee,** *Chonnam National University*; **Gary Kobinger**, *Laval University;* **Shan Lu,** *ISV/UMMS*

Keynote Speakers

(In order of program)

W. Ian Lipkin - Columbia University-USA

BIO

Lipkin is the Director of the Center for Solutions for ME/CFS, the John Snow Professor of Epidemiology at the Columbia University Vagelos College of Physicians and Surgeons, and the Director for the Center of Infection and Immunity with the Mailman School of Public Health at Columbia University.

He is internationally recognized for his contributions to global public health through the innovative methods he developed for infectious diseases diagnosis, surveillance, and discovery. These advances have been critical in replacing culture-dependent methods of global health management by creating new criteria for disease causation and de-linking spurious associations between putative agents and diseases. Such examples include refuting the MMR vaccine having a role in autism and XMRV in ME/CFS.

Lipkin has been at the forefront of outbreak response to many of the world's recent outbreaks, including West Nile Virus in NYC (1999), SARS in China (2003), MERS in Saudi Arabia (2012-16), Zika in the US (2016), encephalitis in India (2017), and COVID-19 (2020).

Lipkin went to China in late January 2020 to consult with colleagues at the China CDC during the early assessment of the SARS-CoV-2 outbreak and contracted the virus via community transmission in March. During the summer of 2020, Lipkin consulted the Democratic National Convention Committee on testing protocols and site safety during the DNC event and for the 93rd Annual Academy Awards event in April 2021. He promotes public health awareness via print and broadcast media and also served as the scientific advisor for the Soderbergh film "Contagion".

Some of his most prestigious honors include Pew Scholar (Biomedical Sciences), Walter Reed Distinguished Lecturer, the Drexel Prize in Translational Medicine, the Mendel Medal (Villanova University), the International Science and Technology Cooperation Award of the Peoples Republic of China, and a recipient of an award of appreciation given by the Chinese government in the 70th anniversary of the People's Republic of China for his service to the country during the SARS epidemic along with the subsequent scientific support he has given since.

ABSTRACT

COVID-19 has exposed our vulnerability to pandemic risk and the urgency of addressing the challenges of climate change, food security, and the viral dissemination of misinformation. New molecular diagnostic platforms, investments in wildlife, domestic animal, and human microbial surveillance, and the advent of social media tools that mine the world wide web for clues to outbreaks of infectious disease are all proving invaluable in early recognition of threats to public health. However, inequities in the distribution of resources required for diagnostics and discovery, and lack of trust and transparency remain threats to biosecurity. To address these challenges we are establishing a global public health consortium comprising of ministries of health and academic institutions. This collaborative global program will focus on creating an infectious disease epidemiology network and has three main objectives: (1) develop a model realizing and extending the goals of the International Health Regulations established by the WHO in 2005 by providing inexpensive, rapid tools for diagnosis discovery, and surveillance of infectious diseases, (2) identify and prioritize infectious agents based on pandemic risk, and (3) share data and build the infrastructure needed to produce, validate and implement drugs and vaccines to reduce morbidity and mortality.

Peter Hotez - National School of Tropical Medicine-USA

BIO

Peter J. Hotez, M.D., Ph.D. is Dean of the National School of Tropical Medicine and Professor of Pediatrics and Molecular Virology & Microbiology at Baylor College of Medicine where he is also the Co-director of the Texas Children's Center for Vaccine Development (CVD) and Texas Children's Hospital Endowed Chair of Tropical Pediatrics**.** He is also University Professor at Baylor University, Fellow in Disease and Poverty at the James A Baker III Institute for Public Policy, Senior Fellow at the Scowcroft Institute of International Affairs at Texas A&M University, Faculty Fellow with the Hagler Institute for Advanced Studies at Texas A&M University, and Health Policy Scholar in the Baylor Center for Medical Ethics and Health Policy.

Dr. Hotez is an internationally recognized physician-scientist in neglected tropical diseases and vaccine development. As head of the Texas Children's CVD, he leads a team and product development partnership for developing new vaccines for hookworm infection, schistosomiasis, leishmaniasis, Chagas disease, and SARS/MERS/SARS-2 coronavirus, diseases affecting hundreds of millions of children and adults worldwide, while championing access to vaccines globally and in the United States. In 2006 at the Clinton Global Initiative, he co-founded the Global Network for Neglected Tropical Diseases to provide access to essential medicines for hundreds of millions of people

He obtained his undergraduate degree in molecular biophysics from Yale University in 1980 (*phi beta kappa*), followed by a Ph.D. degree in biochemistry from Rockefeller University in 1986, and an M.D. from Weil Cornell Medical College in 1987. Dr. Hotez has authored more than 500 original papers and is the author of four single-author books, including *Forgotten People, Forgotten Diseases* (ASM Press); *Blue Marble Health: An Innovative Plan to Fight Diseases of the Poor amid Wealth* (Johns Hopkins University Press); *Vaccines Did Not Cause Rachel's Autism* (Johns Hopkins University Press); and a forthcoming 2020 book on vaccine diplomacy in an age of war, political collapse, climate change and antiscience (Johns Hopkins University Press).

Dr. Hotez served previously as President of the American Society of Tropical Medicine and Hygiene and he is founding Editor-in-Chief of *PLoS Neglected Tropical Diseases.* He is an elected member of the National Academy of Medicine (Public Health Section) and the American Academy of Arts & Sciences (Public Policy Section). In 2011, he was awarded the Abraham Horwitz Award for Excellence in Leadership in Inter-American Health by the Pan American Health Organization of the WHO. In 2014-16, he served in the Obama Administration as US Envoy, focusing on vaccine diplomacy initiatives between the US Government and countries in the Middle East and North Africa. In 2018, he was appointed by the US State Department to serve on the Board of Governors for the US Israel Binational Science Foundation, and is

frequently called upon frequently to testify before US Congress. He has served on infectious disease task forces for two consecutive Texas Governors. For these efforts in 2017 he was named by FORTUNE Magazine as one of the 34 most influential people in health care, while in 2018 he received the Sustained Leadership Award from Research America. In 2019 he received the Ronald McDonald House Charities Award for Medical Excellence

Most recently as both a vaccine scientist and autism parent, he has led national efforts to defend vaccines and to serve as an ardent champion of vaccines going up against a growing national "antivax" threat. In 2019, he received the Award for Leadership in Advocacy for Vaccines from the American Society of Tropical Medicine and Hygiene. Dr. Hotez appears frequently on television (including BBC, CNN, Fox News, and MSNBC), radio, and in newspaper interviews (including the New York Times, USA Today, Washington Post, and Wall Street Journal).

ABSTRACT

Description:

A look at modern 21st-century forces - war, political collapse, climate change, urbanization, anti-science, leading to a return of neglected and vaccine-preventable diseases. My lecture will address my time as US Science Envoy in the White House and US State Department

Objectives:

1. To report on the impact of modern 21st-century forces, including poverty, war, urbanization, climate change, on slowing, halting, or even reversing public health gains.

2. To evaluate the impact of vaccines on combating the diseases arising due to these forces.

3. To summarize the development of new COVID19 vaccines for global Health

Albert Osterhaus - The University of Veterinary Medicine Hannover-DE

BIO

Professor Osterhaus has been Head of the Department of Viroscience at Erasmus MC Rotterdam until 2014, is currently Scientific Director and and Guest-Professor at the Center of Infection Medicine and Zoonosis Research of the University of Veterinary Medicine Hannover. His research follows an integrated "viroscience" concept, with world-leading scientists in molecular virology, immunology, epidemiology, pathogenesis, and intervention studies for human and animal virus infections. His group discovered more than 70 viruses of humans and animals (e.g. human metapneumovirus, coronaviruses, influenza viruses), elucidated the pathogenesis, and developed targeted intervention strategies. The spin-offs, Viroclinics - DDL, Vironovative and CR2O, illustrate additional relevant successes. He has acted as mentor of more than 80 PhD students and holds several key patents. He is the author of more than 1300 papers in peer-reviewed journals, together cited more than 70,000 times, with an H index > 116. As Chair of the European Working Group on Influenza (ESWI) and other international organizations, he organised numerous international conferences on emerging infections. He holds several senior editorships and received numerous prestigious awards. He is member of the Dutch and German National Academies of Sciences, member of the Belgium Academia of Medicine, and Commander of the Order of the Dutch Lion.

ABSTRACT

Complex relationships between human and animal species have resulted in human-animal interfaces that have promoted cross-species transmission, emergence and eventual evolution of a plethora of human pathogens. Remarkably, most of the characteristics of these interfaces have been established long before the end of our species pre-historical development, to be relentlessly shaped throughout the history of our own and animal species. More recently, changes affecting the modern human population worldwide and their dramatic impact on the global environment have taken domestication, agriculture, urbanization, industrialization, and colonization to unprecedented levels. This has created new global multi-faceted human-animal interfaces, associated with major epidemiological transitions, accompanied by an unexpected rise of emerging and re-emerging infectious diseases in humans, that all have their origin in animal reservoirs. Until the beginning of the last century, infectious diseases were the major cause of human mortality. Around 1900 infectious diseases caused about fifty percent of human deaths in the western world. In the following decades, this percentage decreased to less than a few percent. This was largely due to the implementation of public health measures such as sewage installment and development of clean drinking water systems, but also to the development of vaccines and antimicrobials. This success prompted policymakers and scientists to predict that infectious diseases of humankind and of their domestic animals would eventually be brought under control in the industrialized world. Paradoxically the

following decades confronted the world with an ever-increasing number of emerging or re-emerging infectious diseases, some causing true human or animal pandemics. Pathogens spilling over from wildlife reservoirs, either directly or via intermediate hosts, were at the basis of most of these epidemics and pandemics. Striking examples in humans started with the emergence of AIDS from chimpanzees, pandemic influenza from birds and pigs to be followed by Ebola, SARS, MERS, and most recently COVID-19 from bat reservoirs. A complex mix of predisposing factors in our globalizing world, linked to major changes in our societal environment and global ecology, collectively created opportunities for viruses to infect and adapt to new animal and/or human hosts. A better understanding of the underlying processes may eventually lead to better preparedness for outbreaks in humans and animals. Importantly, the increased emergence of viral infections is largely paralleled by medical, veterinary, technological, and scientific progress, continuously spurred by our never-ending drive to combat pathogens. The most recent example is the unprecedented speed with which effective COVID-19 vaccines were developed.

Invited Speakers

Esteban Corley
MAbxience-AR

Peter Dull
Bill & Melinda Gates Foundation-USA

Mireli Fino
MassBiologics of UMMS-USA

Angus Forster
Vaxxas-AU

Rogerio Gaspar
World Health Organization-PT

Cyril Gay
USDA ARS-USA

Jon Heinrichs
Sanofi Pasteur-USA

Subhash Kapre
Inventprise LLC-USA

Neil King
University of Washington-USA

Florian Krammer
Icahn School of Medicine at Mount Sinai-USA

Madhavan Nallani
ACM Biolabs-SG

Colin Pouton
Monash University-AU

Michael Princiotta
EpiVax Therapeutics, Inc.-USA

Sergio Valentinotti
Liomont- CDMX

Andres Wigdorovitz
Bioinnovo SA-AR

Invited Speakers

(Alphabetical Order)

Esteban Corley, *MaBxience*

BIO

Biologist from the University of Buenos Aires and graduate of Management for small and medium companies from the IAE business school of the Austral University

- Director of Mabxience Argentina a company devoted to the production of biosimilar monoclonal antibodies
- Member of the board of Biotecsur, the platform for coordination of biotech development policies dependent of Mercosur countries (Argentina, Brasil, Paraguay and Uruguay
- Member of the board of CABBIO (Centro Argentino Brasilero de Biotecnología)
- Member of the board of the argentine chamber of biotechnology
- Assistant professor of the Universidad Nacional de San Martín in Biopharma startup.
- Member of the Argentine National Pharmacopea for the biopharmaceutical chapter

He initiated his career at the faculty of exact and biological sciences as research and teaching assistant and won a scholarship as a researcher in Fundación Leloir.

He has dedicated more than 35 years to the research, development, and production of similar products starting as R&D analyst in Biosidus, Founder of Genargen, CEO of Rhein Americana, Director of PC-GEN SA, founder of pharmADN and actually Director of mAbxience Argentina

Between 2008 and 2011, he was director of Biotech I a programo f cooperation between EU and Mercosur y La Unión Europea, working in the Ministry of Science, Technology and Innovation of Argentina.

He has also been a senior consultant for the Ministry in a study on the status of Biotech Health Sector in Argentina between 2015 and 2016.

ABSTRACT

mAbxience and Liomont are two Latin American pharmaceutical laboratories that are involved in the production of the AstraZeneca Covid-19 vaccine.

In this presentation we will discuss how this consortium was created as well as the critical factors that were necessary to make this collaboration possible, including the active participation of AstraZeneca and support of the Carlos Slim foundation. These factors will be extrapolated to a broader level exploring the opportunities of having a regional vaccine production program as well as the challenges that need to be overcome for this to become a reality.

(Continue to Next Page)

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Peter Dull, *Bill & Melinda Gates Foundation*

BIO

Peter is Deputy Director for Integrated Clinical Vaccine Development within the Global Health Division at the Bill and Melinda Gates Foundation. In this role he provides technical and strategic guidance on clinical development to the foundation's program strategy teams and external partners. In addition, he leads the foundation's vaccine development activities for HPV vaccines, including efforts on new product development and reduced dose schedules. He joined the foundation after 10 years at Novartis Vaccines where he was the Clinical Franchise Head for Meningitis and Sepsis Vaccines, leading the clinical development global licensure of MenACWY-CRM (Menveo) and 4CMenB (Bexsero). During the ongoing Covid-19 pandemic, in additional to providing direct support for grantees developing new COVID-19 vaccines, he co-leads the COVAX Clinical SWAT team providing product-agnostic support to developers to accelerate vaccine licensure and WHO pre-qualification with an LMIC focus. Prior to joining Novartis, he was an Epidemic Intelligence Service officer in the Meningitis and Special Pathogens Branch at the US Centers for Disease Control and completed subspecialty training in infectious diseases at Emory University.

ABSTRACT

Identifying a correlate of protection for COVID-19 would have significant implications for product developers, regulatory authorities and policy makers to both accelerate new vaccines toward licensure but also guide better use of the existing vaccines. Although evidence has accumulated to support both binding and neutralizing antibodies as relevant biomarkers for protection, new results are being generated continuously over the past 18 months from pre-clinical, natural history and vaccine efficacy studies. This talk will summarize the information collected to date, highlight gaps which necessitate cautious interpretations of where we currently stand and provide a look forward to where additional studies might provide more clarity.

Mireli Fino, *MassBiologics of UMMS*

BIO

In her role as the executive vice chancellor, MassBiologics of UMMS, Mireli W. Fino, MBA, will drive MassBiologics mission through the research and development of internal programs and of UMMS faculty and students while leading its manufacturing facilities in Mattapan and Fall River, and the organization's industry relationships.

Prior to joining MassBiologics in July of 2021, Ms. Fino spent nearly 30 years in the pharmaceutical industry as an accomplished biotech executive with particular expertise in bioprocess development, manufacturing sciences and technology and commercial operations. Most recently, she was with Protein Sciences, in Meriden, CT where she worked since 2012 as senior vice president for manufacturing operations. There, she was instrumental in the approval and launch of the first recombinant influenza vaccine in the US. After Sanofi's 2017 acquisition of Protein Sciences, Ms. Fino became the Site Head of Industrial Operations, Meriden CT and Pearl River NY, where she led the expansion of commercial operations to multiple sites, contract manufacturing organizations and international registrations.

Ms. Fino previously worked for 16 years at Wyeth Pharmaceuticals now Pfizer, Inc., in a variety of senior roles, leading large-scale process development and clinical production of viral and bacterial vaccines; ultimately, she was director of manufacturing sciences and technology for bacterial conjugated vaccines, with focus on innovation and new technology implementation.

Ms. Fino earned an undergraduate degree in biochemical engineering at The Autonomous University of Aguascalientes in Mexico and a Master of Business Administration at MIT.

ABSTRACT

MassBiologics has over 125 years of history producing licensed biologics. During this time, the organization has co-evolved with the life science industry as it delivered on its mission to improve the public health of the people of Massachusetts and the world.

MassBiologics evolution is more tangible than ever as the current revolution in life sciences takes place with new modalities ranging from new approaches to vaccines and antibodies, to gene therapies delivered through nucleic acid and viral vectors. This presentation aims to introduce MassBiologics approach to leveraging our infrastructure and assets for licensed vaccine manufacturing to new modalities. Comparing and contrasting areas that can be easily adapted between modalities to areas where specific challenges require new approaches; we discuss potential avenues where the industry can accelerate the path from the development lab to cGMP production and commercialization.

Angus Forster, *Vaxxas*

BIO

Dr Forster has worked in medical product development and commercialization for 20 years and has overall responsibility for the research, development and operations of Vaxxas. Since 2012, Angus has established the Vaxxas R&D team that includes more than 60 scientists, engineers and professional staff, and led three Phase I clinical studies. He brings considerable experience in pharmaceutics, formulation development, analytical science, medical device design and development, risk management and quality systems. Before joining Vaxxas, Angus commenced his career with GlaxoSmithKline in pharmaceutical development and spent 5 years with PA Consulting (UK) working medical product development projects. Angus has Ph.D. in pharmaceutics and a B.Pharm (Hons) from Otago University, New Zealand.

ABSTRACT

Vaxxas is commercializing a vaccine delivery technology that targets the abundant immune cells present in the top layers of the skin. The technology is based on a small patch, covered in a high-density of micro-projections which are a coated with dried vaccine formulation. When applied to the skin using an integrated single-use applicator, the micro-projections penetrate the stratum corneum to deliver vaccine to the epidermis and upper dermis generating improved immune responses compared to needle and syringe in preclinical and recent clinical studies. Global pandemic vaccination efforts have highlighted the need for significantly improved approaches to vaccination; technologies that simplify vaccination, improve vaccine thermostability and provide alternative distribution channels. Vaxxas' high-density microarray patch (HD-MAP) is being developed to address these goals. The talk will cover the development status of Vaxxas' HD-MAP technology, challenges - with a focus on manufacturing scale-up and opportunities especially in pandemic response.

Rogerio Gaspar, *World Health Organization*

BIO

Dr. Rogério Gaspar from Portugal joined WHO on 6th January as the Director of Regulation and Prequalification Department.

Rogério obtained his PhD in Pharmaceutical Sciences from the Catholic University of Louvain Belgium in 1991, after a graduation as pharmacist from the University of Coimbra Portugal.

He worked as a Full Professor at the Faculty of Pharmacy University of Lisbon until the end 2020, where he was Head of Department and President of the School Council. He was previously leading the Nanomedicine Drug Delivery Systems research group within the Research Institute for Medicines (iMedUL,which he cofounded in 2007), before moving in 2017 to the Institute of Bioengineering and Biosciences where he was until now researcher and part of the Scientific Board

His research focus, at the University of Coimbra and the University of Lisbon, was in the area of new therapeutic strategies using liposomes, polymeric biodegradable nanoparticles, and polymer therapeutics, in several therapeutic areas and more recently in the use of targeted delivery systems for combination therapy in cancer, including nucleic acids delivery, with publications in relevant journals (for reference see ORC ID 0000-0002-5950-0291).

His most recent publication was in August 2020 on “Non-biological Complex Drugs: Complex pharmaceutical in need of individual robust clinical assessment before any therapeutic equivalence decision”, published in Frontiers in Medicine (Regulatory Science).

He was a co-founder of the Master’s degree in Regulatory Science at the University of Lisbon (RAMPS), started in April 2002 and still very active, including relevant international participations.

