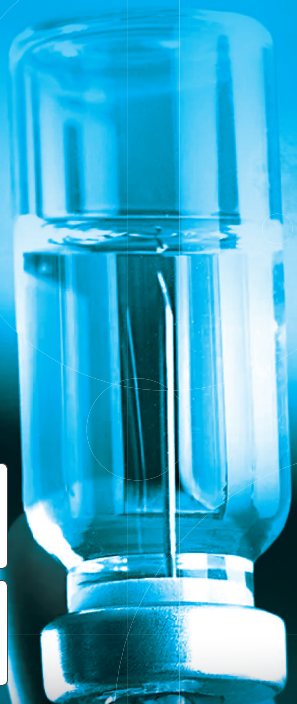
SCIENTIA MEETINGS

BOOK VACCINES 2024



EXHIBITORS

WuXi Vaccines | C.T.L. Cellular Technology Ltd. | FinaBio Fina Biosolutions LLC

labcorp | DesertKing | BIOSYSTEMS Acro

VACCINES SUMMIT-2024

NOVEMBER 13-15, 2024
BOSTON, MA

SCIENTIA MEETINGS
Website: https://scientiameetings.com/conferences/vaccines/ | Ph: 1-815-595-8049 | Email: venky@sciresgroup.net

About Organizer:

Welcome to Scientia Meetings, your gateway to excellence in the world of vaccines and cutting-edge healthcare solutions. Over the past three years, we have been at the forefront of organizing successful Vaccines Summit that bring together industry leaders, professionals, and visionaries to foster innovation, collaboration, and business growth.

About Vaccines Summit-2024:

Scientia Meetings invites participants across the globe to attend its fourth edition of Vaccines Summit which is going to take place during November 13-15, 2024, and is organized around the theme "next-generation vaccines treatment and diagnostics that save lives", Vaccines Summit-2024 is comprised of various sessions designed to offer comprehensive symposiums that address current issues in the field of vaccine research and provides a fantastic opportunity to network with your peers from academia and industry.

Corporate Partnering: Vaccines Summit-2024 help commercialize your innovations and build your business development pipeline through corporate partnering. We will arrange a one-on-one partnering meeting on request. We will share the conference attendees list with you, a month before the conference and arrange for one-on-one meetings with selected corporate representatives.

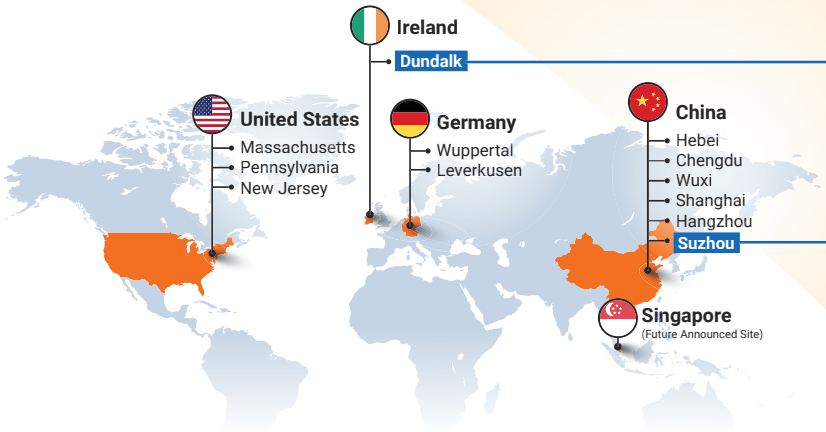
How does this conference help young scientists? Vaccines Summit-2024 not only opens doors to your career, but also opens your eyes to future opportunities, new cultures, and international perspectives. With the majority of the students interested in doing higher studies abroad, the students' marketing forum provides an opportunity for Postgraduate and Undergraduate students to have formal communication with University representatives from around the world. Postgraduate student recruitment is increasingly becoming a strategic priority for higher education institutions. Vaccines Summit-2024 provides an excellent networking opportunity for potential collaboration with businesses and organizations for students.

Investment opportunities: Industry prospectors are looking for breakthrough technologies that are ready for licensing, corporate partnering, or investment opportunities. This can include prototypes, demonstrations, and display booths to showcase your innovative solutions at Vaccines Summit-2024. Pitch your idea to an industrial expert jury to raise the capital you need to get started.

WuXi Vaccines

CDMO for the Development and Manufacturing of Vaccines and Prophylactic Antibodies

Innovation to improve global health



Extensive Capabilities from Preclinical to Commercial BSL-1 and BSL-2

- **Mammalian and Microbial:** mAb, fusion protein, nanoparticles/VLP, OMV, conjugate
- **Viral:** live attenuated viral, viral vector
- **pDNA/cRNA/mRNA**
- **Fill & Finish:** liquid, lyo, suspension, emulsion
- **Standalone Services:** Cell line/strain/virus development and GMP banking; process development, formulation development, biosafety, R&D material generation for vaccines and mAb

WuXi Vaccines, a subsidiary of WuXi Biologics, focuses on vaccine and prophylactic antibody development and manufacturing. With multiple commercial vaccines manufactured at globally GMP-certified facilities, and over 70 projects in development, WuXi Vaccines brings a level of expertise, experience and state-of-the-art facilities to enable your project to be conducted right the first time. As an industry-leading CDMO, we provide world-class integrated development and manufacturing platforms to expedite your preventative products to the clinic and the market.

wuxivaccines.com

Cellular Technology Limited (C.T.L.)

http://www.immunospot.com

is a leading solution provider for immune monitoring supporting both research, pre-clinical and clinical studies phase I, II, III, IV and commercial. We help you to get the best possible results, by offering a wide range of products and services, including:

CONTRACT LABORATORY SERVICES:

Our CLEP/CLIA-certified laboratory can provide logistics (USA as well as globally), cryopreservation of functional PBMC from whole blood (serves as central blood processing laboratory in North America), ELISPOT, ELISA, NAb, multiplex Cytokine Bead Arrays (CBA), Flow Cytometry (phenotyping, ICS, multimer readouts etc.), Killer assays, MAT and more. CTL develops, validates and performs low and high-throughput format testing, tailored to our clients' needs.

INSTRUMENTATION:

Image analyzers (ImmunoSpot^{R}), high-throughput Analysis/Counting: ELISPOT, FluoroSpot, NK Assays, Viral Plaque (PRNT, FRNT, FFA), Bactericidal, Microbial Colony Counting, Genotoxic (MLA, AMES), Yeast Viability analysis, Stem Cell Assays and more….

CONSUMABLES:

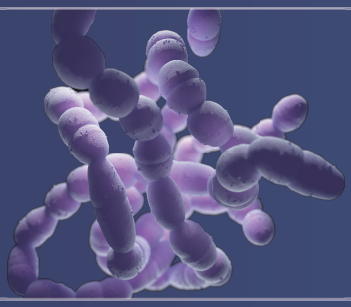
Cryopreserved PBMC Library: Over 150 HLA-typed donors with established reactivity to TH1/Th2 analytes to HLA Class I & Class II-restricted antigens. B and T Cell ELISPOT Kits to multiple species, FluoroSpot Kits ranging from single to multiplexed 4-color analytes and serum-free media, cryopreservation standardization solutions for functional PBMC generation and more…

FinaBio
Fina Biosolutions LLC

a conjugate vaccine R&D company

Promoting (Affordable) Conjugate Vaccines

- Chemistry
- Carrier proteins
- Conjugation Services



*Please join FinaBio for **Happy Hour***
on November 14th
after the conjugate vaccine session is over

NEW ClickCRM™ : *Click Chemistry Conjugation to CRM_{197}*

CARRIER PROTEINS FOR CONJUGATE VACCINES

TTHc Tetanus toxin fragment	**EcoCRM®** CRM_{197}	**8MTT** Modified tetanus toxin	**Qß** VLP
50 kDa	58.4 kDa	150 kDa	28 nm-diameter nanoparticle
heavy chain fragment C	CRM_{197} , a widely used genetically detoxified diphtheria toxin	8MTT is the first genetically detoxified tetanus toxin	High stability
Preclinical	EcoCRM® has been extensively compared to CRM_{197} from other sources[1]	8 mutations to fully detoxify	Contains T cell epitopes
Extensive literature	EcoCRM® available for research & clinical use	$50x10^6$ less toxic than tetanus toxin	High level of symmetry
Anti-TTHc neutralizes toxin		Large size allows for higher hapten: protein ratios	180 identical subunits

FinaBio
Fina Biosolutions LLC

FinaBio.com 877-346-2246 (877-FinaBio) info@FinaBio.com


Gain insights from drug discovery
to commercialization.
Together, let's break through.
Get started at labcorp.com/biopharma/breakthrough
©2024 Labcorp. All rights reserved.
labcorp

The human vaccine-quality benchmark

THE WORLD'S MOST TRUSTED SUPPLY – USED IN 5 GLOBALLY APPROVED VACCINES

YOUR ONLY SOURCE FOR LARGE, READY-TO-SHIP GMP VOLUMES

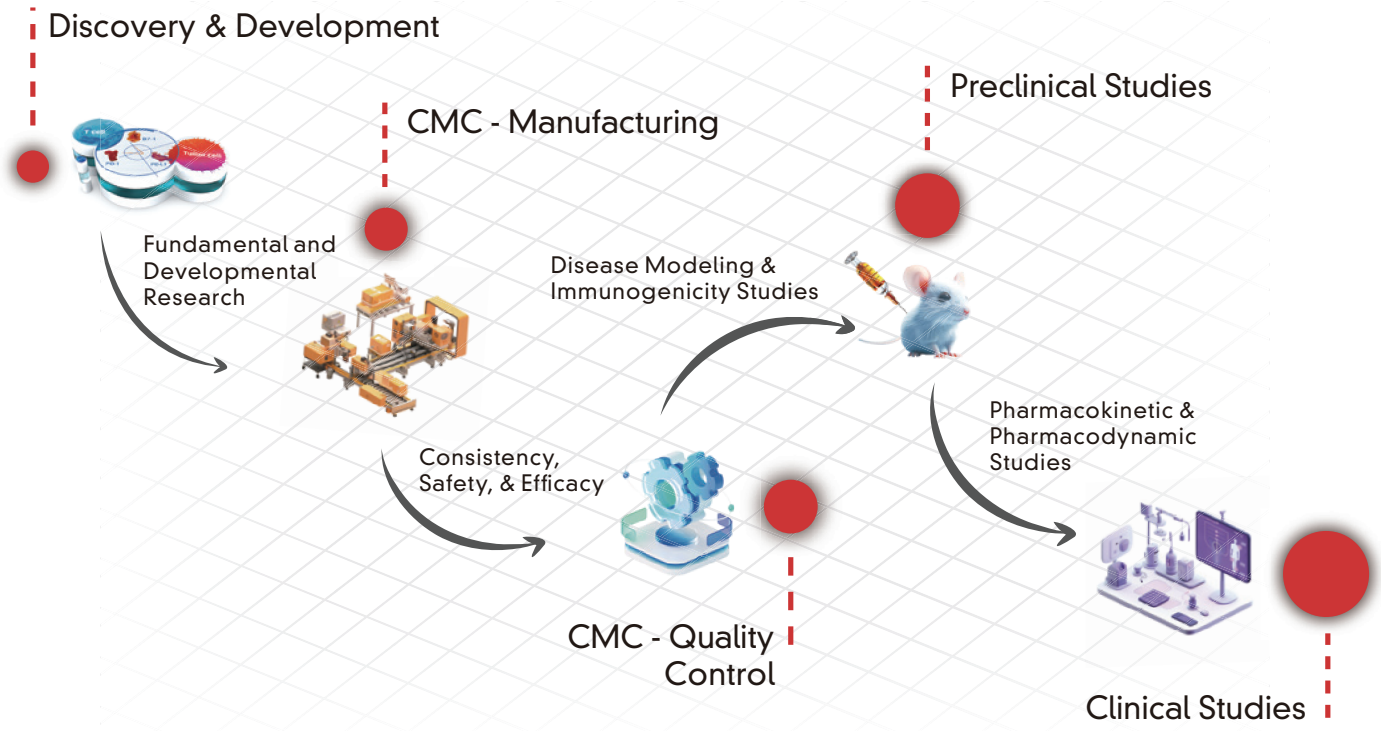
PUTTING 40 YEARS OF INNOVATION TO WORK FOR YOU

Learn more about our QS-21 and other products

WWW.DESERTKING.COM

BIOSYSTEMS
Acro
Where Proteins and Innovation Advance Biomedicine

Overcoming Challenges With Innovation From Discovery To The Clinic



Core Product and Services

Built on Industry-Leading Technology Platforms
Offering Diverse Product Selections for Customers

- Recombinant Proteins
- Antibody
- Enzyme
- Residual Detection Kits
- Cell Lines
- Growth Factors
- Magnetic Beads
- GMP Grade Solutions
- Analytical Services
- Service
- Pathology
- Organoid Toolbox

SCIENTIA MEETINGS

VACCINES 2024

Day 1: November 13, 2024

Keynote Presentations

VACCINES SUMMIT-2024

NOVEMBER 13-15, 2024
BOSTON, MA

SCIENTIA MEETINGS
Website: https://scientiameetings.com/conferences/vaccines/ | Ph: 1-815-595-8049 | Email: venky@sciresgroup.net

Keynote Presentations

Session Chair: **David Weiner**
Executive Vice President, The Wistar Institute, Director, Vaccine & Immunotherapy Center

Title: **Human *in vitro* modeling and systems biology to advance precision vaccines**
Ofer Levy
Staff Physician & Principal Investigator, Director, Precision Vaccines Program, Division of Infectious Diseases, Boston Children's Hospital Professor, Harvard Medical School

Title: **Correlates of protection for COVID-19 and Mpox vaccines**
Dan Barouch
Director, Center for Virology and Vaccine Research, Beth Israel Deaconess Medical Center

Title: **Tailoring vaccine immunity and immune therapy by novel nucleic acid tools incorporating potent delivery and unique formulations**
David Weiner
Executive Vice President, The Wistar Institute, Director, Vaccine & Immunotherapy Center

Title: **Efficacy of dendritic-cell-based cancer vaccines enhanced by development in high omega-3 lipid environment**
Jay A. Berzofsky
Chief, Vaccine Branch, Center for Cancer Research, National Cancer Institute, NIH

Title: **End-to-end development of VSV-based vaccines for outbreak and epidemic preparedness: the road traveled thus far**
Swati Gupta
VP, Emerging Infectious Diseases and Epidemiology, IAVI

Title: **Regulatory perspective on frontiers in vaccine development**
David Kaslow
Director, Office of Vaccines Research and Review, FDA/CBER

Title: **RSV vaccine for maternal immunization: Why did it take more than 60 years?**
William C. (Bill) Gruber
Gruber Vaccine R&D Consulting, LLC

Title: **Accelerating site selection and recruitment for vaccines with AI/ML: From COVID-19 to Beyond**
Michael Lingzhi Li
Technology and Operations Management Unit, Harvard Business School

Title: **Advancement in *Leishmania* vaccination development and its role in global elimination of leishmaniasis**
Hira Nakhasi
Division Director – DETTD, Center for Biologics Evaluation and Research

Title: **Next generation mRNA design – increasing mRNA potency**
Heather Schultheisz
Director of Innovation, Maravai LifeSciences

Title: **Universal vaccines against influenza and other pathogens**
Jerry Sadoff
Chief Medical Officer, Centivax

Title: **How to develop long-lasting vaccines against tough pathogens**
Gongyi Zhang
Professor, Department of Immunology and Genomic Medicine, National Jewish Health

Title: **DNA medicines platform for both prophylactic and therapeutic applications: case studies in Ebola and recurrent respiratory papillomatosis**
Dave Liebowitz
Senior Vice President, Early-Stage Clinical Development, INOVIO

Title: **Genomic integration of SARS-CoV-2 sequences in virus infected and viral RNA transfected human cells**
Rudolf Jaenisch
Professor of Biology, Whitehead Institute, MIT

Human *in vitro* modeling and systems biology to advance precision vaccines

Ofer Levy
Staff Physician & Principal Investigator, Director, Precision Vaccines Program, Division of Infectious Diseases, Boston Children's Hospital Professor, Harvard Medical School

Biography

Dr. Ofer Levy was born to and raised by the artist Benjamin Levy and music composer Hannah Levy in New York City, where he graduated from the Bronx High School of Science. After graduating from Yale College (B.S., Molecular Biophysics and Biochemistry), Dr. Levy entered the Medical Scientist (MD/PhD) Training Program at New York University School of Medicine. There he earned his PhD under the mentorship of Drs. Peter Elsbach and Jerrold Weiss, characterizing neutrophil-derived antimicrobial proteins and peptides including bactericidal/permeability-increasing protein (BPI) and cathelicidins. Inspired by his wife Sharon's example, he chose Pediatrics and completed both residency and fellowship (Infectious Diseases) at Boston Children's Hospital. He is currently Professor at Harvard Medical School as well as principal investigator, staff physician and the Director of the Precisions Vaccine Program in the Division of Infectious Diseases, Boston Children's Hospital. The Precision Vaccines Program is an academic program that fosters international collaboration between academia, government, and industry for development of vaccine formulations optimized to protect vulnerable populations. Dr. Levy's laboratory is focused on modeling vaccine-induced human immune responses in vitro using a variety of platforms including three-dimensional microphysiologic systems as well as global molecular ("OMIC") approaches to accelerate and de-risk development of vaccines optimized for populations with distinct immune responses, including those at the extremes of age who suffer the most infections. He currently leads or co-leads multiple NIH/NIAID-supported studies, including (a) an Adjuvant Discovery Program contract, leveraging robotic and immunologic approaches to discover, characterize, and formulate novel small molecule adjuvants that may enhance vaccine responses of vulnerable populations such as infants and older adults; (b) an international Human Immunology Project Consortium effort employing systems biology to define biomarkers of neonatal vaccine immunogenicity and (c) a project on Immune Development in Early Life (IDEAL). Dr. Levy also serves on the U.S. FDA Vaccines and Related Biologic Products Advisory Committee (VRBPAC) and has appeared in major media including CNN, FoxNews, Scientific American, National Geographic, Wall Street Journal, and USA Today. He lives in Cambridge, Massachusetts along with his wife Dr. Sharon Levy and their three children.

Correlates of protection for COVID-19 and Mpox vaccines

Dan H. Barouch, M.D., Ph.D.
Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

I will review data suggesting that both antibody and T cell responses contribute to COVID-19 vaccine protection in nonhuman primates and humans. I will also discuss new data suggesting the importance of mucosal immunity for next generation COVID-19 vaccines that aim to block acquisition of infection. Finally, I will discuss recent data on immune correlates of protection and durability of the Mpox vaccine.

Biography:

Dr. Dan Barouch received his Ph.D. in immunology from Oxford University and his M.D. from Harvard Medical School. He is currently the William Bosworth Castle Professor of Medicine and Professor of Immunology at Harvard Medical School, Director of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center, a member of the Ragon Institute of MGH, MIT, and Harvard, and part of the Bill & Melinda Gates Foundation Collaboration for AIDS Vaccine Discovery. His laboratory focuses on studying the immunology and virology of HIV-1 infection and developing novel vaccine and eradication strategies. His group has also applied their vaccine expertise to preclinical and clinical studies of other infectious diseases of global significance, including Zika virus, tuberculosis, and most recently SARS-CoV-2. His recent work contributed to the development of the single-shot Johnson & Johnson COVID-19 vaccine, which is now being rolled out in the United States and throughout the world. He was elected to the National Academy of Medicine in 2020.

Tailoring vaccine immunity and immune therapy by novel nucleic acid tools incorporating potent delivery and unique formulations

David B. Weiner, PhD
Wistar Institute Professor & WW Smith Distinguished Chair in Cancer Research,
Director Vaccine & Immunotherapy Center,
Executive Vice President of the Wistar Institute,
Professor Emeritus University of Pennsylvania School of Medicine, Philadelphia PA

The push to expand and enhance novel tools for vaccination and immunotherapy remains a major focus for the field. As an example, gene-vectored vaccines have grown in importance over the past several years, exemplified by the approvals of lipid nanoparticle-formulated mRNA (mRNA-LNPs), viral-vectored vaccines, and a jet-delivered DNA vaccine for SARS-CoV-2. More recently, we see important advances clinically from mRNA and DNA approaches in areas of personalized medicine, and immune therapy of chronic infections. These reports have raised excitement for immune targeting these previously intractable targets. We continue to develop new approaches and formulations that allow the invivo delivery of more effective DNA vaccines. These tools support dose sparing approaches to immunization, with induction of improved humoral immunity. They demonstrate induction of potent effector responses that can impact infectious challenge. These formulations delivery appear well tolerated and are temperature stable. Further, they allow for the inclusion of large genetic stretches supporting the invivo delivery of complex immunogens, while remaining serologistically agnostic thus allowing for consistent redosing. Now through a combination of exciting tools including IM delivery by adaptive, EP, ID delivery using cellectra 3p for induction of focused serological and T cell immunity, and new lipid formulations that further provide development options, a more tailored approach to impact difficult diseases is possible. These multiple tools allow for significant flexibility in the development of novel vaccines and invivo launched biologics. The ability of these approaches allowing for an tailoring for immune response against specific targeting infectious agents or pathogenic cells is a central focus of our program.

