SCIENTIA MEETINGS

VACCINES 2023

BOOK

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EXHIBITORS

VACCINES SUMMIT-2023

NOVEMBER 13-15, 2023
BOSTON, MA

SCIENTIA MEETINGS
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About Organizer:

Scientia Meetings understand the importance of networking and collaboration. Conferences are not just about discussion, but about sharing knowledge and research work, new ideas, and a lot of opportunities. We are launching events in the country to create real networking with scientists and researchers from research institutes, companies, laboratories, and government agencies. We aim to have our events with only a moderate number of invited guests/delegates attending related to discipline and to create a platform for conversations leading to opportunities according to their individual needs. Our aim is to provide a platform for research scholars, scientific leaders, and decision-makers to come together and share their research findings with other scientific professionals which help to improve the sharing of knowledge and easy access to scientific information.

We provide a unique opportunity to share your innovative ideas, evaluate your research works, and promote collaborative work through networking sessions for a brighter future.

About Vaccines Summit-2023:

Scientia Meetings invites participants across the globe to attend its second edition of Vaccines Summit which is going to take place during November 13-15, 2023, and is organized around the theme “next-generation vaccines treatment and diagnostics that save lives”, Vaccines Summit-2023 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-2023 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-2023 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-2023 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-2023. Pitch your idea to an industrial expert jury to raise the capital you need to get started.

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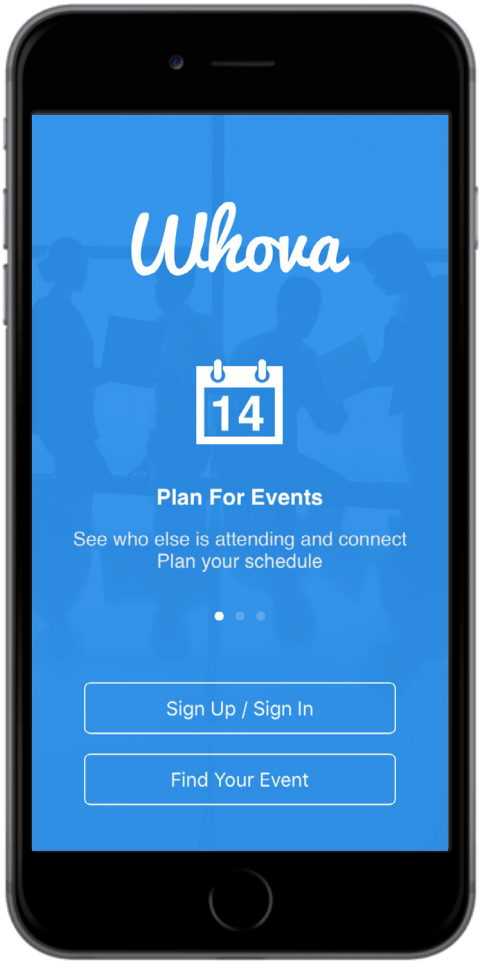

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MUKESH KUMAR, PH.D.
Associate Professor, Department of Biology,
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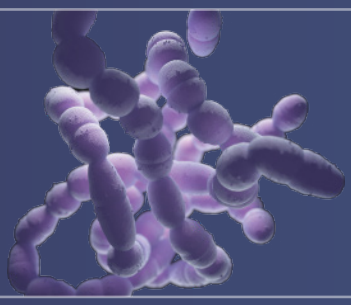

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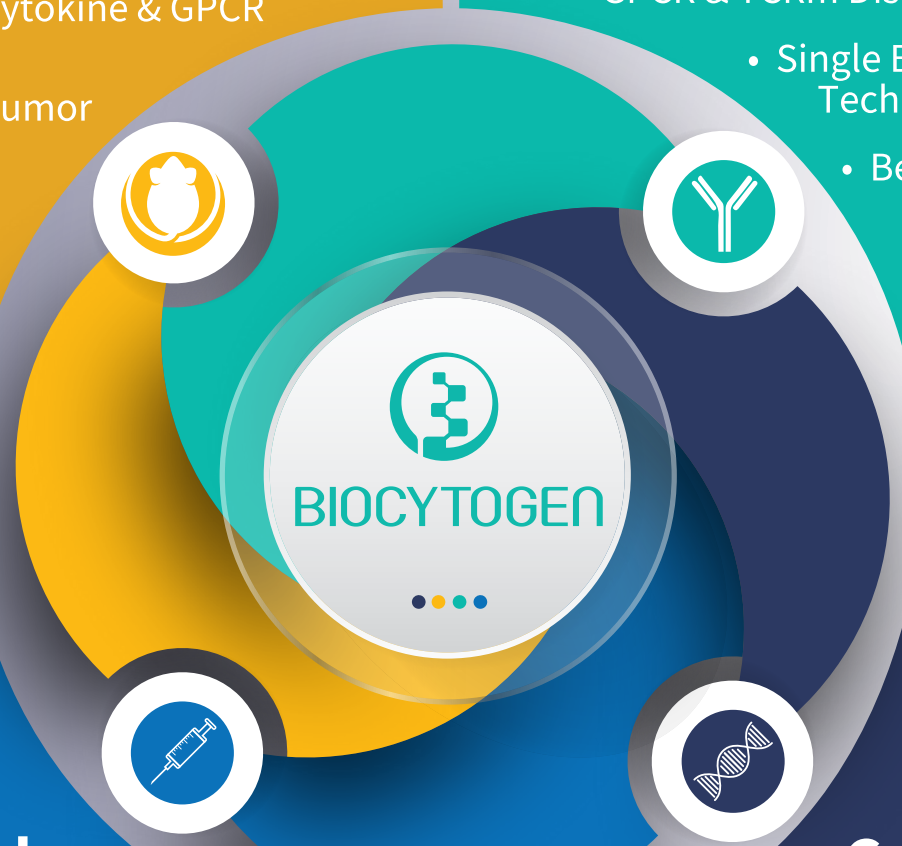