In parallel to his academic career as a researcher, professor and holding academic responsibilities (e.g. Vice Rector and other academic duties), he had a long standing contribution in the regulation of medicines at national regional and international levels, starting at the early phase of the European Medicines Agency in 1995 (London, UK), as a Vice President of the National Medicines Committee (Portugal) and also as a member of EMA’s CPMP and quality working party (QWP).

He has also taken leadership and participation roles in different activities both at the EU-Japan MRA, training in GMPs and Quality Management System for ASEAN National Regulatory Authorities, both public and private sector in Portugal, President of the Portuguese Society of Pharmaceutical Sci ences (SPCF, 2016-2020) and both at the Executive Committee of the European Federation of Pharmaceutical Sciences (EUFEPS, 2009-2013 and 2016-2020, including Vice-President (VP) 2011-2012 and 2018-2020) and

leadership of the EUFEPS Regulatory Science Network (2010-2019) as well as VP of International Pharmaceutical Federation (FIP) Special Interest Group (SIG) in Regulatory Science (2011-2014). Other participation in international collaboration, merging scientific domains and regulatory science, include several countries in the Americas, Africa and Europe.

Rogério was previously a member of the management board of EMA and VP of the management board at Portugal's NRA (INFARMED). In Portugal, he was responsible for the redrawing and installation of the national Official Medicines Control Laboratory (OMCL) and also lead the first ISO 9001 certification for INFARMED (Inspection and Licensing procedures). He had also a relevant participation in activities against medicines counterfeiting and from 2000-2002 lead the participation of Portugal within International Narcotics Control Board (INCB) (UN, Vienna).

ABSTRACT NOT INCLUDED

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Cyril Gay, *USDA ARS*

BIO

Dr. Gay obtained a B.Sc. in Chemistry and a Doctor of Veterinary Medicine from Auburn University, and a Ph.D. in Microbiology from The George Washington University. Dr. Gay has worked in the animal health research field for the last 25 years holding several positions of increasing responsibility in the federal government and the pharmaceutical industry. As Chief, Biotechnology Section, Center for Veterinary Biologics (CVB), United States Department of Agriculture (USDA), Dr. Gay developed the procedures for licensing molecular vaccines that led to the first license for a live recombinant vectored vaccine. In the pharmaceutical industry (SmithKline Beecham and Pfizer Animal Health), Dr. Gay led several cross-functional teams that successfully developed and licensed veterinary vaccines for companion animals and livestock. As Director, Global Product Development, Pfizer Inc., Dr. Gay developed strategic and tactical plans that interfaced R&D, clinical development, manufacturing, marketing, and product life-cycle management. Dr. Gay joined Agricultural Research Service (ARS), USDA, in 2002. Dr. Gay currently holds the position of Senior National Program Leader and provides program direction and national coordination for the Department's intramural animal health research program, with focus on eight research laboratories located in Ames, Iowa, East Lansing, Michigan, Clay Center, Nebraska, Athens, Georgia, Orient Point, New York, Beltsville, Maryland, Pullman, Washington, and Manhattan, Kansas. Dr. Gay provides technical support within the interagency in the implementation of the President's National Biodefense Strategy, including the National Bio and Agro Defense Facility (NBAF). Dr. Gay launched the Global African Swine Fever Research Alliance (GARA) in 2013 and currently serves as its Executive Secretary. Dr. Gay also serves as the Executive Secretary of the Global Foot-and-Mouth Research Alliance (GFRA). Dr. Gay was the 2010 recipient of the USDA Secretary's Honors Award for interagency response to the pandemic H1N1 influenza outbreak; the ARS Special Administrator's Award for outstanding and rapid research support for pandemic H1N1; the USDA Secretary's Honor Award for Emergency Response to the 2013 Chinese H7N9 avian influenza outbreak, and received a U.S Presidential Rank Award in 2017.

ABSTRACT NOT INCLUDED

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Jon Heinrichs, Sanofi Pasteur

BIO

Jon Heinrichs is an Associate Vice President and R&D New Targets Franchise Head in Portfolio Strategy and Execution at Sanofi Pasteur in Swiftwater, PA where he leads vaccine projects in the Pre-and Early-Development spaces as well as serving as the Global Project Head for nirsevimab, a next generation RSV monoclonal antibody in late stage development in collaboration with AstraZeneca. Prior to joining Sanofi, Dr. Heinrichs headed the Microbial Vaccine Research group at Merck Research Labs where he led a team of scientists developing vaccines for several bacterial pathogens. Dr. Heinrichs previously held positions of increasing responsibility at the biotechnology company MedImmune (now part of AstraZeneca), where he contributed to the identification of vaccine candidates and was involved in research on the efficacy of monoclonal antibodies for the prevention of infectious diseases and the treatment of cancer and inflammatory diseases. Dr. Heinrichs earned his doctoral degree in microbiology and molecular genetics from Rutgers University and the University of Medicine and Dentistry of New Jersey and completed a post-doctoral fellowship in the Laboratory of Bacterial Pathogenesis and Immunology at The Rockefeller University.

ABSTRACT

RSV is the leading cause of bronchiolitis and hospitalization in all infants and continues to be an important cause of visits to health-care providers throughout a child's first years of life. Despite more than half a century's efforts, no vaccine has been licensed for prevention of RSV and no preventative options exist for all infants. To address this problem, many companies have been focused on evaluating vaccines and prophylactic antibodies for this indication. Sanofi Pasteur, with our partner AstraZeneca, have tested an antibody targeting the pre-fusion F protein (nirsevimab). This antibody is more potent in preclinical studies than the existing licensed monoclonal (Synagis) and has been engineered to increase its half-life with the goal of providing protection for an entire RSV season for all infants entering their first RSV season, and for children with congenital heart disease or chronic lung disease entering their first and second RSV seasons. This antibody has now demonstrated its ability to protect infants from medically attended LRTI caused by RSV in two large late-stage clinical studies. To further protect all children for their second RSV season and beyond, Sanofi Pasteur is evaluating a live-attenuated RSV vaccine (NS-2 deleted) in collaboration with the NIH. This intranasally-delivered vaccine has been demonstrated to be safe and well-tolerated and preliminary data suggest that this approach may be highly effective in prevention of serious RSV disease in children. These two approaches will, if successful, provide complementary methods to protect all infants and children during their most vulnerable period of life.

Subhash Kapre, *Inventprise LLC*

BIO

Dr. Subhash Kapre established Inventprise in 2012. He brings with him forty-five years of extensive scientific and commercial expertise from his work in at the Serum Institute of India. He is known internationally for his wide-ranging R&D expertise in bacterial and viral vaccines, bio-therapeutics and biopharmaceuticals. Dr. Kapre also has expertise in the establishment of WHO-accredited large-scale vaccine manufacturing plants, capable of supplying doses in the hundreds of millions. Dr. Kapre holds over 70 patents and has several publications to his credit.

ABSTRACT

This a case study of setting up a research unit and then efforts of converting the unit into a manufacturing company. The challenges faced in this endeavor. The possible solutions to such challenges. This roadmap is explained with an example of real life story.

(Continue to Next Page)

Neil King, *University of Washington*

BIO

Dr. King is an assistant professor in the Department of Biochemistry and Institute for Protein Design at the University of Washington. His group uses computational protein design to create new protein technologies for applications in targeted delivery and structure-based vaccine design. Two nanoparticle vaccines from Dr. King's group have entered clinical trials (for SARS-CoV-2 and influenza), with a third planned to enter soon (RSV).

ABSTRACT

Recent advances in computational protein design enable new self-assembling proteins to be designed with atomic-level accuracy. I will describe the development of these methods and their application to structure-based vaccine design. Two clinical-stage nanoparticle immunogens (for SARS-CoV-2 and influenza) will be discussed as examples of the improved potency and breadth that can be elicited by computationally designed nanoparticle vaccines. Finally, we will take a brief look at new classes of nanoparticle scaffolds currently being designed.

(Continue to Next Page)

Florian Krammer, *Icahn School of Medicine at Mount Sinai*

BIO

Florian Krammer, PhD, graduated from the University of Natural Resources and Life Sciences, Vienna (Austria) in 2010. He received his postdoctoral training in the laboratory of Dr. Peter Palese at the Icahn School of Medicine at Mount Sinai, New York working on hemagglutinin stalk-based immunity and universal influenza virus vaccines. In 2014 he became an independent principal investigator and is currently Mount Sinai Professor of Vaccinology at the Icahn School of Medicine at Mount Sinai. Dr. Krammer's work focuses on understanding the mechanisms of interactions between antibodies and viral surface glycoproteins and on translating this work into novel, broadly protective vaccines and therapeutics. The main target is influenza virus but he is also working on coronaviruses, flaviviruses, hantaviruses, filoviruses and arenaviruses.

ABSTRACT NOT INCLUDED

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Madhavan Nallani, ACM Biolabs

BIO

Madhavan obtained his PhD at Jacobs University Bremen, Germany before doing postdoctoral work at the Radboud University Nijmegen, The Netherlands, and finally moved to Singapore. He spent more than 15 years developing the polymersome technology, while an Asst. Professor at Nanyang Technological University Singapore. He has translated the science of polymersomes to a technology platform and founded ACM Biolabs Pte Ltd, in Singapore, in 2013. Since its inception, he developed the company's overall product strategy and product portfolio. He founded ACM's subsidiary AAVACC Pte Ltd in 2017, establishing its veterinary vaccines. In 2020, Madhavan co-founded ACM Biosciences AG in Basel, Switzerland. As its CSO, he pushes the human prophylactic vaccines pipeline towards clinics. The company's lead vaccine is expected to enter clinical trials in Q4 2021.

ABSTRACT

Advancement in nanotechnology can potentially contribute to the development of an efficacious, cost-effective and scalable vaccine platform. Nano-delivery systems that are widely exploited are classified in three categories, polymer based, inorganic and lipid-based delivery systems. Amphiphilic block copolymer self-assembly offers a straightforward, scalable route to well-defined nanoscale vesicles. By controlling the ratio of the different constituent blocks, self-assembly can be tailored to access different nanostructures, including polymersomes. The ability to compartmentalize antigens and adjuvants in the aqueous compartment of polymersomes renders them very attractive for vaccine application. Compared to liposomes, polymersomes have the unprecedented advantage of tuning membrane thickness and property. Owing to their relatively long hydrophobic segments, polymersomes possess enhanced stability without the need for additional stabilization strategies such as cross-linking chemistries. Despite their tremendous potential, only a few reports are available employing polymersomes as a carrier for vaccine application. In the present work, we describe the development of subunit vaccines based on the spike protein of PEDv and applied the lessons learnt for developing SARS-CoV-2 vaccine. We show here that functionally, ACM polymersomes serve as delivery vehicles which are efficiently taken up by DC1 and DC2, which are key initiators of the adaptive immune response. We further investigate the immunological effect of ACM polymersomes on different SARS-CoV-2 spike proteins, namely the ectodomain of the spike protein, the S2 domain only, and a trimeric spike protein. Altogether, we show that our vaccine formulation possesses strong immunogenicity and can elicit robust and durable humoral and cellular immunity against SARS-CoV-2 in C57BL/6 mice that persist for at least 40 days.

Colin Pouton, *Monash University*

BIO

After a series of academic appointment at the University of Bath (UK), Pouton moved to Monash University in 2001 to take up the Chair and Head of Department of Pharmaceutical Biology. Over the past five years he has been Head of Drug Delivery, Disposition and Dynamics (D4) at the Monash Institute of Pharmaceutical Sciences, ranked #2 in the world for research in pharmacy and pharmacology. His department is home to over 200 research scientists. Pouton has published >160 full manuscripts including 53 over the past five years. His work has been cited >10000 times, with over 700 citations per annum for the past five years (Scopus data). In 2015, 2016 and 2018 he was identified by Thompson Reuters as a Highly Cited Researcher in the discipline of Pharmacology & Toxicology. Pouton currently supervises a team of 16 PhD students and 4 grant- funded research assistants. He has supervised 67 PhD completions and supervised over 20 postdoctoral research assistants. Pouton contribute**s** to the research fields of nucleic acid delivery, stem cell technology, drug delivery and vaccine design. In relation to COVID-19 research, he has been using his experience in nucleic acid delivery to design and deliver candidate mRNA COVID-19 vaccines. He has a long-standing interest in the use of differentiated pluripotent stem cells for disease modelling, drug discovery and cell therapy, with an emphasis on neurodegenerative diseases.

ABSTRACT

The COVID-19 pandemic offered an ideal opportunity to test the potential of mRNA vaccines. Their success in protecting against serious illness has been remarkable. The science and technology supporting the commercial products has been in development for well over a decade, both in relation to design of RNA molecules and their packaging into an appropriate delivery system. Lipid nanoparticle (LNP) technology has been a vital part of the success of the mRNA vaccines. Whilst it is a young technology it has generated numerous patents that need to be navigated, either by finding new IP or by licensing patented technology. There is scope for development of new delivery technology as well as improvements in mRNA design. An important aspect of mRNA vaccine design is how best to optimize the level and quality of innate immune responses that are necessary to stimulate adaptive immunity but can work against translation of the mRNA. The relative contributions of the RNA (whether native RNA or modified RNA) and the LNP, as a function of dose and lipid chemistry, will be important topics for future research. Optimizing the biodistribution of the LNPs will also play a vital role in design of improved vaccines.

Michael Princiotta, EpiVax Therapeutics, Inc.

BIO

Michael Princiotta is an immunologist with over 25 years experience studying the processing and presentation of pathogen- and tumor-associated antigens to T cells. He holds a PhD in Microbiology and Immunology from the University of Colorado Health Science Center in Denver, Colorado. Following postdoctoral studies in the Lab of Viral Diseases at NIAID at the NIH, he was a tenure-track faculty member at SUNY Upstate Medical University in Syracuse, NY. Most recently, he was Vice President of Research at Advaxis Immunotherapies, where he oversaw the development of a personalized and shared neoantigen cancer vaccines from conception to phase I clinical trial. Michael is currently the CSO of EpiVax Therapeutics.

ABSTRACT

Advances in whole exome sequencing (WES) have enabled rapid and accurate identification of non-synonymous mutations present in tumor cells, but not expressed by non-cancerous tissues. Having emerged following thymic selection of the T cell repertoire, peptides containing non-synonymous mutations will appear as foreign to the patient's immune system. When presented by MHC class I and II molecules on the surface of tumor cells, these peptides, referred to as neoantigens or neoepitopes, can mark the tumor cell for destruction by effector T cells. It is possible to use neoantigens identified by whole exome sequencing to design personalized therapeutic vaccines targeting an individual's tumor-associated neoantigens. A central challenge to producing effective therapeutic neoantigen vaccines is the identification of peptides that will result in effector T cell responses able to control tumor growth.

Peptide neoantigens are inherently highly similar in sequence to the corresponding native peptides of the non-mutated parental protein from which they are derived. As such, they are less likely to generate strong effector T cell responses and more likely to produce suppressive T cells, such as regulatory (Treg) T cells, or T cells cross-reactive to the native peptide sequence. Failure to exclude cross-reactive or suppressive sequences from vaccine design could reduce or completely abrogate vaccine efficacy.

In this presentation, we will describe the use of AncerTM, a predictive algorithm, that selects neoantigens for recognition by both CD8+ and CD4+ T cells and removes potentially suppressive Treg and cross-reactive self-like epitopes. AncerTM optimizes target selection when designing personalized therapeutic cancer vaccines. We will discuss how AncerTM is being developed as an immunotherapy for the treatment of patients with cancer.

Sergio Valentinotti, *Liomont*

BIO

Dr. Sergio Valentinotti is the Life Sciences director for Laboratorios Liomont where he oversees the vaccine and monoclonal antibodies development programs. Dr. Valentinotti received his BSc. In Chemical Engineering from the National University in Mexico (UNAM) followed by a MSc degree in Biochemical Engineering from Colorado State and a PhD in Applied Science from the Polytechnical School in Lausanne (EPFL).

ABSTRACT

mAbxience and Liomont are two Latin American pharmaceutical laboratories that are involved in the production of the AstraZeneca Covid-19 vaccine.

In this presentation we will discuss how this consortium was created as well as the critical factors that were necessary to make this collaboration possible, including the active participation of AstraZeneca and support of the Carlos Slim foundation. These factors will be extrapolated to a broader level exploring the opportunities of having a regional vaccine production program as well as the challenges that need to be overcome for this to become a reality.

(Continue to Next Page)

Andres Wigdorovitz, *INTA -CONICET*

BIO

- PhD (1996) University of Buenos Aires (Argentina) in the area of sciences - Studying the role of the antigenic presentation of the Foot-and-Mouth Disease Virus

- Coordinator of the Vaccine Area of the Virology Institute , INTA (2003-2014),

- INTA Referent in technological innovation 2015 to the present

- Founder of INCUINTA: THE TECHNICAL-ORGANIZATIONAL PLATFORM FOR THE DEVELOPMENT OF TECHNOLOGICAL PROJECTS.

- Founder and Scientific Director of Bioinnovo SA the public-private technology-based company created by the National Institute of Agricultural Technology (INTA) and Vetanco SA. (www.bioinnovo.com.ar)

- Principal Investigator of the National Council of Scientific and Technical Research (CONICET) of Buenos Aires Argentina

- Professor National University of San Martin 07-01-2014 to the present

- Scientific Advisor Panel Plant Based Vaccines, Antibodies & Biologics (2003 to 20)

- Advisor board Project EU 760331 - Newcotiana: Developing Multipurpose Nicotiana Crops for Molecular Farming using New Plant Breeding Techniques (August 2017 to present)

- Member of the Technological and Social Development Commission for Reports, Promotions and Projects CONICET (March 2017 to 2018)

- Member of the Scientific-Technological Advisory Council of the National Bioeconomy Council of the Ministry of Science, Technology and Productive Innovation of the Nation from November 2017 to the present)

- Member of the Disciplinary Networks Vetarinary Commission of CONICET (RESOLUTION 3227/17). March 2018 to present)

Author in 63 publications in international indexed journals, Author in 7 national and international patents

- International benchmark in Molecular Farming (production of vaccines and antibodies in plants)

- More than 20 agreements of technological connection with national and international companies.

- 14 national and international awards in the last 5 years.

ABSTRACT

Foot-and-mouth disease (FMD) is a highly contagious viral disease of cloven-hoofed animals, which causes severe economic losses and has global importance A novel vaccine against FMDV is desirable considering mostly the costs and regulatory concerns associated with the high biosecurity facilities required for production of the currently used inactivated vaccine. Although many developments have been made, most of them fail when the technology transference steps are considered due to the complexity of the novel technology, the difficulty to scale up the process or because the technology it is not versatile to produce the many serotypes required in FMDV vaccine. We present the use of transient gene expression in 293-6E cells to produce FMDV virus like particles (VLPs) and demonstrated the immunogenicity of the recombinant structures in mice, cattle and pigs

Bovine diarrhea virus (BDV) is considered an important cause of economic loss within bovine herds worldwide.

Vedevax Bock is the first subunit recombinant vaccine in the world approved against Bovine Viral Diarrhea Virus (BVDV), a disease that affects a large part of cattle herds. It is made using a different approach than traditional vaccines: it is a vaccine that combines the E2 glycoprotein of the virus with the APCH antibody, with an affinity for the immune system. This mechanism greatly increases its effectiveness.

Trials were carried out with more than 7000 dairy cattle and breeding in different establishments with different sanitary situations. In conclusion, the Vedevax Block vaccine was highly immunogenic under field conditions, making it a useful tool to reduce the productive and reproductive losses associated with infection by the bovine viral diarrhea virus.

Vedevax is produced by the Bioinnovo Company, a leadership case resulting from a succession of successful cooperation experiences between Inta and Vetanco.