Biography:

Weiner directs a translational molecular immunology research team focused on creating novel immunotherapy approaches for disease prevention and treatment using synthetic nucleic acid technology. Accomplishments of the team and collaborators include the first clinical studies of DNA vaccines, with a focus on advances in gene optimization and electroporation (EP)-mediated DNA delivery. Their work has revitalized the field, rapidly and safely moving new advances into human studies. These include the world's first Zika vaccine, the first MERS vaccine, an advanced Ebola Vaccine, and a novel HIV vaccine, among others. Additionally, the Weiner laboratory has helped to develop immunotherapy approaches that are currently in clinical testing for HPV-associated cancer, prostate and other cancers. The first clinically efficacious therapeutic DNA vaccine for HPV cervical intraepithelial neoplasia CIN) has moved into a Phase 3 trial (REVEAL). Weiner and his lab have received several awards/honors for their accomplishments, including the Vaccine Industry Associations Outstanding Academic Research Laboratory (2015 & 2016), being named one of the Top 20 Translational Research Laboratories of the Year (Nature Biotechnology 2016, 2017 & 2018) and the 2014 Stone family Award for Cancer Research. Weiner was named one of the nation's top 40 most influential vaccine scientists in 2014, received the 2011 NIH Directors Translational Research Award and is an elected fellow of the American Association for the Advancement of Science since 2011 and a fellow of the International Society for Vaccines, for which he served as president from 2018 to 2020. Weiner is an avid trainer, advisor and advocate for students, fellows and junior faculty as he is highly committed to developing the careers of young scientists.

Weiner received his B.S. in biology from Stony Brook University, N.Y., and his M.S. in biology from the University of Cincinnati. He then earned a Ph.D. in developmental biology with a focus on molecular immunology from the University of Cincinnati, College of Medicine. Weiner joined the University of Pennsylvania as a research fellow in the Department of Pathology and Laboratory Medicine, where he rose through the ranks to become Professor. He held a second appointment from The Wistar Institute from 1990 to 1993. At Penn, he served as co-chair of the Tumor Virology Program of the Abramson Cancer Institute and as chair of the Gene Therapy and Vaccine Training Program.

Efficacy of dendritic-cell-based cancer vaccines enhanced by development in high omega-3 lipid environment

Shweta Tiwary[1], Kevin Hsu[1], Katherine C. Goldfarbmuren[1,2], Zheng Xia[1], and Jay A. Berzofsky[1]
[1]Vaccine Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892 USA
[2]Advanced Biomedical Computational Science, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Inc., Frederick, MD 21702 USA

Dendritic cells (DCs), as the most effective professional antigen-presenting cells, also make effective vaccine vehicles. However, optimization of DC vaccines has yet to be achieved. We found that mice expressing the FAT-1 gene from *C. elegans* that converts omega-6 to omega-3 fatty acids have slower tumor growth, prolonged survival, and better responses to syngeneic DC vaccines. We traced the greater DC vaccine efficacy to the FAT-1 bone-marrow-derived DCs themselves, as they are more effective in immunizing wild-type (WT) mice as well. FAT-1 DCs pulsed with antigen slowed tumor growth, prolonged survival and reduced cachexia in TC-1 and B16F10 tumor models in WT mice compared with WT DC vaccines. In vitro, the FAT-1 DCs are also more effective at stimulating T-cell responses. However, we could not find differences in the expression of costimulatory or MHC molecules on the FAT-1 vs WT DCs, although there were differences in cytokine and chemokine expression. Transcriptional differences are being studied by RNAseq. However, the biggest difference was found when we studied the dwell time of antigen-specific CD8 T cells on FAT-1 or WT DCs pulsed with antigen by time-lapse fluorescence microscopy. The dwell time was about 20-fold longer with FAT-1 DCs, suggesting a more prolonged opportunity to transmit signals across the immune synapse. Thus, greater incorporation of omega-3 fatty acids in the DC lipid membrane may account for the greater vaccine efficacy. To determine whether this observation might be translatable to clinical cancer vaccines, we tested WT bone-marrow-derived DCs grown from bone-marrow precursors in the presence of DHA, a precursor omega-3 lipid. Indeed, the greater efficacy to stimulate T cells was imprinted in the DCs by this treatment. Other omega-3 lipids are being tested, but this finding should facilitate translation of the omega-3 effect to make more effective human autologous DC cancer vaccines for treating cancer patients.

Biography:

Dr. Jay A. Berzofsky was appointed Chief, Vaccine Branch, Center for Cancer Research, National Cancer Institute, in 2003, after being Chief, Molecular Immunogenetics and Vaccine Research Section, since 1987. He graduated Summa cum Laude from Harvard (1967), and received a Ph.D.-M.D. from Albert Einstein College of Medicine (AECOM). After interning at Massachusetts General Hospital, he joined NIH in 1974. Dr. Berzofsky's research has focused on antigen processing/presentation, epitope structure, cytokine and regulatory cell control of T cell function and avidity, NKT cells, and translation to the design and clinical trials of vaccines for AIDS, cancer, and viruses causing cancer. He has 521 scientific publications. He was elected President of the American Society for Clinical Investigation (1993-94), a member of the Association of American Physicians, a Fellow of the American Association for the Advancement of Science (AAAS), and Distinguished Alumnus of the Year for 2007 by AECOM. He was elected Chair of the Medical Sciences Section of the AAAS for 2007-2008. He received the NIH Director's Award and the NCI Merit Award in 2008, another NCI Director's Merit Award in 2011, and a Career Award "for his important contribution to tumor immunotherapy" from the European Academy of Tumor Immunology in 2018.

End-to-end development of VSV-based vaccines for outbreak and epidemic preparedness: the road traveled thus far

Swati Gupta
VP, Emerging Infectious Diseases and Epidemiology, IAVI

The ongoing outbreak of Marburg virus (MARV) disease in Rwanda, which follows the Sudanvirus (SUDV) disease outbreak in Uganda two years ago, is a stark reminder that viral hemorrhagic fever (VHF) diseases will continue to emerge and re-emerge with climate change and alterations in human migration patterns. With the exception of ERVEBO®, Merck's licensed single-dose Zaire ebolavirus vaccine, there are no licensed vaccines or therapeutics targeting viruses causing VHF diseases. IAVI has multiple active vaccine development programs based on the recombinant vesicular stomatitis virus (rVSV) vector platform, which uses the same technology as ERVEBO®, intended to address critical unmet needs in countermeasure development against Lassa fever virus, SUDV, and MARV. Vaccination using IAVI's rVSV-based vaccine candidates against these VHF diseases shows promise not only in pre-clinical studies but in ongoing Phase 1 and Phase 2 clinical trials. Updates across the portfolio will be shared, with a specific emphasis on the considerations for end-to-end development of IAVI's Lassa fever rVSV-based vaccine candidate, which is currently being investigated in a Phase 2a study, including discussion of foundational epidemiological and preclinical data, clinical development, and the key partnerships developed while pursuing a path towards licensure.

Biography:

Swati Gupta, DrPH, MPH, leads IAVI's Emerging Infectious Disease product portfolio and the organization's epidemiology work. She has a particular focus in leveraging IAVI's recombinant vesicular stomatitis virus (rVSV) platform and expertise to expand product development efforts beyond HIV, including leading the vaccine development programs for other emerging infectious diseases such as Lassa Fever, Marburg, and most recently SARS-CoV-2.

Previously, Gupta was an executive director with Merck Vaccines, where she worked on the development of innovative partnership models to address cross-cutting issues related to vaccine science and technology. As part of this role, she worked with key external stakeholders to facilitate accelerated Ebola vaccine development efforts to enhance preparedness for the ongoing public health crisis and for potential future outbreaks.

From 2000 to 2014, Gupta was in the Department of Epidemiology at Merck Research Laboratories where she led a number international, prospective cohort studies in support of vaccine and infectious disease products in development, including research on diseases such as HIV, HPV, influenza, dengue, and C.difficile. From 1998 to 2000, Gupta worked as a scientist in HIV Surveillance at the Communicable Disease Surveillance Centre (British equivalent of the U.S. CDC) in the U.K. She has also worked at the Bureau of Tuberculosis Control at the New York City Department of Health.

Gupta holds a doctorate in epidemiology from the Johns Hopkins Bloomberg School of Public Health and a Master of Public Health in infectious disease epidemiology from Yale University School of Medicine.

Regulatory perspective on frontiers in vaccine development

David Kaslow, M.D.
Director, Office of Vaccines Research and Review, FDA/CBER

The U.S. Food and Drug Administration (FDA) is the regulatory authority that has oversight of the safety, effectiveness and quality of vaccines that are used in the United States (U.S.). Within FDA, the Center for Biologics Evaluation and Research (CBER) ensures that FDA's rigorous scientific and regulatory processes are followed by those who pursue the development of vaccines. Within CBER, the Office of Vaccines Research and Review regulates all licensed and investigational vaccines for human use in the U.S. An overview of programs designed to expedite and streamline product development will be presented with a view to the future of vaccine development.

RSV vaccine for maternal immunization: Why did it take more than 60 years?

William C. Gruber, MD
Principal, Gruber Vaccine R&D Consulting, LLC
Adjunct Professor, Depts of Pediatrics and Internal Medicine, School of Medicine
Adjunct Clinical Professor, Department of Epidemiology, School of Public Health
University of Michigan, Ann Arbor, MI

Beginning in the mid-1950s, Respiratory Syncytial Virus (RSV) has come to be recognized as the most important global cause of wintertime lower respiratory tract illness morbidity and hospitalization in infants, particularly in those less than 6 months of age. RSV is a significant contributor to infant deaths in low- and middle-income countries (LMICs). Development of an effective vaccine for protection of infants has been thwarted for decades. The first formalin inactivated vaccine paradoxically resulted in enhanced illness, subsequent inactivated RSV F and G surface protein containing vaccines induced poorly protective immune responses, and early live engineered RSV vaccines proved insufficiently attenuated. Meanwhile, by the 1980s, naturally acquired RSV antibody passed from pregnant mothers to their infants was shown to provide some degree of protection. Licensed polyclonal and monoclonal antibody (mAb) RSV prophylactic approaches followed for selected highest risk infants but were not practical for broad application. The discovery and stabilization of a highly immunogenic RSV F protein in its prefusion state opened the path to improved RSV mAb and vaccine development. Subsequent further stabilization of a bivalent subgroups A and B as an RSVpreF vaccine, and success and acceptance of maternal immunization for Influenza and pertussis, resulted in development of a recently licensed RSVpreF vaccine for maternal immunization to protect infants in the first 6 months of life. This history will be reviewed with a focus on evidence supporting RSVPreF approval, recommendations, and future plans to inform the safety and effectiveness profile of the vaccine.

Biography:

William (Bill) Gruber is currently Principal of Gruber Vaccine R&D Consulting, LLC and has over 40 years of experience in vaccine research and development. He was previously SVP and Head of Pfizer Vaccine Clinical Research and Development (VCRD) and responsible for clinical research and development of vaccines to meet global licensure and post licensure requirements. Dr. Gruber's clinical group was responsible for clinical research and development of licensed pneumococcal conjugate, influenza, SARS-CoV-2 (COVID-19), RSV (older adults, maternal immunization), meningococcal B, C, ACWY, and ABCWY vaccines, as well as numerous investigational vaccines. He retired from Pfizer on December 31, 2023.

Accelerating site selection and recruitment for vaccines with AI/ML: From COVID-19 to Beyond

Michael Lingzhi Li
Technology and Operations Management Unit at Harvard Business School

Site selection and recruitment are critical for all clinical trials, and vaccines are no exception. Compared to classical drug trials, vaccine trials for infectious diseases face significant challenges, particularly in predicting disease incidence rates at potential trial sites. We illustrate a real-world implementation of an AI/ML algorithm, DELPHI, that allowed for the robust acceleration of Janssen's COVID-19 Phase III Trial, which helped to reduce recruitment by 25% and accelerate the trial timeline by 33%.

This case study explores how the interpretability of DELPHI's parameters allowed us to engage in a human-in-the-loop process with decision-makers, enabling rapid scenario analysis and robust site selection amidst evolving COVID-19 conditions. We demonstrate how this approach resulted in the most diverse COVID-19 trial to date and gathered critical variant efficacy data.

We will further discuss the methodology, emphasizing the importance of interpretability in AI for clinical trials. Additionally, we will briefly touch on the broader applicability of our approach, as we are currently collaborating with various organizations to extend this methodology beyond COVID-19 trials, exploring its potential in other areas of drug development.

Biography:

Michael Lingzhi Li is an Assistant Professor in the Technology and Operations Management unit at Harvard Business School. His research focuses on integrating causal inference, optimization, and machine learning to create AI-driven decision algorithms aimed at transforming clinical trials globally. His collaboration with Janssen Pharmaceuticals on using AI/ML to expedite the Phase III trial of a COVID-19 vaccine was awarded the Innovative Applications in Analytics Award and the Edelman Laureate Award. Currently, he partners with several pharmaceutical companies to pioneer and implement advanced AI/ML technologies aimed to transform the clinical trials landscape.

Advancement in *Leishmania* vaccination development and its role in global elimination of leishmaniasis

Hira L. Nakhasi, Ph.D. FASTMH
Division of Emerging and Transfusion Transmitted Diseases, CBER, USFDA, Sliver Spring, MD, USA

Leishmaniasis is a neglected tropical disease caused by infection with the *Leishmania* parasite following transmission by an infected sand fly. It results in different clinical presentations ranging from cutaneous leishmaniasis (CL), that can lead to physical disfigurement, to visceral leishmaniasis (VL; Kala-azar) which is fatal if not treated. Over 600 million people worldwide are at risk of developing leishmaniasis, with an estimated incidence of over 200,000 cases of CL, and over 50,000 cases of VL each year. Kala azar is complicated by post-kala azar-dermal leishmaniasis, a proven reservoir of *Leishmania* parasites. Although progress has been made in reducing VL burden in Southeast Asia through the elimination program, there are numerous recent outbreaks reported from other countries including Chad, Senegal, Tanzania, Ethiopia, Brazil, Nepal, Somalia, Sudan. To achieve global elimination of leishmaniasis, new tools are required, including better surveillance and a safe and effective vaccine. Asymptomatic infection or treatment of VL patients confers life-long immunity in the majority of cases. Moreover, the stability of the *Leishmania* parasite genome indicates that the development of an effective vaccine against leishmaniasis might be possible using a live attenuated vaccine strategy. Because of the sporadic nature of VL outbreaks, we going to test vaccine efficacy using a Controlled Human Infection Model (CHIM) in parallel to field studies using the leishmanin skin test (LST) as a surrogate biomarker of protective cellular immunity. Moreover, the LST is a key surveillance tool to monitor changes in leishmaniasis-endemic countries and occurrence of new outbreaks. I will discuss the advancement of the *LmCen*$^{-/-}$ live attenuated vaccine toward human trials, use of AI tools to identify biomarkers of immunity and the re-introduction of the LST in the field. I will also discuss how these efforts are being integrated to support the elimination of leishmaniasis as a major global public health problem.

Biography:

Dr. Hira Nakhasi is currently the Director of the Division of Emerging and Transfusion Transmitted Diseases (DETTD) at the Center for Biologics Evaluation and Research (CBER) of the US Food and Drug Administration. As the Director of the DETTD, he is responsible for approving assays to screen blood donors for blood borne pathogens and retroviral diagnostic to ensure USA blood safety. He received his Masters and Ph.D. degrees in biochemistry from the M.S. University of Baroda, India and postdoctoral training at the National Institutes of Health, Bethesda, Maryland and Columbia University, New York, USA. His scientific expertise lies in molecular virology, parasitology, cell biology, immunology and vaccinology. His main research is focused on Leishmania pathogenesis and develop methods to evaluate safety and efficacy genetically modified Leishmania vaccines and diagnostic tools. He has published over 150 publications including reviews and book chapters, being a member of the review committees of several high impact journals, reviewer of grants, and being invited to speak at national and international forums. He is also a member of the several scientific organizations. Over the years he has received numerous awards including US Department of Human and Health Services Distinguished Service Award. Recently he was elected to be the Fellow of American Society of Tropical Medicine and Hygiene. He also has been recipient of several grants from International agencies such as Global Health Initiative and Technologies, Japan; Wellcome Trust UK and National Institutes of Health, USA worth millions of dollars for his studies on Leishmania vaccine development.

Next generation mRNA Design – Increasing mRNA Potency

Heather Schultheisz, Ph.D
Director of Innovation, Maravai LifeSciences

mRNA vaccines and therapeutics are expanding rapidly, in part fueled by the success of COVID-19 vaccines. An essential part of any mRNA therapeutic is the 5' cap structure, which is critical to the stability and expression of an mRNA. Learn more about how major capping strategies differ in their manufacturing costs, time, complexity, and availability, and how TriLink BioTechnologies is continuing to

Biography:

Heather Schultheisz is the Director of Innovation at Maravai LifeSciences, where she oversees research collaborations and partnerships to accelerate the development of new technology for RNA medicines. Heather completed her Ph.D. in Biology at The Scripps Research Institute, and has over 15 years experience in biotechnology with an emphasis on RNA applications from development and scale up of nucleic acid enzymatic syntheses to identification of key microRNA targets in pluripotent stem cells. Before joining Maravai LifeSciences, Heather worked at Genomatica where she led R&D program and alliance management.

Universal vaccines against influenza and other pathogens

Jerald Sadoff*, Rishi Bedi, Sawsan Youseff, Nicholas Bayless, Sang Il Kim, Gus Zeiner, Sujeong Kim, James Zengel, Jacob Glanville
Chief Medical Officer, Centivax

Developing universal vaccines against broadly cross-reactive protective epitopes in pathogens such as influenza, SARS-CoV-2, and malaria has been difficult because many of these epitopes are immuno-recessive. A method has now been developed to focus the humoral immune response on such immuno-recessive epitopes. Likewise, broadly cross-reactive T-cell epitope targets which can be presented by HLAs from almost all humans can be combined with this antigen focusing technology to further enhance the vaccine. As an example, a universal mRNA LNP influenza vaccine consisting of 10 highly divergent H1N1 HAs, 10 highly divergent H3N2 HAs, a single B HA and T cell epitopes from 5 influenza antigens has been developed. The HAs are expressed as stabilized trimers presented as transmembrane proteins, the combination of which enhances immunogenicity by 20-40-fold. This mRNA LNP vaccine is dosed to expresse low non-immunogenic levels of the individual H1 and H3 HAs, which prevents immune responses to the highly variable immunodominant epitopes of each individual HA, while the combination of 10 HAs results in enough conserved antigen in the HA head and stem to induce strong immune responses. In a variety of pre-clinical models, including human organoids, this vaccine induces HAI and neutralizing responses against a wide variety of H1N1, H3N2 strains and the B strain, protection in mice, ferrets and pigs as well as binding antibody against exotic potential pandemic strains and neutralizing antibody against the current H5N1 circulating strains. The same approach has been utilized to develop a Universal Covid vaccine which consists of a variety of highly divergent coronavirus RBDs at low doses to target the common neutralizing site. A malaria vaccine that targets the immuno-recessive epitope that protective Mabs are directed against in Malaria CS antigen, as well as the immuno-recessive protective epitope of VAR2CSA, which is the antigen that enhances placental malaria infection has been designed. These new technologies provide the possibility of producing vaccines against pathogens that thus far have evaded standard vaccine approaches and have the efficacy of vaccines against measles, mumps, rubella smallpox and others where control of these pathogens has been possible.

Biography:

Dr. Jerald Sadoff, M.D. as Chief Medical Officer with immediate effect. Dr. Sadoff has more than fifty years of experience in vaccine development. He has overseen or played a key role in the approval of more vaccines than any other currently active vaccine developer, including vaccines against Hepatitis A “VAQTA ®”; Haemophilus,“Liquid Pedvax”; Varicella,“ Varivax II®”; Measles, Mumps, Rubella and Varicella combination “ProQuad®”; Zoster, “Zostavax™”; Rotavirus “Rotateq®”; Human Papilloma Virus, “Gardasil®”; Ebola, “Zabdeno®+Mvabea®” and Covid-19, “Jcovden”. In total, there are fourteen vaccines for which he has played a key developmental role, with one additional vaccine now in late-stage clinical studies. He currently serves on several Scientific Advisory Boards for NIH-sponsored HIV and Malaria vaccine efforts, including the NIAID AIDS Vaccine Research Working Group. Over the last 35 years, he has authored over 350 articles, book chapters, and abstracts, and has 29 issued patents.

Most recently, Dr. Sadoff served as Senior Advisor Vaccine Development for Janssen Infectious Diseases and Vaccines, a division of Johnson & Johnson, where he held various leadership roles for more than a decade, leading the clinical development efforts for universal flu vaccines as well as for monoclonal antibodies and vaccines against HIV, Malaria, RSV, Ebola and Covid-19. For these efforts, he received the Johnson Gold Medal for Science and Technology. Prior to Janssen, Dr. Sadoff spent seven years at the AERAS Global TB Vaccine Foundation as President and CEO, where he helped develop and test the first new TB vaccines (4) in more than 40 years. Previous to AERAS, he spent eight years at Merck Co as Head of Clinical Vaccine development where he led and played a key role in licensing 9 vaccines. Prior to Merck, Dr. Sadoff spent 22 years at the Walter Reed Army Institute of Research (WRAIR), where he became head of vaccine development after working on a variety of vaccines against Malaria, Hepatitis A, Dengue, Shigella, Cholera, Gonorrhea, Pseudomonas, Klebsiella and E. Coli. At Walter Reed, Dr. Sadoff was awarded the Paul A. Siple Memorial Medallion: Army Science Conference (1st Place), as well as placing first and second in the two other Army Science conferences he participated in, and was awarded the Army Legion of Merit for his service to the Nation.