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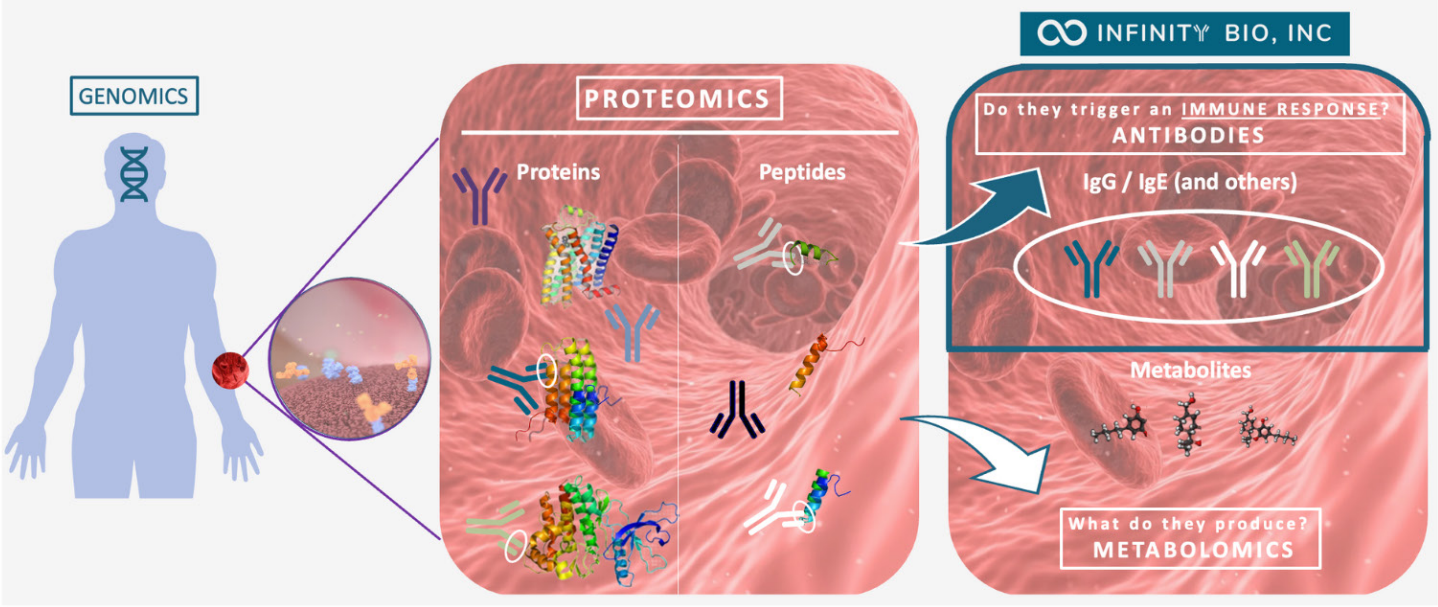

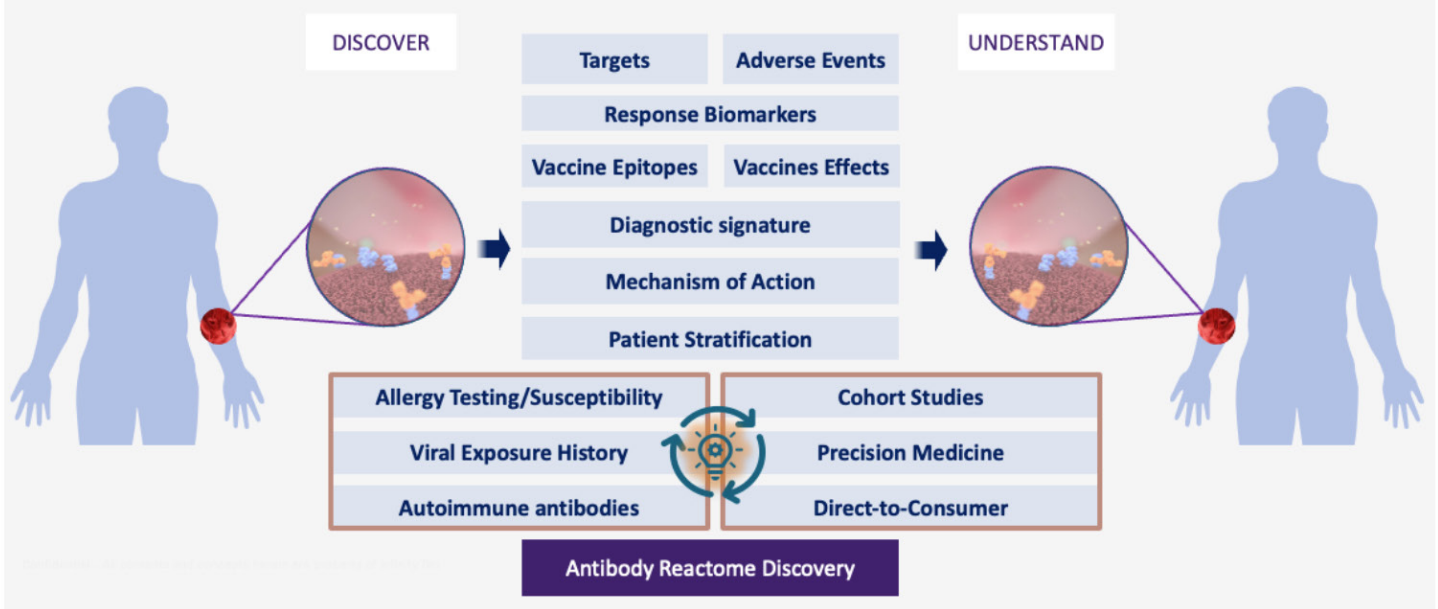

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SCIENTIA MEETINGS

VACCINES 2023

Day 1: November 13, 2023

Keynote Presentations

VACCINES SUMMIT-2023

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Keynote Presentations

Title: **Prospects for vaccination against human cytomegalovirus**
Stanley A. Plotkin
Consultant and Emeritus Professor of the University of Pennsylvania, Vaxconsult, LLP