Select Your Masterclass Speakers

(Alphabetical Order)

Barry Buckland, *BiologicB*

BIO

PhD in Biochemical Engineering at University College London obtained in 1974. Joined the Merck Research Laboratories (MRL) in 1980 and built a world class Bioprocess R&D group. Leader of process development of all biologically made product candidates within the MRL pipeline and manufacture of Clinical Supplies during a 20 year time frame. Products developed within this period include MEVACOR®, ZOCOR®, IVOMEC®, CANCIDAS®, RECOMBIVAX HB®, VAQTA®, VARIVAX®, COMVAX®., ROTATEQ® (Rotavirus vaccine), ZOSTAVAX® (shingles vaccine) and GARDASIL® (HPV vaccine).

External awards and appointments include being elected to the National Academy of Engineering in 1997 and Fellow of University College London in 1998. Awarded PhRMA Discoverer of the Year award in April,2009 for development of the Merck HPV vaccine (along with Eliav Barr and Kathrin Jansen).

Starting in May 2009; CEO, BiologicB. Since this time have provided consultancy worldwide to a number of companies and not-for-profit institutions, in all areas of Biologics including Vaccines and Therapeutic Proteins. Chair of Board for a not-for-profit organization, Engineering Conferences International. Continue as Visiting Professor at University College London and as Executive Director of NIIMBL (National Institute for Innovation in Manufacturing Biopharmaceuticals).

Katherine Kedzierska, *University of Melbourne*

BIO

Prof Katherine Kedzierska is Deputy Head of the Department of Microbiology and Immunology, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity.

Katherine received her PhD from Monash University in 2002 for her studies on the mechanisms underlying defective immune functions after HIV infection. Her PhD work was recognised by the 2001 Premier's Commendation for Medical Research, 2002 Monash University Mollie Holman Doctoral Medal and an NHMRC Peter Doherty Postdoctoral Fellowship to pursue her postdoctoral research with Laureate Professor Peter Doherty at University of Melbourne. Her postdoctoral work was focused on the early establishment of influenza-specific $CD8^+$ T cell memory, TCR repertoire diversity and viral escape in a mouse model of influenza virus infection. In 2007, she got awarded an NHMRC RD Wright Fellowship and grant funding to establish her own research team.

She is currently an NHMRC Investigator Fellow and a group leader of 'Human T cell Laboratory' in Department of Microbiology and Immunology at University of Melbourne. Her research interests include human T cell immunity to pandemic, seasonal and newly emerged influenza viruses, anti-viral immunity in the young, the elderly and Indigenous Australians, viral escape and generation of immunological memory in human influenza infection. She also studies human immunity to SARS-CoV2 in COVID-19 patients.

Katherine is a recipient of a number of prestigious awards, including 2016 Australian Academy of Science Jacque Miller Medal, 2011 NHMRC Excellence Award and 2011 Scopus Young Researcher of the Year Award. She is a Co-Head of Indigenous Health at the Doherty Institute. In 2019, she was elected as a Fellow of the Australian Academy of Health and Medical Science (AAHMS).

Janet R. Rea, *AVM Biotechnology*

BIO

Janet R. Rea, M.S.P.H., has over 40 years of experience in clinical development through commercialization of biologic and small molecule drug products, vaccine and IVDs. Her areas of expertise include GXP compliance, aseptic production, and health authority interactions, notably while at Immunex (Amgen), AVI BioPharma (Sarepta), Protein Sciences (Sanofi), Targeted Genetics and Atossa Therapeutics. She received her B.S. degree in Microbiology and Masters of Science of Public Health from the University of Washington, where she has also served as Clinical Assistant Professor in the Biomedical Regulatory Affairs Certificate and Master's Program.

Indresh Srivastava, *Novavax*

BIO

Dr. Srivastava has joined NOVAVAX as Vice President of Vaccine Development after spending about 10 years at Protein Sciences Corporation, A Sanofi company where he served in various capacities. He has a strong background in vaccine development particularly in immunogen design, process development, process scale up, tech transfer to Manufacturing sites, analytical and formulation development. He has published extensively in these areas. In 2017, Dr. Srivastava was elected a Fellow for ISV and was also selected "Fellow of the Month." He has many honors among which two Fellowships from Indian Council of Medical Research, Swiss Government Scholarship, Swiss National Foundation Program project to support his doctoral and post-doctoral research. Dr. Srivastava served on NIH Special Emphasis Panels for vaccine development for more than 15 years, completed a 4-year term as the standing member of regular Vaccine Study Section (VACC), and 2011 co-edited a book entitled, "Development of Vaccines: Discovery to Clinical Testing." Dr. Srivastava spent more than 12 years at Chiron Corporation/Novartis Vaccines and Diagnostics, Inc., in various capacities including Head (AI), Protein Biochemistry; Head, Vaccine Manufacturing, and Head, Protein Expression and Analytics. Prior to joining Protein Sciences, he spend two years at Vaccine Research Center, National Institutes of Allergy and Infectious Diseases, where he led the process development, analytical and formulation development of vaccine candidates for clinical evaluation. Prior to joining Biotechnology Industry, he was an Assistant Professor of Research in the department of Microbiology and Immunology at Medical college of Pennsylvania. He holds a Ph.D., degree from Central Drug Research Institute, Lucknow India, and completed his post-doctoral training with Prof. Luc Perring at Hospital Cantonal, University of Geneva. Dr. Srivastava is serving as a reviewer/Editorial Board member for several journals; served as a member of Scientific Advisory Boards; and served as a Chair/Co-Chair of National and International meetings.

Meet the Fellows

(In Order of Program)

BIOS

David Weiner, *The Wistar Institute*

Dr. Weiner directs a translational molecular immunology research team focused on creating novel approaches for disease prevention and treatment using synthetic nucleic acid technology. With help from collaborators, his group is one of the pioneering research teams in the field of DNA vaccines and immunotherapies and has developed the first clinical studies of DNA vaccines.

The Weiner lab has made synthetic DNA platform advances by creating the world's first Zika vaccine, the first and most advanced MERS coronavirus vaccine and developing an advanced Ebola vaccine, among others.

In oncology, the Weiner lab has helped to develop immunotherapy approaches for HPV-associated cancers, prostate cancer and glioblastoma multiforme (GMB), among others, which are currently in clinical testing. His work has led to the first clinically efficacious therapeutic DNA vaccine (VGX3100) for HPV cervical intraepithelial neoplasia (CIN), which is now in licensure trials (REVEAL).

The Weiner lab has published more than 428 papers, chapters and reviews, and members have participated in hundreds of scientific lectures.

Dr. Weiner is a Professor Emeritus at the University of Pennsylvania Perelman School of Medicine and sits on multiple academic and industry advisories and review panels. He has received several awards and honors for these accomplishments, including inclusion as one of the top 40 most influential vaccine scientists in the world (2015), the W.W. Smith Charitable Trust Professorship in Cancer Research (2016), and the Vaccine Industry Excellence Award for Best Academic Research Team (2015 & 2016). Dr. Weiner was named among the Top 20 Translational Researchers by Nature Biotechnology in 2016, 2017 and 2018 (ranked #2), and received the Stone Family Award for Cancer Research (2014), the NIH Director's Translational Research Award (2011), and the Life Sciences PA Scientific Achievement Award (2018). He is a Fellow of the American Association for the Advancement of Science (2011), Fellow of the International Society for Vaccines and President of the International Society for Vaccines (2018-2020).

Dr. Weiner is highly committed to developing of the careers of young scientists and has been an avid trainer, advisor, and advocate for students, fellows and junior faculty.

Sarah Gilbert, *University of Oxford*

Dr. Sarah Gilbert is Professor of Vaccinology in the Nuffield Department of Medicine at the University of Oxford. She completed her undergraduate studies at the University of East Anglia and her doctoral degree at the University of Hull. Following four years as a research scientist at the biopharmaceutical company Delta Biotechnology she joined Oxford University in 1994 and became part of the Jenner Institute (within NDM) when it was founded in 2005. Her chief research interest is the development of viral-vectored vaccines that work by inducing strong and protective T and B cell responses. She works on vaccines for many different emerging pathogens, including influenza, Nipah, MERS, Lassa, Crimean-Congo haemorrhagic fever, and SARS-CoV-2. Working with colleagues in the Jenner Institute research labs, the Clinical Biomanufacturing Facility and Centre for Clinical Vaccinology and Tropical Medicine, all situated on the Old Road Campus in Oxford, she has advanced important novel vaccines from design to clinical development, with a particular interest in the rapid transfer of vaccines into manufacturing and first in human trials. She is the Oxford Project Leader for ChAdOx1 nCoV-19, an important vaccine (being codeveloped with AstraZeneca) against the novel coronavirus, SARS-CoV-2, which likely can play an important role in this current pandemic. Sarah has had an exceptionally impactful vaccine career and has contributed service to ISF in by participating in past ISV conferences, serving on the organizing committee for the annual ISV meeting held in 2020, as well as being able to serve on the organizing committee for the ISV 2021 meeting.

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BIOS

Linda Klavinskis, *King's College London*

Linda Klavinskis is a Professor of Viral Immunology in the Faculty of Life Sciences and Medicine at King's College London. She is a Fellow of the International Society for Vaccines and serves as General Secretary and Executive Board member of the Society.

Professor Klavinskis obtained her PhD in Immunology at the University of London (UCL) followed by postdoctoral training in viral pathogenesis in Michael Oldstone's laboratory at the Scripps Research Institute. The research in her laboratory focuses on adaptive immune responses to vaccination and virus infection. This work has led to deciphering an alternative mode of antigen presentation, termed 'cross-dressing' and unravelling mechanisms contributing to epitope selection and CD8 T-cell immunodominance with relevance to vaccine design. Translationally, she has made inroads in understanding the biology of skin immunisation and developed a microneedle vaccine delivery platform. During the COVID-19 pandemic her lab has focused on the role of innate immunity in the hyperinflammatory response in severe COVID-19 and applying therapeutic approaches.

Xavier Saelens, *Ghent University*

Dr. Xavier Saelens obtained his PhD degree from the University of Ghent (Ghent, Belgium) in 1990 in the laboratory of Walter Fiers. After postdoctoral training in the influenza research group of Willy Min Jou, and in the Molecular Signaling and Cell Death group of Peter Vandenabeele, both at Ghent University, he became an assistant professor in Molecular Virology in 2008. Currently, he is a full professor in the Department of Biochemistry and Microbiology at Ghent University and a principle investigator at the VIB-UGent Center for Medical Biotechnology.

The research team of Xavier Saelens applies modern biotechnology methods to develop new vaccines and antivirals against important human respiratory viruses such as influenza, respiratory syncytial virus and, more recently, coronaviruses. In addition, his group uses interactomics tools to gain new insights in the molecular interplay between host and viral factors.

His research group pioneered the development of a universal influenza A vaccine candidate based on the viral matrix protein 2 and elucidated it's mechanism of protection. More recently, his team proposed a new human respiratory syncytial vaccine candidate that is based on the small hydrophobic protein of this virus. This vaccine candidate has successfully passed a Phase I clinical study. The group also develops single

domain antibodies and formats thereof as new candidate biologics to control infections by human respiratory viruses. A recently started research focus point is the development of respiratory delivery technologies for antibody-based antivirals.

In 2015 he received the biennial price in Virology from the Study Centre Princess Joséphine- Charlotte from the Flanders and Walloon Research Foundations of Belgium. In 2019 and 2020 Xavier Saelens obtained excellence awards from VIB for outstanding scientific and technology transfer output.

He is a board member and the treasurer of the Belgian Society for Microbiology and member of the board of the International Society for Vaccines where he has contributed in many ways to the society.

BIOS

Manon Cox, *NextWaveBio*

Dr. Manon M.J. Cox, MBA founded NextWaveBio early 2018 initially providing scientific and strategic direction to various biopharmaceutical companies. NextWaveBio' mission is to bridge the gap between preclinical and clinical development by offering infrastructure and education around quality systems required for clinical development and manufacturing.

Prior to that she led the development of Flublok®, the only FDA approved recombinant influenza vaccine at Protein Sciences Corporation where she served as President and Chief Executive Officer since April 2010 and Director since 2008. She joined Protein Sciences in 1998 as Director of Business Development and became Chief Operating Officer in 2003. Previously she was with Gist-brocades, a large Dutch company specialized in fermentation, where she held various management positions, most recently in New Business Development and before that in Production and Research and Development. Prior to joining Gist-brocades, she worked as a Molecular Biologist on the development of a PCR screening test for cervical cancer at the University of Amsterdam.

She serves on the Board of Directors of Vaxxas, the Netherland-America Foundation including its Education Committee, the International Society of Vaccines, and various Scientific Advisory Boards in the vaccine development space.

Dr. Cox has received many honors and awards recognizing her stature as a leader in innovation and influenza, including in 2014 receiving a Doctorate in Humane Letters honoris causa from St. Joseph University and the Woman of Innovation award from the Connecticut Technology Council and was elected fellow in the International Society of Vaccines in 2015. Dr. Cox holds a Doctorate from the University of Wageningen, received her MBA with distinction from the University of Nyenrode and the University of Rochester, NY and holds a Doctorandus degree in Molecular Biology, Genetics and Biochemistry from the University of Nijmegen, The Netherlands.

Ted Ross, *University of Georgia*

Ted M. Ross, Ph.D. is the Director of the Center for Vaccines and Immunology and Georgia Research Alliance Eminent Scholar and Professor of Infectious Diseases at the University of Georgia. Dr. Ross earned his undergraduate and graduate studies in Zoology and Microbiology at the University of Arkansas and he received a Doctorate in Microbiology and Immunology from Vanderbilt University in 1996. He was awarded the inaugural Sidney P. Colowick Award in Outstanding Graduate Research while at Vanderbilt. Dr. Ross performed post-doctoral fellowships at Duke University on HIV biology of viral entry and at Emory University on vaccine development for HIV and influenza viruses. He then started his own laboratory as Principal Investigator at East Carolina University and in 2003 moved the laboratory to the University of Pittsburgh in the Departments of Medicine-Infectious Diseases, Microbiology and Molecular Genetics, and as a founding member of the Center for Vaccine Research where he served the University for 10 years. In 2015, he joined the faculty at the University of Georgia. Dr. Ross explores new vaccine technologies intended to protect against all strains of influenza – an endeavor that could potentially eliminate the need for seasonal flu shots. Dr. Ross and his colleagues are applying similar strategies to fight other serious viruses such as, Dengue, SARS-CoV-2, Chikungunya, and HIV Type-1 viruses.

Dr. Ross has published more than 225 papers and book chapters on infectious disease and vaccine development. He has been an invited speaker at more than 130 national and international conferences and participates in several vaccine working groups, including at the U.S. NIH, U.S. Centers for Disease Control and Prevention and the World Health Organization. He is an editorial 100 board member of Vaccine. He previously served as Editor-in-Chief of the journal Current HIV Research. In addition, he has been an ad-hoc reviewer on NIH study sections and a reviewer for 24 different journals.

Dr. Ross is currently the President of International Society for Vaccines from 2020-2021 and has served as the Co-Chair of the ISV Congress in Philadelphia (8th), Seoul (9^{th}), and Atlanta (12^{th}).

Denise Doolan, *James Cook University*

Dr. Denise Doolan received her undergraduate degree in Science majoring in Biochemistry in 1985 at the University of Queensland, Brisbane, Australia. She subsequently completed a Masters in Life Sciences at Griffith University, Brisbane, while working as an Experimental Scientist at Australia's Commonwealth Scientific and Industrial Research Organisation (CSIRO). She completed a Ph.D. in Molecular Immunology in 1993 at the University of Queensland, under the supervision of Dr. Michael F. Good at the Queensland Institute of Medical Research. She was awarded a postdoctoral fellowship from the United States National Research Council, The National Academies, to pursue studies on malaria vaccines with Dr. Stephen L. Hoffman at the Naval Medical Research Center (NMRC) in Rockville, MD USA. For more than ten years Dr. Doolan stayed affiliated with the NMRC's Malaria Program, beginning as a postdoctoral fellow, then being promoted to Director of Basic Research and later Director of Basic and Preclinical Research & Development and finally Scientific Director. During this time she also was affiliated with the Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD USA. Dr. Doolan was awarded a Pfizer Australia Research Fellowship in 2007 and returned to Australia to head the Molecular Vaccinology

Laboratory, Division of Immunology, at The Queensland Institute of Medical Research. In 2008 she was appointed as a Credentialed Professor at the Griffith Medical Research College, Griffith University, and as an Adjunct Professor in the School of Medicine, University of Queensland.

Throughout her scientific career, Dr. Doolan has provided critical insights into multiple facets of malaria immunology and vaccine development, extending to the more general fields of immunology, vaccinology and the advancement of public health. Dr. Doolan has received numerous awards and honors, the most recent ones being *Who's Who in America 61st Edition* (2007) and *IBC Leading Scientists of the World* (2008). She served as Associate Editor of *The Journal of Immunology* and is an Academic Editor of *Public Library of Science* (PLoS) One. In the course of her scientific career Dr. Doolan has coauthored over 70 articles in well-established journals including Science and *Nature Medicine*. She also contributed several chapters to books in the field of malaria vaccine development and has edited a book on malaria methods and protocols. Dr. Doolan is inventor on a number of patents in the areas of antigen discovery, immune assays, or vaccination strategies.

Shan Lu, *UMASS Medical School*

Dr. Shan Lu is a profess and Director, Laboratory of Nucleic Acid Vaccines (since 1996) in Department of Medicine, University of Massachusetts Medical School, Worcester, Mass, USA.

Dr. Lu was one of the early pioneers to demonstrate the feasibility of DNA immunization in early 1990s and advocated the further advancement of this field in the last 3 decades, including the development of novel polyvalent DNA/protein HIV vaccines into human clinical studies which showed the robust and broadly cross-reactive immune responses.

Dr. Lu is the founding Editor-in-Chief, Emerging Microbes and Infections (EMI), published by Nature and Taylor & Francis respectively. He is also a member of editorial boards for Journal of Virology, Current Opinion of Virology, Vaccine, NPj Vaccine, Human Vaccines and Immunotherapeutics

Dr. Lu joined International Society for Vaccines (ISV) in 2008 and served as a board member or officer including president (2011-2013). He was elected as a Fellow of ISV in 2013. He played a key role in the design and management of ISV congresses including 2021 Annual Virtual Congress.

BIOS

Margaret Liu, *ProTherImmune*

Professor Margaret A. Liu, obtained an M.D. from Harvard Medical School, a B.A. in Chemistry, summa cum laude, from Colorado College, and passed the Epreuve pour le Diplôme d'Enseignement, à l'unanimité (judges' unanimous decision), in piano from the Ecole Normale de Musique de Paris, and is the recipient of an honorary Medical Degree (MD *honoris causa)* from the Karolinska Institutet in Stockholm, and an honorary Doctorate of Science from Colorado College. She completed Internship and Residency in Internal Medicine and a Fellowship in Endocrinology, all at Massachusetts General Hospital/Harvard Medical School. She received Board Certification in Internal Medicine and in Endocrinology and Metabolism. Dr. Liu was a Visiting Scientist at the Massachusetts Institute of Technology, Instructor at Harvard Medical School, Adjunct Assistant Professor of Medicine at the University of Pennsylvania, a Visiting Professor at the Karolinska Institutet in Stockholm, and the recipient of an NIH Physician Scientist Award. She served as Senior Director at Merck Research Laboratories, Vice President of Vaccines Research and Gene Therapy at Chiron Corporation, Vice-Chairman of Transgène, Senior Advisor in Vaccinology at the Bill & Melinda Gates Foundation, Executive Vice-Chair of the International Vaccine Institute, and was on the US NIH NIAID Council.

Her research has focused on novel technologies for vaccines and immune treatments for cancer. She pioneered the development of DNA vaccines, which are now in clinical trials for many human diseases and are licensed for several veterinary applications. She also was an innovator in the field of bispecific antibodies to activate T cells for tumor cell killing. The Nobel Committee invited her to lecture in the Karolinska Research Lecture series, and she was named by Discover magazine as one of the 50 most important female scientists. She consults world-wide for companies, investment firms, non-governmental organizations, and governmental scientific advisory bodies, and has held positions as an Adjunct Professor at UCSF, and as a Foreign Adjunct Professor at the Karolinska Institutet. Dr. Liu was previously the President of the International Society for Vaccines for the 2015- 2017 term, then President Emerita, and is currently the Chairman of the Board of ISV (2020-2021).