How to develop long-lasting vaccines against tough pathogens

Gongyi Zhang, Ph.D.
Professor, Department of Immunology and Genomic Medicine
National Jewish Health
Founder, NB Life Laboratory, LLC, Colorado, USA

Re-infection still occurs after a previous infection of SARS-CoV-2 or after vaccinations with multiple boosts, which becomes an entangling problem for people all over the world to fight the COVID-19 pandemic caused by SARS-CoV-2. This is also true for the influenza vaccine. Furthermore, we still do not have a potent vaccine against HIV and some other tough pathogens. It seems impossible to generate herd immunity with either a higher rate of infection or universal vaccination of populations, emerging variants of viruses always seek to break through the protection. Here, I will try to dissect the underlying working mechanisms of vaccinations, which are involved in the participation of germinal center B cells, transcription factor BCL-6, native forms of antigens presenting by follicular dendritic cells to B cells, and the critical roles of T follicular helper cells to the maturation process of B cells. I will also address the challenges we face in generating long-lasting vaccines against SARS-CoV-2, influenza, HIV, HBV, HCV, etc. Based on the above fundamental understanding, I will present a universal solution to solve this century-long conundrum. Toward the end, I will present some successful examples such as SARS-CoV-2, Influenza A, and Influenza B, etc. We may have potentially resolved this century-long puzzle in the vaccine field (US Patent: 11,690,917: Methods and Compositions for a universal and long-lasting vaccine. Inventor: Gongyi Zhang. It was issued on July 4, 2023)

Biography:

Dr. Gongyi Zhang obtained his Ph.D. from the Institute of Biophysics, Chinese Academy of Sciences in 1993. He was a visiting fellow at NIDDK, NIH from 1993 to 1996. He did a postdoctoral fellowship at the Rockefeller University from 1997 to 1999. He set up his own research group at the Department of Immunology (currently named, Department of Immunology and Genomic Medicine) at National Jewish Health in 1999 and stayed there since then. He is currently a Professor in the Department of Immunology and Genomic Medicine, at National Jewish Health in Denver, Colorado, and has a joint appointment at the Department of Immunology and Microbiology at the University of Colorado Anschutz Medical Campus. He set up a company, NB Life Laboratory, to develop long-lasting vaccines against tough pathogens such as influenza, HIV, SARS, and others in 2018.

DNA medicines platform for both prophylactic and therapeutic applications: case studies in Ebola and recurrent respiratory papillomatosis

Dave Liebowitz, **M.D & Ph.D**
Senior Vice President, Early-Stage Clinical Development, Inovio Pharmaceuticals, Inc.

Inovio's DNA Medicines Platform is suited for multiple prophylactic and therapeutic applications. The platform has demonstrated the ability to generate antigen-specific humoral and cellular immune responses. The versatility of the platform enables prophylactic applications in the infectious disease setting, therapeutic approaches for chronic viral diseases and cancer, and more recently, *in vivo* long-term protein (monoclonal antibody; mAb) expression, which, in addition to prophylactic and therapeutic applications for mAbs, the platform may also be used for protein replacement therapies. Other important features of the DNA Medicines platform are: (1) it has been well-tolerated in approximately 19,000 administrations in ~6,000 participants; (2) it allows rapid plasmid construct, design, and manufacture; (3) it doesn't require frozen storage or shipping (stable for >5 years at 2-8ºC); and, (4) it can be repeatedly re-dosed, due the lack of anti-vector immunity, allowing boosting of immune responses, and, as needed, to boost protein expression.

INO-4201, a Zaire Ebola virus (ZEBOV) vaccine, is composed of plasmid pGX4201 encoding for a synthetic consensus sequence of ZEBOV GP spanning outbreaks from 1976 to 2008. It is administered as a single intradermal injection (0.1 mL) followed by electroporation (EP). It is being studied as a heterologous booster for individuals who have previously received primary immunization with rVSVΔG-ZEBOV-GP (ERVEBO®; Merck). The rVSVΔG-ZEBOV-GP vaccine is highly effective as a primary immunization for protection against ZEBOV. However, rVSVΔG-ZEBOV-GP is not indicated for boosting in individuals who received the vaccine for primary immunization. The World Health Organization's Strategic Advisory Group of Experts on Immunization (SAGE) has noted the lack of data on the benefit–risk of administering more than two doses of rVSVΔG-ZEBOV-GP vaccine. Furthermore, with outbreaks occurring periodically, multiple boosters might be needed during the lifetime of a person. While formal studies regarding repeated booster doses of the rVSVΔG-ZEBOV-GP vaccine have not been undertaken, as a VSV-vectored vaccine, it may not be optimally suited for repeat boosting to maintain long term protection. INO-4201 has been studied as a booster dose for adults who have previously received rVSVΔG-ZEBOV-GP primary immunization ≥ 2 years prior to boosting. The data indicates that, in the INO-4201 boosted individuals, titers were significantly elevated by week 2 and remained elevated through week 24 (the last timepoint collected). INO-4201 was well-tolerated, with the most common adverse event being injection site pruritis (25%). There were no SAEs. Based on the promise of this data, INO-4201 is being studied further for a booster indication.

INO-3107, an HPV-6/HPV-11 vaccine, which is composed of plasmids encoding the HPV-6 and HPV-11 E6/E7 proteins as well as human interleukin-12, is being developed for the treatment of Recurrent Respiratory Papillomatosis (RRP), a rare disease characterized by small, wart-like growths (papillomas) in the respiratory tract. RRP is caused by HPV-6/HPV-11 and surgery is the standard of care. Patients with RRP have an average of four surgical procedures a year to treat the disease. Surgery can irreversibly damage the vocal cords early in the disease course, and patients with severe RRP may require hundreds of surgical interventions over the course of their lifetime. In a Phase 1 / 2 trial, INO-3107 demonstrated promising clinical benefit with 28% complete responders and 44% partial responders, yielding an overall response rate (ORR) of 72% (23/32) and an overall clinical response (OCR) rate of 81% (26/32). INO-3107 induced HPV-6 and HPV-11-specific T-cell responses and drove peripheral T cell clonal expansion. Treatment with INO-3107 was well tolerated in this trial. Twenty patients (62.5%) reported TEAEs . All related TEAEs were Grade 1or 2 in severity, and the most common related TEAE was injection site pain (10 patients); all other related TEAEs were seen in three patients or fewer. In summary, INO-3107 provides clinical benefit to adults with RRP through a reduction in surgeries, is well tolerated, and generates an antigen-specific immune response against HPV types 6 and 11. INO-3107 has received Breakthrough Therapy Designation and Inovio plans to submit a BLA in mid-2025 under FDA's accelerated approval program.

Biography:

Dr. Dave Liebowitz has over 27 years of industry experience in clinical and preclinical development in Oncology, Infectious Diseases (Virology), Vascular Biology, Inflammation and Metabolic Disorders with protein, small molecule, cellular therapeutic, and vaccine modalities. He was previously Senior Vice President, Clinical Development – Infectious Diseases at INOVIO. Prior to returning, Dr. Liebowitz was Senior Vice President, Clinical Development and Medical Affairs at Xencor, leading several immune-oncology programs. Prior to that, Dr. Liebowitz held numerous senior positions, including Chief Medical Officer at DNAtrix, an oncolytic virotherapy company in San Diego, CA; Chief Medical Officer at Vaxart, Inc. and Chief Scientific and Medical Officer for Vivaldi Biosciences, an influenza vaccine and therapeutics biotechnology company.

During his time at Vaxart, Inc., he led the successful application and negotiation process for acquiring a BARDA contract and served as the Principal Investigator of the award, leading its completion. In addition, he was an early recipient of a grant from the Bill and Melinda Gates Foundation.

Dr. Liebowitz began his academic career as an Assistant Professor of Medicine and Virology at the University of Chicago and was the Director of the Bone Marrow Transplantation Program. Dave has B.S. and M.S. degrees in Biology from Emory University, an M.D. with Honors, and a Ph.D. in Molecular Genetics and Cell Biology (Virology), both from the University of Chicago.

Genomic integration of SARS-CoV-2 sequences in virus infected and viral RNA transfected human cells

Rudolf Jaenisch
Whitehead Institute and MIT

SARS-CoV-2 sequences can be reverse-transcribed and integrated into the genomes of virus-infected cells by a LINE1-mediated retrotransposition mechanism. Whole genome sequencing (WGS) methods revealed the footprints of LINE1 mediated retrotransposition (target site duplication, presence of a LINE1 endonuclease recognition consensus sequence and presence of a polyadenylation sequence at the integration site) indicating integration by the well-defined "target-site primed reverse transcription" mechanism (1). We have recently confirmed these results (2). Indirect evidence also indicates that retrotransposition of viral sequences occurs in tissues of virus infected patients. Because virus infection is toxic to the infected cells we were not able to isolate cells with retrotransposed NC RNA copies. In my talk I will summarize new results that extend our published work.

We have established an RNA-based reporter system to study LINE1-mediated retrotransposition. The RNA reporter system enables direct assaying retrotransposition of RNA introduced into cells, and avoids the need to define parameters of RNA production and processing from transfected DNA plasmid used in the classic DNA plasmid reporter assay. We compared retrotransposition of human LINE1 (L1PA1), SARS-CoV-2 Nucleocapsid (NC), GFP and human globin RNA. We found that *in-cis* retrotransposition of LINE1 RNA was 10 to 100-fold more frequent than *in-trans* retrotransposition of the other RNA species, consistent with previous results. The reporter assay showed that SARS-CoV-2 NC subgenomic RNA was retrotransposed by LINE1, validating our previous results in virus-infected cells (1). The 3' UTR sequence of SARS-CoV-2 enhanced *in-trans* retrotransposition of all tested RNA species, suggesting that sequence context of the RNA influences the efficiency of LINE1-mediated retrotransposition. The RNA-based reporter was sensitive and robust as it readily identified not only *in-cis* but also *in-trans* retrotranspositions which were not detected by the DNA-based reporter assay. Thus, the RNA reporter assay provides a useful and sensitive tool for studying LINE1-dependent trans-mobilization of RNA.

1. Zhang L, Richards A, Barrassa MI, Hughes SH, Young RA and Jaenisch R. Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues. Proc. Nat. Acad. Sci. USA **118** (21) e2105968118. (2021). PMCID: PMC8166107
2. Zhang L, Punam B, Flamier A, Barrasa I, Richards A, Hughes S and Jaenisch R. LINE1- mediated reverse transcription and genomic integration of SARS-CoV-2 mRNA detected in virus-infected but not in viral mRNA-transfected cells, Viruses 15, 629, 10.3390/v15030629 (2023)

Biography:

Jaenisch and his lab focus on understanding epigenetic regulation of gene expression (the biological mechanisms that affect how genetic information is converted into cell structures but that don't alter the genes in the process). Jaenisch uses patient-derived induced pluripotent stem cells to develop sophisticated models of conditions, such as Alzheimer's disease and diabetes. The lab is also investigating epigenetic mechanisms for certain types of cancer and for brain development, studying how conditions such as Rett Syndrome occur. This work has led to major advances in our understanding of embryonic stem cells and induced pluripotent stem (IPS) cells, which appear identical to embryonic stem cells but can be created from adult cells without using an egg. IPS cells offer major promise for use in regenerative medicine, potentially supporting the growth of healthy cells and tissues derived from a patient's own cells.

Most recently, Jaenisch and his lab have focused on the biology of SARS-CoV-2. The lab showed that SARS-CoV-2 sequences can be reverse-transcribed and integrated into the genomes of virus-infected cells by a LINE1-mediated retrotransposition mechanism. This could explain the frequent finding that patients show high titers of infectious virus in the first 10 days after infections but often for many months remain positive for viral RNA by PCR in the absence of detectable virus. The lab has developed a sensitive assay for identifying integration of transfected viral RNA, an assay they will use to detect possible integration of vaccine RNA.

SCIENTIA MEETINGS

VACCINES 2024

Day 1: November 13, 2024

Poster Presentations

VACCINES SUMMIT-2024

NOVEMBER 13-15, 2024
BOSTON, MA

SCIENTIA MEETINGS
Website: https://scientiameetings.com/conferences/vaccines/ | Ph: 1-815-595-8049 | Email: venky@sciresgroup.net

Poster Presentations

Title: **Characterization and comparison of immunity against MPXV for individuals infected with MPXV or vaccinated with modified vaccinia Ankara vaccines**
Aurelie Wiedemann
INSERM/VRI

Title: **Conjugated pneumococcal vaccination yields broadly functional, mucosal-directed responses in aged adults**
Qixin Wang
Ragon Institute of MGH
MIT and Harvard

Title: **Monovalent XBB.1.5 mRNA vaccine recalls a more durable and coordinated antibody response to SARS-CoV-2 spike than the bivalent WT/BA.5 mRNA vaccine**
Ryan McNamara
Harvard T. H. Chan School of Public Health

Title: **Development of a Marburg self-amplifying mRNA-lipid nanoparticle vaccine: differential immune responses when co-formulated with toll-like receptor agonists**
Erik de Leeuw
Labcorp

Characterization and comparison of immunity against MPXV for individuals infected with MPXV or vaccinated with modified vaccinia Ankara vaccines

Aurélie Wiedemann[1,2¥], Mathieu Surénaud[1,2¥], Mathieu Hubert[3], José-Luis Lopez Zaragoza[4], Alexandre Ribeiro[1,2], Cécile Rodrigues[1,2], Emile Foucat[1,2], Harouna Diombera[1,4], Corinne Krief[1,2], Olivier Schwartz[1,3], Jean-Daniel Lelièvre[1,2,4], and Yves Lévy[1,2,4*]

[1]Vaccine Research Institute, Université Paris-Est Créteil, France
[2]INSERM U955, Institut Mondor de Recherche Biomedicale (IMRB), Team Lévy, Créteil, France
[3]Institut Pasteur, Université Paris Cité, Virus and Immunity Unit, CNRS UMR3569, 75015 Paris, France
[4]Assistance Publique-Hôpitaux de Paris, Groupe Henri-Mondor Albert-Chenevier, Service Immunologie Clinique, Créteil, France

The 2022 monkeypox virus (MPXV) outbreak has revitalized questions about immunity against MPXV and vaccinia-based vaccines (VAC-V), but studies are limited. We analyzed immunity against MPXV in individuals infected with MPXV or vaccinated with the licensed modified vaccinia Ankara vaccine (MVA)-BN or an experimental MVA-HIVB vaccine. The frequency of neutralizing antibody (NAb) responders was higher among MPXV-infected individuals than MVA vaccinees. Both MVA vaccines induced similar and strong humoral responses. Similarly, we show a higher frequency and magnitude (5-fold) of T-cell responses, mainly mediated by CD8+ T cells, against a peptide pool containing selected sequences from MPXV, Variola, and VAC-V in MPXV-infected individuals than MVA vaccinees. We describe a hierarchy of cross-reactive T-cell responses against five peptide pools that are highly homologous between VAC-V and MPXV 2022, with the highest frequency of responders against MVA-121L and MVA-018L proteins. Both vaccines stimulated a notable frequency of polyfunctional CD4+ and CD8+ T-cell responses, with a subset of CD4+ T cells showing a mixed cytokine profile. Finally, we found that smallpox vaccination in childhood positively affected humoral but not T-cell vaccine responses, whereas these responses were not affected in people living with HIV. These findings contribute to deciphering and monitoring the profile of immunity to MPXV and MVA. In the context of a potential threat of the reemergence of smallpox following bioterrorism, the diversification and availability of potent vaccines is crucial. The comparable immunogenicity of both MVA vaccines emphasizes the potential utility of MVA-HIVB as a valuable new tool for controlling MPXV outbreaks.

Biography:

Dr. Aurelie Wiedemann is a Senior Scientist at the Vaccine Research Institute (VRI)/INSERM in Paris, France. Specializing in immunology, she leads the Cellular Division at VRI, where she evaluates immune cellular responses among participants in vaccine clinical trials and cohorts of infected patients. Dr. Wiedemann also spearheads the coordination of multiple clinical trials spanning Europe and Africa.

Conjugated pneumococcal vaccination yields broadly functional, mucosal-directed responses in aged adults

Qixin Wang[1], Ross Blanc[1], Kate S. Levine[1], Hadar Malca[1], Lindsay R. Grant[2], Ashley Miller[2], Bradford D. Gessner[2], and Ryan P. McNamara[1]
[1]Ragon Institute of Mass General, MIT, and Harvard. Cambridge, MA, 02139, USA. [2]Pfizer, Inc., Collegeville, PA, 19426, USA

Streptococcus pneumoniae (*S. pneumoniae*) is a respiratory pathogen that can cause severe pneumonia, particularly in infants and older persons that have become immunosenescent. To characterize mechanisms of protection afforded by the 13-valent conjugated (13vPnC) or 23-valent pneumococcal polysaccharide (23vPS) vaccines, we applied systems serology to deeply profile antibody responses against select serotypes (1, 3, 6A, 6B, 7F, 19A, 19F, and 23F). These responses included Fab binding antibody titers, Fc-receptor binding antibody titers, and antibody-dependent-complement deposition (ADCD), -cellular phagocytosis (ADCP), and -neutrophil phagocytosis (ADNP) against the selected *S. pneumoniae* antigens in older adults prior to vaccination and 1-, 12-, and 42-months post-vaccination with either 13vPnC or 23vPS. Antibody responses between the two treatment arms diverged as early as 1-month post-vaccination, and multivariate signatures of humoral output retained separation up to 12-months post-vaccination. At the 1-month post-vaccination, 13vPnC yielded overall higher IgG and IgA binding levels and ADCD than 23vPS, especially with significant differences against serotype 6A. At 12-months post-vaccination, the *S. pneumoniae* serotypes 1, 6A, 6B, and 7F were targeted by both IgA and IgG mediated ADCD function induced by 13vPnC, while only serotype 7F was targeted by both mechanisms induced by 23vPS. At 42-months post-vaccination, correlations between IgA and ADCD remained against serotypes 1 and 6B for 13vPnC vaccinees; whereas, no correlations persisted at this time point for any serotypes between IgA and ADCD among those vaccinated with 23vPS. In conclusion, 13vPnC provided more complete humoral responses to serotypes at 12- and 42-months post-vaccination. Moreover, 13vPnC appears to skew class-switching/recall responses to IgA, the primary antibody subclass at the mucosal surface.

Monovalent XBB.1.5 mRNA vaccine recalls a more durable and coordinated antibody response to SARS-CoV-2 spike than the bivalent WT/BA.5 mRNA vaccine

Susanna E. Barouch[1,3], Kate S. Levine[1,3], Ross Blanc[1], Qixin Wang[1], Xin Tong[1], and Ryan P. McNamara[1,2,4,*]
[1]Ragon Institute of Mass General, MIT, and Harvard. Cambridge, Massachusetts, United States of America
[2]Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, United States of America
[3]These authors contributed equally to this work
[4]Lead author
*Correspondence: rpmcnamara@mgh.harvard.edu

In the fall of 2023, the monovalent XBB.1.5 mRNA vaccine for COVID-19 became available. However, the comparative magnitude, durability, and functionality of antibody responses induced by the XBB.1.5 vaccine compared with the 2022-2023 bivalent wildtype (WT) + Omicron BA.5 vaccine remains to be fully determined. In this study, we compared antibody profiles generated by these two vaccines in healthcare workers. We show that the monovalent XBB.1.5 vaccine induced higher magnitude binding, neutralizing, and Fc-gamma receptor (FcgR) binding antibodies to the XBB.1.5 spike compared with the bivalent vaccine against the WT and BA.5 spikes, both at both peak immunogenicity and at 6 months post-vaccination. Moreover, antibody interaction architectures and correlations remained more robust at 6 months post-vaccination with the XBB.1.5 vaccine, whereas these correlations were largely lost at 6 months with the bivalent vaccine. Our results suggest that the XBB.1.5 vaccine led to a more durable and functionally coordinated antibody response compared to the bivalent vaccine.

Development of a Marburg self-amplifying mRNA-lipid nanoparticle vaccine: differential immune responses when co-formulated with toll-like receptor agonists.

Anas Tomeh, Gillian Hoover, Sarah Horst, Erik de Leeuw, Murty Chengalvala & Allan Watkinson
Labcorp

Self-amplifying RNA (sa mRNA) formulated in lipid nanoparticles (LNPs) is an innovative vaccine modality and is being used to develop a Marburg Virus vaccine comprising the Marburg Virus Glycoprotein (MARV GP) sa mRNA. Toll-like Receptor (TLR) agonists, which boost the innate immune response, have been used as adjuvants in subunit vaccines; however, it is uncertain as to whether these TLR agonists will provide adjuvanticity with the mRNA-LNP vaccines. To test the role of the TLR agonists, we have formulated MARV GP sa mRNA-LNPs encapsulating a CpG oligonucleotide (TLR 9 agonist), Telratolimod (TLR7 agonist) and Monophosphoryl-lipid A (MPLA) (TLR 4 agonist). Formulation development was performed to optimize the critical quality attributes (CQAs) of particle size (<150nm), polydispersity index (PDI)(<0.2), TLR agonist %encapsulation efficiency (%EE) (>80%) and sa mRNA %EE (>90%). Empty LNPs and MARV GP sa mRNA-LNPs were also formulated as controls. Morphology analysis was performed on each formulation using cryoEM. Each formulation was tested for immunogenicity in BALBc mice with an immunization and boost regimen (T=0 and T=d21). On day 35 the mice were euthanized, and blood and spleen samples were taken. Anti-MARV GP IgG was measured by ELISA as was the IgG1/IgG2a ratio. Additionally, T-cell responses were determined using isolated splenocytes and a IFNγ/IL-5 ELISpot assay. At 0.2ug sa mRNA dose, the control MARV GP sa mRNA-LNP demonstrated a strong anti-MARV GP IgG response. Interestingly, this was significantly inhibited by the presence of the CpG TLR9 agonist and the Telratolimod TLR7 agonist. In contrast, the MPLA TLR4 agonist, significantly boosted the IgG response compared to the agonist free control. The IgG1/IgG2a ratio indicated that the MPLA converted a generally Th1 response to one more representative of Th2. ELISpot analysis of the T-cell response revealed that each of the TLR agonists inhibited IFNγ+ cells compared to the MARV GP sa mRNA agonist free control. The inhibition was particularly evident with Telratolimod TLR7 agonist, with levels equivalent to the naïve control. With the IL-5 T-cell response, the MARV GP sa mRNA agonist free control was equivalent to the naïve control and inhibited with the TLR agonist. Overall, the data showed that the MARV GP sa mRNA-LNP vaccine was effective at inducing a B- and T-cell response. In contrast, the co-presentation with TLR 7 agonists had an inhibitory effect, except for the MPLA formulation, which boosted anti-MARV GP IgG responses in a Th2 manner.