Title: **Development of a COVID-19 vaccine**
Sir Andrew J. Pollard
Ashall Professor of Paediatric Infection and Immunity and Director of Oxford Vaccine Group

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

Title: **Precision Vaccines: Bringing Precision Medicine to Vaccinology**
Ofer Levy
Staff Physician & Principal Investigator, Director, Precision Vaccines Program, Division of Infectious Diseases, Boston Children's Hospital Professor, Harvard Medical School

Title: **Monitoring COVID-19 vaccine safety during the pandemic: successes, opportunities, and outstanding challenges**
Walter Straus
Vice-President, Clinical Safety, Moderna

Title: **Nanoparticle intranasal vaccine prevents forward airborne transmission to naïve recipient hamsters**
Jay A. Berzofsky
National Cancer Institute, NIH

Title: **Use of VSV vaccine platform for epidemic preparedness and response; update from current studies and innovative partnership strategies**
Swati Gupta
VP, Emerging Infectious Diseases and Epidemiology, IAVI

Title: **NIAID, vaccine research center's pandemic preparedness and emergency response: Looking at the past to shape our future**
Karin Bok
Acting Deputy Director, Director of Pandemic Preparedness and Emergency Response, Vaccine Research Center, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Title: **Translating the COVID-19 learnings into long-lasting innovation: how new technologies could help address global health issues and improve pandemic preparedness**
Ruben Rizzi
Vice President of Global Regulatory Affairs, BioNTech

Title: **Ad26 viral vector based vaccines for COVID-19 and HIV-1**
Hanneke Schuitemaker
VP, Head of Viral Vaccine Discovery and Translational Medicine, Janssen Vaccines and Prevention B.V

Title: **Data-science-supported formulation development creates value for vaccine products**
Sabine Hauck
Leukocare

Title: **Next generation mRNA Design-Increasing mRNA Potency with a New Cap Analog**
Kate Broderick
Chief Innovation Officer, Maravai LifeSciences

Title: **Durable immunity, lessons from measles and mumps**
Richard B. Kennedy
Professor of Medicine, Co-Director, Mayo Clinic Vaccine Research Group

Title: **Nucleic acid tools for driving vaccine immunity and gene delivery for improved immune impact**
David Weiner
Executive Vice President, Director, Vaccine & Immunotherapy Center, The Wistar Institute

Title: **UVC: Universal Vaccine Cell**
Tom Henley
Chief Scientific Officer, Intima Bioscience

Title: **A strategic model and industry collaboration for sustainable development of vaccines against neglected diseases**
Francesco Berlanda Scorza
VP, Global Health R&D Vaccines Head and GVGH Institute Director, GSK Vaccines Institute for Global Health

Title: **Accelerating recombinant protein vaccine development and manufacturing for disease X**
Jian He (Jason)
CMC Head, WuXi Vaccines

Prospects for vaccination against human cytomegalovirus

Stanley A. Plotkin, MD
University of Pennsylvania, USA

Attempts to develop vaccines against the human cytomegalovirus have been going on for the last 50 years. Vaccination for organ transplant recipients has shown promise of efficacy over the years but has not been established. However, vaccination before pregnancy to protect the fetus has not yet been shown to be successful. Nevertheless, several promising candidates are now being tested and may improve on the approximately 50% efficacy already shown for prevention of infection during pregnancy.

Biography

Dr. Stanley A. Plotkin is Emeritus Professor of the University of Pennsylvania. Until 1991, he was Professor of Pediatrics and Microbiology at the University of Pennsylvania, Professor of Virology at the Wistar Institute and at the same time, Director of Infectious Diseases and Senior Physician at the Children's Hospital of Philadelphia. For seven years he was Medical and Scientific Director of Sanofi Pasteur, based at Marnes-la-Coquette, outside Paris. He is now consultant to vaccine developers and non-profit research organizations.

He is a member of the Institute of Medicine of the National Academy of Sciences and the French Academy of Medicine. His bibliography includes over 800 articles and he has edited several books including a textbook on vaccines. Dr. Plotkin has received honorary doctoral degrees from the University of Pennsylvania, the University of Rouen and the Complutense University of Madrid, He also has received the French Legion of Honor. Dr. Plotkin developed the rubella vaccine now in standard use throughout the world, is codeveloper of the pentavalent rotavirus vaccine, and has worked extensively on the development and application of other vaccines including anthrax, oral polio, rabies, varicella, and cytomegalovirus

Development of a COVID-19 vaccine

Professor Sir Andrew J Pollard | PhD FRCPCH FMedSci
Director | Oxford Vaccine Group
Ashall Professor of Infection and Immunity
Pandemic Sciences Institute | University of Oxford
Department of Paediatrics | University of Oxford | Children's Hospital

Biography

Sir Andrew is Director of the Oxford Vaccine Group at the University of Oxford and an honorary consultant paediatrician (infectious disease and immunology) at Oxford Children's Hospital. He received a knighthood in the Queen's Birthday Honours in 2021 for services to Public Health and the Order of Medical Merit from the Federal Republic of Brazil in 2022.