Gary Kobinger, *Laval University*

Dr. Gary Kobinger obtained his PhD magna cum laude from the University of Montreal was recruited by the Public Health Agency of Canada where he became Chief of the Special Pathogens Biosafety Level 4 program. He is now a Professor at the Université Laval and is Director of the Centre de Recherche en Infectiologie. He also holds appointments at the University of Manitoba and the University of Pennsylvania.

Dr. Kobinger supported the development the rVSV-ZEBOV vaccine as well as the monoclonal antibody cocktail ZMapp which was advanced to treat Ebola virus infection, the first such antibody approach advanced for Ebola, thus helping to advance the MAb approach for EID in resource limited settings. His preclinical NHP work and service to WHO helped advance rVSV-ZEBOV, which is an important tool for control of Ebola. He also pioneered simple mobile diagnostic laboratories for field use for Ebola testing during outbreaks facilitating public health controls of outbreaks, and used these diagnostic tools in the current SARS-CoV2 outbreak in Canada. For this and other contributions he has been granted several awards including the 2015 scientist of the year award from Radio Canada (CBC), the Order of Manitoba and the Meritorious Service Cross (civil division) of the Governor General of Canada in 2016, and the Manning principal award in 2017. Dr. Kobinger has co-authored over 300 peer-reviewed scientific manuscripts, and has given numerous invited seminars in Universities, national and international funding agencies, departments of national defenses, the White House, and the World Health Organization (WHO) concerning research on high consequence pathogens and the development of new public health policies and recommendations. His work presently focuses on developing and testing new vaccine platforms and immune treatments against pathogens of high consequences to global public health.

Serving the international community, Gary sits on several committees such as the IHR roster of experts in Viral Haemorrhagic Fever, the WHO's High Priority Pathogen advisory board, the STAG-IH advisory board to the Deputy Director-General and ad-hoc advisor to the SAGE committee. He has contributed to ISV meeting through speaking, helping to organize sessions, and providing speakers. In addition Dr. Kobinger serves on the ISV Board.

BIOS

Annie De Groot, *EpiVax*

Anne (Annie) Searls De Groot is a graduate of Smith College and University of Chicago, where she obtained her BA and MD respectively. After medical school, she completed her residency in internal medicine at Tufts New England Medical Center, and then participated in a research fellowship in vaccinology at the NIH, and a second fellowship in infectious disease back at the New England Medical Center. Having become an Infectious Disease specialist and obtained her first NIH Grant, she joined the medical and research faculty at Brown University. She started EpiVax while still a faculty member at Brown and gradually shifted her effort from primarily academic research at Brown to translational research at EpiVax. She retains an active academic presence, most recently at the University of Georgia, Center for Vaccines and Immunology, where she is currently professor and senior scientist at the University of Georgia, collaborating with researchers and training the next generation of vaccinologists.

Annie has served as Chief Executive Officer and Chief Scientific Officer of the biotech company EpiVax, which she cofounded with Bill Martin, COO/CIO, for the past 22 years. This company is privately held, employs approximately 30 high-level research scientists, and is a globally recognized immunoinformatics and vaccine design company. One of the company's more fundamental discoveries was that human pathogens use "human-like" sequences to camouflage themselves from immune response, and that removing these sequences from vaccines makes them more effective. The EpiVax team also discovered what are now known as "Tregitopes"—peptides that activate natural regulatory T cells.

De Groot is the author of more than 240 publications and 50 patents, and has generated more than $35M in US federal funding. In addition to her research, Dr. De Groot continues to work to improve access to healthcare by volunteering evenings and weekends at Clinica Esperanza/Hope Clinic, which provides free medical care and preventive health services to uninsured adults living in Rhode Island. De Groot is also the founder and scientific director of the GAIA Vaccine Foundation, a nonprofit organization that aims to improve the health of women, children and families in Mali, West Africa.

Tonya Villafana, *AstraZeneca*

Dr. Tonya Villafana has dedicated her career to developing vaccines and drugs against some of the most difficult infectious diseases and sought to improve global health through significant contributions spanning the public, non-governmental and private sectors. In her current role as Vice President, Global Franchise Head, Infectious Diseases at AstraZeneca, Dr. Villafana has led the accelerated late-stage development of Vaxzevria (COVID-19 Vaccine AstraZeneca), working closely with the University of Oxford, health authorities, the US government, US National Institutes of Health and COVAX (a partnership between CEPI, Gavi, WHO and UNICEF), to enable broad and equitable access to the vaccine around the world at no-profit during the pandemic. This complex development program has enabled supply of more than 1 billion doses in more than 170 countries around the world in just 18 months.

During her 12 years with AstraZeneca, Dr. Villafana has led late-stage development for a number of vaccine and monoclonal antibody infectious disease programs including nirsevimab, a novel monoclonal antibody for the prevention of RSV disease in all infants. From 2011-2013, she was seconded to the World Bank and served as the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) World Bank Fellow. In this role, Dr. Villafana supported the Global Medicines Regulatory Harmonization Initiative with a focus on strengthening regulatory systems in Africa and co-authored the Bank's position on Non-Communicable Diseases for the 2011 UN High Level Meeting on NCDs. Prior to joining AstraZeneca, Dr. Villafana was Director of Portfolio Management at the PATH Malaria Vaccine Initiative (MVI), where she had oversight of MVI's vaccine candidate portfolio. She served as Chair of MVI's Portfolio Management Committee and was a member of the RTS,S malaria vaccine team (GSK's Mosquirix, which received positive scientific opinion from the EMA), leading teams for PATH in Tanzania and Gabon. From 2001-2006 Tonya was the Site Director of the HIV Vaccine Initiative at the Botswana Harvard School of Public Health AIDS Initiative Partnership for HIV Research and Education in Gaborone, Botswana, where she established clinical sites to conduct the first HIV vaccine studies in the southern African nation, in collaboration with the US NIH HIV Vaccine Trials Network. While in Botswana, she served on the Botswana National HIV Vaccine Committee collaborating with local and international institutions including WHO, the Debswana Mining company and Botswana Police Service.

Dr. Villafana has served on several important scientific committees and advisory boards including the Malaria Clinical Trials Alliance, International Society of Vaccines and the NIH Integrated Preclinical/Clinical Vaccine Development Program. She has worked closely on global health initiatives with the Bill and Melinda Gates Foundation, PAHO, WHO, IFPMA, and UK Development Agency for International Development. She has contributed to ISV meetings and participated in several over the years. She was a member of the ISV Scientific Committee for the 2017 meeting held in Paris, where she helped to create a forum for young investigators interested in vaccines. Dr. Villafana is supportive of ISV's role in training and elevating the work of young researchers, particularly those from developing countries.

She received a PhD in immunology from Weill Cornell University Graduate School of Medical Sciences and an MPH from Harvard School of Public Health. Dr. Villafana is committed to developing novel vaccines and drugs to prevent diseases in the most vulnerable populations around the world.

Oral Abstracts

(Selected from Scientific Committee)

(Alphabetical Order by First Author)

Improved protection against multidrug *Pseudomonas aeruginosa* following administration of an Fc engineered DNA-encoded monoclonal antibody (DMAb) with enhanced complement activity

Jihae Choi1, Rishabh Sharma1, Elizabeth M Parzych1, Susanne N Walker1, Nicholas J Tursi1, Gabrielle Villafana1, Jacqueline Chu1, Daniel W Kulp1, Farokh Dotiwala1, David B Weiner1, Ami Patel1
1The Wistar Institute, Philadelphia, PA, USA

Antimicrobial resistance is a serious threat to global health across all age groups. While there has been progress towards new antibacterial agents, *Pseudomonas aeruginosa* remains one of the most common bacterial infections in both healthy and immune compromised people. At-risk groups include patients with skin injuries (burns/wounds), medical implants, long-term ventilation, HIV, and cystic fibrosis. The discovery and development of non-traditional strategies for multi drug resistant strains of *Pseudomonas aeruginosa* is needed. Alongside recent advances in nucleic acid platforms for vaccination and immunotherapy, DNA-encoded monoclonal antibodies (DMAbs) are demonstrating prophylactic and therapeutic efficacy in preclinical models of infectious disease and cancer. Previously, we demonstrated *in vivo* delivery and protective efficacy of DMAbs targeting the *Pseudomonas aeruginosa* type III secretion injectosome protein, PcrV. Here, we describe Fc engineering of anti-PcrV DMAbs to enhance antibody-dependent complement deposition as a strategy to promote clearance of *Pseudomonas aeruginosa*. The Fc portion of plasmid DMAb-αPcrV was engineered to encode the Fc modification(s) E345K and/or E430G that enhance IgG hexamerization and complement deposition upon pathogen binding. Engineered Fc variants were first evaluated *in vitro*, followed by *in vivo* delivery to BALB/c mice by intramuscular electroporation to produce fully functional mAb directly in muscle. Wildtype DMAb-αPcrV and Fc variants DMAb-αPcrV-E345K and DMAb-αPcrV-E430G showed comparable serum antibody expression *in vivo*, at levels >20ug/mL. Using an opsonophagocytic killing assay, we demonstrate that DMAb-αPcrV-E345K and DMAb-αPcrV-E430G induce higher complement activity than wild type DMAb. In a lethal murine intraperitoneal PA14 *Pseudomonas aeruginosa* challenge model, the complement-enhanced variant DMAb-αPcrV-E430G showed superior protection compared to wild type, with decreased bacterial colonization in the spleen liver, kidney, lungs, and brain. Overall, our studies support the important role of complement in *Pseudomonas aeruginosa* clearance and support further characterization of Fc engineered DMAbs that enhance effector function against other antimicrobial resistant pathogens.

T cell epitope content comparison (EpiCC) analysis between PCV2 vaccines and field strains

Andres H. Gutierrez1, Frances Terry1, William D. Martin1, Alvaro Aldaz2, Jose Angulo2, Dennis L. Foss3
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Background: As porcine circovirus type 2 (PCV2) continues to evolve, the genetic gap between available vaccines and field strains grows. Vaccines that contain T cell epitopes well-matched to the circulating strains are more likely to induce strong T cell-mediated memory responses upon challenge or field exposure. To quantify the relatedness between PCV2 vaccines (three monovalent and one bivalent) and contemporary field strains, we predicted and compared the T cell epitope content contained in their capsid proteins.
Methods: Six hundred and fifteen PCV2 field strains, including genotype PCV2a (n=108), PCV2b (n=111), and PCV2d (n=396) viruses from Asia (n=76), Europe (n=246), and America (n=293), were compared to three PCV2a-based monovalent vaccines (VacAlt1, VacAlt2, and VacA) and one bivalent vaccine (VacAB). The bivalent vaccine is a combination of PCV2a and PCV2b. Utilizing PigMatrix, the field strains and vaccine

strains were screened to identify putative class I and class II T-cell epitopes restricted by Swine Leukocyte Antigen (SLA). The field strains were then compared to the vaccine strains to generate a relatedness score. These T cell epitope content comparison (EpiCC) scores evaluate the shared epitope content between field strains and vaccine strains. Each field strain was also compared to itself to determine its T cell epitope density (baseline score). For each comparison, the EpiCC score was then divided by the field strain baseline score to determine the percent T cell epitope coverage of the field strain by the vaccine strain.
Results: Overall, the combination PCV2a-PCV2b vaccine (VacAB) had, on average, the highest EpiCC scores globally (8.72) and by geographical region (Asia=8.36, Europe=8.80, and America=8.73). At the genotype level, VacAB had higher EpiCC scores than the monovalent vaccines for field strains from each analyzed genotype (PCV2a=8.89, PCV2b=10.09, and PCV2d=8.28). Globally, and considering all the analyzed strains, putative VacAB epitopes shared with the PCV2 field strains covered 82.4% of their total epitope content. VacAB T cell epitope coverage was 16%, 19.2%, and 13.3% higher than VacAlt1, VacAlt2, and VacA coverages, respectively.
Conclusions: This study demonstrated that the bivalent PCV2 vaccine has greater T cell epitope overlap with field strains than monovalent PCV2 vaccines. This result suggests that the bivalent vaccine might offer broader T cell-mediated immune response and protection against circulating PCV2 strains.

An mRNA vaccine against SARS-CoV-2: Polyethylene Glycol-free, liposome-based vaccine candidate EG-COVID induces high levels of virus neutralizing antibodies

H. Christian Hong1, Kwang Sung Kim2 , Shin Ae Park3 , Min Jeong Chun1, Eun Young Hong5 , Seung Won Chung1 , Hyun Jong Kim4 , Byeong Gyu Shin2 , Abdennour Braka7, Jayaraman Thanappan7, Sunghoon Jang7 , Sangwwok Wu7,8, Yang Je Cho6 , SeokHyun Kim1, 2
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In addition to the traditional method of vaccine development, the mRNA coronavirus vaccine, which is attractive as a challenging vaccination, recently opened a new era in vaccinology. Here we describe the EG-COVID which is a novel liposome-based mRNA candidate vaccine that encodes the spike (S) protein of SARS-CoV-2. It was successful to develop the mRNA vaccine platform that can be lyophilized using liposome-based technology instead of currently employed lipid nanoparticle (LNP) mRNA carrier. Intramuscular injection of the EG-Covid-MR021 elicited robust neutralizing antibodies against SARS-CoV-2 spike protein. Moreover, our experimental evidence clearly showed that the lyophilized EG-COVID is stable at 4°C in contrast to other available SARS-CoV-2 mRNA vaccines which require storage temperature far below 0°C. In this report, we demonstrate a novel preparation of an mRNA vaccine EGCOVID, which is potent and safe against SARS-CoV-2, that can be stored for a prolonged time in a conventional refrigerator.

High throughput biosensor technology to establish dosing frequency and concentration for an mRNA-LNP genital herpes vaccine

Lauren M. Hook1*, Sita Awasthi1, Tina M. Cairns2, Mohamad-Gabriel Alameh1, Bernard T. Fowler1, Molly M.H. Sung3, Drew Weissman1, Gary H. Cohen2, and Harvey M. Friedman1
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Translational Sciences, School of Dental Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, United States of America 3Acuitas Therapeutics Inc, Vancouver, British Columbia, Canada

We recently demonstrated remarkable success in preclinical studies with a trivalent nucleoside-modified mRNA-LNP vaccine consisting of HSV-2 glycoproteins gC2, gD2, and gE2. Here we evaluated antibody responses to gD2 alone in female BALB/c mice that were immunized IM 2 times 1-month apart with 100ng, 300ng, 1μg, 3μg, or 10μg of gD2 mRNA-LNP or 2 times IM with 10μg Poly(C) RNA-LNP as a control. Mice were challenged intravaginally with 5x103 PFU HSV-2 strain MS (275 LD50) and evaluated for clinical disease measured by death, weight loss, and genital lesions, and subclinical infection assessed by day 2 and day 4 vaginal virus titers, and HSV-2 DNA copy number in DRG. By all measures, the gD2 mRNA-LNP animals were completely protected from clinical disease (50/50) and 96% protected from subclinical infection (48/50). Sera were collected to evaluate antibody responses to gD2 four weeks after the first and second immunizations and indicated a dose-dependent increase in gD2 antibody titer with a significant boost after the second immunization. We used a high throughput biosensor competition assay to measure epitope-specific responses to seven distinct functional epitopes on gD2 involved in virus entry and spread. Few mice produced antibodies to these epitopes after the first immunization, while nearly all mice produced antibodies in a dose-dependent manner after the second, highlighting the importance of the second immunization for the development of epitope-specific antibody responses. The high throughput biosensor technology enabled us to evaluate the effects of the number of immunizations and dose concentrations on the generation of epitope-specific antibody responses. In combination with similar studies with gC2 and gE2 in the future, this approach will help inform formulation of our trivalent HSV-2 vaccine.

DNA delivery of immune-focused SARS-CoV-2 nanoparticle vaccines drives rapid and potent immunogenicity and achieves single-dose protection

Kevin Liaw, K Konrath, Y Wu, X Zhu, S Walker, Z Xu, K Schultheis, N Chokkalingam, NJ Tursi, M Purwar, V Machado, I Maricic, E Reuschel, D Frasse, K Broderick, L Humeau, TRF Smith, DB Weiner, DW Kulp

Antibodies from SARS-CoV-2 vaccines may target epitopes that reduce durability or increase antigenic escape. Using a novel synthetic vaccinology pipeline, we developed rationally immune-focused SARS-CoV-2 vaccines by incorporating glycans into the Spike receptor binding domain (RBD). We assessed the antigenic profiles of these multivalent glycan modified RBDs and demonstrated that they can focus antibody responses towards neutralizing epitopes and away from non-neutralizing epitopes. We then designed nanoparticle vaccines by fusing these immune focused RBDs with nanoparticle scaffolds. We demonstrated that when encoded in synthetic plasmid DNA and administered intramuscularly via adaptive electroporation, these DNA-launched nanoparticles (DLNPs) self-assembled *in vivo*. These DLNPs induced rapid seroconversion and strong neutralizing antibody responses across guinea pig, hamster, and multiple mouse models. They also induced greater CD8+ mediated cellular responses compared to non-focused, non-nanoparticle vaccination. A single, dose-sparing immunization protected against lethal SARS-CoV-2 challenge. In addition, we show that DLNPs are broadly neutralizing against emerging SARS-CoV-2 variants and can also be easily modified to produce DLNPs targeted to these variants. Single-dose coronavirus vaccines via DNA-launched nanoparticles provide a promising platform for rapid clinical translation.

Perception of Vaccination of Filipino Mothers in The NCR Area Post-Dengvaxia

Naomi K. Pompa, Patricia L. Carrillo, Wynona Jane T. Go Cue, Jairone N. Jacobe, Jonel Jen E. Jorge, Hosea Mae F. Loquias, Melissa Mae M. Magsino, and Julia Audrey M. Peralta

Vaccine hesitancy of mothers is a significant public health concern especially after the Dengvaxia controversy in the Philippines which resulted in lower vaccine confidence from 2015 to 2018. Reasons for vaccine hesitancy are multifaceted, culture-specific, and often not completely understood. Hence, it calls for a need to determine the complex factors and influences affecting the perception of Filipino mothers in terms of vaccination. This cross-sectional study assessed the demographic profile, vaccination factors, and influences of Filipino mothers (n =384) aged 19-65 that have a living child in the National Capital Region (NCR). Descriptive and inferential statistics were used to analyze the obtained data, and significant factors in vaccine hesitancy of mothers (μ = 42.12 y/o) were revealed. The Pearson's Chi-square Test was utilized to find the variation of the hesitancy status of the participants with different variables. Factors in the demographic profile such as educational attainment ($p = 0.035$) and monthly income ($p = 0.034$) have affected their perception of vaccination. Vaccine hesitancy (20.1%) of the participants is relatively increased in the Philippines despite their relatively high level of knowledge and a positive attitude regarding vaccination. Most of the participants trust the government ($p = 0.037$) and pharmaceutical companies ($p = 0.002$) for their vaccines. Majority followed the recommended vaccination schedule of their child ($p = 0.001$) and half suppose that there are more ways for disease prevention other than vaccination ($p = 0.015$). Vaccine cost ($p = 0.012$) and accessibility ($p = 0.005$) also influenced the decisions of the participants. The participants showed a positive perception towards vaccination despite high vaccine hesitancy prevalence. However, there remains a need for the government and health professionals to prioritize parental education not only to correct false information on vaccination but also to gain the public's trust while improving the public health system against its fight with vaccine hesitancy.