SCIENTIA MEETINGS

VACCINES 2024

Day 2: November 14, 2024

Conjugate Vaccine

VACCINES SUMMIT-2024

NOVEMBER 13-15, 2024
BOSTON, MA

Conjugate vaccine

Session Chair: **Andrew Lees**
CEO/CSO, Fina Biosolutions

Session Co-Chair: **Robert van der Put**
Director Business Development, Intravacc

Title: **Overview of conjugate vaccines and conjugate vaccine development**
Andrew Lees
CEO/CSO
Fina Biosolutions

Title: **Turbo: an adjuvant platform for bacterial glycoconjugate vaccines**
Kishore Alugupalli
Founder & Chief Executive Officer
TurboVax Inc

Title: **Data in the target population for a *Shigella* flexneri 2a glycoconjugate support the development of a broad serotype coverage synthetic glycan-based vaccine candidate for shigellosis**
Laurence A. Mulard
Institut Pasteur

Title: **Development of the first quadrivalent synthetic oligosaccharide-based conjugate vaccine against *Shigella***
Fiona Lin
Vaccine Process Development and Manufacturing Lead
GATES MRI

Title: **A modular vaccine platform for prophylactic and therapeutic vaccines: exogeneous decoration of bacterial outer membrane vesicles with synthetic peptide antigens**
Robert van der Put
Director Business Development, Intravacc

Title: **Design of a glycoconjugate vaccine against *Salmonella* Paratyphi A**
Renzo Alfini
Senior Scientist
GVGH Preclinical – Vaccine Chemistry
GSK Vaccines Institute for the Global Health

Title: **Study of CDAP chemistry as generic conjugation for development of glycoconjugate vaccines**
Carlo Giannelli
Lab Head Vaccine Chemistry
GSK Vaccines Institute for the Global Health

Title: ***In vivo* polysaccharide protein conjugation using *E. coli* as host with a next generation conjugating enzyme system**
Christian Harding
Omniose

Title: **The fentanyl epidemic: costs, currency, and who pays the check**
Shon Remich
Chief Medical Officer
Ovax

Title: **Heroin and fentanyl vaccines adjuvanted with army liposome formulation**
Gary R. Matyas
Chief
Adjuvants and Formulation
US Military HIV Research Program, Walter Reed Army Institute of Research

Overview of conjugate vaccines and conjugate vaccine development

Andrew Lees
Fina Biosolutions LLC, Rockville MD 20850. USA

Protein-polysaccharide vaccines are highly protective but remain complex to manufacture and are expensive. Since the first conjugate vaccine for Hib was licensed in 1987, conjugate vaccines of increasing valency for *S. pneumoniae* and *N. meningitidis* have been introduced as part of routine childhood vaccination. In addition to infectious diseases, conjugate vaccines addressing diverse indications are in development. In this talk, I will introduce topics covered in the Vaccines Summit Conjugate Vaccine Agenda, provide an overview of conjugate vaccine chemistry and carrier proteins, and discuss developing conjugate vaccines. In addition, I will present Fina Biosolutions' efforts to make conjugate vaccines more affordable through better chemistry and more affordable carrier proteins. We have sought to make conjugation know-how more accessible and increase carrier protein availability. Advancements in applying CDAP chemistry to polysaccharide activation have made this chemistry easier to use. Our EcoCRM®(CRM_{197}) has driven down the cost of this widely used carrier protein. We have introduced 8MTT, the first commercially available, full-length genetically detoxified tetanus toxin, and we have just introduced site-specific 3rd generation click chemistry that is commercially available.

Biography:

Andrew Lees is the founder and CEO of Fina Biosolutions LLC (Rockville, MD), a company focused on promoting affordable conjugate vaccines by making the technology available to emerging market vaccine manufacturers. Among his contributions in the field, Andrew developed an efficient linking chemistry that is widely used in conjugate vaccines, a class that includes vaccines for S. pneumoniae and meningococcal disease. The chemistry has helped to reduce the cost of these vaccines. Andrew is also an adjunct professor at the University of Maryland School of Medicine Center for Vaccine Development, the Uniformed Services University, Dept. of Medicine, and the University of Toledo, Dept of Chemistry. He has over 75 publications and 25 patents, mainly in the area of conjugate vaccines. Andrew received his BS in chemistry from Harvey Mudd College (1976) and his Ph.D. in Biophysics from Johns Hopkins (1984). Honors include the Uniformed Services Meritorious Service Award, the Harvey Mudd College Outstanding Alumni Award, the Johns Hopkins Distinguished Alumni Award, and the American Chemical Society Horton Award for Outstanding Contributions to Industrial Carbohydrate Chemistry. On graduating from Hopkins, he was on the cover of Baltimore Magazine as one of "84 people to watch in '84" due to his role as a leading Baltimore area magician.

Turbo: an adjuvant platform for bacterial glycoconjugate vaccines

Kishore R. Alugupalli, PhD
CEO, TurboVax Inc.

Activation of the adaptive immune system requires the engagement of co-stimulatory pathways in addition to the primary B or T cell antigen receptor signaling, and adjuvants play a central role in this process. Despite of the importance of this fundamental immunological tenet, surprisingly many bacterial polysaccharide subunit vaccines do not incorporate adjuvants (PMID: 35118012). As expected, such vaccines induce suboptimal antibody responses and require multiple boosters, particularly in infants. We found that the presence of endotoxin, a Toll-Like Receptor (TLR) 4 ligand in the typhoid Vi polysaccharide and Vi polysaccharide-conjugate vaccine accounts for their immunogenicity (PMID: 38180344). Consistent with this, we have previously shown that coordinated signaling by B cell antigen receptor and TLR is required for antibody production and long-lasting immunity (PMID: 15357949; PMID: 17339472). Based on these rationales, we developed a safe and non-toxic TLR4, or TLR2 ligand-based liposome formulations called Turbo, as an adjuvant for glycoconjugate vaccines (PCT WO 2024/124052 A1).

The adjuvanticity of Turbo was rigorously tested using both inbred and outbred mice of all ages. We found that admixing Turbo to FDA-approved or WHO-prequalified typhoid vaccines e.g. TyphimVi and Typbar TCV, and multivalent meningococcal vaccines e.g. MENVEO and MenQuadfi promotes robust antibody responses across all ages and eliminates or minimizes the need for boosters (PMID: 38799439; PMID: 38625118). In contrast to the commonly used adjuvant alum, Turbo promoted affinity maturation and class switching of all four IgG isotypes, and the magnitude of all these IgG responses was sustained for one year, accompanied by the presence of long-lived plasma cells homing to bone marrow. Unlike alum Turbo adjuvanticity is not dependent on canonical or non-canonical inflammasome activation and pyroptosis, an inflammatory cell death rather than immune cell survival. As expected, Turbo adjuvanticity is dependent mainly on the MyD88, an adaptor protein required for TLR2 and TLR4 signaling. Turbo upregulated the expression of the co-stimulatory molecules CD40 and CD86 on B cells and Turbo-driven adjuvanticity is lost in mice deficient in CD40 or CD86, indicating that Turbo drives by activating the required co-stimulatory pathway (PMID: 38625118). The effector function of an antibody is dependent on its isotype and the control of a given bacterial pathogen is based on the isotype of the IgG produced by the vaccine. Therefore, the incorporation of Turbo as an adjuvant in polysaccharide or glycoconjugate vaccines will generate a wide range of complement and Fc receptor-mediated protective mechanisms and will make Turbo-adjuvanted vaccines highly immunogenic and efficacious.

Biography:

Dr. Kishore Alugupalli PhD did his undergraduate studies in India, post-baccalaureate training in Hungary and PhD at the Lund University, Sweden. Following post-doctoral training at UMASS Medical School, Worcester, USA, Dr. Alugupalli became Research Assistant Professor at the same institution. During this time, driven by an idea that "the quality control of our understanding on immune responses cannot be intellectual seduction but should be protection against infections", Dr. Alugupalli focused his entire academic research on the "What is missing in immunology to understand Immunity". Dr. Alugupalli discovered the function of B1b cells, a subset of B lymphocytes that can generate long-lasting immunity. This discovery led to the identification for pathways and parameters crucial for immunological memory, a key aspect for making effective and safe subunit vaccines that can provide durable immunity. In 2005, he accepted a tenure-track faculty position in the department of Microbiology and immunology, Thomas Jefferson University, Philadelphia. At the Thomas Jefferson University he served as the Director of the Immunology and Microbial Pathogenesis PhD program and became the Immunology Director of the PharmD program at the Jefferson College of Pharmacy. His 20 years of academic research was continuously funded by the National Institutes of Health. With a focused goal of making efficient and cost-effective bacterial subunit vaccines, in 2023 Dr. Alugupalli founded TurboVax Inc, a Delaware C-corporation and left academia and became the full-time CEO of TurboVax Inc to dedicate his time on a goal to minimize the threat of antimicrobial resistance, and the reduce bacterial disease burden globally. TurboVax Inc is interested in commercialization of an indispensable and path-breaking vaccine adjuvant named Turbo for glycoconjugate subunit vaccines. Bacterial polysaccharide or glycoconjugate subunit vaccines when adjuvanted with Turbo induces long-lasting and highly protective immune responses across all ages and eliminates the need for boosters. By partnering with Vaccine developers, TurboVax Inc will help prevent a wide range of bacterial infections.

Data in the target population for a *Shigella* flexneri 2a glycoconjugate support the development of a broad serotype coverage synthetic glycan-based vaccine candidate for shigellosis

Laurence A. Mulard, Ph.D
Institut Pasteur

The burden caused by endemic shigellosis calls for a *Shigella* vaccine that would induce broad serotype protection especially in children under five from low- and middle-income countries. Protective immunity is believed to be achieved to a major extent by antibodies targeting the O-antigen (O-Ag) moiety of the *Shigella* lipopolysaccharide. A multidisciplinary strategy aimed at vaccine candidates encompassing well-defined synthetic glycans mimicking the putative protective determinants carried by the O-Ag of selected *Shigella* serotypes has led to SF2a-TT15, a glycoconjugate designed to help protect against *S. flexneri* 2a.

In a first-in-human clinical trial run in Israel, SF2a-TT15 was demonstrated to be well tolerated and immunogenic in healthy adult volunteers. The induced immune response was sustained in magnitude and functionality in the majority of volunteers followed for two and up to three years post-vaccination.

A phase 2a age-descending study was set up in Kenya to assess the safety and immunogenicity of SF2a-TT15 against *S. flexneri* 2a in adults, children and infants. Safety and immunogenicity data were obtained for 200 9-month-old infants randomized into four arms to test two vaccine dosages with or without adjuvant, including placebo recipients.

Promising clinical data for SF2a-TT15 in the target population support further development toward a *Shigella* synthetic glycan-based conjugate vaccine candidate fulfilling chemical feasibility, strain coverage and immunogenicity criteria. The successful strategy was thus extended to other prevalent serotypes of interest. A quadrivalent Shigella vaccine candidate that could provide broad protection against circulating pathogenic strains was achieved and delivered thanks to promising pre-clinical data.

Biography:

Laurence A. Mulard graduated as an engineer (ESPCI, Paris, France). She obtained her PhD in Chemistry (UPMC, France). After postdoctoral studies at NIH (MD, USA), she joined the Institut Pasteur, where she was appointed Head of the Chemistry of Biomolecules Unit. Her research interests deal with the development of chemical tools and bioactive compounds aimed at interfering with molecular phenomena governing infectious diseases. Focus is on advancing conjugate vaccine development against diarrheal diseases. A first *Shigella* synthetic glycan-based vaccine developed in her group was demonstrated safe and immunogenic in the target population, enabling a promising quadrivalent *Shigella* vaccine candidate.

Development of the first quadrivalent synthetic oligosaccharide-based conjugate vaccine against *Shigella*

Fiona Lin, Ph.D
Vaccine Process Development and Manufacturing Lead at the Gates Medical Research Institute (GMRI)

In this presentation we will provide an overview of the process development, optimization, and the GMP production of four synthetic oligosaccharide-carrier protein conjugates, components of a quadrivalent vaccine candidate for *Shigella*. This work was a collaboration between Gates MRI and Institut Pasteur to develop an efficacious *Shigella* vaccine with broad coverage for infants under 5 years of age in low-and-middle income countries (LMICs). The proposed quadrivalent *Shigella* vaccine composition includes synthetic oligosaccharide components acting as surrogates of the heterogeneous *Shigella* surface polysaccharide antigens characteristic of serotypes *S. flexneri* 2a, *S. flexneri* 3a, *S. flexneri* 6, and *S. sonnei.* Unlike traditional glycoconjugate vaccines where the carbohydrate component is typically derived from bacterial cell wall components, the carbohydrates of the subject oligosaccharide conjugates are made entirely by chemical synthesis, and the conjugation to a carrier protein is also done via chemical reactions. As such, high level of control in the structures of the oligosaccharide haptens and the degree of conjugation was achievable, allowing better characterization of this type of complex products compared to traditional polysaccharide glycoconjugate vaccines. We will highlight some challenges encountered, key considerations for this unique approach, and provide a high-level cost of goods assessment to demonstrate the feasibility of a commercially viable product suitable for LMICs. Immunogenicity studies in preclinical animal models using the quadrivalent vaccine formulations demonstrate robust immune responses elicited by these glycoconjugates. These quadrivalent vaccine formulations represent the first multivalent glycoconjugate vaccine candidate based on fully synthetic oligosaccharide haptens with strong potential for clinical efficacy against *Shigella*.

Biography:

Fiona Lin is a Vaccine Process Development and Manufacturing Lead at the Gates Medical Research Institute (GMRI). She obtained her Ph.D. in Chemistry from UC-Berkeley under the guidance of Prof. Carolyn Bertozzi, 2022 Nobel Laureate, focusing on bioorthogonal chemistry and carbohydrate synthesis and characterization. She has spent more than 15 years in the biopharma industry working in CMC functions, primarily in analytical development and quality control, and supported therapeutic modalities including conjugate vaccines, proteins/peptides, RNAs, small molecules. She has contributed to the development of licensed vaccines including Prevnar 20™ and Penbraya™, and several investigational vaccine candidates (anti-nicotine, Group B Streptococcal, high-valent Pneumococcal, Tb, and malaria).

A modular vaccine platform for prophylactic and therapeutic vaccines: exogeneous decoration of bacterial outer membrane vesicles with synthetic peptide antigens

Robert van der Put, Ph.D
Director Business Development, Intravacc

Pandemics cause significant social instability and millions of deaths. It is necessary to be prepared for such events in the future. Accelerating vaccine development is one means of addressing pandemic preparedness. Vaccines have a valuable role in the protection against infectious diseases. Accelerated vaccine development based on well-established platforms is an approach that could be useful. For example, conjugate vaccines can be tailored towards highly specific antigens and can be developed quickly. In this study, we determined the feasibility of using outer membrane vesicles (OMVs) as carriers of a conjugated vaccine antigen and we developed an upscaled GMP production process. A SARS-CoV-2 peptide that was designed and synthetically produced was used as the antigen. This report provides information on the characterization of OMVs before and after antigen conjugation and on approaches that improve the conjugation to the OMVs. While initially 2.1 µg of peptides was conjugated to OMVs, after a design of experiments (DoE) 7.5 µg of peptides was conjugated to 25 µg OMV. Furthermore, the process was successfully upscaled 2000-fold using a GMP-qualified reactor. Finally, the OMV-conjugated peptide product was evaluated in a stability study. This production platform is likely to be a valuable tool for rapid development of new vaccines.

Biography:

Robert van der Put holds both a PhD in conjugate vaccine development and a master's degree in drug innovation and has over 20 years of experience in the vaccine industry. He is a passionate and driven Director of Business Development at Intravacc, a leading institute for translational vaccinology. His mission is to advance the development and production of safe and effective vaccines for global health, by leveraging his expertise in conjugate vaccine development, process optimization, quality control, and technology transfer.

Design of a glycoconjugate vaccine against *Salmonella* Paratyphi A

Renzo Alfini*, Martina Carducci, Luisa Massai, Daniele De Simone, Marco Mariti, Omar Rossi, Simona Rondini, Francesca Micoli, Carlo Giannelli
Senior Scientist, GVGH Preclinical – Vaccine Chemistry, GSK Vaccines Institute for the Global Health

S. Typhi and Paratyphi A together are responsible for over 13 million cases and 133 thousand deaths per year, most of which occur in children in South and South-East Asia. After the successful development of a Typhoid Conjugate Vaccine (TCV), which is manufactured by Biological E in India and was WHO prequalified in 2020, we are attempting to broaden its coverage by incorporating the *S.* Paratyphi A component.

Here we describe the development of the glycoconjugate vaccine obtained by linking the serovar-specific O-antigen (O:2) to CRM_{197} carrier protein (O:2-CRM_{197}). A random approach was preferred to a selective chemistry to generate the conjugate, based on simplicity of manufacturing and stability data collected. Then we investigated the impact of potential critical quality attributes. The preclinical data collected allowed to define which parameters are most appropriate for an immunogenic O:2-CRM_{197} conjugate, supporting the optimal design of a Paratyphi A glycoconjugate component to be combined with TCV in a bivalent formulation against enteric fever.

Biography:

Renzo Alfini PhD in chemistry awarded at the University of Florence, Italy, in 2010. Since 2013 working in the field of vaccines as a scientist and senior scientist, focusing his research on the development of vaccines against neglected diseases (e.g., Salmonella Typhi, Salmonella Paratyphi A, non-typhoidal Salmonella, Shigella, Group A Streptococcus, and klebsiella pneumonia) in GSK Vaccines Institute for Global Health (GVGH, Siena, Italy). The expertise is related to the synthesis, purification, and characterization of glycoconjugates and outer membrane vesicles (OMV), investigating different platforms and innovative technologies applied to glycoconjugation, Generalised Modules for Membrane Antigens (GMMA), Multiple Antigen-Presenting Systems (MAPS) and recombinant protein.

Study of CDAP chemistry as generic conjugation for development of glycoconjugate vaccines

Rebecca Nappini[a,b], Renzo Alfini[b], Salvatore Durante[b], Maria Michelina Raso[b], Elena Palmieri[b], Roberta Di Benedetto[b], Martina Carducci[b], Omar Rossi[b], Paola Cescutti[b], Francesca Micoli[b], Carlo Giannelli[b]
[a] Università delgi studi di Trieste, Dipartimento di Scienze della Vita, Trieste, Italy
[b]GSK Vaccines Institute for Global Health (GVGH), Siena, Italy

Glycoconjugation is a well-established technology for vaccine development: linkage of the polysaccharide (PS) antigen to an appropriate carrier protein allows to overcome the limitations of PS T-independent antigens, making them effective in infants and providing immunological memory. Glycoconjugate vaccines have been successful in reducing the burden of different diseases globally; however many diseases still remain to be controlled and alarming concern is emerging toward antibiotic resistant bacteria. Considering the variety of glycan antigens displayed on the surface of the pathogens for which vaccines are still not available, high-valency glycoconjugate vaccines need to be developed.

CDAP chemistry was identified with the aim to develop a generic conjugation strategy that can be easily applied to PS having different structures. This chemistry works with hydroxyl groups on the PS and amino groups on the protein, moieties that are common to a large range of PS and all proteins[1]. Here new fast analytical tools to study the reaction have been developed and, starting from a published procedure[2,3], reaction conditions for PS activation and conjugation have been extensively investigated. Mathematical models have been built to identify reaction conditions to generate conjugates with preferred characteristics and successfully applied to a large number of bacterial PS from different pathogens, e.g., *Klebsiella pneumoniae*, *Salmonella* Paratyphi A, *Salmonella* Enteritidis, *Salmonella* Typhimurium, *Shigella sonnei* and *Shigella flexneri*.

Furthermore, using *Salmonella* Paratyphi A O-antigen and CRM_{197} as models, a Design of Experiments approach has been used to study the impact of conjugation conditions and conjugate features on the immunogenicity in rabbit, and identify conjugate critical quality attributes and optimal design for an effective vaccine candidate. The approach used can be rapidly extended to other PS and accelerate the development of high-valency glycoconjugate vaccines.

Biography:

Carlo Giannelli. PhD in industrial organic chemistry awarded at the University of Florence, Italy, in 2004. From 2009 working in the field of vaccines, focusing his research on the development of vaccines for neglected diseases. Involved in the development of vaccines against *Salmonella* Typhi, *Salmonella* Paratyphi A, non-typhoidal *Salmonella*, *Shigella*, Group A Streptococcus and *klebsiella pneumoniae*. Analytical lab head at GVGH from 2009 to 2021, working on the characterization and stability of drug substances and drug products based on three main platforms: glycoconjugation, Generalised Modules for Membrane Antigens (GMMA) and recombinant protein. Six Sigma Green Belt certification obtained in 2018 and Black Belt in 2021.

From 2021, Vaccine Chemistry lab Head working on design and development of glycoconjugates, Multiple Antigen-Presenting Systems (MAPS) and Nanoparticle based vaccines.