His research includes the design, development and clinical evaluation of vaccines including those for typhoid, meningococcus, *Haemophilus influenzae* type b, pneumococcus, plague, pertussis, influenza, rabies, coronavirus and Ebola. His work on pneumococcal and meningococcal vaccines has been used in global public health policy. His studies on typhoid both using the human challenge model and in field sites supported the WHO prequalification of a new typhoid conjugate vaccine and WHO recommendations for its use in countries with a high burden of disease with more than 50 million vaccinated since 2021. He was the chief investigator for the clinical trials of the Oxford-AstraZeneca vaccine in 2020 in 24,000 participants in UK, South Africa and Brazil, which led to authorisation of the vaccine for use in more than 180 countries with over 3.5 billion doses distributed and award of the Copley Medal by the Royal Society in 2022. He has supervised 48 PhD students and his publications includes over 600 manuscripts. He chairs the UK Department of Health and Social Care's Joint Committee on Vaccination and Immunisation, was a member of WHO's Strategic Advisory Group of Experts (2016-2022). He chaired the European Medicines Agency scientific advisory group on vaccines (2012–2020). He received the Bill Marshall Award of the European Society for Paediatric Infectious Disease (ESPID) in 2013, the ESPID Distinguished Award for Education and Communication in 2015 and the Rosén von Rosenstein medal in 2019 from the Swedish Society of Medicine, the James Spence Medal from the Royal College of Paediatrics and Child Health in 2022. He is chair of the Knoop Charitable Trust and is a trustee of the Jenner Vaccine Foundation, the Academy of Medical Sciences and the Oxford Philharmonic Orchestra.

Correlates of protection for COVID-19 vaccines

Dan Barouch, M.D., Ph.D.
William Bosworth Castle Professor of Medicine, Professor of Immunology, Harvard Medical School
Ragon Institute of MGH, MIT, and Harvard
Director, Center for Virology and Vaccine Research

Beth Israel Deaconess Medical Center Three and a half years into the COVID-19 pandemic, the nature and durability of protection against SARS-CoV-2 still remains unclear. Current COVID-19 mRNA vaccines have been shown to provide minimal protection against infection with current variants but substantial protection against severe disease. However, such protection appears to wane quickly. I will describe preclinical and clinical evidence that vaccine protection is mediated by both antibody and T cell responses.

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.

William Bosworth Castle Professor of Medicine, Harvard Medical School, Ragon Institute of MGH, MIT, and Harvard, Director, Center for Virology and Vaccine Research, Beth Israel Deaconess Medical Center

Precision Vaccines: Bringing Precision Medicine to Vaccinology

Ofer Levy MD, PhD
Director, *Precision Vaccines Program*, Department of Pediatrics Boston Children's Hospital
Professor of Pediatrics, Harvard Medical School
Associate Member Broad Institute of MIT & Harvard

Vaccines are typically discovered and developed based on a "one size fits all" approach, yet vaccine safety, immunogenicity and efficacy varies substantially in relation to demographic features including age, sex and co-morbidity. For example, due to distinct immunity, infants and older adults (≥65 years of age) are both at heightened risk of severe infection and tend to mount lower vaccine responses. To address this challenge, the *Precision Vaccines Program* (PVP) at Boston Children's Hospital (BCH) has assembled a multi-disciplinary team to employ novel approaches to discover and develop vaccines to protect vulnerable populations. Supported in part by NIH/NIAID, the Bill & Melinda Gates Foundation, the Coalition for Epidemic Preparedness Innovations (CEPI), and industry-derived sponsored research agreements, the PVP leverages multiple innovative vaccinology approaches including: (a) multi-omic systems biology to define signatures predictive of vaccine safety and efficacy, (b) population-specific human *in vitro* modeling to study vaccine safety, immunogenicity and mechanism of action (MOA) and as a tool for high throughput screening for bespoke adjuvants, (c) age- and morbidity-specific animal models and (d) targeted clinical trials in diverse international populations. Recent advances by the PVP include: 1) supporting the NIH/NIAID Immunophenotyping of a Coronavirus Cohort (IMPACC) COVID biomarker discovery effort (PMID: 37327781), 2) conducting systems vaccinology studies to define signatures predictive of vaccine safety and immunogenicity in newborns (PMID: 32426309) and adults (PMID: 36316476), 3) Identification and optimization of novel small molecule adjuvants that activate pattern recognition receptors (PRRs) via high throughput screening and medicinal chemistry and formulation (PMID: 37453068), 4) defining adjuvantation systems that enhance age-specific antiviral immunity (PMIDs: 34783582 & 35918315), and 5) advancing adjuvanted vaccines against opioid overdose deaths (PMID: 35579508). Precision vaccinology approaches tailored to enhance vaccine safety and efficacy in vulnerable populations hold promise in addressing current and future infectious and non-infectious disease challenges in vulnerable populations across the globe.

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.

Monitoring COVID-19 vaccine safety during the pandemic: successes, opportunities, and outstanding challenges

Walter Straus, MD, MPH, FACP
Vice-President, Clinical Safety, Moderna

In the setting of the greatest pandemic of a century, the successful development, emergency use authorization, manufacture, and deployment of several COVID-19 vaccines within one year following the first description of the novel SARS-CoV-2 virus counts as a remarkable and extraordinary public health achievement. Doing so required regulatory, industry, academia, and public health sectors throughout the world to collaborate intensively to ensure that vaccine safety was monitored and in an exceptionally timely and comprehensive manner so that the benefits and risks of COVID-19 vaccines were known and communicated real-time. This presentation will provide an overview of novel as well as established tools and networks used to monitor COVID-19 vaccine safety, highlighting effective collaborations across the vaccine research ecosystem. A case example will be provided.