Poster Abstracts

(See Poster Index for Order)

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1. Novel immunogen design elicits increased protection against avian H7N9 influenza that is associated with mobilization of seasonal influenza T cell memory

Mayara Grizotte-Lake1, Hyesun Jang2, Andres H. Gutiérrez1, Christine Boyle1, Lauren Myers1, Nese Kurt Yilmaz3, sharing Hou3, Celia Schiffer3, Ted M. Ross2,4, Anne S. De Groot1,2, Leonard Moise1,2
1EpiVax, Inc., Providence, RI, USA 2Center for Vaccines and Immunology, University of Georgia, Athens, GA, USA 3Department of Biochemistry and Molecular Pharmacology, UMass Medical School, Worcester, MA, USA 4Department of Infectious Diseases, University of Georgia, Athens, GA, USA

Background: Cross-conserved hemagglutinin (HA)-specific CD4+ T cell epitopes support protective B cell responses against seasonal influenza. However, in the case of avian H7N9, which poses a pandemic threat, HA elicits only weak neutralizing antibody responses in infection and vaccination without adjuvant. Strategies to optimize H7N9 HA immunogenicity are therefore critical for pandemic preparedness. Because cross-conserved T cell epitopes augment seasonal influenza, we hypothesized that an immune-engineered H7N9 HA incorporating broadly reactive H3N2 HA-specific memory CD4+ T cell epitopes would boost protective antibody responses and increase protection.
Methods: We designed and produced two optimized H7N9 HA constructs: OPT1 (three amino acid substitutions replace a reported regulatory T cell (Treg) epitope with a highly conserved and broadly reactive CD4+ T cell epitope from H3-HA) and OPT2 (integrates six H3-HA CD4+ T cell epitopes, one Treg epitope removed). Structure modeling and molecular dynamics simulations of the engineered constructs were performed to assess perturbation of antibody target structures and predict folding stability. Vaccination studies were carried out in HLA-DR3 transgenic mice pre-immune to H3N2 (A/Hong Kong/4108/2014). Mice were primed and boosted IM with wildtype or engineered H7N9 rHA without adjuvant eight weeks post-H3N2 exposure. T cell phenotypes, total IgG, and HAI titers to H3 and H7 were monitored. Mice were challenged IN with H7N9 virus (A/Anhui/1/2013) four weeks following boost and followed for weight loss and survival.
Results & Conclusions: Vaccination of H3N2 pre-immune mice with OPTimized rH7 immunogens expanded TCM (CD44+CD62L+) and TEM (CD44+CD62L-) levels over wildtype rH7. A higher increase was induced by the OPT2 vaccine, which is consistent with its higher H3 epitope load and ability to recruit more H3-HA-specific CD4+ T cells than OPT1. A similar increase in Tfh (CXCR5+PD1+ICOS+Bcl6+) in animals that received OPTimized rH7 immunogens was observed, with no significant difference between OPT1 and OPT2. Anti-H7 IgG responses are found after prime-boost with OPT1 and OPT2 while no antibody response to wildtype vaccine is found before a third immunization. Both OPTimized vaccines completely protected against lethal H7N9 virus infection while in contrast, wildtype vaccinated animals had a survival rate that was similar to unvaccinated pre-immune controls. OPT1 and OPT2 lowered average weight loss post-infection with OPT2 animals maintaining >95% of their weight. Collectively, we find increased vaccine-induced protection against a pandemic influenza strain is associated with enhanced T cell immunity elicited by a novel immunogen design strategy that harnesses seasonal influenza CD4+ T cell memory. Structure-guided T cell epitope modification may also be useful to develop more effective vaccines against seasonal influenza strains.

2. DNA priming immunization is more effective than recombinant protein vaccine in eliciting antigen-specific B cell responses

Shixia Wang1, Haiying Li1, Guangnan Hu1, Lu Zhang2, Shuying Liu3 and Shan Lu1 1Laboratory of Nucleic Acid Vaccines, Department of Medicine, University of Massachusetts Medical School, Worcester, Massachusetts, USA 2First Affiliated Hospital, Nanjing Medical University, Nanjing, Jiangsu, China 3SYL-Consulting, Thousand Oaks, California, USA

While DNA prime-protein boost vaccination approach has been widely used in preclinical and clinical studies especially in the field of HIV vaccine development, the exact role of DNA immunization has not been fully identified. Our previous work demonstrated that DNA immunization was able to elicit T follicular helper (Tfh) cell responses and germinal center (GC) B cell development in a mouse model. In the current report, a mouse immunogenicity study was conducted to further ask whether DNA immunization is able to elicit antigen-specific B cell responses. Using HIV-1 Env as model antigen delivered in the form of DNA prime – protein boost, our data demonstrated that DNA prime was able to enhance the antigen-specific B cell responses for both Env-specific antibody secreting cells (ASC) and memory B cells. Furthermore, the DNA priming can greatly reduce the need of including an adjuvant as part of the recombinant protein vaccine boost formulation. Our findings revealed one mechanism that supports the value of DNA priming in assisting the induction of high affinity and long-lasting antigen specific antibody responses.

3. Polymersomes as stable nanocarriers for a highly immunogenic and durable SARSCoV-2 spike protein subunit vaccine

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Multiple successful vaccines against SARS-CoV-2 are urgently needed to address the ongoing Covid-1 pandemic. In the present work, we describe a subunit vaccine based on the SARS-CoV-2 spike protein co-administered with CpG adjuvant. To augment the immunogenicity of our formulation, both antigen and adjuvant are encapsulated with our proprietary artificial cell membrane (ACM) polymersome technology. Structurally, ACM polymersomes are self-assembling nanoscale vesicles made up of an amphiphilic block copolymer comprising of polybutadiene-b-polyethylene glycol and a cationic lipid 1,2- dioleoyl-3-trimethylammonium-propane. Functionally, ACM polymersomes are nonimmunogenic, non-toxic, highly stable, delivery vehicles that are efficiently taken up by dendritic cells (DC1 and DC2), which are key initiators of the adaptive immune response. In the context of a Covid-19 vaccine, we have shown ACM encapsulation to be compatible with the spike protein and does not impair its ACE2-binding activity. Importantly, vaccinating with ACM-spike significantly enhances the IgG response compared to the free spike protein. ACM encapsulation is also compatible with CpG adjuvant, resulting in superior DC activation compared to the free adjuvant. To capitalize on these benefits, ACM-spike and ACM-CpG are co-administered. Two doses of this formulation, at 5 μg per dose, elicit 100% seroconversion in C57BL/6 mice at uniformly high neutralizing antibody titers that persist at least 40 days. In contrast, neutralizing antibodies elicited by co-administration of free spike and free CpG quickly wane after the peak time point. Furthermore, we confirm the presence of functional memory CD4+ and CD8+ T cells that produce Th1 cytokines (TNFα, IFNγ and IL-2) 40 days after final administration. Our preclinical work demonstrates a safe and highly efficacious vaccine formulation that activates both the humoral and cellular arms of the adaptive immune system. This represents an important step towards the development of a Covid-19 vaccine in humans.

4. IMMUNIZATION COMPLIANCE TO ROUTINE PEDIATRIC VACCINATIONS AMONG SERVICE PATIENTS IN A TERTIARY HOSPIAL IN CEBU BEFORE (SEPTEMBER 2019 TO MARCH 2020) AND DURING (APRIL 2020 TO SEPTEMBER 2020) THE COVID-19 PANDEMIC

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Background: Despite the fact that vaccination remains the most efficient public health tool in preventing diseases, there is still a decline in vaccination compliance especially during the COVID-19 pandemic.
Objective: To determine the immunization compliance among service patients in a tertiary hospital in Cebu before and during the COVID-19 pandemic
Design: A descriptive, cross-sectional study
Subjects: Pediatric service patients delivered in a private hospital in Cebu from September 2019 to September 2020
Methodology: Participants were randomly assigned into two groups: 105 out of 438 patients in the pre-COVID-19 and 50 out of 207 in the during COVID-19 group. Consent was secured in both groups before including them in the study. Participants were either interviewed by phone, or asked to answer an online questionnaire adapted from the Vaccine Confidence Interval (VCI) Survey Tool. Data was then encoded in the master data sheet, tallied and presented in percentages.
Statistical Analysis: Sample size was calculated using 95% CI at 0.05 margin of error using Cochran's formula. In analyzing results between groups, a p-value of <0.05 was considered significant.
Results: For both cohorts, none had a record of no vaccination at all. For the group born before COVID-19, only 5% were partially vaccinated for age, and 95% were fully vaccinated for age. In contrast, there were only 26% who were only partially vaccinated while 74% were fully vaccinated for age in those born during the pandemic. Both groups mostly had easy access to a health facility, and scored high in vaccine confidence. Failure to recall immunization schedule was the main reason for missed vaccinations in the pre-COVID-19 group while in the during COVID-19 group, it is the fear of exposure to COVID-19 during well baby follow-ups.
Conclusion: There is a high compliance to routine pediatric vaccinations among service patients in a tertiary hospital in Cebu for both pre and during COVID-19 groups in mothers who were young and college educated. Fear of catching the COVID-19 virus was the main reason for vaccine hesitancy.

5. A novel heterologous prime-boost immunotherapy protects against hepatitis B and D co-infection and hepatitis D super-infection.

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Chronic hepatitis B and D virus (HBV/HDV) infections are a major cause of severe liver disease and cancer. Current HBV therapies with nucleoside analogue reversed transcriptase inhibitors (NAs) are life-long and interferon therapy has a sustained effect only in a few patients. A hallmark of chronic HBV infection is the profound T cell dysfunction/tolerance to viral proteins. It is widely accepted that to achieve a sustained off-therapy response, an activation of the host immune response is needed. Here we describe a novel immunotherapy that effectively raises antibodies that block viral entry and healthy HBV-specific T cells, driven by T cells to the HDV antigen (HDAg), acting as a heterologous antigen to circumvent the HBV-specific T cell tolerance. The immunotherapy consisting of a DNA prime - protein boost strategy was evaluated in mice and rabbits for induction of antibodies to the PreS1 domain of HBV and T cells specific

for HBV and HDV. We found that the prime-boost strategy was more effective in inducing both antibodies and T cells, as compared to either DNA or protein alone. Importantly, the prime-boost strategy induced superior levels of neutralizing antibodies to HBV. These antibodies were able to neutralize both HBV and HDV *in vitro* and were protective against HBV mono-infection, HBV/HDV co-infection, and HDV super-infection *in vivo* in a humanized mouse model. This approach is a promising complement to current combination therapies targeting viral maturation in order to achieve a functional cure against chronic HBV. In addition, the therapy has also the potential to protect against HDV super-infection.

6. Highly conserved, non-human-like, and cross-reactive SARS-CoV-2 T cell epitopes for COVID-19 vaccine design and validation

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Background: Efficacy trials and real-world data unexpectedly show that approved mRNA COVID-19 vaccines protect 14 days after one dose and one week before neutralizing antibodies appear. This remarkable finding suggests that early protection may be mediated by T cells and that neutralizing antibodies are not absolutely required for protection. As T cells support the SARS-CoV-2 antibody response, clear virus-infected cells, and may be required to block transmission, we set out to identify conserved peptide epitopes associated with SARS-CoV-2 T cell immunity and assess their immunogenicity in an HLA transgenic mouse model to support development of a T cell-directed COVID-19 vaccine.

Methods: SARS-CoV-2 spike, membrane and envelope sequences were analyzed for potential binding to HLA class I and class II supertype alleles using EpiMatrix. JanusMatrix was used to identify SARS-CoV-2 epitopes that share TCR-face conservation with epitopes restricted by the same alleles, but found in the human proteome, and related alpha- and beta-coronaviruses. Conservation of epitopes with circulating SARS-CoV-2 was assessed using the Epitope Content Comparison (EpiCC) algorithm. Selected epitopes were assayed for antigenicity by ex vivo and cultured IFN□ ELISpot assays using PBMCs from SARS-CoV-2 convalescent donors and healthy individuals. Serology was assessed by MSD assays. Immunogenicity of peptide epitopes co-formulated with poly-ICLC adjuvant was evaluated by prime-boost immunization of HLA-DR3 transgenic mice. Immune recall was assessed by IFN□/IL-4 ELISpot assay using whole splenocytes. Frequencies, mean fluorescence intensity and differentiation of IFN□/IL-4/IL-5 producing T cell subpopulations were assessed using intracellular cytokine staining and flow cytometry.

Results & Conclusions: Sixty-six percent of 32 predicted epitopes were recognized in direct ex vivo assays by persons who mounted a protective immune response to SARS-CoV-2 infection. T cell responses correlated with total spike-specific IgG and neutralizing antibody responses (p<0.01). Persons with no SARS-CoV-2 experience demonstrated ex vivo responses to only 9% of epitopes. However, following a period of epitope-specific T cell expansion in culture, these individuals demonstrated robust T cell responses to 97% of SARS-CoV-2 epitopes, similar to convalescents. These data suggest that pre-existing immunity, potentially to common cold coronaviruses, may contribute to natural immunity and enhance vaccine efficacy. Intradermal immunization of HLA-DR3 transgenic mice with a pool of 20 peptides co-formulated with poly-ICLC demonstrated the vaccine generates an epitope-specific memory population in coronavirus-naïve animals and sharply focuses the T cell response on Th1 and Tc1 populations. Robust type 1 immunity skewing (>100-fold over type 2; p<0.05) alleviates concern that this T cell-targeted vaccine may enhance respiratory disease commonly associated with Th2 responses. EpiCC analysis shows the vaccine epitopes match >90% of the corresponding sequences in representative B.1.1.7, B.1.351, P.1, and B.1.617.2 variants. Taken together, these epitopes may be used to improve our understanding of

natural and vaccine-induced immunity and to facilitate the development of T cell-targeted vaccines that harness pre-existing SARS-CoV-2 immunity and avoid T cell escape.

7. Comparison of Mucosal and Intramuscular Immunization against SARS-CoV-2 with Replication-Defective and Replicating Single-cycle Adenovirus Vaccines

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SARS-CoV-2 is a mucosal pathogen that enters at surfaces such as the lungs and nasal passages. Currently, there are 3 vaccines for SARS-CoV-2 approved for use in the United States and 20 approved worldwide. All vaccines currently approved for SARS-CoV-2 are being administered intramuscularly. We developed a single cycle adenovirus (SC-Ad) vector expressing the full-length SARS-CoV-2 spike protein. This vector allows for the antigen gene to be replicated up to 10,000-fold, and 100-fold more than matched replication defective adenovirus (RD-Ad) vectors. Despite being able to replicate the antigen gene up to 100-fold more than RD-Ad vectors, it cannot produce infectious particles, circumventing the risk of adenoviral disease posed by replication competent adenovirus (RC-Ad) vectors. Single intranasal (IN) and intramuscular (IM) immunizations in hamsters each generated significantly higher antibody responses against wild-type SARS-CoV-2 as compared with those produced by RD-Ad vectors. These significant antibody responses were also observed against variant SARS-CoV-2 spike proteins, including that of the full-length receptor binding domain (RBD) of the beta variant. In addition, hamsters infected with SARS-CoV-2 that had been vaccinated with SC-Ad Spike IN or IM 10 months prior experienced significant protection against COVID-19 disease as compared with PBS and RD-Ad Spike matched vectors. These data suggest that a single IN or IM immunization with SC-Ad Spike is sufficient to produce efficacious antibody responses against wild-type and variant SARS-CoV-2 strains, as well as protection against disease in hamsters infected with wild-type SARS-CoV-2.

8. Combination therapy with PTT and FlaB-Her2 Vax in DD-her2/neu breast cancer mice model

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Immunotherapy is an emerging modality for breast cancer treatment, as evidenced by the plethora of preclinical and clinical concepts and ongoing trials. Therapeutic cancer vaccines (TCVs) are elucidating to induce tumorspecific T cell responses in cancer immunotherapy. However, combination with other therapeutic modalities is expecting to improve the limitations of clinical outcomes of TCV. *Photothermal therapy* is a minimally invasive cancer therapeutic modality, which uses hyperthermia generated by photothermal agents from laser energy to kill cancer cells. Our previous studies showed that the TLR5 agonist flagellin served as an excellent adjuvant inducing effective cell-mediated immunity (CMI) against co-administered TAA peptide epitopes flagellin-secreting bacteria modulated TME to induce an effective anti-tumor immune response. This study established a platform for combination therapy of flagellin-adjuvanted peptide vaccine (FlaB-Her2 Vax) and PTT to induce an effective antitumor immune response in a breast cancer model. For PTT optimization, nanoparticles (NP) prepared to contain clinically approved near-infrared (NIR) photothermal agent (indocyanine green; ICG), cyclin arginine-glycineaspartate (cRGD) peptide, and flagellin adjuvant. To evaluate the potentiation of FlaB-Her2 Vax with the combination of the optimized PTT, we used the DD-her2/neu breast cancer in the mice abscopal model. The effect of combination therapy evaluated by the survival and tumor growth in both primary and abscopal sites of mice. The effector cytokines that promote the activation of CD8+ T cells in the spleen and tumor-draining lymph nodes (TDLNs) were analyzed. In addition, to investigate the TME-modulating effect of flagellin in the optimized PTT therapy, DD-her2/neu tumor-bearing mice were injected with flagellin in the peritumoral region and then evaluated anti-tumor effects. For optimal PTT treatment, primary tumors were irradiated with 808nm laser with 50ºC, 2W for 10 mins. To amplify and induce this robust immune response, we incorporate the combination of FlaB-Her2Vax given before and after PTT, which contribute to priming and boosting the immune system to influence the free tumor-associated antigen and epitope expansion. Our results suggest that compared to PTT alone treated or FlaBHer2 Vax alone treated animals, overall survival has significant improvement in the group receiving combination therapies (PTT+FlaB-Her2 Vax). In particular, treatment with combination therapy (PTT+FlaB-Her2 Vax) and FlaB peritumor treatment showed a significant anti-tumor immune response in their treated primary and untreated secondary tumors by inducing immunogenic cell death and subsequent tumor-specific immune response. The activation of CD8+ T cells in the spleen and tumor-draining lymph nodes (TDLNs) shows the significant potential immune response of the combination therapy by promoting the effector cytokine. In conclusion, these results suggest that FlaB adjuvanted-tumor-specific peptide vaccines effectively induce tumor-specific T and B cell repertoire combined with PTT's precise tumor targeting. This study indicated that a combination of local PTT and TCV induced a systemic immunity against established tumors and metastases in an aggressive breast cancer model, leading to a potential clinical method for her2 positive breast cancer patients

9. Agent-based investigation of the impact of low rates of influenza on next season influenza cases

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Introduction: Interventions to curb the spread of SARS-CoV-2 during the 2020-21 influenza season essentially eliminated influenza during that season, thus reducing residual population immunity against influenza. The implication for the subsequent, 2021-22 influenza season is unknown.

Methods: We used an agent-based model of influenza implemented in the FRED (Framework for Reconstructing Epidemiological Dynamics) simulation platform to estimate cases and hospitalization over two succeeding influenza seasons. The impact of reduced residual immunity was estimated in light of

increased protective measures (e.g., social distancing and school closure) in the first season. The impact was contrasted by the level of cross-immunity between influenza strains over the seasons.
Results: When second season strains had a low level of cross-immunity with first season strains, a low first season has limited impact on second season cases. When a high level of cross-immunity exists between strains in the 2 seasons, the first season has a much greater impact on the second season. In both cases this is modified by the transmissibility of strains in the 2 seasons and by the level of cross-immunity. In the context of 2020-21 and 2021-22 seasons, the worst case scenario is highly transmissible strain causing increased cases and hospitalizations, with a possible significant increase in second season cases in some scenarios. The most likely overall scenario is a more modest increase.
Discussion: Influenza is highly variable in number of cases and hospitalizations per season. The most prevalent influenza subtype often switches from one season to next and this is not necessarily accompanied by a significant rise in cases in the second season. Modeling suggests that low 2020-21 season will result in higher incidence in 2021-22 but probably not reaching levels expected if there is no population immunity, such as in the case of a pandemic strain. Young children may be especially at risk in 2021-22 since very young children were unlikely to have had any exposure to infection and all immunity in that age group would be from vaccination, which wanes quickly. Achieving high vaccination levels in all age groups but particularly the very young will be important in 2021-22.