Author of 30 scientific publications and two patent applications.

In vivo polysaccharide protein conjugation using *E. coli* as host with a next generation conjugating enzyme system

Cory Knoot[1], Lloyd Robinson[1], Rachel Edwards[1], Jenna McGuffey[1], Isra Darwech[1], Paeton Wantuch[2], David Rosen[2], and Christian Harding[*1]
[1]Omniose, Saint Louis, MO, USA
[2]Washington University School of Medicine, Saint Louis, MO, USA

In vivo polysaccharide protein conjugation is an enzymatic process used to generate conjugate vaccines whereby an oligosaccharyltransferase attaches a polysaccharide to a carrier protein. Recently, *in vivo* conjugation technologies have emerged as commercially viable alternative manufacturing processes for conjugate vaccine production. Although *in vivo* conjugation has been commercially adopted, only two oligosaccharyltransferases, PglB and PglL, are currently employed at the industrial level. Given the diversity of bacterial glycosylation systems, we hypothesized that new, uncharacterized oligosaccharyltransferases may exist. Here, we present on the characterization and use of a novel O-linked oligosaccharyltransferase, termed PglS, to produce next-generation bioconjugate vaccines *in vivo.* Using *E. coli* models for heterologous glycosylation, we demonstrate that PglS can glycosylate multiple carrier proteins engineered to contain small 23 amino acid GlycoTags (also known as sequons) with a diverse array of bacterial polysaccharides. Moreover, we demonstrate that PglS transfers polysaccharides previously shown to be incompatible with other *in vivo* conjugation technologies due to the limited substrate specificities of those conjugating enzymes. These findings have opened the door for next generation bioconjugate vaccines against bacteria like *Klebsiella pneumoniae* and Group B Streptococcus (GBS). Specifically, we show that *K. pneumoniae* capsule-based bioconjugate vaccines are highly immunogenic, eliciting potent serotype specific immune responses that mediate functional protection. Additionally, we show that the Omniose bioconjugation platform has been successfully engineered to produce a decavalent, pan-serotype GBS capsular polysaccharide bioconjugate vaccine with 100% retention of sialic acid residues, which are vital for eliciting antibody responses that mediate opsonophagocytic killing.

Biography:

Dr. Harding received his undergraduate B.S. in Biology from the College of Charleston in 2009 and his Ph.D. in Biomedical Sciences with an emphasis in Microbial Pathogenesis from the Ohio State University in 2015. Subsequently, he went on to complete a postdoctoral fellowship in the laboratory of Dr. Mario F. Feldman located in the Department of Molecular Microbiology at Washington University School of Medicine, St. Louis. After his fellowship, Dr. Harding became the primary founder of VaxNewMo LLC (doing business as Omniose) dating back to 2016. Since then, he has established multiple R&D programs developing polysaccharide-protein conjugate vaccines targeting bacterial pathogens with unmet medical need. He is the main innovator and driver for all Omniose research activities, including its bioconjugation platform. Currently, he leads a team of 16 scientists focusing on bacterial vaccine development. Over the last eight years, Dr. Harding has refined Omniose's bioconjugation technology for use in developing bioconjugate vaccines against multiple bacterial targets, including, Streptococcus pneumoniae, Group B Streptococcus and Klebsiella pneumoniae. He has devised seven awarded NIH SBIR/STTR grants totaling more than $11 million USD in non-dilutive funding. The refinements and improvements to the Omniose bioconjugation platform developed under his leadership culminated in a three-year exclusive, strategic research collaboration with AstraZeneca starting in Q1 of 2024.

The fentanyl epidemic: costs, currency, and who pays the check

Shon Remich
Chief Medical Officer, Ovax

Fentanyl is a synthetic opioid that is up to 100 times more potent than morphine and significantly stronger than heroin. It was originally developed in the 1960s for pain management and is still used medically for the treatment of severe pain. However, illegal production and distribution of fentanyl have led to a nationwide opioid crisis, often referred to as the fentanyl epidemic. Verified data from CDC reported over 124,000 deaths due to opioid poisoning from 2020 to 2022 with an age adjusted rate average of 34.2/100,000 persons. More than 88% of these deaths were due to illegally produced Fentanyl over the same period (>109,000 deaths). Less than 37% of all overdose deaths in the same time period were among individuals with a history of opioid use, and less than 8% were among individuals who recently returned to opioid use. Alarmingly, over 67% of all deaths from overdose between 2020-2022 had 1 or more potential opportunities for intervention prior to their death (despite the approval of Naloxone in 2015). Recently, provisional counts of the number of deaths over the past 12 month period ending April 2024 have declined significantly constituting a hopeful trend. Naloxone, is an effective antidote to opioid death, however, the number of deaths due to fentanyl poisoning despite substantial investments and aggressive access and educational programs remains unacceptable. An effective prospective treatment method could have potentially averted over 67% of the 124,162 opioid poisonings from 2020 to 2021constituting more than 83,000 lives. Death due to Fentanyl poisoning reaches well beyond individuals suffering from addiction and an effective prospective countermeasure would save numerous lives in addition to heavy healthcare and societal resources utilized for the treatment of fentanyl poisoning.

Biography:

Dr. Shon Remich is a passionate physician-scientist who has dedicated more than 25 years of his career to public and global health. He has been at the forefront of some of the largest public health challenges of the last century. During his 23-year military career, he completed board certification in Pediatrics and postdoctoral programs in Clinical Pharmacology (Georgetown/Walter Reed) and Allergy/Immunology (Walter Reed/NIH). He completed two overseas postings in Kenya, totaling eight years, where he directed the clinical development of both drugs (GMP IV artesunate) and vaccines (RTS,S) as countermeasures for malaria. During his second posting, he led the President's Emergency Plan for AIDS Relief (PEPFAR) for the Department of Defense.

Upon returning to the Walter Reed Army Institute of Research (D.C.), he directed the Translational Medicine department and Bioproduction facility and chaired the military's largest Institutional Review Board. As the director of Translational Medicine, his team conducted multiple clinical trials for complex and debilitating diseases (HIV, Anthrax, Malaria, Hantavirus, Plague, Shigella, E. coli, and Influenza), including the first Ebola vaccine (VZV-Ebola) trial in the U.S.

After his military career, he joined Pfizer's clinical development team, supporting the U.S. licensure of the Japanese Encephalitis vaccine (Ticovax) and later played a key role in the development of the nation's first COVID vaccine (Comirnaty). He then joined the vaccine business unit at Takeda to support the EMA approval of Qdenga, a dengue vaccine. After a short time at BioNTech, where he led its latent viral program, Dr. Remich joined a newly formed biotech company, Ovax. Ovax is committed to developing solutions to address the current epidemic and public health emergency related to overdose deaths.

Heroin and fentanyl vaccines adjuvanted with army liposome formulation

Gary R. Matyas*[1], Essie Komla[1,2], Agnieszka Sulima[3], Arthur E. Jacobson[3], Kenner C. Rice[3]
[1]U.S. Military HIV Research Program, Center for Infectious Disease Research, Walter Reed Army Institute of Research
[2]Henry M. Jackson Foundation for the Advancement of Military Medicine
[3]Drug Design and Synthesis Section, Molecular Targets and Medications Discovery Branch, Intramural Research Program, National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Department of Health and Human Services

Opioid use disorder (OUD) and fatal overdose due to consumption of fentanyl-laced drugs are global concerns. Data from the US Centers for Disease Control and Prevention indicate that fatal overdose cases were 97,306 over the last year with 65,787 due to synthetic opioids, predominantly fentanyl and fentanyl derivatives. Although this is a significant decline in deaths from a high of 111,448 in 2023, it still represents overwhelming number of preventable deaths. Currently, 902,000 Americans are using heroin, which in now is laced with fentanyl. The major barrier towards mitigation of opioid use disorder, particularly in the case of fentanyl-laced heroin, remains the unavailability of effective treatment modalities. There are only 3 pharmacotherapies approved to treat OUD including methadone, buprenorphine, and naltrexone or their combinations. Their efficacies are diminished by the availability of more potent fentanyl analogues. This is particularly true with overdose rescue antagonist, naloxone. Current efforts are focused on active immunizations using opioid conjugate vaccines as alternatives or complementary treatment strategies to currently available drugs against OUD. The architecture of conjugate vaccines consists of a hapten, which is a structural analogue of the target drug conjugated to an immunogenic carrier protein, mixed with a potent adjuvant. Our laboratory developed 6-AmHap as a hapten for a heroin vaccine and para-FenHap as a hapten for fentanyl vaccine. The haptens were conjugated to tetanus toxoid (TT) using SM-(PEG)2 linker. Army Liposome Formulation (ALF) containing monophosphoryl lipid A mixed with aluminum hydroxide were used as the adjuvants for mouse and rat studies. The heroin vaccine protected mice and rats from both subcutaneous and intravenous heroin challenge and induced antibodies that cross-reacted with heroin, morphine, and other opioids, but not the therapeutics for OUD. The heroin vaccine had a good safety profile in a GLP rabbit pharmacology-toxicology study and induced antibody endpoint titers ≥1 million. A phase 1 clinical trial of the heroin vaccine will be conducted in the beginning of next year. The fentanyl vaccine protected mice from fentanyl challenge and induced antibodies that cross-reacted with other fentanyl analogs commonly found in confiscated substances of abuse, but not the therapeutics for substance abuse. When combined to form a bivalent vaccine, both heroin's and fentanyl's effects were attenuated in mice models. The binding affinities (K_d) of induced antibodies to heroin and fentanyl from the bivalent vaccine were less than 0.5 nM, demonstrating high affinity antibody production.

Biography:

Dr. Gary Matyas received his Ph.D. in biology from Purdue University and completed his postdoctoral studies at the National Institute Neurological, Communicative Disorders and Stroke at the National Institutes of Health. His postdoctoral research and his Ph.D. studies were centered on the biochemistry and function of glycolipids. In 1988, Dr. Matyas joined the Walter Reed Army Institute of Research as a research chemist in the Department of Membrane Biochemistry, Division of Biochemistry, which later merged with US Military HIV Research Program. The focus of his research was on vaccines for various infectious diseases, using liposome adjuvants and transcutaneous immunization. He has studied liposomes as adjuvants for vaccines, including HIV, malaria, Campylobacter and COVID-19. He oversees the cGMP manufacture of Army Liposome Formulations (ALF) including ALF43 and ALFQ. Dr. Matyas' research efforts focus on the development of adjuvants for HIV vaccines. He is the principal investigator for a comparative adjuvant phase 1 clinical trial that studies the effect of various adjuvants on DNA immunization and HIV-1 envelope protein boosts. The trial is being conducted in Kenya. Dr. Matyas has participated in multiple clinical trials with ALF and ALFQ for HIV, malaria, Campylobacter and COVID-19. In July 2012, Dr. Matyas was awarded the Avant-Garde Award for Medications Development from the NIH National Institute on Drug Abuse to develop a combination heroin/HIV vaccine. As part of this award and extended research, Dr. Matyas has developed an ALF-based vaccines that blocks the biological effects of opioids such as heroin and fentanyl. His heroin vaccine has proven effective in preventing overdose in animal studies and is funded for a phase 1 clinical trial.

Session Chair: **Xingmin Sun**
University of South Florida

Title: **Durability of antibody responses following SARS-CoV-2 booster vaccination**
Mehul S. Suthar
Associate Professor
Emory Vaccine Center
Emory University

Title: **Computational design of a potent pre-fusion protein as a human metapneumovirus vaccine**
Michael Kishko
Principal Scientist
Global Antigen Design, Sanofi

Title: **The state of herpes simplex virus vaccine R&D**
Simon Delagrave
Herpes Cure Advocacy

Title: **A simple, safe, affordable, and scalable intracellular delivery platform for "naked" RNA/DNA vaccines and therapeutics**
Eleftheria Michalaki
Senior Scientist
Piezo Therapeutics

Title: **Recombinant fusion protein vaccine containing *Clostridioides difficile* FliC and FliD protects mice against *C. difficile* infection**
Xingmin Sun
Professor
Dept. of Molecular Biosciences; Dept. of Chemistry, University of South Florida

Title: **Preclinical studies on single injection slow-released silica matrix HIV-protein trimer vaccine**
Milla RUNSALA
Business Development Manager
DelSiTech Ltd

Title: **Whole-cell *Acinetobacter baumannii* vaccine candidates induce a protective response and appear well-tolerated in mice**
Stephen J. Dollery
Director of Research and Development
Biological Mimetics, Inc

Title: **Swift defense, long offense: rVSV-based vaccines against Nipah and Lassa viruses**
Courtney Woolsey
Assistant Professor of Microbiology and Immunology
University of Texas Medical Branch

Title: **Adaptive immunity to Bordetella pertussis in vaccination and infection**
Ricardo da Silva Antunes
Instructor at La Jolla Institute for Immunology

Durability of antibody responses following SARS-CoV-2 booster vaccination

Mehul S. Suthar[1,2,3]
[1]Center for Childhood Infections and Vaccines, Children's Healthcare of Atlanta, Division of Infectious Diseases, Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA
[2]Emory Vaccine Center, Emory University, Atlanta, GA, USA
[3]Emory National Primate Research Center, Atlanta, GA, USA

Infection with SARS-CoV-2 in humans has caused a pandemic of unprecedented dimensions. Immunological memory against SARS-CoV-2 is critical for protection against severe disease and death. However, the efficacy of vaccines has been jeopardized by the emergence of SARS-CoV-2 variants and subvariants with mutations in the spike protein that evade antibody-mediated neutralization. We report the durability of antibody responses to mRNA primary and booster vaccines administered throughout the course of the pandemic. The COVID-19 mRNA vaccines in the United States have included a two dose primary series followed by one or two monovalent booster doses encoding the WA1 spike, one or two doses of a bivalent booster dose encoding the WA1 and BA.5 spike, and more recently a monovalent booster dose encoding the XBB.1.5 spike. As compared to the previous vaccination, the XBB.1.5 vaccine generates durable binding and neutralizing antibodies that persist for at least 6 months post-booster vaccination. We observed minimal decay in neutralizing antibodies against WA1 or XBB.1.5. However, contemporary circulating Omicron variants diminished the neutralizing activity of the XBB.1.5 booster after 6 months. These findings show that the recent booster vaccine improves antibody durability, however, immune evasive variants with mutations in the spike protein continue to jeopardize the efficacy of COVID-19 vaccines.

Biography:

Mehul S. Suthar is an Associate Professor in the Department of Pediatrics-Infectious Disease at the Emory University School of Medicine. He is also a member of the Emory Vaccine Center and the Emory National Primate Research Center. He is also the Director of the Center for Childhood Infections and Vaccines. Dr. Suthar's lab is focused on understanding the molecular and immunological mechanisms by which emerging viral infections are controlled by the host. His lab uses a multidisciplinary approach to understand virus-host interactions that regulate innate immune signaling and viral control, understand how CD8+ T cells mediate viral control and clearance, and understand the antibody response to virus infection. More recently, Dr. Suthar has been involved in a major effort to study the antibody response to SARS-CoV-2 infection and vaccination. His group is focused on identifying, characterizing, and assessing the risk of SARS-CoV-2 variants on vaccines currently in use.

Computational design of a potent pre-fusion protein as a human metapneumovirus vaccine

Michael Kishko*[1], Antonia Stuebler*[1], Sukanya Sasmal*[£], Yvonne Chan*[€], Dean Huang*[1], Christopher Reyes*[1], Owen Price*[$] Ana Kume*[1], Christine Bricault*[1], Judith Alamares-Sapuay*[1], Linong Zhang*[1]
*Sanofi, 38 Sidney Street, Cambridge, MA, USA
[1]Current address: Sanofi, 200 West Street, Waltham, MA, USA
[£]Current address: Amazon, 525 Market Street, San Francisco, CA, USA
[€]Current address: Nested Therapeutics, 1030 Massachusetts Avenue, Cambridge, MA, USA
[$]Current address: Blavatnik Institute, Harvard Medical School, 45 Shattuck Street, Boston, MA, USA

Human metapneumovirus (hMPV) is a leading cause of respiratory infections in the elderly, with high morbidity and mortality, for which no vaccines or specific therapies are available. The hMPV Fusion protein (F) is the main target of neutralizing antibodies, and its pre-Fusion conformation (pre-F) is considered the optimal vaccine target. Utilizing the computational design strategy of intraprotomer interface stabilization, we designed a pre-F hMPV recombinant subunit vaccine candidate that yields 14.4 mg/L with a melting temperature of 79.3°C as compared to 5.7 mg/L and 70.4°C for the prototypical pre-F benchmark stabilized by an introduction of a proline at site 185. Our construct retained all pre-F specific sites and was stable at +4°C for up to 6 months. Immunization with our construct induced high binding and neutralizing Ab titers in the mouse model, with the higher neutralizing titers stemming at least in part from increased levels of site Ø and site II competing Abs than those induced by immunization with the 185P pre-F benchmark or post-fusion F. Further, our subtype A2 based construct induced cross-neutralizing Abs against all four hMPV subtypes. In summary, this promising candidate warrants further evaluation.

COMPETING INTERESTS: All authors are current or former employees of Sanofi and may hold Sanofi stock. M.K., A.S, S.S, Y.C., J.AS. and LZ are inventors on patent WO 2023/102373 A1 that describes the hMPV pre-F antigens here presented.

FUNDING: This study was funded by Sanofi.

Biography:

Michael Kishko completed his PhD at the Morningside Graduate School of Biomedical Sciences at the University of Massachusetts, USA, in 2011. He is a Principal Scientist with Sanofi Pasteur, based in Massachusetts, USA, where he performs vaccine discovery for respiratory viruses. He has made numerous contributions to vaccine research and development, and is the author of numerous publications in international scientific journals.

The state of herpes simplex virus vaccine R&D

Simon Delagrave, Ph.D.
Board Member, Herpes Cure Advocacy, a 501(c)(3) non-profit

Thanks to new technologies and discoveries of the last several years, vaccines are now available against SARS-CoV-2 and respiratory syncytial virus. However, a vaccine against herpes simplex virus (HSV) remains elusive despite compelling commercial and health economic needs. This presentation will give an overview of the latest developments in structural biology, protein design, and other fields, that enable the creation of new vaccine candidates against HSV. Past HSV vaccine discovery efforts as well as ongoing clinical trials will also be discussed. The growing body of knowledge on vaccines and HSV may finally be reaching the threshold of clinical and commercial success, and non-profit patient advocacy organizations such as Herpes Cure Advocacy are urging the scientific community to redouble its efforts to develop prophylactic and therapeutic vaccines against herpes simplex virus.

Biography:

Simon Delagrave, Ph.D., is a life sciences R&D executive, consultant, and board member at Herpes Cure Advocacy. His 28 years of professional experience include numerous contributions in the fields of infectious diseases and gene therapy. He holds a BSc in biochemistry from McGill University and a Ph.D. from MIT in biological chemistry. While at Sanofi Pasteur North America, Dr. Delagrave was head of virology research, interim head of research, and Project Leader for HSV529, a vaccine against genital herpes which completed phase I clinical testing. He later served as SVP at a Flagship Pioneering company, and now consults for various organizations such as a major venture creation firm, a highly respected research hospital network's gene and cell therapy institute, and seed-stage biotechs. His work has led to 16 issued U.S. patents, several pending applications, as well as over 30 peer-reviewed scientific articles, including the recent discovery of the first atomic structure of a human anellovirus.

A simple, safe, affordable, and scalable intracellular delivery platform for "naked" RNA/DNA vaccines and therapeutics

Eleftheria "Ria" Michalaki
Senior Scientist at Piezo Therapeutics

The urgency to combat emerging infectious diseases, as exemplified by the COVID-19 pandemic, and the ongoing challenges in oncology medicines due to tumor heterogeneity and low treatment responses necessitate the development of novel vaccines and delivery platforms. Nucleic acid (NA)-based medicines – notably mRNA vaccines – have been proposed as an agile, economical, and scalable alternative to traditional methods. Their current intracellular delivery mechanism (lipid nanoparticles; LNPs) is limited by high costs, complex screening and manufacturing, limited durability, and poor reactogenicity. Developing a drug delivery platform that can address these challenges can revolutionize mRNA vaccines and other NA-based medicines, enabling their broader application.

At Piezo Therapeutics, we seek to develop and commercialize a novel intracellular delivery platform (called Piezopen), which combines electroporation (EP) and microneedle (MN) electrodes to administer RNA/DNA without LNPs, viral vectors, or other formulations. Piezopen stands unparalleled in terms of cost (<$1/device) and size (<50 g/device) while operating without a power source and being close to painless. Piezopen concentrates pulses and antigen expression to the epidermis to maximize immunogenicity and minimize reactogenicity. EP adjuvants humoral and cellular responses without unfavorable reactogenicity/inflammation or off-target effects seen with LNPs or viral vectors.

We believe Piezopen can enable rapid deployment, scale-up, and enactment of global vaccination programs by eliminating LNPs and viral vectors from RNA/DNA vaccines. In the long term, we aim to improve the simplicity, safety, affordability, and scalability of both RNA and DNA vaccines.

Biography:

Eleftheria "Ria" Michalaki is a Senior Scientist at Piezo Therapeutics. She has extensive experience in vaccine delivery, lipid nanoparticles (LNPs) formulations, and biomaterialsbased techniques. She holds a BS and Ph.D. from the University of Patras and Stanford University, respectively, both in Chemical Engineering. During her postdoctoral training in the Mechanical Engineering department at the Georgia Institute of Technology, she worked on screening and identifying LNPs in vivo for lymphatic system-specific targeted delivery, while she also participated in the Certificate Program in Translational Research at Emory University through the NIH-funded Georgia Clinical & Translational Science Alliance. During her career, she has received numerous honors and awards including the Richard Skalak Award – The American Society of Mechanical Engineers (ASME) (2022), the Lymphatic Education & Research Network (LE&RN) Young Investigator Conference Scholarship Award (2022), Nerem International Travel Award (2022), AHA Postdoctoral Fellowship (2021-2023), and Berkeley Rising Star in Mechanical Engineering (2020).