Biography

Walter is an internist, gastroenterologist-hepatologist and epidemiologist, who has spent much of his career working in vaccines, supporting programs from translational research through post-authorization safety assessment. His career spans academia, government (CDC, where he served as an Epidemic Intelligence Officer), and industry. At Moderna, he led the team overseeing the safety of its COVID-19 vaccine program and is now team leader for safety of its latent virus and public health vaccine program. At Moderna and previously at Merck, his teams have provided safety oversight for more than 20 vaccines – licensed or in development. Outside of Moderna, he is a member of the CIOMS Working Group on Artificial Intelligence in Pharmacovigilance.

Nanoparticle intranasal vaccine prevents forward airborne transmission to naïve recipient hamsters

Yongjun Sui[1], Swagata Kar[2], Bhavna Chawla[2], Tanya Hoang[1], Hanne Andersen[2], and Jay A. Berzofsky[1]
[1]Vaccine Branch, CCR, National Cancer Institute, NIH, Bethesda, Maryland USA
[2]Bioqual Inc. Rockville, Maryland USA

Natural transmission of SARS-CoV-2 is primarily airborne, through the respiratory mucosal route. However, current licensed COVID-19 vaccines are all intramuscular (IM), and induce more systemic than mucosal immunity. We have developed a nanoparticle mucosal intranasal (IN) vaccine containing the S1 spike protein of SARS-CoV-2 combined with TLR ligands and IL-15 as adjuvants. We found that this vaccine is more effective than the same S1 in alum given IM at reducing viral load (VL) in the naso/oropharynx in both rhesus macaques and Golden Syrian hamsters. Although macaques don't get COVID disease, hamsters do, and the IN mucosal nanoparticle vaccine protected hamsters against COVID disease better than the IM one. Based on these results, we hypothesized that the IN mucosal vaccine might protect better against forward transmission to naïve recipients, a key public health goal. We tested this in hamsters by immunizing two groups with a licensed mRNA-1273 vaccine IM and then boosting one group with the same and the other with the naso/oral nanoparticle Spike vaccine. Both vaccines reduced VL in the oropharynx and lungs and prevented weight loss after SARS-CoV-2 challenge. A day after challenge, the animals were cohoused with a naïve hamster separated by a permeable barrier that allowed airborne transmission but not touching or sharing of secretions. The naïve group exposed to the hamsters who had the nanoparticle mucosal boost had markedly lower transmission as measured by VL in oral swabs and lung. Moreover, this reduction in VL correlated with higher neutralizing antibody measured by ACE2 inhibition in the oral secretions, but did not correlate with serum antibodies. Thus, the mucosal nanoparticle vaccine was a more effective boost than a second dose of mRNA vaccine IM at preventing forward airborne transmission, a key public health necessity, and correlated with local mucosal antibody.

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.

Use of the VSV vaccine platform for epidemic preparedness and response; updates from current studies and innovative partnership strategies

Swati Gupta
VP, Emerging Infectious Diseases and Epidemiology, IAVI

Outbreaks of viral hemorrhagic fever (VHF) diseases are increasing in frequency, including the occurrence of Marburg virus (MARV) disease outbreaks in Equatorial Guinea and Tanzania and a Sudanvirus (SUDV) disease outbreak in Uganda within the last year alone. With the exception of ERVEBO®, Merck's licensed single-dose Zaire ebolavirus vaccine, there are no licensed vaccines or therapeutics targeting viruses causing hemorrhagic fever 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 SUDV, MARV, and Lassa fever virus. 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, and updates across the portfolio will be shared. Furthermore, recent experience with mobilization of doses of IAVI's SUDV vaccine drug product in response to the outbreak of SUDV disease in Uganda in late 2022 highlights the need for collaboration, partnership, and alignment of public health stakeholders to ensure the availability of safe and effective vaccines against future outbreaks of VFH diseases. As products progress closer to licensure, different partnership models will need to be created in order to do end to end product development for vaccines with limited commercial markets.

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.

NIAID, vaccine research center's pandemic preparedness and emergency response: Looking at the past to shape our future

Karin Bok, MS, PhD
Acting Deputy Director, Director of Pandemic Preparedness and Emergency Response, Vaccine Research Center, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Lessons from responding to multiple emergencies, including Ebola virus outbreaks and the Coronavirus Pandemic will be examined to shape the way we prepare for future emergencies.

Biography

Dr. Karin Bok is the Director of Pandemic Preparedness and Emergency Response at the Vaccine Research Center, National Institutes of Health. She provides expertise for the preclinical and clinical development of several preparedness and response medical countermeasures, including preventive and therapeutic products against Ebola, Zika, Nipah, Influenza, and Coronavirus. Karin collaborates with government colleagues and external stakeholders to prepare and accelerate the response to an infectious disease emergency and advance the study of preventive measures that target unmet medical needs. She is currently part of H-CORE (former Operation Warp Speed) contributing to accelerating the development and testing of vaccines against SARS-CoV-2 in the US. She is also part of the senior team working on the advanced development of broadly neutralizing monoclonal antibodies for HIV, as well as universal influenza and RSV vaccines.

Previously, Dr. Bok was a Senior Vaccine Scientific Advisor at the National Vaccine Program Office, within the Office of the Assistant Secretary for Health. Dr. Bok led the vaccine safety portfolio and advised on vaccine research and development issues. She also directed research and policy studies on vaccines administered to pregnant women. Karin represented NVPO and HHS in several executive scientific advisory committees, such as the Vaccines and Related Biological Products Advisory Committee (VRBPAC, FDA), the Advisory Commission on Childhood Vaccines (ACCV, HRSA), and the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC, NICHD) to name a few.