10. Exploratory analysis of the humoral immune response to ChAdOx1 MERS-CoV.
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Introduction: Coronaviruses remain a threat to humanity. Previous outbreaks caused by Middle East respiratory coronavirus (MERS-CoV) with the highest mortality among coronaviruses, highlight the need for an effective vaccine. ChAdOx1 MERS is a viral vector vaccine candidate with a backbone of a replication-deficient simian adenovirus encoding the full-length MERS spike protein. We have previously reported safety and immunogenicity data of a first in human, dose escalation, phase 1 trial of the ChAdOx1 MERS vaccine (NCT03399578) in healthy UK adults, aged 18–55 years. The vaccine was safe and immunogenic demonstrating a significant increase from baseline in T-cell response and IgG titres, with induction of MERS-CoV neutralizing antibody. Here we report data from exploratory analysis of the humoral immune response induced by single vaccination of ChAdOx1 MERS using three different doses in both UK and Saudi populations.
Methods: Replicate open-label, non-randomised, dose-escalation, phase 1/phase 1b clinical trials were conducted in healthy adults (18-55 years) at the Centre for Clinical Vaccinology and Tropical Medicine (Oxford, UK) and King Abdulaziz Medical City (Riyadh, Saudi Arabia). ChAdOx1 MERS was administered as a single intramuscular injection at three different doses: Low dose (5×10 viral particles (vp), n=12), intermediate-dose (2·5×10 vp, n=18) and high-dose (5×10 vp, n=18). ChAdOx1 MERS specific IgM, IgG and IgA antibodies as well as IgG response against the MERS-CoV spike S1 and S2 subunits after vaccination, were quantified using an in-house standardized indirect ELISA. Affinity maturation of IgG antibodies was determined by an avidity assay using a sodium thiocyanate (NaSCN)-displacement ELISA.
Results: A single dose of ChAdOx1 MERS elicited MERS specific IgM and antibody class switching to IgG and IgA across all doses in both cohorts. All isotypes maintained a significant increase from baseline up to 6 months after vaccination ($p<0·0001$, $p<0·05$ and $p<0·001$ for IgG, IgM and IgA respectively using Kruskal-Wallis test). The magnitude of IgG and IgM antibodies exhibited a dose-dependent response, inducing antibody titres significantly higher than baseline at all time points; day 14, day 28, day 56 and day 182 for IgG and up to day 56 for IgM in the recipient of the high dose. Anti-MERS spike-specific IgG avidity increased by 1.1- fold, 1.2-fold and 1.1-fold between day 28 and day 56 after vaccination with the low, medium and high doses respectively. The avidity index at day 56 was greater in the high dose group (median 0.84, IQR 0.60–1.01) followed by the medium dose group (0.80, 0.73–0.92) and the low dose

group (0.79, 0.56–0.94). In the volunteers receiving the high dose, a significant response towards the S1 spike subunits (median 1179 ELISA units [EU], IQR 764.7-1587) compared to S2 subunit (729.8 EU, 453.5-1094) was observed at day 28 ($p < 0.05$, two-tailed Wilcoxon matched pairs test).
Conclusion: Immunization with a single dose of ChAdOx1 MERS induces a robust and durable antibody response. The humoral immunogenicity profile of different doses supports using the 5×10 vp dose for future phase II and efficacy trials.

11. A Theoretical Strategy for Heterologous Prime-Boost COVID-19 Vaccination

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The control of the pandemic by the SARS-CoV-2 coronavirus requires the design and implementation of innovative and cost-effective epidemiological measures. One of these measures with growing support, is that of heterologous prime and boost using the set of vaccines against Covid-19 approved worldwide. In the present work, based on computational techniques of knowledge representation, a set of 19 combinations is suggested using the BBIBP-CorV, JANSSEN, CORONAVAC, SPUTNIK, MODERNA, PFIZER, and VAXZEVRIA vaccines. The feasibility of the proposed schemes is analyzed in the light of recent results of clinical trials with heterologous vaccination, suggesting that this strategy can be a safe and effective way to carry out future massive vaccination campaigns.

12. Effects of Body Mass Index on the Response to SARS-CoV-2 Vaccination

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Obesity is a significant co-morbidity for SARS-CoV-2 infection. Because of the higher potential for negative outcomes following infection of individuals with high body mass index (BMI), the effect of high BMI on vaccine immunogenicity and efficacy is an important public health concern. However, few studies have been conducted measuring vaccine immunogenicity and the durability of the response to vaccination in relation to BMI. We measured the RBD-specific serum IgG and surrogate neutralizing titers in a cohort of 202 vaccinated individuals with no history or serological evidence of SARS-CoV-2 infection two months and seven months following vaccination. RBD-specific IgG titers and surrogate neutralizing titers did not vary significantly as a function of BMI two months following immunization. Seven months following immunization antibody titers in all groups had declined by approximately 90%. Responses were also similar between male and female participants and did not vary significantly across age groups. These results indicate that the immunogenicity of mRNA-based vaccines and the durability of the antibody response to them is unaffected by the BMI of the vaccinee.

13. A single-dose live-attenuated YF17D-vectored SARS-CoV-2 vaccine candidate

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The explosively expanding COVID-19 pandemic urges the development of safe, efficacious and fast-acting vaccines to quench the unrestrained spread of SARS-CoV-2 and its emerging variants. Several vaccine platforms are leveraged for a rapid emergency response to COVID-19. We employed the live-attenuated yellow fever 17D (YF17D) vaccine as a vector to express a non-cleavable prefusion form of the SARS-CoV-2 Spike antigen. The vaccine candidate, tentatively named YF-S0, has a remarkable safety profile and induced in hamsters and mice, as well as in cynomolgus macaques, high levels of SARS-CoV-2 neutralizing antibodies (and immunity protecting from YFV infection). Humoral immunity is complemented by a favorable Th1 cell-mediated immune response as profiled in mice. In a stringent hamster SARS-CoV-2 challenge model as well as in non-human primates, vaccine candidate YF-S0 prevents infection with SARS-CoV-2. Moreover in hamsters, a single dose confers protection from lung disease in most vaccinated animals within 10 days.
The emergence and spread of new variants of SARS-CoV-2 has produced enormous concern due to their possible implication in the improved transmissibility of the virus, their pathogenicity, as well as the possible escape from the immunity generated by the current vaccines. Our vaccine candidate induces high neutralizing antibody titers against the emerging variants of concern (VoC) B.1.1.7 (UK) and B.1.351 (South-African). Furthermore, in our stringent hamster, YF-S0 confers full protection against infection by as well as a marked reduction in transmission of B.1.1.7, while partially protecting against B.1.351. These results warrant further development of YF-S0 as a potent SARS-CoV-2 vaccine candidate.

14. Developing Low-cost, Safe and Effective Bi-antigen SARS-CoV-2 Vaccine comprising S1 subunit and N protein expressed in *Pichia pastoris* for Developing Countries.

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The SARS-CoV-2 Spike (S) Glycoprotein is directly recognized by the immune system, representative antigen for T-cell response and key target for neutralizing antibodies. S1 subunit has receptor binding domain (RBD) which binds to the host ACE-2 receptor mediating attachment. RBD is a target of neutralizing antibodies and contains multiple dominant neutralizing epitopes. NTD present within S1 is also a target for virus neutralizing antibodies. Nucleocapsid (N) protein is a highly conserved protein, abundantly expressed during infection and representative antigen for T-cell response. Both S1 and N protein induce stable immune response and presents the idea of a bi-antigenic recombinant subunit SARS-CoV-2 vaccine. *Pichia pastoris* is the most desirable expression platform in recombinant technology to produce cost effective product with high yield and easy to scale up process. Furthermore, *Pichia pastoris* is a suitable host for high expression with several posttranslational modifications and offers easy technology transfer to developing countries. Therefore, we have developed a bi-antigenic recombinant subunit SARS-CoV-2 vaccine comprising S1 and N protein using *Pichia pastoris* as the platform technology. As SARS-CoV-2 continues to unleash mayhem globally, there is an urgent need to develop accessible and low-cost vaccine for the developing countries. Our technology addresses several challenges in vaccine design by providing economic and effective option for preventing SARS-CoV-2 infections in developing countries. The platform used to develop the technology has the advantage of not requiring dedicated or specialized facility making it an affordable option using existing manufacturing facilities without significant capital investments. The highly conserved N protein across coronavirus species makes it a potential target for a universal coronavirus vaccine.

15. In vivo evaluation of nanoparticulate combined adjuvant systems based on *Salmonella Thyphi* porins-chitosan

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Subunit antigens are usually not sufficiently immunogenic to induce protective immunity, and they are often combined with adjuvants to provide high immune responses. Particulate systems have been widely used for delivery/adjuvant purposes to enhance the immune responses against pathogens (1,2). In our previous study, we have developed a combined adjuvant system based on chitosan and *Salmonella Typhi* porins (outer membrane proteins) in nanoparticle form and demonstrated in vitro the enhanced cellular uptake and immune responses in J774A.1 macrophage cell line (3). In this study, we have performed immunization studies in BALB/c mice and investigated the effect of nanoparticles on humoral immune responses against a model antigen, ovalbumin, in comparison to microparticle and gel forms of the porins+chitosan combination, which were investigated in our previous study (4). Nanoparticles based on water soluble chitosan (Protasan UP Cl213, Novamatrix) were prepared using ionic gelation method. Porins (*Salmonella Typhi* 9,12, Vi:d ATCC9993) and ovalbumin (EndoFit ovalbumin, Invivogen) were incorporated into the nanoparticles during preparation. Nanoparticles with particle size of 337,7±1,7 nm for porins loaded, 239,6±3,3 nm for OVA loaded and 429,9±6,8 nm for porins+OVA loaded were obtained. The zeta potentials of nanoparticles were positive and decreases were observed in presence of porins and/or OVA. Mice were immunized intraperitoneally on Days 0 and 15 with nanoparticles containing

20 µg porins and/or 100 µg OVA. IgG and IgM levels were determined in sera collected by submandibular route on 0, 8, 12 and 30 days. All animal care and experimental protocols were approved by Animal Experimentations Local Ethics Board (protocol no:2015/75-14). IgM levels with the porins+chitosan nanoparticles were observed to increase on Day 30, whereas with gel and microparticle forms, IgM levels were observed to increase significantly beginning from Day 8. With porins+chitosan nanoparticles, IgG levels were observed to increase gradually over time and reach to the highest levels after the booster, similar to that obtained with the microparticles, whilst with the gel, IgG levels were significantly higher when compared to micro and nanoparticles. Our results showed that nanoparticles produce IgM antibodies as the first immune response and further the IgG antibodies are produced as the basis of long-term protection. Higher IgM levels obtained at early stage by microparticles compared to that of nanoparticles can be attributed to the particle size difference, which was shown in vitro to result in higher uptake of microparticles (with particle size of 2.49 ± 0,03□m) than the nanoparticles, and consequently significant stimulation of macrophages (3). Our results suggested that nanoparticulate porins+chitosan combined system stimulates the humoral immune responses and can be suggested as a promising adjuvant/delivery system with a potential of providing long term protection.

16. H1N1 G4 swine influenza T cell epitope cross-conservation in swine and human vaccines and circulating strains

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Pandemic influenza may emerge from animal reservoirs and spread among humans when there is poor antibody protection in the human population, as occurred in 2009 with the emergence of swine-origin H1N1 influenza. Recent swine influenza surveillance revealed a novel emergent genotype 4 Eurasian avian-like H1N1 virus, bearing 2009 pandemic and triple-reassortant-derived internal genes, that does not cross-react with antibodies that recognize currently circulating human influenza strains. When vaccines and emergent strains are poorly matched, flu vaccines containing highly cross-conserved T cell epitopes have been shown to reduce morbidity and limit spread in the absence of antibodies. Here, we assess the risk of pandemic emergence of G4 in the US and European swine populations, as well as the cross-protective potential of swine and human vaccine strains to limit spread using immunoinformatics tools. H1N1 HA sequence data, including G4, swine, and human influenza strains circulating in the US were retrieved. European swine flu and vaccine strains were downloaded to assess their potential to protect the European swine population. For computational reasons, customized script was used to subsample to preserve representative clades and four subsets of sequence data were compiled. Each final reduced dataset combining the G4 data was translated into amino acid sequences and assigned into three single analyses: (1) European circulating swine flu virus and G4 strains; (2) US circulating swine flu and G4 strains and (3) US circulating human influenza virus and G4 strains. T cell epitope mapping was performed to define high binding likelihood T cell epitopes based on the binding preferences of class II Swine Leukocyte Antigen (SLA) and Human Leukocyte Antigen (HLA) alleles. Swine and human vaccine strains were added respectively for comparison to phylogenetic representative sequences from each host/region using the T cell Epitope Content Comparison (EpiCC) tool which evaluates T cell epitope relatedness between vaccine and circulating strains. We discerned three important findings: (1) High EpiCC scores were observed for comparisons of European swine flu vaccines and H1N1 G4 swine strains. As EpiCC scores have been shown to be directly associated with vaccine protection against circulating strains, high T cell epitope relatedness suggests that European vaccines might protect European swine against the emergent virus. (2) US commercial swine vaccines and COBRA vaccines, however, showed poor T cell cross-conservation against H1N1 G4 swine strains. This indicates that the US swine population may be susceptible to emergent G4

and may be protected by vaccination with a European swine flu vaccine. (3) Human flu vaccine T cell epitopes were also poorly conserved with G4 suggesting that emergent strain has pandemic potential with both an absence of cross-reactive antibody and cross-reactive T cell immune potential. In summary, emergent G4 influenza poses a greater threat to the US pork industry than the European pork industry. European swine vaccines should be tested for efficacy against emergent G4. Emergent G4 influenza also poses a threat to humans in the US and further studies are required to establish the utility of the EpiCC tool to better control the spread of emergent G4.

17. Adenosine deaminase co-delivery rescues age-associated impairment of SARS-COV-2 synDNA vaccine-induced responses

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SARS-CoV-2 is responsible for a global pandemic claiming over 2 million lives and infecting over 100 million people. Elderly patients display increased COVID-19 morbidity and mortality. Vaccine candidates have been studied and deployed in the clinic. However, age-associated immune deficits are known to cause sub-optimal responses, and the longevity of vaccine-induced responses is under investigation. Germinal center follicular helper T cells (TFH) promote affinity maturation of B cell receptors and memory B cell differentiation and are defined by expression of adenosine deaminase-1 (ADA-1). We investigated the adjuvant properties of plasmidencoded adenosine deaminase (pADA) in the context of SARS-CoV-2 spike synDNA antigens. Young and aged mice were immunized with plasmid-encoded spike (pS) alone or co-immunized with pS and pADA and cellular and humoral responses were evaluated. When immunized with pS alone, aged mice had decreased spikebinding IgG and neutralization titers. However, young and aged animals co-immunized with pADA had similar humoral responses. We observed similar trends in serum antibody affinity as measured by SPR. pADA coimmunization also rescued age-associated decreases in spike-specific IFNy secretion in the spleens and lungs of co-immunized aged mice as measured by ELISpot. pADA co-immunization also rescued age-associated increased in secretion of inflammatory TNFα and supported CD4+ and CD8+ T cell polyfunctionality as measured by intracellular cytokine staining. Finally, preliminary data analysis indicates that co-immunization with pADA significantly impacts viral load in a model of SARS-CoV-2 infection. These data suggest that pADA enhances antigen-specific cellular and humoral immunity in aged mice and supports further study of this molecule as an immunoadjuvant for vaccines targeting elderly populations.

18. Live attenuated influenza virus vaccine expressing an IgA-inducing protein reduces virus replication and transmission in pigs

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The rapid evolution of influenza A viruses (IAV) complicates the disease control for animal and public health. Although vaccination is an effective way to control influenza, available vaccines result in limited protection against antigenically distinct viruses. These vaccines usually stimulate IgG antibodies but not a strong mucosal IgA response, which is typically more cross-reactive. We developed a live attenuated influenza virus (LAIV) vaccine containing IgA-inducing protein (IGIP) as an adjuvant to enhance the mucosal IgA response against influenza. This Flu-IGIP LAIV was tested in a bivalent formulation (H1N1 and H3N2) against challenge with antigenically drifted viruses in pigs. Pigs were vaccinated intranasally with either a bivalent Flu-IGIP or a bivalent Flu-LAIV without IGIP and boosted two weeks later. Three weeks post boost, pigs were challenged with antigenically drifted H1N1 or H3N2 virus. Pigs vaccinated with both Flu-IGIP and Flu-LAIV shed significantly less virus after H1N1 or H3N2 challenge compared to non-vaccinated pigs. Vaccination with LAIV reduced transmission to respiratory contacts, while Flu-IGIP fully blocked transmission regardless of challenge virus. Both Flu-IGIP and Flu-LAIV vaccines reduced virus replication in the lungs and lung lesions after challenge with either virus. Vaccinated pigs had increased numbers of influenza-specific IgA-secreting cell two weeks post boost and at the day of infection there were increased CD21+ B cells in the blood of the Flu-IGIP pigs compared to Flu-LAIV and naïve pigs. IgG and IgA levels in bronchoalveolar lavage fluid and nasal wash of vaccinated pigs were boosted after challenge as soon as 5 days post infection (dpi) and remained high at 14 dpi. Our results indicate that Flu-IGIP LAIV has the potential to upregulate protective mucosal responses leading to protection from clinical signs, replication and shedding after antigenically drifted influenza virus infection.

19. DNA Launched Native Like Trimer Env immunogen induced Tier 2 neutralizing antibodies and revealed a new murine Env C3/V5 epitope

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Designing an efficacious HIV vaccine remains a challenge despite extensive efforts over the years. HIV-1 Envelope protein (Env) is present on the membrane of the virus particle and is of interest as an immunogen as it is a target of all known neutralizing antibodies. Recombinant proteins as vaccine candidates based on the native-like trimer (NLT) conformation of the Env have been shown to induce autologous neutralizing antibodies (nAbs) against difficult to neutralize tier-2 HIV strains in rabbits and non-human primates, but not mice. In this work we designed and characterized a DNA launched NLT immunogen based on BG505 strain (BG505 DL-NLT) and studied the induction of humoral and cellular response in mice as it is the most cost effective and widely used vaccine model. Extensive antigenic profiling demonstrated DL-NLT BG505 expresses well and maintains native like trimeric profile in vivo. We saw induction of autologous tier-2 nAbs in mice as well as potent antigen specific CD8 T cell responses. The epitope mapping of the induced neutralizing antibodies in the anti-serum revealed a new murine neutralizing Env C3/V5 epitope. We were able to isolate and further characterize five murine monoclonal antibodies. The structures of Env-nAbs complexes probed using cryo-EM further confirmed the identity of the target epitope. Beyond potential functional immunity gains, DNA vaccines permit in vivo folding of structured antigens and provide significant cost and speed advantages for enabling rapid evaluation of new HIV vaccines.