Recombinant fusion protein vaccine containing *Clostridioides difficile* FliC and FliD protects mice against *C. difficile* infection

Shaohui Wang, Xianghong Ju, Joshua Heuler, Xingmin Sun*
Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa, FL, USA.

Bacterial flagella are involved in infection through their roles in host-cell adhesion, cell invasion, auto-agglutination, colonization, and formation of biofilms, as well as in the regulation and secretion of non-flagellar bacterial proteins involved in the virulence process. In this study, we constructed a fusion protein vaccine (FliCD) containing *Clostridioides difficile* flagellar proteins FliC and FliD. Immunization of mice with FliCD induced potent IgG and IgA antibody responses against FliCD, protected mice against *C. difficile* infection (CDI) and decreased *C. difficile* spores and toxin levels in the feces after infection. Additionally, anti-FliCD serum inhibited the binding of *C. difficile* vegetative cells to HCT8 cells. These results suggest that FliCD may represent an effective vaccine candidate against CDI.

Biography:

Dr. Sun is a professor with tenure in the Department of Molecular Medicine, College of Medicine at the University of South Florida (USF). He holds courtesy appointments in the Department of Internal Medicine, Department of Cell Biology, Microbiology & Molecular Biology, Department of Chemistry at USF, and USF Genomics. He received his PhD in Natural Sciences from the University of Kiel, Germany, and his master's degree in veterinary microbiology and Immunology from Nanjing Agricultural University, China. He received his postdoctoral training in Molecular Microbiology and Biochemistry at Brown University, USA. The research in his laboratory is focused on the pathogenesis of Clostridioides difficile and the development of novel therapeutics including vaccines to prevent / treat C. difficile infection (CDI). He was an NIH (National Institutes of Health) Career Development K01 Awardee. His laboratory has been continuously supported by the NIH. He has been actively serving NIH study section panels including chairing the NIH study section panel in 2020. He serves as an Associate Editor for "Molecular Medicine", Associate topic editor for "Frontiers in Microbiology", and editorial boards for "Infection and Immunity" and "Applied and Environmental Microbiology". He received the Tufts Institute for Innovation Inaugural Award in 2014. In 2018, he was awarded the "Faculty Outstanding Research Achievement Award" at USF. In 2019, he was awarded the "Excellence in Innovation Award" at USF. He chaired the Research Committee of the College of Medicine at USF from 2019 to 2020. Currently, he serves as the President for the USF Chapter, National Academy of Inventors, USA

Preclinical studies on single injection slow-released silica matrix HIV-protein trimer vaccine

Milla Runsala*[1], Namit Chaudhary[2], Darrell J. Irvine[2], Aleksi Lehtinen[1], Jari Mikkola[1], Linda Wirman[1] and Lasse Leino[1]
[1]DelSiTech Ltd, Turku, Finland
[2]Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology, Cambridge, MA

Introduction: Slow-released HIV vaccines are under extensive study as prolonged immunization is reported to induce stronger immune responses. Prolonged antigen delivery also increases neutralizing antibody production which is an essential humoral response to fight against HIV. This study aimed to formulate a single injection slow-release Silica Matrix HIV-protein trimer vaccine and test the prototype vaccine in a mouse immunization model.

Methods: A stabilized SOSIP HIV Env-protein trimer immunogen and saponin adjuvant were encapsulated in separate Silica Matrix microparticles utilizing the sol-gel process and spray drying. Microparticles were mixed in Silica Matrix hydrogel to produce an injectable vaccine depot. The immunogen/adjuvant release time was designed to be 4 weeks in vivo after subcutaneous dosing of the depot. C57BL/6 mice were divided into four groups and immunized with s.c. injections. The Bolus group received an injection containing 5 µg of immunogen and adjuvant, respectively, in PBS. As a positive control, an escalating dose group (7ED) received the same total vaccine amounts, but the dose was delivered in 7 exponentially increasing immunogen/ adjuvant dosages over 2 weeks. The first Silica Matrix group received 5 µg of immunogen and adjuvant, respectively, encapsulated in Silica Matrix depot (IA-Silica Matrix). The second Silica Matrix group received only 5 µg of immunogen (I-Silica Matrix) in the depot. The mice were studied in two cohorts. Serum samples were collected until 6 weeks and analyzed for antibody titers with ELISA.The second cohort followed mice until 3 weeks, after which the lymph nodes were collected for FACS analysis of germinal center B cells.

Results: All groups showed robust antibody responses through 5 weeks. Germinal center (GC) B cell (B220+, CD38low, GL7+) number, on the other hand, was significantly higher in both the 7ED and IA-Silica Matrix group when compared to the Bolus group. Interestingly, the I-Silica Matrix group had a similar GC B cell number to the Bolus group. When the count of antigen-specific GC B cells (B220+, CD38low, GL7+, antigen+) was compared between the groups, again, the I-Silica Matrix group had a similar GC B cell number than the Bolus group. However, the antigen-specific GC B cell counts were significantly higher in the 7ED and IA-Silica Matrix groups compared to the Bolus group.

Conclusion: The preliminary results show that a single injection slow-release Silica Matrix HIV-protein trimer immunogen vaccine with adjuvant induces a robust antibody titer response and comparable GC B cell response as the 7ED immunization, which both were superior to the Bolus vaccine.

Acknowledgements: This study was funded by Bill & Melinda Gates Foundation Grant Agreement INV-053170.

Whole-cell *Acinetobacter baumannii* vaccine candidates induce a protective response and appear well-tolerated in mice

Stephen J. Dollery[1]*, Daniel V. Zurawski[2], Ruth V. Bushnell[1], John K. Tobin[1], Taralyn J. Wiggins[1], David A. MacLeod[1], Jonathon Mclaughlin[3], Naomi J. P. E. R. Tasker[1], Yonas A. Alamneh[2], Rania Abu-Taleb[2], Christine M. Czintos[2], Wanwen Su[2], Mariel G. Escatte[2], Heather N. Meeks[4], Michael J. Daly[5], and Gregory J. Tobin[1]

[1]Biological Mimetics, Inc., 124 Byte Drive, Frederick, MD, USA

[2]Wound Infections Department, Bacterial Diseases Branch, Center for Infectious Disease Research, Walter Reed Army Institute of Research, Silver Spring, MD, USA.

[3]Personalised Medicine Centre, School of Medicine, C-TRIC, Altnagelvin Hospital, Ulster University, Derry, Londonderry, United Kingdom

[4]Defense Threat Reduction Agency, Ft. Belvoir, VA, USA.

[5]Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD, USA;

Acinetobacter baumannii is an environmental bacterium infamous for its pathogenicity. *Acinetobacter* infections contribute to an estimated one-million deaths per year. Decontamination of infected sites is challenging; the bacterium is not only desiccation-resistant, but also resistant to multiple antibiotics and drugs of last resort including carbapenem, colistin, and sulbactam. Amongst many concerned stakeholders, the WHO places *A. baumannii* at the top of their critical pathogen list in a bid to direct urgent countermeasure development. Several early-stage vaccines have shown a range of efficacies in healthy mice, but no vaccine candidates have advanced into clinical trials. Herein, BMI presents updates on our *A. Baumannii* vaccine research program. We present findings from inactivated whole-cell vaccine candidates and show high levels of protection in neutropenic mice from pulmonary challenge with virulent AB5075, a particularly pathogenic isolate. We demonstrate that a humoral response is sufficient for this protection via the passive immunization of neutropenic mice and present preliminary toxicology study data. We also explore capsule driving mutations and next generation vaccine candidates as avenues for further research.

Biography:

Stephen J. Dollery, Ph.D., is the Director of Research and Development at Biological Mimetics Incorporated (BMI). This role includes serving as the principal investigator for several innovative immunogen design and vaccine testing projects. Before joining BMI, he studied infectious diseases as a research fellow in the U.S. National Institutes of Health (NIH) Laboratory of Viral Diseases (LVD). His previous work includes discoveries regarding the entry mechanisms of several viruses and the development of model systems of infection.

Swift defense, long offense: rVSV-based vaccines against Nipah and Lassa viruses

Courtney Woolsey*[1,2], Alyssa Fears[1,2], Jacquelyn Turcinovic[1,2], Daniel J. Deer[1,2], Viktoriya Borisevich[1,2], Krystle N. Agans[1,2], Jasmine Martinez[1,2], Mack B. Harrison[1,2], Natalie S. Dobias[1,2], Abhishek N. Prasad[1,2], Karla A. Fenton[1,2], Robert W. Cross[1,2], Thomas W. Geisbert[1,2]
[1]Galveston National Laboratory, University of Texas Medical Branch, Galveston, TX, USA.
[2]Department of Microbiology and Immunology, University of Texas Medical Branch, Galveston, TX, USA.

Nipah virus (NiV) and Lassa virus (LASV) are highly pathogenic viruses that pose serious public health threats, highlighting the urgent need for vaccines that can provide rapid and durable protection. Recombinant vesicular stomatitis virus (rVSV)-based vaccines have shown significant promise in combating these deadly pathogens in preclinical non-human primate models.

Earlier studies demonstrated that a single-cycle rVSVΔG-NiV-G vaccine conferred rapid (within 7 days) and long-lasting (over 1 year) protection against NiV in African green monkeys. In the present study, we conducted a dose down experiment to determine the minimum effective dose for protection, offering key insights into correlates of immunity. For LASV, prior research showed that the rVSVΔG-LASV-GPC vaccine induced rapid protection as early as 3 days post-vaccination in cynomolgus monkeys. We further evaluated the durability of the immune response, showing robust protection one-year post-vaccination, and conducted a dose down study to define the minimum dose required for effective immunity. Notably, low doses of both vaccines were sufficient to achieve protection.

Both vaccines are advancing through clinical trials, with the NiV vaccine in Phase I and the LASV vaccine progressing to Phase II trials. These findings are critical for confirming the vaccines' ability to induce fast-acting and long-lasting immunity, reinforcing their potential to curb transmission and prevent future outbreaks.

Biography:

Dr. Woolsey's research focuses on preclinical vaccine development and understanding the immunopathology of emerging and re-emerging viruses requiring maximum biocontainment (BSL-4) including ebolaviruses, marburgviruses, henipaviruses, and arenaviruses. She employs advanced immunological tools to dissect natural and vaccine-mediated host immunity to these pathogens. The overall objective is to harness this knowledge to improve medical countermeasures. Her specific interests include 1) generating rapid-acting and durable recombinant Vesicular stomatitis virus (rVSV)-based vaccines, 2) characterizing how these vaccines elicit early and sustained protection, and 3) exploring mechanisms of virus persistence and sequelae.

Adaptive immunity to Bordetella pertussis in vaccination and infection

Ricardo da Silva Antunes, Ph.D
Instructor at La Jolla Institute for Immunology

Whooping cough, also known as pertussis, is a highly contagious respiratory tract infection caused by Bordetella pertussis (BP) and remains a significant global challenge as a vaccine-preventable disease, despite widespread vaccination. Understanding the immune system's response to pertussis vaccines and infection is crucial for improving current vaccine efficacy. While there's growing evidence suggesting the role of T cells in controlling and preventing symptomatic disease, most data on human BP-specific T cells relate to the four antigens contained in acellular Pertussis (aP) vaccines, leaving a gap in understanding T cell responses to other non-aP antigens. We conducted a whole-genome mapping of human BP-specific CD4+ T cell responses in healthy vaccinated adults. Our findings revealed a broad range of responses, targeting hundreds of BP antigens, including fifteen distinct non-aP vaccine antigens with reactivity comparable to that of aP vaccine antigens. Moreover, the pattern and magnitude of CD4+ T cell reactivity to both aP and non-aP vaccine antigens were identical regardless of whether aP or inactivated whole-cell Pertussis (wP) vaccines were administered during childhood priming vaccination. This indicates that T cell reactivity in adults is likely driven by widespread subclinical undetected infections, with adults serving as a reservoir for ongoing BP circulation. An increased BP reservoir, resulting from the decreased capacity of aP vaccination to prevent subclinical infection could be a contributing factor for the increased incidence of clinical disease and recurrent outbreaks. Additionally, we examined T cell responses following whooping cough disease and found that wP-vaccinated individuals who experienced symptomatic/clinical infections had lower memory T cell responses compared to wP controls. We also identified T cell responses unique to antigens associated with symptomatic infection, which could potentially provide longer-lasting protection compared to vaccination and/or asymptomatic infections. Overall, the tools and epitopes identified will facilitate the characterization of response durability in longitudinal monitoring, helping to distinguish the effects of asymptomatic reinfections. The novel antigens discovered may also serve as promising targets for designing next-generation pertussis vaccines.

Biography:

My research integrates the disciplines of T cell biology and clinical immunology to gain new and fundamental understanding of human diseases and developing better immunotherapeutic strategies. This involves the study and characterization of T cell responses, against several emergent pathogens relevant to worldwide global health, such as whooping cough (pertussis), COVID-19, dengue, and common allergens that cause allergic asthma. I have a strong track record of studying vaccine responses and developing new approaches and innovative ways to measure biological processes such as the establishment of a T cell-based immunodiagnostic system to distinguish SARS-CoV-2 infection and COVID-19 vaccination history and the development of a Bordetella pertussis genome-wide epitope screening strategy. In particular, my focus in pertussis research led to several seminal contributions such as exploring how differences in T cell responses contribute to the time-dependent decline in protection by the acellular pertussis vaccine and the observation that asymptomatic infections are highly prevalent in human vaccinated populations. These studies also established me as a recognized leader in the field of pertussis adaptive immunity.

SCIENTIA MEETINGS

VACCINES 2024

Day 3: November 15, 2024

Cancer Vaccines & Immunotherapy

VACCINES SUMMIT-2024

NOVEMBER 13-15, 2024
BOSTON, MA

Cancer Vaccines & Immunotherapy

Session Chair: **Robert O. Dillman**
Chief Medical Officer, AIVITA Biomedical, Inc.

Title: **A platform for personal cancer vaccine immunotherapy targeting tumor-initiating cells**
Robert O. Dillman
Chief Medical Officer
AIVITA Biomedical, Inc.

Title: **Immune response measurements of antigen-specific B-cells by ELISPOT**
Andrea Maul-Pavicic
Scientist
CRO
Cellular Technology Limited

Title: **Novel biologics platform for antigen-specific T cell modulation**
Steven Almo
Chair
Department of Biochemistry
Albert Einstein College of Medicine

Title: **T-cell signalling pathways that enhance chimeric antigen receptor (CAR) therapy against in cancer**
Christopher E. Rudd
Professeur
Faculte de Medicine, Universite de Montreal

A platform for personal cancer vaccine immunotherapy targeting tumor-initiating cells

Robert O. Dillman, M.D.
Chief Medical Officer, AIVITA Biomedical, Inc.
Clinical Professor of Medicine, University of California Irvine

Antigen-loaded dendritic cells (DC) evoke an immune response to the antigens that they are loaded with. *Ex vivo* antigen loading into patient DC offers advantages over *in vivo* antigen uptake and processing by endogenous DC for initiating a targeted adaptive immune response. Loading with antigens from self-renewing tumor-initiating cells (TICs) yields a uniquely personal vaccine. Peripheral blood mononuclear cells are differentiated into DC *in vitro*, then the patient's DC are incubated with a lysate of their own irradiated TICs established from a short-term cell line derived from surgically resected tumor. These personal cancer vaccines are manufactured at 97% efficiency and have been tested in Phase 1 and Phase 2 clinical trials in patients with a variety of advanced cancers, including melanoma, glioblastoma, ovarian, renal, and hepatocellular cancers. Feasibility, safety, enhanced immune responses, and evidence of efficacy have been demonstrated. Phase 3 and adaptive Phase 2-3 trials have been approved by the United States FDA.

- TIC antigens offer unique targeting
- Personal immunotherapies can be reliably manufactured at a low cost of goods
- In a randomized trial the DC platform was superior to direct injection of tumor cell antigens
- Phase 2 clinical trials have demonstrated safety and efficacy including objective tumor responses, increases in progression-free survival and increases in overall survival

Biography:

Dr. Robert O. Dillman, M.D., is Chief Medical Officer of AIVITA Biomedical. Previously, Dr. Dillman served as Vice President of Oncology at Caladrius Biosciences, Inc. (formerly Neostem, Inc.), a leading development and manufacturing partner to the cell therapy industry. From May 2014 to January 6, 2016 he also served as Member of Caladrius' Melanoma Scientific Advisory Board. Dr. Dillman has served as the Executive Medical Director of the Hoag Hospital Institute for Research and Education, in Newport Beach, California, a position he has held since 2011. Prior to this position he served as Executive Medical Director of the Hoag Family Cancer Institute from 2008-2011, and was Medical Director of the Hoag Cancer Center from 1989-2008. He has also served as a Clinical Professor of Medicine at the University of California, Irvine ("UCI") since 1989. He also held the position of Assistant Director of the UCSD Cancer Center and Chief of Hematology/Oncology at the San Diego VA Medical Center, then Director of Experimental Clinical Oncology and Associate Director of the Ida M. Green Cancer Center of Scripps Clinic and Research Foundation in La Jolla, California.

Dr. Dillman chaired the Cancer Biotherapy Research Group from 1990 to 2002, and is a past President and board Member of the International Society for Immunotherapy of Cancer. He directed a cell biology research laboratory focused on patient-specific cell therapies for more than 20 years, and is an internationally recognized leader in cancer immunotherapy approaches, including monoclonal antibodies, adoptive cell therapies, IL-2, and cancer vaccines. He has authored more than 300 medical publications and is recognized internationally for his work in lung cancer, lymphoma, Chronic Lymphocytic Leukemia (CLL), melanoma, and kidney cancers. He was the first physician in Orange County, California to be selected as one of the Best Doctors in America in Hematology and/or Oncology. In 2006, Dr. Dillman was named Orange County Physician of the Year by the Orange County Medical Association. In 2008, he received Hoag Hospital's first endowed chair, the Grace E. Hoag Endowed Chair of Oncology and in 2010, he became one of only five recipients in the world to receive the Distinguished Service Award from the Society for Immunotherapy of Cancer.

Dr. Dillman received his undergraduate degree from Stanford University and medical degree from Baylor College of Medicine. He also completed both his internship and residency in Internal Medicine at Baylor College of Medicine, and served as a Chief Resident. He completed his fellowship in Hematology/Oncology at University of California, San Diego Medical Center.

Immune response measurements of antigen-specific B-cells by ELISPOT

Andrea Maul-Pavicic*, Lingling Yao, Anton Gorbachev, Noemi Becza, Greg Kirchenbaum, Paul-Lehmann, Magdalena Tary-Lehmann
Cellular Technology Limited

Cellular Technology Limited, The plasma and memory B-cell ELISPOT is an extremely sensitive assay based on the detection of antigen-specific secreted antibodies of cryopreserved or fresh PBMCs. The B cell response encompasses four immunoglobulin (Ig) classes (IgG1-4) and four IgG subclasses (IgG, IgA, IgM and IgE), each contributing to fundamentally different effector functions. For clinical studies assessment of humoral immunity to infectious agents and hence to antigen-specific B cell responses is most often confined to the antibodies present in serum, as evaluated by ELISA or NAb assays. It neglects monitoring memory B cells (if present in PBMCs), which could mount a faster and more efficient antibody response after antigen re-encounter.

In immunotherapy evaluations, ELISA measurements of total IgG are usually performed without taken into consideration the detection of the appropriate Ig classes or IgG subclasses, which are critical for successful host defense and avoidance of immunopathology.

Our multiplexed ELISPOT/FluoroSpot (collectively ImmunoSpot®) assay platform is ideally suited for antigen-specific B-cell enumeration since it provides a single-cell resolution for counting individual antibody-secreting cells (ASC), might this be from plasma or memory B cells. This information cannot be provided by ELISA assays.

In summary, we will show successful measurements of antigen specific B cells in clinical settings after infection or vaccination, facilitating high-throughput immune-monitoring efforts of large donor cohorts.

Biography:

Andrea Maul-Pavicic, Ph.D., biologist with a strong background in immunology.

Academic career in Germany, post-doctoral positions at the German Cancer Research Center, Heidelberg, Germany; at the Max-Planck-Institute of Immunobiology, Freiburg, Germany and at the Center for Chronic Immunodeficiency, Medical Center-University of Freiburg, Germany.

From 2012 – 2022 Senior Staff Scientist at the Center for Chronic Immunodeficiency and Department of Rheumatology and Clinical Immunology, Medical Center-University of Freiburg, Germany.

Member of the integrated research training group (IRTG): “B cells and beyond/Plasma cells: Culprit and treatment target in antibody mediated diseases” (DFG: German research association).

In June 2022, move from Germany to Cleveland, USA. Since then, Contract Laboratory Scientist at Cellular Technology Limited, Cleveland, Ohio, USA.