In addition, Dr. Bok has more than 20 years' experience working on research and discovery programs, leading her own scientific studies focused on vaccines, antibody products, antivirals, diagnostics, and virus evolution of gastrointestinal viruses.

Her international scientific experience includes managing and conducting research through Argentina's national gastroenteritis surveillance program, the clinical testing of the rotavirus vaccine, and the reimplementation of the National Smallpox Vaccine Program.

Translating the COVID-19 learnings into long-lasting innovation: how new technologies could help address global health issues and improve pandemic preparedness

Ruben Rizzi, MD
Vice Present Global Regulatory Affairs, BioNTech SE

The COVID-19 pandemic posed a unique threat to global health, prompting national and supranational institutions to deploy restrictive measures to curb infections and triggering a worldwide demand for prophylactic vaccines. The development of vaccines against SARS-CoV-2 rapidly became a high priority among governments as well as academia and the pharmaceutical industry. As a result of the extraordinary efforts, less than a year after COVID-19 was declared a pandemic, the first vaccines received emergency approvals and vaccination campaigns were initiated worldwide. Two years later, COVID-19 vaccines have become standard of care, principally being supplied through traditional regulatory pathways, and potentially updated on an annual basis to ensure the closest possible match to circulating SARS-CoV-2 variants. During the development of COVID-19 vaccines, pre-existing regulatory tools were used and learnings from prior pandemic developments were leveraged. Additionally, most regulators adopted a very open communication approach with vaccine developers, providing specific guidance to clarify requirements and expectations through all development phases. We will analyze the importance of this regulatory framework for rapid vaccine development, evaluating the key factors that led to the unprecedented rapid development of COVID-19 vaccines, discussing which principles could help address unmet global health needs and how regulatory science will evolve and adapt to the emerging technologies, such as messenger RNA. Furthermore, platform-inspired approaches have been used to enable the early start of FIH studies for COVID-19 vaccines as well as to support approval of variant-adapted vaccines, and this experience could be used to improve existing pandemic preparedness models.

Biography

Ruben Rizzi, MD, is VP of Global Regulatory Affairs at BioNTech. He joined the company in December 2019 and he has worked on both infectious diseases and immune-oncology programs, being the global regulatory lead for BioNTech for the COVID-19 vaccine developed in collaboration with Pfizer (COMIRNATY). Today, Ruben is still supporting the lifecycle of COVID-19 vaccines and leading the teams working on the development of BioNTech´s pipeline, post-approval activities and labeling.

Ad26 viral vector-based vaccines for COVID-19 and HIV-1

Hanneke Schuitemaker, PhD
VP Viral Vaccine Discovery & Translational Medicine
Professor in Virology
Janssen Vaccines & Prevention

Replication incompetent adenoviral vectors have been used as vaccine platform for the genetic delivery of transgenes encoding viral proteins. To circumvent impact of pre-existing immunity against the adenoviral vector, we selected Adenovirus 26, a low-seroprevalent Adenovirus, for the generation of the vector. The complementing PER.C6® cell-line was optimized for vector manufacturing. This platform was used in multiple vaccine programs, including our HIV-1 vaccine program, and for a COVID-19 vaccine in response to the pandemic.

The Ad26 based HIV-1 vaccine consisting of mosaic gag, pol and env immunogens, complemented with env proteins, provided protection in a NHP SHIV challenge model. However, a phase 2b study in southern Africa in women at high risk for HIV infection, and a phase 3 study in men who have sex with men (MSM) and transgender individuals, also at high risk for HIV infection, did not reveal protection from the vaccine.

The Ad26 based COVID-19 vaccine expressing a pre-fusion stabilized SARS-CoV-2 Spike protein demonstrated protection in a NHP challenge model which did translate in protection against COVID-19 in humans. Protection was durable and further enhanced by a second dose with a 2-month interval and correlated strongly with the presence of Spike specific humoral immunity.

A rare but serious adverse event of thrombosis with thrombocytopenia syndrome has been associated with Adenovector based COVID-19 vaccines and may limit the further use of the adenoviral vector platform. The pathogenesis of TTS is being investigated.

Biography

Hanneke Schuitemaker, Ph.D., is the Head of Viral Vaccine Discovery and Translational Medicine at Janssen Vaccines & Prevention B.V. She has been in this role since 2010 and oversees Janssen's viral vaccine programs including investigational vaccine candidates for HIV, respiratory syncytial virus (RSV), Ebola, Zika, Influenza and COVID-19. In addition, she is a Professor of Virology at the Amsterdam University Medical Center.

Hanneke Schuitemaker is a medical biologist by training, received her Ph.D. in Medicine in 1992 at the University of Amsterdam and worked for more than 20 years on the pathogenesis of HIV-1 infection, first at Sanquin (1989-2007), the blood supply foundation in the Netherlands, where she was the Chair of the department of Clinical Viro-Immunology (1998-2007), and then at the Amsterdam University Medical Center (2008-2010), where she was the Chair of the Department of Experimental Immunology. From mid-2003 to mid-2004, she worked as a visiting scientist at The Scripps Research Institute in La Jolla, California. She successfully trained more than 30 Ph.D. students and co-authored more than 340 peer-reviewed scientific articles.

Data-science-supported formulation development creates value for vaccine products

Sabine Hauck
Leukocare, Germany

Formulation development was considered an art for a long time. High Throughput Screening (HTS) improved evidence-based formulation development, and today, Next Generation Formulation Development combines scientific data with data science. By utilizing molecular modeling, machine learning elements, and advanced Design of Experiments (DoE), excipients are specifically combined, leading to stabilizing formulations tailored to the drug product's needs. *In silico* analyses also expedite timelines, even with a limited amount of vaccine.