20. FluB-RAM and FluB-RANS: Genome re-arrangement as safe and efficacious live attenuated influenza B virus vaccines

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Influenza B virus (IBV) is considered a major respiratory pathogen responsible for seasonal respiratory disease in humans, particularly severe in children and the elderly. Seasonal influenza vaccination is considered the most efficient strategy to prevent and control IBV infections. Live attenuated influenza virus vaccines (LAIVs) are thought to induce both humoral and cellular immune responses by mimicking a natural infection, but their effectiveness have recently come into question. Thus, the opportunity exists to find alternative approaches to improve overall influenza vaccine effectiveness. Two alternative IBV backbones were developed with re-arranged genomes, re-arranged M (FluB-RAM) and a re-arranged NS (FluB-RANS). Both re-arranged viruses showed temperature sensitivity in vitro compared to the WT type B/Bris strain, were genetically stable over multiple passages in embryonated chicken eggs and were attenuated in vivo in mice. In a prime-boost regime in naïve mice, both re-arranged viruses induced antibodies against HA with hemagglutination inhibition titers considered of protective value. In addition, antibodies against NA and NP were readily detected with potential protective value. Upon lethal IBV challenge, mice previously vaccinated with either FluB-RAM or FluBRANS were completely protected against clinical disease and mortality. In conclusion, genome re-arrangement renders efficacious LAIV candidates to protect mice against IBV.

21. Novel ocular delivery of whole inactivated influenza virus with *L. lactis* bacterium-like particle as a mucosal adjuvant

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Influenza A virus (IAV) is the cause of seasonal epidemics, zoonotic outbreaks, and probably next unpredictable pandemics. The major entry is mucosal surface, and mucosal immunoglobulins are main contributors to specific immune responses and cross-protections. Inactivated vaccines are generally administered subcutaneously/intramuscularly, which do not induce specific secretory IgA. Attempts are made to develop mucosal adjuvants for easier and non-invasive administration, especially for animal mass vaccinations. Gram-positive and nonpathogenic lactic acid bacteria are promising mucosal delivery candidates for therapeutic/prophylactic molecules with advantages over other systems in many aspects. Recently, the adjuvanticity of non-genetically modified, non-living, and non-recombinant *Lactococcus lactis*, bacterium-like particle (BLP), has been well studied. BLPs can be combined with recombinant hybrid antigenprotan fusion proteins or either simply admixed with antigens. Most recently, phenotypic characterizations of mice responses after intranasal, intramuscular, and gastrointestinal co-administration of BLP and highly pathogenic IAV antigens have been demonstrated: high TLR2-dependent potential to boost systemic/mucosal responses, better Th1/Th2-type balanced response, and comparable protective efficacy. For the first time, we inoculated four treatment groups of day-old SPF chicks (12 bird/group) ocularly with whole inactivated virus particles (389 HAU) plus different dry weights of BLPs

(75, 150, 300, 600µg/dose) against low pathogenic H9N2 IAV, an economically important pathogen of poultry industry which occasionally infects humans and other mammals. Weekly performance parameters, clinical manifestations, immune responses, and protection were compared to four control groups immunized similarly but with any of PBS, virus particles, BLP, or a subcutaneous benchmark vaccine. All chicks were immunized at 7 and 21 DOA (days of age). Half of each group were euthanized at 35 DOA, and the remaining were challenged oculo-nasally with a field H9N2 isolate. Sampling framework included weekly sera and tears; tracheal washings and tissues at 35 and 45 DOA; and nasopharyngeal swabs at 35, 39, 42, and 45 DOA. Results showed that tear IgA titers in treatment groups increased after each dose, while no increase was seen in control groups. A similar finding was evident about tracheal washings. No sera-specific IgG was detected by ELISA/HI before the challenge except for the benchmark-vaccinated chicks; however, mucosal IgA and serum IgG titers elevated post-challenge. Considering the low pathogenicity of H9N2 IAV, no difference was found in presence/intensity of clinical manifestation among groups, but a mild and transient conjunctivitis was noticeable only in BLP-treated chicks in days post inoculations. Moreover, a slight weekly decrease in weight gain/uniformity was evident in all groups compared to PBS-inoculated chicks. Notably, only the benchmark vaccine inhibited virus shedding concurrent with a viral peak in other groups (39 DOA); however, no comparable difference was seen among other groups. The strong point of study lies in the significant induction of mucosal immune response (best: 150µg BLP/dose) and the absence of systemic response. It seems that reduced performance in all groups is attributed to the inoculation stressor factor rather than the inoculum content. With an eye to the direct correlation of protection with humoral response, further studies to achieve a balance between toxicity and adjuvanticity of mucosal vaccination would be of great value.

22. Development of a novel Live Attenuated Influenza A Virus vaccine encoding the IgA-inducing protein.

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Live attenuated influenza virus (LAIV) vaccines elicit a combination of systemic and mucosal immunity by mimicking a natural infection. To further enhance protective mucosal responses, we incorporated the gene encoding the IgA-inducing protein (IGIP) into the LAIV genomes of the cold-adapted A/Leningrad/134/17/57 (H2N2) strain (caLen) and the experimental attenuated backbone A/turkey/Ohio/313053/04 (H3N2) (OH/04att). Incorporation of IGIP into the caLen background led to a virus that grew poorly in prototypical substrates. In contrast, IGIP in the OH/04att background (IGIP-H1att) virus grew to titers comparable to the isogenic backbone H1att (H1N1) without IGIP. IGIP-H1att- and H1caLen-vaccinated mice were protected against lethal challenge with a homologous virus. The IGIP-H1att vaccine generated robust serum HAI responses in naïve mice against the homologous virus, equal or better than those obtained with the H1caLen vaccine. Analyses of IgG and IgA responses using a protein microarray revealed qualitative differences in humoral and mucosal responses between vaccine groups. Overall, serum and bronchoalveolar lavage samples from the IGIP-H1att group showed trends towards increased stimulation of IgG and IgA responses compared to H1caLen samples. In summary, the introduction of genes encoding immunomodulatory functions into a candidate LAIV can serve as natural adjuvants to improve overall vaccine safety and efficacy.

23. Administration of Four Different COVID-19 pcDNA 3.1 DNA Vaccine Prototypes Using Intradermal Electroporation and Assessment of Their Immunogenicity in BALB/c mouse

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Since December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to more than 208 million infections and more than 4.3 million deaths worldwide as of July 19th, 2021. The disease has greatly affected the world economically, socially, and politically. As a result, many countries have given priority to vaccine studies to control COVID-19. In this study, we developed four prototype DNA vaccines expressing RBD, S1, S2 and Spike regions of SARS-CoV-2. Initially, we screened the most prevalent strain in Turkey using sequencing from clinical patients. Then, we examined the Spike region of the SARS-CoV-2 using bioinformatics to determine the antigenic epitopes. Then, we designed the RBD, S1, S2 and Spike regions to be included to the vector pcDNA 3.1 (Thermofisher, USA). Moreover, a human signal peptide and kozak sequence was inserted in frame to 5' terminus. The *in-vitro* expression potency of the prototype vaccines was examined using HEK293T cell transfected with Lipofectomine 3000 (Thermofisher, USA) and Western blot using anti-polyHIS antibody (Sigma). Thereafter, six groups (four DNA vaccine groups, an empty plasmid and PBS control group) of BALB/c mice (8 mice/group) were vaccinated thrice (25 µg plasmid/dose), first two at two weeks intervals and the last dose was administered six weeks after last dose using intradermal (ID) electroporation device (BTX Agilepulse ID, USA). The humoral immunity was analyzed using peptide-ELISA for IgG, IgG1 and IgG2a, recombinant S1 ELISA for IgG, SARS-CoV- 2 surrogate virus neutralization assay (sVNT) for neutralizing antibodies (Affinity Immuno, Canada), and Western blot for IgG responses (recombinant S1 and S1+S2 were used as antigen). The cellular immunity was determined from lymphocyte cell culture (stimulated by recombinant S1+S2 and peptide mix) by flow cytometer targeting CD8+ cells secreting IFN-γ and CD4+ cells secreting IFN-γ and IL-4, MTT proliferation assay and cytokine ELISA detecting IFN-γ and IL-4 secretion. The results showed that pcDNA 3.1-RBD, pcDNA 3.1-S1, pcDNA 3.1-S2 and pcDNA 3.1-Spike have expressed recombinant proteins detectable at 24.9 kDa, 82.9 kDa, 72.1 kDa and 148 kDa. All of the vaccines induced significant comparable IgG response ($P<0.001$) and except pcDNA 3.1-S2, three protoyptes induced higher and comparable levels of IgG2a ($P<0.01$). Recombinant S1 and S1+S2 antigens probed with sera from vaccinated mouse showed reactivity as shown by Western blot at the expected molecular weights. Cellular immune response assays showed that pcDNA 3.1-RBD, pcDNA 3.1-S1, and pcDNA 3.1-Spike induced significantly higher amounts of secreted IFN-γ ($P<0.01$), CD8+ and CD4+ cells secreting IFN-γ ($P<0.05$ and $P<0.01$). IL-4 levels were only higher in pcDNA 3.1-S2. Altogether, among the DNA vaccine encoding RBD, S1 and Spike proteins, pcDNA 3.1-Spike induced higher IgG, IgG2a and IFN-γ levels. sVNT using sera collected 3 weeks after last vaccination with pcDNA 3.1-Spike showed 20-40% neutralization. Overall, among four prototypes, DNA vaccine encoding Spike induced a strong protective immune response in mice and can be used to develop a DNA vaccine for human use.

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24. Importance of IFN-λ1 levels in COVID-19 patients and implications on vaccine efficacy against SARS-CoV-2

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Cytokine storm in COVID-19 patients is most likely induced by interleukin-6 (IL-6) and IL-6 levels seem to be an indicator disease severity [1]. On the other side, interferon lambda 1 (IFN- λ1; also known as IL-29) levels have an immunoregulatory function in COVID-19 patients that that suppresses inflammation [2]. IFN-λ1 is a type III interferon which serves as first defense line for SARS-CoV-2 since their specific receptors are mainly found in respiratory epithelial cells [3]. There are clinical studies four studies that are testing the clinical efficacies of recombinant IFNλ in COVID-19 patients [4]. An important question arouses while vaccine are being developed against COVID-19 which is “Do we have to induce IFN-λ1 by vaccination and to what level?” this question can be answered by analyzing consequitive sera of COVID-19 patients. For this purpose, in this study we analyzed the IFN-λ1, IL-6 (using cytokine ELISA kits, Thermoscientific, USA), neutralizing antibodies (using microneutralization assay) and Anti S1 IgG antibodies (using ELISA, Euroimmun, Germany) in hospitalized COVID-19 patients (n: 226). Among these patients we had analyzed consecutive sera of 107 patients (71 of them has two, 26 has three and 20 had more than four sera) and remaining 119 patients had only one serum sample. The COVID-19 patients were categorized based on clinical presentation which is described as mild-moderate-severe disease as described in “Treatment Guidelines for Adult Patient with COVID-19” prepared by the Ministry of Health, Turkey [5]. The results showed that IFN-λ1 is predominantly secreted in almost all patients (87%) who recovered the illness especially at the beginning of infection whereas IL-6 was not detected in most of them (74%). In these patients, anti S1 antibodies and neutralizing antibodies were prominent. In some severely infected patients, IL-6 were secreted at higher levels compared to IFN-λ1. Interestingly the amount of neutralizing antibodies that exists at the beginning of infection but does not correlate with the amount of anti-S1 antibodies. Overall, inducing IFN-λ1, neutralizing antibodies and anti S1 IgG antibodies have utmost importance to recover from COVID-19. Therefore, efficacy of vaccines can be monitored by IFN-λ1 secretion after administration vaccine doses.

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25. Immunogenicity of a DNA Vaccine Encoding Chimeric Multi-Epitope HER2 antigen against HER2+ Breast Cancer by Targeting the Chimeric Antigen to Dendritic Cells

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Breast cancer was ranked first among global cancer incidence in 2020. It is an important public health problem among women considering that it is accounts for one in four cancer cases. Even the survival rate of HER2+ breast cancer patients have increased with current treatments such as chemotherapy, monoclonal antibodies or tyrosine kinase inhibitors, disease progression continues in patients resistant to treatments. More recently, more efforts have focused on using HER2 vaccines, any vaccine has not been approved yet. The use of HER2 protein as a vaccine antigen causes immunological tolerance and this represents a major barrier to effective vaccination against HER2. DNA vaccine encoding chimeric multiepitope may circumvent immune tolerance and elicit stronger and more specific anti-tumor response in addition to opsonization activity. Moreover, DNA vaccines currently induce relatively weak immune responses in humans so it may be targeted to dendritic cells (DCs) to improve immunogenicity. To overcome immune tolerance and increase immunogenicity of DNA vaccine, we generated a DNA vaccine encoding a fusion protein comprised of the chimeric HER2 multi-epitope antigen and a single-chain antibody fragment (scFv) specific for the DCrestricted antigen-uptake receptor DEC205 (ScFvDEC). Extracellular domains of human and rat HER2 proteins were used to identify antigenic epitopes and construct a chimeric multiepitope vaccine. Chimeric multi-epitope DNA vaccine (pMeHer2) encodes five T-cell epitopes and three linear B-cell epitopes, pScFvDEC-MeHer2 vaccine encodes ScFvDEC and introduced at the N terminus of the chimeric multiepitope HER2 antigen. ScFvDEC-MeHer2, ScFvDEC and MeHer2 proteins expressed by HEK 293T cells have molecular weights of 42.8 kDa, 25.9 kDa and 16.9 kDa. To determine immunogenicity, mice were immunized intramuscularly with pScFvDEC-MeHer2 and pMeHer2 as vaccine groups, pScFvDEC, pEmpty and PBS as control groups. pScFvDEC-MeHer2 vaccine induced strong IgG response compared to pMeHer2 and the control groups ($P<0.0001$). The pScFvDEC and pMeHer2 groups also showed a significant increase compared to the PBS ($P<0.0001$ and $P=0.0001$) and pEmpty ($P<0.0001$ and $P=0.0003$) groups. pScFvDEC-MeHer2 and pMeHer2 immunized mice showed Th1 biased or Th1/Th2 balanced immune responses. The percentages of both CD4/IFN-ɣ and CD8/IFN-ɣ secreting T cells were higher in mice immunized with pScFvDECMeHer2 compared with the pMeHer2. pScFvDEC-MeHer2 and pMeHer2 elicited significantly higher levels of IFN-γ compared with to control groups (pScFvDEC, pEmpty and PBS)

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26. DESIGN OF A VACCINE AGAINST ZIKA AND DENGUE VIRUSES BASED ON MIMOTOPES OF THE ENVELOPE DIMER EPITOPE

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Zika (ZIKV) and dengue (DENV) viruses are members of the Flavivirus genus that can cause severe reactions, as hemorrhages (DENV), congenital syndrome (ZIKV), or even death. After an infection, virus-specific antibodies are generated by the immune system; however, because of the structural similarity between these viruses, some antibodies can cross-react with different members of the flavivirus family. After a secondary infection with other flavivirus, the cross-reactive antibodies can lead to severe forms of the disease, through a mechanism named antibody-dependent enhancement of infection (ADE). Recently, some broadly neutralizing antibodies (antibodies that neutralize both DENV and ZIKV), have been isolated and it has been demonstrated that they do not induce ADE 2,3. These antibodies are directed to a discontinuous quaternary epitope named the Envelope Dimer Epitope (EDE)1, located in the envelope (E) protein of both viruses. This study aims to generate peptides that emulate the EDE structure (mimotopes), to use them as vaccine candidates for ZIKV and DENV infection, without inducing ADE.
Using the broadly neutralizing antibody EDE1 C8 2,3 and a phage display library, we identified three peptides that are recognized by EDE1 C8 but have very low or no similarity with the E protein from DENV and ZIKV. The analysis by circular dichroism of the free peptides showed mainly a random coil folding, characterized by a lack of secondary structure. EDE1 C8 did not recognize these mimotopes attached chemically to a carrier protein, and free or phage-displayed peptides did not induce antibodies against native viruses when administered to mice. To improve the stability and folding of the peptides, we designed and produced adeno-associated virus-like particles (VLPs) that display the mimotopes on their surface. VLPs had a similar size and structure to the native adeno-associated virus, as determined by cryo-electron microscopy. Cryo-EM maps showed that the peptides displayed on VLP are flexible and their structure could not be determined. Comparison of the volume difference with the control particles showed that mimotopes were adequately displayed on the surface of the VLPs with a repetitive and ordered array. Modified VLPs were recognized by the EDE1 C8 antibody in a native dot-blot, but not in denaturing conditions, demonstrating that the three-dimensional structural conformation of the peptides displayed in the VLPs can mimic EDE. VLPs displaying mimotope 2, but not mimotope 3, elicited antibodies against ZIKV and DENV when injected to mice. Sequence alignment identified important residues that are conserved between mimotope 2 and residues of the E protein that bind EDE1 C8, suggesting that they are important to mimic the EDE.
We demonstrated that it is possible to emulate a very conserved epitope in ZIKV and DENV with peptides unrelated to the E protein. This information is valuable for the design of a safer dengue and Zika vaccine without ADE. More research is necessary and undergoing to study the neutralizing and ADE effect of the antibodies produced in response to the immunization with the VLP displaying mimotope 2.

27. Development of SARS-CoV-2 Neutralizing Antibodies by Constructing Highly Diverse Antibody Libraries from Indian Population.

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Introduction: Passive immunization with neutralizing monoclonal antibodies (nMAbs) represents a promising therapeutic approach to reduce SARS-CoV-2 impact on public health worldwide. The development of single-chain variable fragments (scFv) antibodies or nanobodies can be an attractive alternative to costly full IgG MAbs. The blood samples from COVID-19 survivors can be a rich source for

amplification and cloning of anti-SARS-CoV-2 antibody genes for Antibody Phage Display library construction and ultimately screening and scFv production.
Objective: The aim of our study was to develop anti-SARS-CoV-2 specific scFv antibody library from blood samples of COVID-19 survivors using phage display technology.
Methods: Blood samples were collected from ten COVID-19 recovered patients. The lymphocytes were separated by Ficoll separation and used for isolation of total RNA. Antibody specific genes (Variable Heavy and Variable light chains) were PCR amplified and cloned in appropriate phage display expression vector and transformed in specific *E. coli* strain. Bacteriophage was used for expression of phagemid vector. The libraries were panned against SARS-CoV-2 proteins viz: S1, S2 & RBD. Bio-panning against N protein is in progress.
Results: Stringent bio-panning with decreasing concentration of antigens were performed and around 500 clones were isolated for each target antigens. As a result of ELISA screening, about 1% positive clones were obtained against target proteins (RBD, S1 and S2) which are further being characterized. The best binders will be tested for virus neutralization assay, toxicological studies, preclinical and clinical studies.
Conclusion: Anti-SARS-CoV-2 specific scFv antibody library was successfully constructed from blood samples of COVID-19 survivors from Indian population. The library includes one billion different clones of antibody genes (VHs-Vκs and VHs-Vλs) with high probability to get high affinity fully human antibodies. After validation, the discovered antibodies against SARS-CoV-2 can be used for therapeutic and diagnostic purposes.

28. Broadly protective computationally designed influenza neuraminidase vaccine in the ferret animal model

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The influenza neuraminidase (NA) surface protein is often a secondary target for vaccine designs, following the hemagglutinin (HA). The N1-I computationally optimized broadly reactive NA antigen (N1-I COBRA) resulted from combining avian, human, and swine isolated N1 viruses. Previously, mice vaccinated with the N1-I COBRA elicited sera that elicited NA inhibition titers across a panel of N1 viruses. In this study, N1-I COBRA was further tested in the naive and preimmune ferret animal models with A/California/07/2009 (H1N1; CA/09) and A/Vietnam/1203/2004 (H5N1; Viet/04) influenza challenges. Ferrets were naive or preimmune with A/Singapore/6/1986 (H1N1). The ferrets were prime-boost vaccinated with 15ug NA or HA protein with Addavax adjuvant including: mock, N1-I COBRA NA, Viet/04 NA, CA/09 NA, and CA/09 HA. The CA/09 challenge resulted in the naive N1-I COBRA vaccinated ferrets having similar weight loss to the CA/09 HA control and maintaining weight after day 2 post-infection (p.i.). The Sing/86 preimmune vaccinated ferrets were all protected from CA/09 challenge, with no weight loss, and lower nasal wash titers compared to the mock animals. The mock animals had less weight loss, clinical scores, and percent mortality when compared to the challenged naïve animals. The Viet/04 challenge resulted in both the naive N1-I COBRA and Viet/04 NA vaccinated ferrets maintaining weight. The CA/09 NA group lost weight, and also had 25% mortality. Of the 16 ferrets that were preimmunized with Sing/86, only one mock vaccinated preimmune ferret reached a minimum body weight percentage at day 4 p.i. of 90% with recovery to 100% by day 10 p.i., all others were greater than 95%. Overall, the N1-I COBRA elicited protection in the naïve and preimmune ferret model with H1N1 and H5N1 infections. The current results indicate that the N1-I COBRA performed similarly to the CA/09 HA control, and a promising outlook for the N1-I COBRA for mixture and clinical studies.