Novel biologics platform for antigen-specific T cell modulation

Steven Almo, Ph.D
Chair of the Department of Biochemistry at the Albert Einstein College of Medicine

Selectivity is the underpinning of biological function and is an essential consideration for the development of therapeutic strategies. We describe the Immuno-STAT biologics platform, which provides a highly modular scaffold for the antigen selective delivery of functionality to immune cells. By doing so, the Immuno-STAT platform enables selective modulation of the relatively rare disease-relevant T cells *in vivo*, while avoiding broad immune activation/suppression. Thus, in contrast to other existing immunotherapies, which elicit global and non-selective responses, Immuno-STATs are TCR-selective engagers that target, expand and activate disease relevant T cell populations, while leaving the vast majority of the repertoire untouched. The modularity of the Immuno-STAT platform allows for the facile targeting of different indications by simply changing the sequence of the antigenic peptide and incorporating protein modules that deliver a range of stimulatory (e.g., CD28 agonist, 4-1BBL, IL-15) or inhibitory (e.g., PD-L1)_signals to T cells. This scaffold has enabled biologics for a wide range of viral, oncology and autoimmune targets, and CUE-101, which delivers engineered IL-2 cytokine to tumor-specific T cells, is currently being evaluated in a multi-arm clinical trial for HPV-driven head and neck cancer. The modular design of the Immuno-STAT platform is highlighted by the recent initiation of a phase I trial for CUE-102, which targets Wilms Tumor-1 (WT1)-associated tumors; CUE-101 and CUE-102 are 99% identical in sequence, differing only in the nine amino acid antigenic peptides, which afford significant regulatory and clinical trial efficiencies for therapeutic development of Immuno-STATs.

Biography:

Steven Almo is the Chair of the Department of Biochemistry at the Albert Einstein College of Medicine, where he is Professor of Biochemistry and co-leader of the Cancer Therapeutics Program for the Montefiore Einstein Comprehensive Cancer Center. Dr. Almo holds the Wollowick Family Foundation Chair in Immunology and is Director of Einstein's Macromolecular Therapeutics Development Facility, a resource dedicated to the development and optimization of protein-based therapeutics. Dr. Almo is recognized for his broad contributions to structural biology, immune regulatory mechanisms and technology development. After obtaining his Bachelor of Science in biology from the Massachusetts Institute of Technology, Dr. Almo earned his Doctor of Philosophy in biophysics from Harvard University. He then completed postdoctoral training in cell biology and biophysics at Johns Hopkins University School of Medicine. His highresolution structural and functional analyses of the mammalian immune system have resulted in the unprecedented understanding of the molecular mechanisms that control immunity and are guiding the development of novel antigen-selective strategies for the treatment of infectious diseases, autoimmune diseases and cancers.

T-cell signalling pathways that enhance chimeric antigen receptor (CAR) therapy against in cancer

Christopher E. Rudd[1-3]
[1]Département de Medicine, Université de Montréal, Montreal, Quebec H3C 3J7, Canada
[2]Division of Immunology-Oncology, CR-HMR, Montreal, Quebec H1T 2M4, Canada
[3]ImmunAb Research Inc, Montreal, Canada H4X1K3

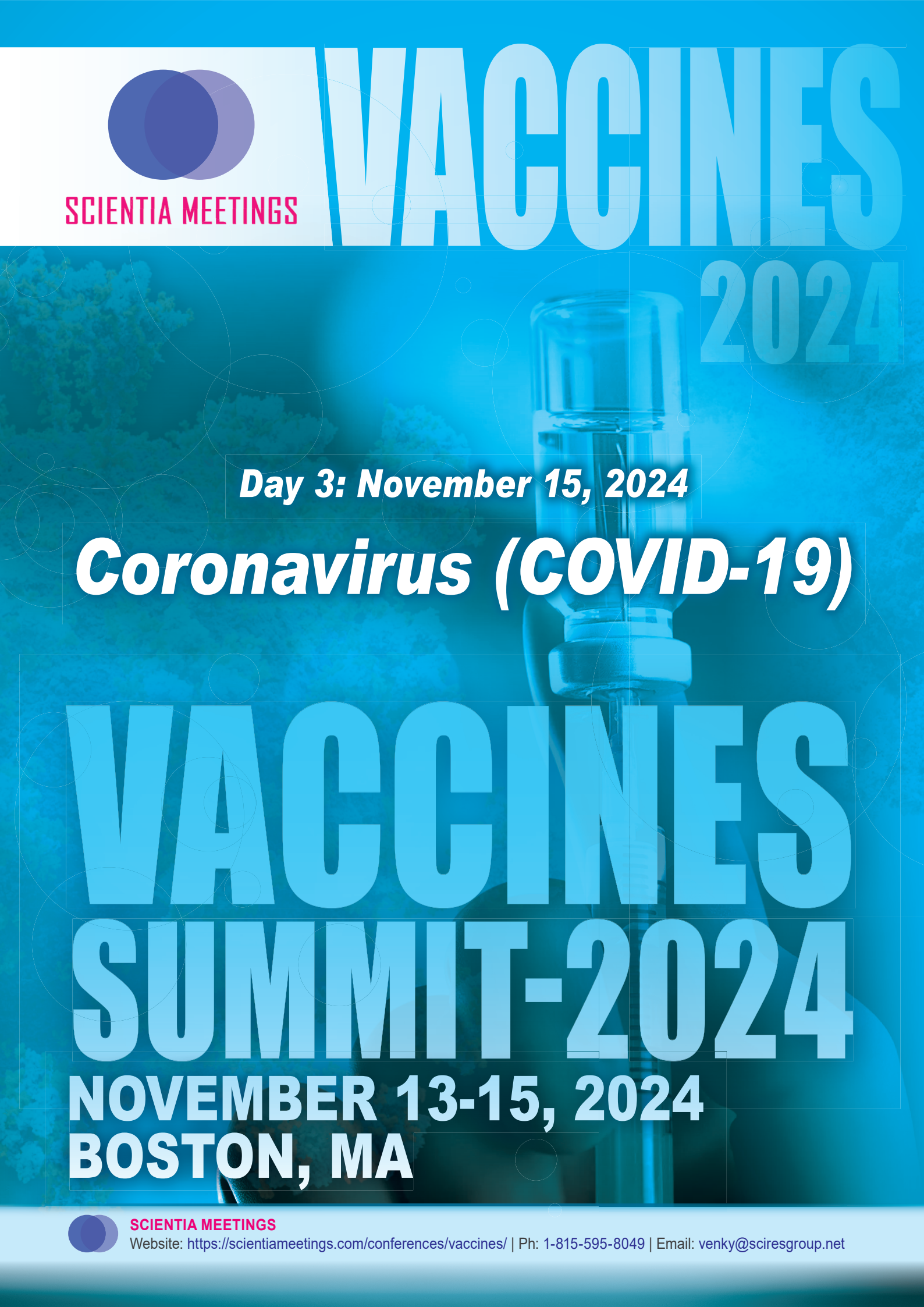
A successful response of the immune system to infection and vaccines is critically dependent on the receptors and pathways that induce the activation and effector functions of T-cells. In my presentation, I will describe novel signaling mechanisms involving adaptors and kinases, which play crucial roles in driving diverse T-cell responses to antigens. By uncovering these mediators, exciting opportunities arise for the development of novel chimeric antigen receptor (CAR) strategies in the realm of infection and tumor immunity.

Biography:

Dr. Rudd is currently a Professor at Université de Montréal. He previously served as faculty at Harvard Medical School, Dana-Farber Cancer Institute, and the University of Cambridge in the UK. He currently serves as the Director of the Signalling in Immunotherapy unit at the Centre de Recherche Maisonneuve Rosemont. His work uncovered key components of the T-cell receptor and co-receptor signalling cascade for the activation and development of effector functions of T-cells. This pioneering research on p56lck and tyrosine phosphorylation substrates has served as the foundation for drug design targeting cancer, autoimmunity and viral infections. It also informed the development of key signalling motifs needed in chimeric antigen receptor (CAR) therapy.

SCIENTIA MEETINGS

VACCINES 2024



Day 3: November 15, 2024

Coronavirus (COVID-19)

VACCINES SUMMIT-2024

NOVEMBER 13-15, 2024
BOSTON, MA

SCIENTIA MEETINGS
Website: https://scientiameetings.com/conferences/vaccines/ | Ph: 1-815-595-8049 | Email: venky@sciresgroup.net

Coronavirus (COVID-19)

Session Chair: **Zhaohua Zhou**
Senior Scientist, Office of Pharmaceutical Quality Research, CDER/FDA

Title: **SARS-CoV-2 B epitope-guided neoantigen nanovaccines enhance tumor-specific CD4/CD8 T cell immunity through B cell antigen presentation**
Duxin Sun
Director of Pharmacokinetics Core
The University of Michigan

Title: **The secreted SARS-CoV-2 ORF8 protein drives a systemic pro-inflammatory cytokine response via NLRP3 pathways in patients with severe COVID-19**
Xiaosheng Wu
Assistant Professor
Hematology Research, Mayo Clinic Rochester

Title: **Hypersensitivity caused by mRNA/LNP COVID vaccines: Role of PEG and anti-PEG antibodies**
Zhaohua Zhou
Senior Scientist
Office of Pharmaceutical Quality Research, CDER/FDA

Title: **From light to insight: Harnessing bioluminescence imaging to track SARS-CoV-2 spread and antiviral therapies in mouse models**
Pradeep D. Uchil
Research Scientist
Yale University School of Medicine

Title: **Immunogenicity and protective efficacy of RSV G central conserved domain vaccine with a prefusion nanoparticle**
Linong Zhang
Sanofi

Title: **A pre-immune ferret model for influenza demonstrates enhanced neutralizing antibody titers following vaccination**
Ashley C. Beavis
Sanofi Vaccine Research and Development

Title: **Long-term cellular immunity of vaccines for Zaire Ebola virus diseases**
Aurelie Wiedemann
Vaccine Research Institute / Inserm

Title: **Targeting Langerhans cells using trimeric Env of HIV triggers a swift and robust production of Env-specific IgG antibodies and neutralizing antibodies through a Tfh/germinal center (GC) reaction**
Sylvain Cardinaud
Vaccine Research Institute / Inserm

Title: **Providing solution for novel vaccine development and manufacturing for a healthier 21st century**
Xinhao Ye
Director
CMC lead of WuXi Vaccines

SARS-CoV-2 B epitope-guided neoantigen nanovaccines enhance tumor-specific CD4/CD8 T cell immunity through B cell antigen presentation

Duxin Sun, PhD
Associate Dean for Research, College of Pharmacy
Charles Walgreen Jr. Professor of Pharmacy
Professor of Pharmaceutical Sciences, Medicinal Chemistry program, Chemical Biology Program, University of Michigan, Ann Arbor, MI 48109

Current neoantigen cancer vaccines activate T cell immunity through dendritic cell /macrophage-mediated antigen presentation. It is unclear whether incorporating B cell-mediated antigen presentation into current neoantigen vaccines could enhance CD4/CD8 T cell immunity to improve their anticancer efficacy. We developed a SARS-CoV-2 B cell epitope-guided neoantigen peptide/mRNA cancer nanovaccines ($B_{SARS}T_{NeoAg}$Vax) to improve anticancer efficacy by enhancing tumor-specific CD4/CD8 T cell antitumor immunity through B cell-mediated antigen presentation. $B_{SARS}T_{NeoAg}$Vax crosslinked with B cell receptor, promoted SARS-CoV-2 B cell-mediated antigen presentation to tumor-specific CD4 T cells, increased tumor-specific follicular/non-follicular CD4 T cells, and enhanced B cell-dependent tumor-specific CD8 T cell immunity. $B_{SARS}T_{NeoAg}$Vax achieved superior efficacy in melanoma, pancreatic, and breast cancer models compared to the current neoantigen vaccines. Our study provides a universal platform, SARS-CoV-2 B epitope-guided neoantigen nanovaccines, to improve anticancer efficacy against various cancer types by enhancing CD4/CD8 T cell antitumor immunity through viral-specific B cell-mediated antigen presentation.

Biography:

Dr. Duxin Sun is the Associate Dean for Research, the Charles Walgreen Jr. Professor of Pharmacy and Pharmaceutical Sciences in the College of Pharmacy at the University of Michigan. He serves as the Director of the Pharmacokinetics (PK) Core. Dr. Sun also has a joint appointment in the Chemical Biology program, the Interdisciplinary Medicinal Chemistry program, and University of Michigan's Comprehensive Cancer Center.

Dr. Sun's research interests focus on drug development, cancer nanomedicine, cancer vaccine, and pharmacokinetics. Dr. Sun established the STAR system (Structure-Tissue/Cell Selectivity-Activity Relationship) to enhance drug development success rate by addressing the 90% failuar rate. He designed albumin based nanomedicines to enhance clinical efficacy of immuno-oncology drugs by targeting immune cells in the lymphatic system and tumors. He also developed SARS-CoV-2 B epitope-guided neoantigen peptide or mRNA vaccines to enhance their efficacy by activating CD4/CD8 T cell immunity through B cell-mediated antigen presentation.

Dr. Sun earned his BS in Pharmacy, MS in Pharmacology, and PhD in Pharmaceutical Sciences, and has also received training in Molecular Biology as a visiting scientist. With research experience in both academia and the pharmaceutical industry, Dr. Sun has published over 280 papers, and has mentored 40 PhD students and 75 postdoctoral fellows/visiting scientists. Dr. Sun is an elected Fellow of both the American Association for the Advancement of Science (AAAS) and the American Association of Pharmaceutical Scientists (AAPS). He has served on the FDA Pharmaceutical Science and Clinical Pharmacology Advisory Committee and participated in study sections for the NIH and FDA.

The secreted SARS-CoV-2 ORF8 protein drives a systemic pro-inflammatory cytokine response via NLRP3 pathways in patients with severe COVID-19

Xiaosheng Wu*, Gordon J. Ruan, Michelle K. Manske, Kimberly A. Gwin, Dongni Yi, Kevin E. Nowakowski, Jithma P. Abeykoon, Thomas E. Witzig
Division of Hematology, Department of Medicine, Mayo Clinic, Rochester, MN 55905, USA.

Despite extensive research, the precise cause of the severe inflammatory cytokine response in critical COVID-19 cases remains uncertain. Our study has demonstrated that the virus-encoded Open Reading Frame 8 (ORF8) protein is secreted as a glycoprotein both in vitro and in the bloodstream of symptomatic patients with COVID-19. ORF8 specifically binds to the NOD-like receptor family pyrin domain-containing 3 (NLRP3) in CD14+ monocytes, triggering inflammasome-driven cytokine and chemokine responses, including IL1β, IL8, and CCL2. Elevated ORF8 levels in the blood are associated with greater disease severity and mortality in acute SARS-CoV-2 infections, while assays of monocyte responsiveness to ORF8 stimulation predict the infection outcomes. Importantly, the inflammasome response activated by ORF8 was effectively suppressed by NLRP3 inhibitors like MCC-950. These findings identify ORF8 as a critical factor in COVID-19 pathogenesis, provide insight into the underlying mechanisms, and suggest a potential therapeutic target for severe cases. Our study suggests that ORF8 protein vaccination may help prevent the onset of cytokine storms and reduce mortality.

Hypersensitivity caused by mRNA/LNP COVID vaccines: Role of PEG and anti-PEG antibodies

Zhaohua Zhou, Ph.D.
Office of Pharmaceutical Quality research, CDER/FDA

Investigation on the potential involvement of polyethylene glycol (PEG) in anaphylactic reactions associated with lipid nanoparticle (LNP) use, especially in mRNA-based COVID-19 vaccines, has yielded conflicting outcomes. While both clinical and laboratory evidence has suggested PEG's role in type 1 hypersensitivity reactions, studies have presented inconsistent findings regarding its immunogenicity in COVID-19 vaccines.

In response, the FDA and CDC conducted a comprehensive public health investigation utilizing a robust dual cytometric bead assay (DCBA) anti-PEG method to evaluate anti-PEG IgE, IgG, and IgM levels in individuals who reported anaphylactic reactions after receiving their first dose of mRNA/LNP COVID vaccines. While anti-PEG antibodies were identified in some allergic cases, they were also present in vaccinated individuals without any symptoms. Other studies utilizing ELISA-based anti-PEG assays indicated correlations with elevated anti-PEG IgG and IgM levels in allergic cases. Certain research suggested non-IgE mechanisms, such as anti-PEG IgG detection, leading to complement activation-related pseudoallergy (CARPA). However, this contradicts the observation that the majority of individuals with detectable anti-PEG IgG/M do not manifest allergic reactions to PEG-containing products, including mRNA/LNP vaccines.

This study emphasizes two critical factors contributing to the conflicting and erroneous findings. First, it underscores the limitations of anti-PEG assays, especially ELISA-based methods, which lack accuracy in sensitivity and specificity due to the unique hydrophilic properties of PEG backbones. Second, it highlights the importance of accurate clinical diagnosis in identifying genuine hypersensitivity reactions. Our recent analysis by DCBA of samples from a well-controlled NIAID clinical trial demonstrated a direct connection between PEG and anti-PEG IgE, specifically, in repeatable allergic reactions triggered by mRNA/LNP vaccine boosters.

Disclaimer: "This presentation reflects the views of the author and should not be construed to represent FDA's views or policies"

Biography:

Dr. Zhou is a Senior Research Scientist at the Office of Pharmaceutical Quality Research, CDER, US Food & Drug Administration. His research is dedicated to developing laboratory models for identifying and predicting drug-induced acute allergic reactions, with a particular focus on elucidating the root causes and devising in vitro diagnostic methods for polyethylene glycol (PEG)-induced drug allergies. This includes PEG-contained drug delivery systems, such as lipid nanoparticle-based drugs and vaccines like the mRNA/LNP COVID vaccines.

By utilizing comprehensive models, Dr. Zhou can efficiently assess whether drug quality contributes to allergic reactions and predict patient sensitivity to specific therapeutics. Furthermore, he possesses regulatory expertise within the FDA, including biotherapeutic CMC assessment and immunogenicity method assessment.

From light to insight: Harnessing bioluminescence imaging to track SARS-CoV-2 spread and antiviral therapies in mouse models.

Pradeep D. Uchil[1], Irfan Ullah[2], Walther Mothes[1], Priti Kumar[2], Marzena Pazgier[3], Andrés Finzi[4]
[1]Department of Microbial Pathogenesis, Yale University School of Medicine, New Haven CT 06510, USA
[2]Department of Internal Medicine, Section of Infectious Diseases, Yale University School of Medicine, New Haven, CT 06520, USA
[3]Infectious Disease Division, Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA
[4]Département de Microbiologie, Infectiologie et Immunologie, Université de Montréal, Montreal, QC, H2X0A9, Canada

Bioluminescence imaging (BLI) has emerged as a valuable technique for assessing antiviral treatments as it offers a real-time readout for the impact on viral replication and spread. In a series of studies, we harnessed BLI-guided analyses to track SARS-CoV-2 replication in K18-hACE2 mice for obtaining both basic and translational insights on various antiviral modalities including mAbs, convalescent plasma, ACE2 decoys, vaccines and anti-SARS-CoV-2 drugs. Our studies revealed that neutralizing antibodies (nAbs) need both Fab and Fc-effector functions for optimal protection in vivo underscoring the significance of Fc-mediated activities in clearing established infection. In addition, BLI demonstrated the importance of cross-reactive Fc-effector functions in COVID-19 convalescent plasma (CCP) as a second line of defense against evolving VOCs when viral neutralization is compromised. This knowledge can inform the selection of convalescent plasmas for future disease outbreaks. Additionally, modified ACE2-Fc fusion proteins exhibited potential as broad therapeutic agents, utilizing both neutralization and Fc-effector functions to prevent fatal SARS-CoV-2 VOC infections. We also applied BLI to evaluate the effectiveness of direct-acting antivirals (DAAs) targeting SARS-CoV-2 replication. While monotherapy using favipiravir, molnupiravir, and nirmatrelvir showed limited success in eliminating the virus, combination therapies such as molnupiravir with nirmatrelvir, caspase inhibitors or convalescent plasma with Fc functions resulted in significant viral clearance and improved survival rates. Together, these findings emphasize the versatility of BLI in rapid evaluation of antiviral therapies and its potential to accelerate therapeutic development and implementation.

Biography:

Dr. Pradeep Uchil, a Research Scientist at Yale University in the Department of Microbial Pathogenesis. Dr. Uchil investigates virus replication, spread, and host interactions using mouse models. He employs whole-body bioluminescence imaging to identify key tissues and cell types involved in virus spread, pathogenesis, immune control as well as elucidate the impact of anti-SARS-CoV-2 strategies (convalescent plasma, antibodies, antiviral drugs, vaccines) on virus clearance. Dr. Uchil is recognized for his imaging expertise in uncovering fundamental and translational aspects of virus infection in mouse models. He earned his PhD in Flavivirus Molecular Virology from the Indian Institute of Science, Bangalore. He completed his postdoctoral work at Yale university focusing on Retrovirus Cell Biology and Innate Immunity.

Immunogenicity and protective efficacy of RSV G central conserved domain vaccine with a prefusion nanoparticle

Jennifer N. Rainho-Tomko[#1], Vincent Pavot[#2], Michael Kishko[#3], Kurt Swanson[#4,6], Darin Edwards[1,7], Heesik Yoon[1], Lilibeth Lanza[1], Judith Alamares-Sapuay[3], Robert Osei-Bonsu[3], Sophia T. Mundle[3], Dave A. Murison[3,8], Scott Gallichan[5], Simon Delagrave[3,10], Chih-Jen Wei[4,9], Linong Zhang[3], and Gary J. Nabel[4,9]

[1]Sanofi, 2501 Discovery Drive, Suite 300, Orlando, FL 32826 USA
[2]Sanofi, 1541 Avenue Marcel Mérieux, Marcy l'Etoile, France
[3]Sanofi, 38 Sidney Street, Cambridge, MA 02139 USA
[4]Sanofi, 270 Albany, Cambridge, MA 02139 USA
[5]Sanofi, 95 Willowdale Blvd, Toronto, ON Canada
[6]Present Address: Ring Therapeutics Inc., 620 Memorial Drive, Cambridge, MA 02139 USA
[7]Present Address: Moderna Inc., 200 Technology Square, Cambridge, MA 02139 USA
[8]Present Address: Souffle Therapeutics, 35 Cambridgepark Dr., 2nd Floor, Cambridge, MA 02140
[9]Present Address: ModeX Therapeutics, an OPKO Health Company, 20 Riverside Road, Weston MA 02493
[10]Present Address: Delagrave Life Sciences Consulting, Sudbury, Massachusetts, USA.