Value creation has been shown for various vaccines: Molecular modeling of an antibody revealed the lead molecule with the least aggregation propensity, and *in silico* comparison of Fv models to established antibodies pointed out property outliers. A machine-learning tool guides the time-saving selection of suitable excipients. For a formulated antibody, kinetic modeling allowed for shelf-life prediction based on wet-lab short-term stability data. Inactivated viral vaccines benefitted from higher processing stability: An influenza vaccine was re-formulated using DoE to support continuous manufacturing with terminal sterilization, and another vaccine was protected against antigenicity loss during irradiation-based inactivation. Tailored formulations for vaccines based on live viruses achieved longer shelf-life in liquid dosage form or high-temperature stability as lyophilized products.

Employing advanced data science maximizes insights from wet-lab experiments, enhances drug substance understanding, and enables more comprehensive conclusions than only wet- lab experiments. This knowledge supports the informed selection of the right lead candidate and the design of a formulation that stabilizes the vaccine during processing, storage, and transport. Furthermore, improved stability can reduce degradation and related activity loss or unwanted effects of potential degradation products, thus de-risking preclinical and clinical trials.

Biography

Sabine Hauck is Executive Vice President Corporate Development at Munich-based biotech company Leukocare AG. She has 20+ years of experience in the biotech industry, in which she held various positions in pharmaceutical development, quality assurance and regulatory affairs. Her experience spans from small molecules to cell therapies and includes a variety of dosage forms. In the current position, Sabine is responsible for digitalization activities at Leukocare AG as well as for Business Process and Quality Management. In this role, she supports the ongoing digital transformation of the organization related to the algorithm-based formulation development approach at Leukocare.

Next-generation mRNA Design – Increasing mRNA Potency with a New Cap Analog

Kate Broderick, Ph.D.
Chief Innovation Officer, 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 major capping strategies differ in their manufacturing costs, time, complexity, and availability, and how TriLink BioTechnologies is continuing to innovate in this technology as we debut a novel Cap1 structure.

Biography

Dr. Kate Broderick is the Chief Innovation Officer at Maravai LifeSciences, leading their Office of Science and Innovation. Dr. Broderick has a broad background in product development in the DNA therapeutic and drug delivery field. Prior to joining Maravai in 2022, Dr. Broderick spent 15 years at Inovio Pharmaceuticals, and has served as a principal investigator for a variety of grants and awards from government agencies and non-profits, including the National Institutes of Health. She received her PhD from the University of Glasgow in Scotland and completed her post-doctoral research at the University of California, San Diego.

Durable immunity, lessons from measles and mumps

Richard B. Kennedy, Ph.D.
Professor of Medicine
Co-Director, Mayo Vaccine Research Group
Division of General Internal Medicine
Mayo Clinic

Two paramyxoviruses: measles and mumps continue to cause outbreaks in the US and globally. In the US, both viruses are given as part of the MMR vaccine; however, immunization has resulted in remarkably different outcomes between the two viruses—eliciting essentially life-long immunity to measles, with high titer neutralizing antibody (neut. Ab) responses that persist for decades, and an immune response to mumps that only provides protection for about a decade. As a result of this waning immunity, the US is experiencing a resurgence of mumps disease, characterized by the largest outbreaks in decades and >10,000 reported mumps cases in the US in the past two years alone. Our current lack of understanding of why long-term immunity to mumps is not maintained is a critical obstacle preventing us from addressing this public health concern.

The different clinical outcomes between these viruses may be driven by the significant differences that exist in both the innate and adaptive arms of the response to these two vaccine viruses. These, in turn result in divergent antibody titers, memory B cell numbers, and differences in the quantity/quality of the responding T cells. We have investigated the residual immune response decades after 2nd dose MMR vaccine and the response to a 3rd dose of MMR. The functional characterization of these disparate immune responses is a first step in understanding the molecular mechanisms leading to durable vs transient immunity.

Biography

Dr. Kennedy earned his B.S. degree in Microbiology from Brigham Young University and his Ph.D. in Immunology from Mayo Clinic with postdoctoral training in immunogenetics and vaccinology. Dr. Kennedy is a Professor of Medicine and the Co-Director of the Mayo Clinic Vaccine Research Group. He has over 140 peer-reviewed publications in journals including: Lancet Infectious Diseases, the Journal of Infectious Diseases, and Frontiers in Immunology, 8 book chapters, and has participated in well over 100 scientific posters, abstracts, and presentations at national and international vaccine, virology, and immunology meetings. He is the Deputy Editor-in-Chief of Vaccine: X and an Associate Editor at Vaccine. He is a member of the American Association of Immunologists and the American Society for Microbiology. He has served as an ad hoc reviewer on dozens of NIH study sections and has participated in multiple international review panels (e.g., Wellcome Trust, Research Councils UK, Science Foundation of Ireland, European Research Council).

Dr. Kennedy has 4 R01 grants from NIH funding his work on viral vaccine immunology. He is also the PI of a CDC contract using single cell technologies to evaluate the T cell response to influenza vaccination and is a site PI for one of three NIAID Collaborative Influenza Vaccine Innovation Centers. Dr. Kennedy's research emphasis is on understanding the factors driving the tremendous diversity in human immune responses to vaccines against viral pathogens including: influenza, measles, mumps, rubella, SARS-CoV-2, smallpox, varicella, and zika. His group focuses on the role of host genetic variation, age and immunosenescence, nutrition, and other factors on the development and maintenance of immunity following vaccination. The laboratory employs systems biology and vaccinomics approaches to better understand the complex interactions that occur during the development of vaccine response with the goal of predicting and controlling vaccine-induced immune responses. Dr. Kennedy also investigates the use of peptide-based vaccines for SARS-CoV-2, vaccinia, Mpox, influenza, and zika virus.