29. One mucosal administration of a live attenuated recombinant COVID-19 vaccine protects non-human primates from SARS-CoV-2

Mariana Tioni
Meissa Vaccines

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the causative agent of the COVID-19 global pandemic. Vaccines are needed to control the disease and bring an end to the pandemic. SARS-CoV-2 is an enveloped RNA virus that relies on its trimeric surface glycoprotein, spike, for entry into host cells. Here we describe the COVID-19 vaccine candidate MV-014-212, a live attenuated, recombinant human respiratory syncytial virus (RSV) expressing a chimeric SARS-CoV-2 spike as the only viral envelope protein. MV-014-212 was attenuated and immunogenic in African green monkeys (AGMs). One mucosal administration of MV-014-212 in AGMs protected against SARS-CoV-2 challenge, reducing the peak shedding of SARS-CoV-2 in the nose by more than 200-fold. MV-014-212 elicited mucosal immunity in the nose and neutralizing antibodies in serum that exhibited cross neutralization against two virus variants of concern. Intranasally delivered, live attenuated vaccines such as MV-014-212 entail low-cost manufacturing suitable for global deployment. MV-014-212 is currently in phase I clinical trials as a single-dose intranasal COVID-19 vaccine.

30. Approaches to therapeutic DNA vaccination against squamous cell carcinomas associated with HPV infection

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Introduction SARS-CoV-2 pandemics demonstrated the potential of genetic vaccines. Human papilloma viruses of high oncogenic risk are the main etiologic agents associated with squamous cell carcinomas (SCC), motivating therapeutic HPV vaccination. Ideal targets are viral oncoproteins E6 and E7. Genetic vaccines against HPV-induced lesions are currently in development, but none has yet demonstrated potential to treat established tumors.

Aim To determine the dominant genotype of HPV, sequence its E6/E7 oncoproteins, develop respective DNA immunogenes and evaluate their therapeutic potential in a mouse model of HPV-induced SCC.

Experimental Clinical study and animal experiments were approved by the ethical committees of performing institutes. DNA extracted from cervical smears and FFPE of SCC was analyzed for the presence of 12 HR HPV types, DNA from 32 cervical smears was sequenced by the Sanger method, and from 7 FFPE samples, by NGS. Sequences were used to build an amino acid consensus of E6 and E7, and further synthesize the respective expression-optimized genes. Genes were cloned into pVax1 to obtain DNA-immunogens pVaxE6 и pVaxE7. Groups of C57Bl/6 mice (n=5) were sc implanted with 2×10000 TC-1luc2 cells expressing E6/E7 (kind gift of Prof TC Wu, John Hopkins University) and after 5 days immunized with pVaxE6, or pVaxE7, or pVaxE6+pVaxE7 introduced either separately or in a mix, or with DNA encoding reverse transcriptase domain of TERT (pVaxrtTERT; Jansons J et al, Microorganisms, 2021 doi: 10.3390/microorganisms9051073). Control mice received empty pVax1. DNA was introduced by id injections followed by electroporation. Tumor growth was followed by bioluminescence iamging (BLI) and morphometrically. After 18 days, mice were sacrificed, infiltration of TC-1luc2 cells into organs was

assessed by ex vivo BLI. Organs were fixed, paraffinized, H&E-stained FFPE sections were assessed for metastases. Immune response of splenocytes to stimulation with E6/E7-derived peptides was assessed by flow cytometry for IFN-g, IL-2 and TNF-a production by CD4+ and CD8+ T-cells.
Results We studied 189 cervical smears and 40 FFPE SSC samples, also from patients with HIV-1 and TB infections. Most prevalent was HPV16 detected in 4% healthy, 36% HIV-infected and 43% HIV/TB-coinfected women. Consensus E6/E7 protein sequence was built after analysing DNA from 25 cervical smears and 7 SCC samples. Synthetic genes encoding E6 and E7 were characterized for the capacity to express respective mRNA. Therapeutic DNA-immunization with E6 and rtTERT hindered tumor growth, reducing tumor size by 30% and ifiltration of tumor cells into organs by 50%, while not inducing E6-specific immune response. E7 alone, and E6 and E7 as separate injections, induced specific CD8+ T-cell response, but had no effect on tumor growth.
Conclusions: We have developed therapeutic DNA-immunogen based on HPV16 E6 capable to suppress tumor growth in murine model of SCC. Anti-tumor effect can be potentiated by co-vaccination with reverse transcriptase domain of TERT.

31. An Intranasal OMV-based vaccine induces high mucosal and systemic protecting immunity against a SARS-CoV-2 infection

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The development of additional and effective COVID-19 vaccines next to the currently marketed mRNA, viral vector and whole inactivated vaccines, is essential to curtain the SARS-CoV-2 pandemic. A major concern is reduced vaccine-induced immune protection to emerging variants, and therefore booster vaccinations to broaden and strengthen the immune response might be required. Currently, all registered COVID-19 vaccines and the majority of COVID-19 vaccines in development are intramuscularly administered, targeting the induction of systemic immunity. Intranasal vaccines have the capacity to induce local mucosal immunity as well, thereby targeting the primary route of viral entry of SARS-CoV-2 with the potential of blocking transmission. Furthermore, intranasal vaccines offer greater practicality in terms of cost and ease of administration. Currently, only eight out of 112 vaccines in clinical development are administered intranasally. We developed an intranasal COVID-19 subunit vaccine, based on a recombinant, six proline stabilized, D614G spike protein (mC-Spike) of SARS-CoV-2 linked via the LPS-binding peptide sequence mCramp (mC) to Outer Membrane Vesicles (OMVs) from *Neisseria meningitidis*. The spike protein was produced in CHO cells and after linking to the OMVs, the OMV-mC-Spike vaccine was administered to mice and Syrian hamsters via intranasal or intramuscular prime-boost vaccinations. In all animals that received OMV-mCSpike, serum neutralizing antibodies were induced upon vaccination. Importantly, high levels of spike-binding immunoglobulin G (IgG) and A (IgA) antibodies in the nose and lungs were only detected in intranasally vaccinated animals, whereas intramuscular vaccination only induced an IgG response in the serum. Two weeks after their second vaccination hamsters challenged with SARS-CoV-2 were protected from weight loss and viral replication in the lungs compared to the control groups vaccinated with OMV or spike alone. Histopathology showed no lesions in lungs seven days after challenge in OMV-mC-Spike vaccinated hamsters, whereas the control groups did show pathological lesions in the lung. The OMV-mC-Spike candidate vaccine data are very promising and support further development of this novel nonreplicating, needle-free, subunit vaccine concept for clinical testing.

32. Age-associated defects in the adaptive immune response to *Clostridioides difficile* vaccination and infection impair the development of a protective immune response in the elderly

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Clostridioides difficile is the number one cause of healthcare-associated infection in the United States and the most lethal acute enteric pathogen. The elderly (≥65) have the greatest risk of *C. difficile* infection (CDI) and severe morbidity and mortality due to CDI. Additionally, most recurrent CDIs occur within the elderly. Although previous studies have shown that strong humoral responses against *C. difficile* Toxin A/B (TcdA/B) during primary CDI or vaccination are protective against severe disease and recurrence, the elderly have impaired humoral responses against TcdA/B during both primary CDI and vaccination, leaving the elderly vulnerable to severe disease and recurrence. Using an aging mouse model of CDI, we show that there is significantly greater morbidity and mortality in aged mice during primary CDI when compared to young adult mice, mirroring what is seen in elderly CDI patients. Additionally, in response to both primary CDI and vaccination with TcdA/B-encoding DNA, aged mice have significantly lower anti-TcdA/B antibody titers. This impaired humoral response is the result of poor Tfh and B cell responses following infection and vaccination as aged mice have a significantly lower frequency of Tfh cells and number of anti-TcdA/B B cells when compared to young adult mice. While these age-related defects in the humoral response allow for increased morbidity and mortality from CDI, we also show that these defects can be restored with the addition of the molecular adjuvant ADA-1 during vaccination of aged mice with TcdA/B-encoding DNA. When ADA-1 is used as an adjuvant in aged mice, the anti-TcdA/B antibody response is restored to levels seen in young adult mice. Additionally, the use of ADA-1 as an adjuvant boosts the frequency of Tfh cells in aged mice following vaccination, suggesting that ADA-1 is able to help restore the development of the aged germinal center reaction following vaccination. Importantly, this restoration of the aged humoral response to TcdA/B is achieved with just two vaccinations of aged mice. As CDI is a significant burden on the health of the growing global population of elderly individuals and vaccine responses in the elderly are typically dampened, our studies excitingly suggest that the addition of the molecular adjuvant ADA-1 can overcome age-related defects in the aged immune response to vaccination and restore humoral responses to those seen in the young.

33. Enhanced immunity to SARS-CoV-2 variants of concern following heterologous prime-boost vaccination with INO-4802 in nonhuman primates

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More than one year after being declared a pandemic, COVID-19 remains a public health emergency. The emergence of multiple SARS-CoV-2 variants that show evidence of escaping immune recognition in vaccinated and convalescent individuals necessitates the development of next-generation vaccines that offer enhanced protection against present and future variants. We have developed such a vaccine using our SynCon® DNA platform. INO-4802 encodes a pan-Spike immunogen and was designed to induce broad immunity across SARS-CoV-2 variants of concern (VOCs). Given that a large portion of the global population harbors some level of immunity to the original SARS-CoV-2 strain, either through infection or immunization with vaccines that have received emergency use authorization (EUA) clearance, raising the question going forward of whether a boost with next-generation vaccines can effectively broaden immune

coverage against VOCs. In the current study, we addressed this question by evaluating the immunogenicity of a prime-boost regimen in nonhuman primates. Rhesus macaques received primary immunization with INO-4800, a first-generation DNA vaccine matched to SARS-CoV-2 Spike protein of the original strain and currently in clinical development. One year later, the immunized animals were randomized and received either homologous boost with INO-4800 or heterologous boost with INO-4802. Following the boost, all animals showed significantly increased levels of functional antibody responses with neutralizing and ACE2 blocking activity against multiple SARS-CoV-2 VOCs. These data indicate homologous or heterologous prime-boost strategies with the INO-4800 and INO-4802 DNA vaccines enhance broad humoral responses against emerging SARS-CoV-2 variants.

34. Determining Adenosine Deaminase 1 (ADA-1) Impact on Immune Memory and Durability as a Molecular Adjuvant in a SARS-CoV-2 DNA Vaccine Formulation.

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The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for coronavirus disease of 2019 (COVID-19), has infected millions of people causing a global pandemic. SARS-CoV-2 vaccines candidates have demonstrated acute immunogenicity and protection however, it has yet to be demonstrated whether natural or vaccine induced immunity against SARS-CoV-2 induces long term, protective immunity. In this study we sought to understand if adenosine deaminase (ADA), as a molecular adjuvant, can enhance immune memory and durability in the context of a SARS-CoV-2 DNA vaccine. Mice were immunized with a plasmid encoding for SARS-CoV-2 spike alone or in combination with plasmid encoded ADA (pADA). Subsequent B and T cell responses were measured until d60pi. In mice co-immunized with ADA, there were increased concentrations of spike receptor binding domain (RBD)-specific IgG in the sera which were found to bind RBD at an increased affinity as well as exhibit increased neutralization capability against SARS-CoV-2 pseudotyped viruses. Additionally, ADA co-immunized mice exhibited increased frequency of RBD specific memory B cells. In regard to T cell responses, mice co-immunized with ADA exhibited increased spike-specific IFN-γ, TNF-□ and IL-2 as measured by flow cytometry and ELISpot. The ADA-enhanced anti-spike antibody durability over time was associated with increased frequencies of T follicular helper cells (TFH). Preliminary analysis supports that co-immunization with pADA impacts viral load in a SARSCoV-2 infection model. These data suggest that ADA enhances immune memory and durability and supports further study with translational focus for enhancement of vaccines.

35. A Clinical Review of INO-4800: DNA plasmid vaccine elicits neutralizing humoral responses and cross reactive cellular immune responses that target multiple epitopes within the spike protein, increasing the potential for immunologic response to new strains

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Background: DNA vaccines are safe, tolerable, elicit cellular and humoral responses, allow for repeated dosing over time, are thermostable at room temperature, and are easy to manufacture. We present the Phase 1 data of Inovio's US COVID-19 DNA Vaccine (INO-4800) targeting the full-length Spike antigen of SARS-CoV-2.
Methods: Participants in the open-label Phase 1 trial received INO-4800 in doses that included 1.0 mg and 2.0 mg each administered intradermally (ID) followed by electroporation (EP) at Days 0 and 28. ClinicalTrials.gov identifier: NCT04336410
Findings: The majority of adverse events (AEs) related to INO-4800 were mild in severity and did not increase in frequency with age and subsequent dosings. In Phase 1, 78% (14/18) and 84% (16/19) of subjects generated neutralizing antibody responses with geometric mean titers (GMTs) of 17.4 (95%CI 8.3, 36.5) and 62.3 (95% CI 36.4, 106.7) in the 1.0 and 2.0 mg groups, respectively. By week 8, 74% (14/19) and 100% (19/19) subjects generated T cell responses by Th1- associated IFNγ ELISPOT assay. Importantly, using a flow cytometry assay SARS-CoV-2 specific cells were able to produce cytolytic markers such as granzyme A and B. The cellular immune responses when tested against variants demonstrated no decrease in the magnitude.
Discussion: INO-4800 appears to be safe and tolerable with the induction of both humoral and cellular immune responses. In addition to eliciting neutralizing antibodies, INO-4800 induced T cell immune responses as demonstrated by IFNγ ELISpot and flow cytometry. The cellular responses increase the likelihood that as future variants arise, INO-4800 can induce an immune response to overcome immune escape.

POSTER ABSTRACT INDEX

Poster Number	Title	Name
1	Novel immunogen design elicits increased protection against avian H7N9 influenza that is associated with mobilization of seasonal influenza T cell memory	Mayara Grizotte-Lake
2	DNA priming immunization is more effective than recombinant protein vaccine in eliciting antigen-specific B cell responses	Shixia Wang
3	Polymersomes as stable nanocarriers for a highly immunogenic and durable SARS-CoV-2 spike protein subunit vaccine	Lam Jian Hang
4	Immunization Compliance to Routine Pediatric Vaccinations Among Service Patients in a Tertiary Hospital in Cebu Before (September 2019 to March 2020) and during (April 2020 to September 2020) the COVID-19 Pandemic	Syrelle Corazon G. Deiparine
5	A novel heterologous prime-boost immunotherapy protects against hepatitis B and D co-infection and hepatitis D super-infection.	Lars Frelin
6	Highly conserved, non-human-like, and cross-reactive SARS-CoV-2 T cell epitopes for COVID-19 vaccine design and validation	Leonard Moise
7	Improved Protection against SARS-CoV-2 by Mucosal Vaccination with a Single-cycle Adenovirus	Haley Mudrick
8	Combination therapy with PTT and FlaB-Her2 Vax in DD-her2/neu breast cancer mice model	Jayalakshmi Thiruppathi
9	Agent-based Investigation of the Impact of Low Rates of Influenza on Next Season Influenza Infections	Mary Krauland
10	Exploratory Analyses of The Humoral Immune Response to ChAdOx1 MERS-CoV Vaccine	Sarah Batawi
11	A Theoretical Strategy for Heterologous Prime-Boost COVID-19 Vaccination	Javier Burgos Salcedo
12	Immunogenicity of mRNA-based SARS-CoV-2 vaccines in healthy weight, overweight, and obese adults.	John T. Bates
13	A single-dose live-attenuated YF17D-vectored SARS-CoV-2 vaccine candidate	Lorena Sanchez Felipe
14	Developing Low-cost, Safe and Effective Bi-antigen SARS-CoV-2 Vaccine comprising S1 subunit and N protein expressed in Pichia pastoris for Developing Countries	Ganesh Kumraj
15	In Vivo Evaluation of Nanoparticulate Combined Adjuvant Systems Based on Salmonella Thyphi Porins-Chitosan	Selin Parmaksız
16	Emergent H1N1 G4 swine influenza virus may pose a threat to the US pork industry and human population	Swan Tan
17	Co-immunization with adenosine deaminase rescues age-associated impairment of SARS-CoV-2 synDNA vaccine-induced responses	Ebony Gary
18	Live attenuated influenza virus vaccine expressing an IgA-inducing protein reduces virus replication and transmission in pigs	Daniela Rajao
19	DNA Launched Native Like Trimer Env immunogen induced Tier 2 neutralizing antibodies and revealed a new murine Env C3/V5 epitope	Mansi Purwar
20	FluB-RAM and FluB-RANS: Genome Rearrangement as Safe and Efficacious Live Attenuated Influenza B Virus Vaccines	Stivalis Cardenas-Garcia
21	Novel ocular delivery of whole inactivated influenza virus with L. lactis bacterium-like particle as a mucosal adjuvant	Iman Salamatian
22	Development of a novel Live Attenuated Influenza A Virus vaccine encoding the IgA-inducing protein	C. Joaquin Caceres
23	Administration of Four Different COVID-19 pcDNA 3.1 DNA Vaccine Prototypes Using Intradermal Electroporation and Assessment of Their Immunogenicity in BALB/c mouse	Muhammet Karakavuk

24	Importance of IFN-Î»1 levels in COVID-19 patients and implications on vaccine efficacy against SARS-CoV-2	Mert Doskaya
25	Immunogenicity of a DNA Vaccine Encoding Chimeric Multi-Epitope HER2 Antigen Against HER2+ Breast Cancer by Targeting the Chimeric Antigen to Dendritic Cells	Aytul Gul
26	Design of a Vaccine Against Zika and Dengue Viruses Based on Mimotopes of the Envelope Dimer Epitope	Esmeralda Cuevas Juárez
27	Development of SARS-CoV-2 Neutralizing Antibodies by Constructing Highly Diverse Antibody Libraries from Indian Population	Kafil Ahmed
28	Broadly protective computationally designed influenza neuraminidase vaccine in the ferret animal model	Amanda Lee Skarlupka
29	One mucosal administration of a live attenuated recombinant COVID-19 vaccine protects non-human primates from SARS-CoV-2	Mariana Tioni
30	Approaches to therapeutic DNA vaccination against squamous cell carcinomas associated with HPV infection	Maria Isaguliants
31	An Intranasal OMV-based vaccine induces high mucosal and systemic protecting immunity against a SARS-CoV-2 infection	Corine Kruiswijk
32	Age-associated defects in the adaptive immune response to Clostridioides difficile infection impair the development of a protective immune response in the elderly	Matthew Bell
33	Prime-boost vaccination regimens with INO-4800 and INO-4802 augment and broaden immune responses against SARS-CoV-2 in nonhuman primates	Blake Schouest
34	Co-Immunization with Adenosine Deaminase-1 as a Molecular Adjuvant Supports Robust and Durable Protective Anti-SARS-CoV-2 Immunity In Vivo	Gina Cusimano
35	Clinical Review of INO-4800: DNA plasmid vaccine elicits neutralizing humoral responses and cross reactive cellular immune responses that target multiple epitopes within the spike protein, increasing the potential for immunologic response to new strains	Jean Boyer

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