Respiratory syncytial virus (RSV) is a significant cause of respiratory illness in both young children and older adults. Recently, licensed RSV vaccines based on a surface antigen, RSV prefusion F (pre-F), have exhibited high protective efficacy during the first season. However, the vaccine efficacy declined substantially in the subsequent season. Recognizing the protective role of another surface antigen, RSV G, particularly within the central conserved region (Gcc), we wanted to better understand the role of Gcc and the pre-F antigens as the incorporation of Gcc into existing RSV vaccines conceptually may augment the protective efficacy of the prefusion alone vaccines. Here we designed three constructs to display the G central conserved domain (Gcc), with a focus on inducing broad and potent neutralizing antibodies. One construct displaying Gcc from both RSV subgroups trimerized via a C-terminal foldon (Gcc-Foldon) was highly immunogenic in mice and in MIMIC, a pre-immune human in vitro model. To explore an optimal RSV vaccine, we combined the Gcc-Foldon antigen with a stabilized pre-F nanoparticle (pre-F-NP) as a bivalent vaccine and detected no antigenic interference between the two antigens in the MIMIC model. In RSV-primed macaques, the bivalent vaccine elicited potent humoral responses. Furthermore, Gcc-Foldon and pre-F NP demonstrated comparable, nearly complete protection against virus challenge in mice while the bivalent vaccine ultimately resulted in full protection. This two-component vaccine may hold promise in increasing the protective efficacy and warrants further clinical evaluation.

Acknowledgements: We thank Y. Lewis for protein expression and purification support. We thank R. Bodinizzo, K. Balko, E. Hunter, M. Pike, H. Bisceglia, S. Montano, and F. Guillaume for their contributions to the animal experiments and analytical assays. We thank I. Ordonez and L. Zheng for assistance with statistical analysis. We thank J. Moser for support with the MIMIC® studies. We thank J. Zhang, C. DeMaria, and J. Ni for CHO cell line generation and purification support.

Author Contributions: J.N.R.-T., V.P., M.K., and L.Z. wrote the paper, acquired and reviewed the data, and designed research studies. K.S., D.E., H.Y., and S.T.M. acquired and reviewed the data and designed research studies. L.L., J.A.-S., R.O.-B., and D.A.M., acquired and reviewed the data. S.G., S.D., C.-J.W., G.J.N. designed research studies and reviewed and analyzed data.

Competing Interests: All authors are current or former employees of Sanofi, and may hold Sanofi stock. K.S., C.-J.W., and G.J.N. are inventors of patents WO2020205986A1 and WO2019195291 that describe the Gcc and pre-F-NP antigens here presented.

Biography:

Linong Zhang, a virologist, holds a Ph.D. in Molecular Virology from the University of Zurich, Switzerland. Since joining Sanofi in 2000, he initially served as a senior scientist in Toronto, Ontario, Canada. In 2020, he was relocated to Cambridge, Massachusetts, USA. Currently, Linong holds the position of senior expert scientist. Linong has made significant contributions to a variety of vaccine development projects and has published numerous papers in relevant fields.

A pre-immune ferret model for influenza demonstrates enhanced neutralizing antibody titers following vaccination

Ashley C. Beavis*, Katherine Roebke, Bianca Baum, Svetlana Pougatcheva, John Hamberger, Philip Davidson, Wen Cheng, Thorsten U. Vogel, Irina V. Ustyugova, Ana Goncalvez, Raul Gomila, William Warren, Konstantin Zeldovich, Maryann Giel-Moloney
Sanofi Vaccine Research and Development, 200 West Street, Waltham, MA, 02451.

Influenza is a highly contagious, acute respiratory disease that affects all age groups and causes additional burden with health impacts including cardiovascular events and the exacerbation of underlying chronic conditions. Vaccination is the most effective strategy to protect against seasonal influenza infection and further complications. Current quadrivalent (QIV) influenza vaccines are administered as a single dose and contain two type A strains (H1 and H3) and two type B strains (Yamagata and Victoria lineages). Due to constant antigenic drift, the components of the vaccine require updating on an annual basis for the northern and southern hemispheres. The naive ferret model is used for antigenic mapping of circulating influenza viruses, for understanding strain cross reactivity, and to assess immunogenicity of vaccine candidates, which typically requires multiple immunizations. However, most humans have been exposed to influenza, either via infection or vaccination, and have pre-existing immunity. Thus, it is important to utilize a pre-clinical animal model that is more translational and reflective of a non-naïve population to assess influenza vaccine candidates as single dose regimen. Previous studies have established anti-influenza immunity in ferrets with consecutive single strain infections or infection with two influenza strains. Here, we established a pre-immune ferret model by single intranasal co-infection with four historical viruses representing the four subtypes to more closely mimic human pre-existing immunity. Following co-infection, ferrets generated neutralizing antibodies against viruses from all four subtypes, demonstrating successful imprinting. To assess the effect of pre-immunity on influenza vaccination, the imprinted ferrets were administered a single dose of quadrivalent recombinant or mRNA influenza vaccine. mRNA vaccination of imprinted ferrets provided similar results to protein vaccination, inducing a significant increase in homologous neutralizing antibody titers compared to naïve ferrets post single dose. Following a second dose of mRNA at day 215, imprinted ferrets had higher homologous neutralizing antibody titers against flu B compared to naive ferrets. Lastly, to explore how pre-immunity impacts breadth of responses, we evaluated antibody titers against a panel of ten antigenically diverse influenza A H3 viruses. Compared to naïve ferrets, pre-immune ferrets had higher magnitude of titers against all ten H3 strains following vaccination, and the breadth of responses against a diverse H3 heterologous read out virus panel were comparable between the mRNA and non-adjuvanted protein-based vaccine platforms. This study demonstrates that pre-existing immunity elevates vaccine-induced neutralizing antibody titers and highlights the translational benefits of this single dose pre-immune ferret model for further vaccine research and development.

This work was financially supported by Sanofi.

Ashley C. Beavis, Katherine Roebke, Bianca Baum, Svetlana Pougatcheva, John Hamberger, Philip Davidson, Wen Cheng, Thorsten U. Vogel, Irina V. Ustyugova, Ana Goncalvez, Raul Gomila, William Warren, Konstantin Zeldovich, and Maryann Giel-Moloney are Sanofi employees and may hold shares and/or stock options in the company.

Biography:

Ashley Beavis obtained her PhD in Infectious Diseases from the University of Georgia and is a Principal Scientist on Sanofi's Global Antigen Design Influenza HA Design team. Her research interests include respiratory viruses, RNA viruses, vaccine research and development, intranasal vaccines, and viral vectors.

Long-term cellular immunity of vaccines for Zaire Ebola Virus Diseases

Aurélie Wiedemann[1,2¥], Edouard Lhomme[1,3,4¥], Mélanie Huchon[1,3,4], Emile Foucat[1,2], Marion Bérerd-Camara[5], Lydia Guillaumat[1,2], Marcel Yaradouno[5], Jacqueline Tambalou[5], Cécile Rodrigues[1,2], Alexandre Ribeiro[1,2], Abdoul Habib Béavogui[6], Christine Lacabaratz[1,2], Rodolphe Thiébaut[1,3,4], Laura Richert[1,3,4], Yves Lévy[1,2,7]*, Prevac study team[a]

[1]Vaccine Research Institute, Université Paris-Est Créteil, France
[2]INSERM U955, Institut Mondor de Recherche Biomedicale (IMRB), Team Lévy, Créteil, France
[3]University of Bordeaux, Inserm, CHU Bordeaux, CIC 1401, EUCLID/F-CRIN Clinical Trials Platform, F-33000 Bordeaux, France
[4]Univ. Bordeaux, Inserm, Population Health Research Center, UMR 1219, INRIA SISTM, Bordeaux, France
[5]Alliance for International Medical Action
[6]Centre National de Formation et de Recherche en Santé Rurale (CNFRSR), Maferinyah, Guinea
[7]Assistance Publique-Hôpitaux de Paris, Groupe Henri-Mondor Albert-Chenevier, Service Immunologie Clinique, Créteil, France

Recent Ebola outbreaks underscore the importance of continuous prevention and disease control efforts. The European Medicines Agency (EMA) has authorized two vaccines: Merck's Ervebo (rVSV-ZEBOV) and Johnson & Johnson's two-dose combination (Ad26.ZEBOV/MVA-BN-Filo). In a five-year follow-up of the Partnership for Research on Ebola Vaccinations (PREVAC) randomized trial (NCT02876328), we evaluated the long-term functionality, breadth, and magnitude of vaccine-induced memory T cell responses of three vaccine regimens: Ad26.ZEBOV followed by MVA-BN-Filo (Ad26–MVA group), rVSVΔG-ZEBOV-GP followed by placebo (rVSV group), and rVSVΔG-ZEBOV-GP followed by rVSVΔG-ZEBOV-GP (rVSV–booster group) in 92 participants. We found ex vivo polyfunctional EBOV-specific CD4+ T cell responses increased after the Ad26 prime, enhanced by the MVA boost, while minimal responses were observed in the rVSV groups, declining one year later. This observation contrasted with the detection of a significant increase in IP-10 and TRAIL serum markers at day 7 post rVSV injection, indicating an activation effect. Through 8-day in vitro culture, we showed both Ad26-MVA and rVSV single vaccination sustained EBOV-specific T cell responses for up to 60 months post-initial vaccination, with no decline observed. CD8+ T cell responses were absent in the long-term follow-up of the rVSV booster group. Analysis of cytokine production revealed shared biomarkers between Ad26-MVA and rVSV groups, including Th1 cytokines, granzyme, and T cell activation markers (PDL-1). While the number of factors produced in vitro decreased over time, at month 60, G-CSF, a marker of T-cell activation, remained detectable in both the Ad26-MVA and rVSV groups. The low production of T-cell cytotoxic and activation markers by PBMCs from the rVSV booster group was consistent with the low frequency of ex vivo CD8+ T cell responses. Finally, we demonstrated a correlation between EBOV-specific T cell responses and anti-EBOV IgG responses suggesting the need for a long-term boost to maintain memory responses.Markers of long-term protection against Ebola Virus Disease (EVD) are still lacking. Our findings may provide insights into the low vaccine responders and/or observations of breakthrough infections despite EBOV vaccination. Additionally, they could help in shaping recommendations for booster vaccination and identifying populations that are likely to benefit from revaccination.

Biography:

Dr. Aurelie Wiedemann is a Senior Scientist at the Vaccine Research Institute (VRI)/INSERM in Paris, France. Specializing in immunology, she leads the Cellular Division at VRI, where she evaluates immune cellular responses among participants in vaccine clinical trials and cohorts of infected patients. Dr. Wiedemann also spearheads the coordination of multiple clinical trials spanning Europe and Africa.

Targeting Langerhans cells using trimeric Env of HIV triggers a swift and robust production of Env-specific IgG antibodies and neutralizing antibodies through a Tfh/germinal center (GC) reaction

Adele Hammoudi[1,2], Mathieu Surenaud[1,2], Florence Picard[1,2], Jade Legros[1,2], Guillaume Hypolite[1,2], Sebastian Brami[1,2], Emma Sicherre[1,2], Borys Pedenko[3], Delphine Guilligay[3], Christiane Moog[1,4], Sandra Zurawski[1,5], Gerard Zurawski[1,5], Winfried Weissenhorn[3], Mireille Centlivre[1,2], Véronique Godot[1,2†], Yves Levy[1,2,6†*], Sylvain Cardinaud[1,2†*]

[†]These authors contributed equally

[1]Vaccine Research Institute (VRI)

[2]Inserm U955, Team 16, Institut Mondor de Recherche Biomédicale, Université Paris-Est Créteil, Créteil, France

[3]University Grenoble Alpes, CEA, CNRS, Institut de Biologie Structurale (IBS), Grenoble, France

[4]University of Strasbourg, INSERM UMR_S 1109, Interdisciplinary Thematic Institute (ITI) of Precision Medicine of Strasbourg, France

[5]Baylor Institute for Immunology Research (BIIR), Dallas, Texas, United States of America,

[6]Assistance Publique-Hôpitaux de Paris, Groupe Henri-Mondor Albert-Chenevier, Service Immunologie Clinique, Créteil, France

Background: Although approved vaccines are successful in generating long-lasting antibody responses, the development of HIV vaccines still faces challenges. While the RV-144 trial demonstrated limited efficacy by focusing on certain HIV antigens, subsequent studies struggled to reproduce these findings. Novel approaches that target antigens directly to dendritic cells (DCs) and activate the skin's immune system show promise. Previous research that targeted epidermal Langerhans cells (LCs) with anti-Langerin mAbs fused to HIV-1 Envelope monochains (LC.Env, Kervevan PLoS Path 2021) triggered antigen-specific immune responses in both mice and human LC:T/B cocultures. In this study, our objective is to refine LC targeting by designing trimeric Env constructs (LC^3.Env^3) or BG505-like structures (LC^3.SOSIP) to explore their potential to induce germinal center (GC) and Tfh cell reactions, thereby enhancing Env-binding IgG and the production of HIV neutralizing antibodies (NeutAb) in vivo.

Methods: LC.Env, LC^3.Env^3, and LC^3.SOSIP were manufactured in CHO cells and subjected to quality control measures. B6 mice received intradermal immunizations of LC^3.Env^3 or control LC.Env mAb (5 mcg of Env antigen) on day (D) 0 and D21 without adjuvant. Antibody and cellular responses were evaluated post-prime (PP) and post-boost (PB) using Luminex and FACS techniques. Germinal center (GC) and Tfh reactions in draining lymph nodes (dLN) were observed using immunofluorescence. Additionally, rabbits were subcutaneously vaccinated with 30 mcg of LC^3.Env^3or LC^3.SOSIP without adjuvant, and serum levels of neutralizing antibodies (NeutAb) were measured.

Results: Following LC^3.Env^3 immunization, notable alterations were observed in Tfh and B-cell populations within the dLN, characterized by a substantial expansion of Env-specific germinal center (GC) B-cells postboost ($P<0.01$) and the rapid development of structured GCs, indicating a robust immune reaction. Envspecific IgG antibodies were detectable post-prime, with LC^3.Env^3 immunization resulting in a progressive increase in IgG avidity over time. Importantly, Env IgG titers were notably higher compared to non-targeting Env^3 HIV-1 trimer. Fluorescent vaccine studies revealed LC-specific antigen uptake associated with potent T- and B-cell Env-specific immune responses. Rabbit immunization with LC^3.Env^3 and LC^3.SOSIP demonstrated elevated levels of Env-specific IgG and sera capable of neutralizing tier-1 HIV-1 viruses.

Conclusions: This research presents an innovative approach to propel HIV vaccine development forward by utilizing Langerhans cells as a delivery system, leading to heightened humoral responses and the generation of neutralizing antibodies. These results underscore the importance of continual refinement and exploration of various strategies to achieve comprehensive and e^icacious immunization against HIV.

Providing solution for Novel Vaccine Development and Manufacturing for a Healthier 21st Century

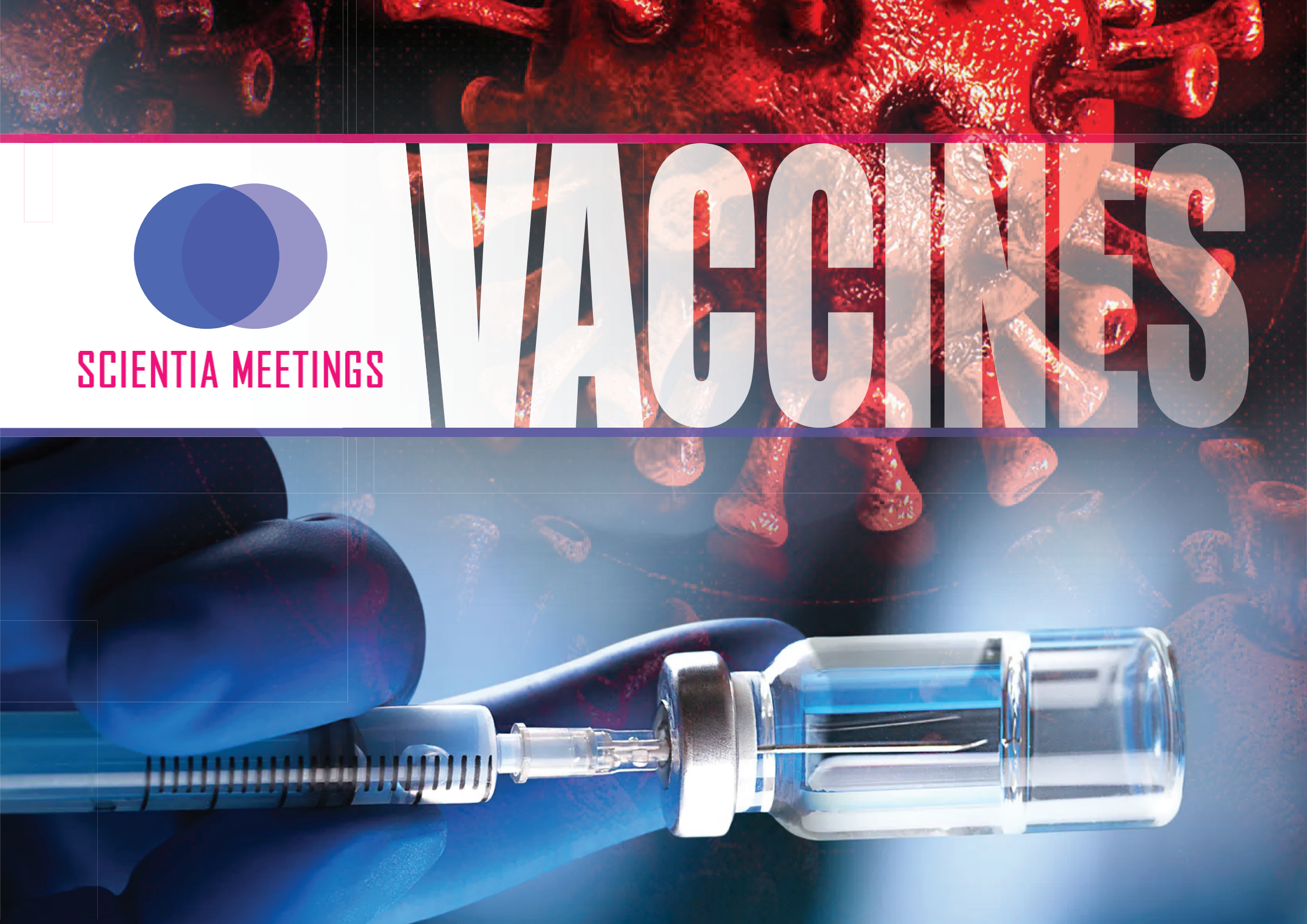
Xinhao Ye, PhD
Director, CMC lead of WuXi Vaccines

In the past century vaccination has played a pivotal role in reducing mortality and morbidity caused by infectious diseases. Leveraging innovations from emerging technologies, vaccines are poised to meet evolving demands of a 21st-century society characterized by increased life expectancy, the emergency of new infections, and persistent poverty in low-income countries. Consequently, next-generation vaccines must be more effective, safer, and better tolerated across all ages, especially for children, the elderly, and other populations with compromised immune system. Moreover, vaccine access and equality remain problematic in low- and middle-income countries (LMICs). Addressing this long-standing issue will require affordable vaccine supplies and local manufacturing capabilities. As a world-leading CRDMO, we'd like to take the opportunity to present how we get prepared, enabling our clients, whether multinational corporations or biotech startups, to tackle these challenges. It includes comprehensive efforts to support structure-based immunogen design, to accelerate novel vaccine development, to enhance adjuvant accessibility and screening, and to enable low-cost small-footprint manufacturing. Ultimately, the end-to-end platform aims to empower next-generation vaccine development, foster global collaboration, and support efforts in areas critical for epidemic and pandemic preparedness.

SCIENTIA MEETINGS

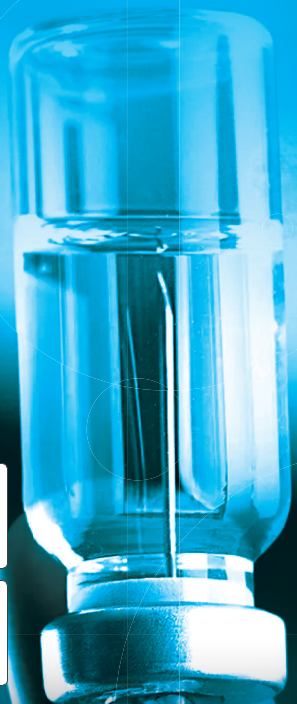
VACCINES 2024

Index


SCIENTIA MEETINGS
VACCINES

SCIENTIA MEETINGS

BOOK VACCINES 2024



EXHIBITORS

WuXi Vaccines | C.T.L. Cellular Technology Ltd. | FinaBio Fina Biosolutions LLC

labcorp | DesertKing | BIOSYSTEMS Acro

VACCINES SUMMIT-2024

NOVEMBER 13-15, 2024
BOSTON, MA

SCIENTIA MEETINGS
Website: https://scientiameetings.com/conferences/vaccines/ | Ph: 1-815-595-8049 | Email: venky@sciresgroup.net