Nucleic acid tools for driving vaccine immunity and gene delivery for improved immune impact

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

New approaches for immunization and immunotherapy through nucleic Acid platforms and tools has never been more important. Advances in this area can impact both infectious disease and are growing in interest for cancer therapeutics. We have been developing enhancements for synthetic nucleic Acid (DNA) strategies and moved tools into clinical studies for infectious disease, as well targeting cancers for immune clearance. These approaches are simple to produce, very well tolerated, have inherent temperature stability, and can incorporate large genetic stretches without immune interference they provide flexibility for repeat administrations. AS therapeutics for cancer including studies in HPV disease, we have observed reduction in disease and immune based clearance. We also build on this approach allowing for the design and expression of invivo launched biologics as well as immune adjuvants. Combined these approaches allows for an enhanced ability to tailor the immune response against specific targeting infectious agents or pathogenic cells.

Biography

Dr. Weiner directs a translational molecular immunology research team focused on synthetic nucleic acid based approaches for disease prevention and treatment. His early work developed new mAb targeting tumor antigens as well as viruses. His group went on to be one of the founding research teams in the field of Nucleic Acid Vaccine and Immune therapies. With collaborators he developed a pathway to the clinic enabling the first DNA vaccine trails for infectious diseases and for Cancer immune-therapy and opening up clinical approaches for other nucleic acid vaccines. Using cutting edge antigen design with a focus on invivo assembly + modifications of delivery, including EP, his team has helped expand multiple clinical DNA studies. These developments included advancing countermeasures for Emerging infectious Diseases, development of novel gene biologics and therapeutic vaccines for treatment of cancer, as well as advancing genetic approaches for delivery of mAb as broad new tools to further build upon.

Dr. Weiner's resume includes publication of over 510 papers/chapters & reviews and more than 650 lectures. He has received several awards/honors, including the WW Smith Family Chair in Cancer Research - 2016, Vaccine Industry Association Outstanding Academic Research Laboratory (2015 & 2016) (runner up 2017, 2018, 2019), Named Top 20 Translational Research Laboratories of the Year (Nature Biotechnology 2016, 2017, 2018, 2019 & 2020), the Stone family award for Cancer Research 2014, Received an NIH Directors Translational Research Award 2011, the Pennsylvania Life Sciences Achievement Award (2019), the Pennsylvania Drug Industry Award for Excellence (2022), the Genescript outstanding lab award 2023. He is currently the WW. Smith Distinguished Professor in Cancer Research at the Wistar Institute, Director of the Vaccine and Immunotherapy Center and the Executive Vice President of the Wistar Institute, and a Professor Emeritus at the University of Pennsylvania-SOM.

UVC: Universal Vaccine Cell

Tom Henley, Ph. D
Chief Scientific Officer, Intima Bioscience

Despite rapid clinical translation of COVID-19 vaccines in response to the global pandemic, an opportunity remains for vaccine technology innovation to address current limitations and meet challenges of inevitable future pandemics. We describe a universal vaccine cell (UVC) genetically engineered to mimic natural physiological immunity induced upon viral infection of host cells. Cells engineered to express the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike as a representative viral antigen induce robust neutralizing antibodies in immunized non-human primates. Similar titers generated in this established nonhuman primate (NHP) model have translated into protective human neutralizing antibody levels in SARSCoV-2-vaccinated individuals. Animals vaccinated with ancestral spike antigens and subsequently challenged with SARS-CoV-2 Delta variant in a heterologous challenge have an approximately 3 log decrease in viral sub genomic RNA in the lungs. This cellular vaccine is designed as a scalable cell line with a modular poly-antigenic payload, allowing for rapid, large-scale clinical manufacturing and use in an evolving viral variant environment.

Cooper *et al.* A genetically engineered, stem-cell-derived cellular vaccine Cell Rep Med. 2022 Dec 20;3(12)

Biography

Dr. Tom Henley received his Ph.D. in immunology from Cambridge University and has spent over 18 years utilizing gene editing technologies to genetically engineer human cells for applications in human health. He is currently Chief Scientific Officer at Intima Bioscience, a clinical stage gene and cell therapy company focused on curative intent in solid tumor cancer. By leveraging gene and cell therapy expertise in oncology applied to vaccinology, he co-created one of the first cellular vaccine technology platforms which is being developed for evaluation in the human clinic by Praesidium Bioscience.

A strategic model and industry collaboration for sustainable development of vaccines against neglected diseases

Miren Iturriza and Francesco Berlanda Scorza, Ph.D
GSK Vaccines Institute for Global Health, Siena, Italy

Infectious diseases pose a significant burden on low- and middle-income countries (LMICs), particularly affecting children under 5 years old. The GSK Vaccines Institute for Global Health (GVGH), part of GSK commitment to Global Health, is a science-driven organization dedicated to developing affordable vaccines for neglected infectious diseases that disproportionately impact impoverished communities. GVGH prioritizes the development of public health priority vaccines where commercial incentives are lacking. The main objective is to mitigate risks in the early stages of technical and clinical vaccine development, ensuring a sustainable vaccine supply for LMICs through collaboration with commercial partners.

The GVGH operating model involves several key elements. Firstly, vaccine targets are selected based on their disease burden and potential for public health impact, considering the probability of technical success and the likelihood of implementation if proven safe and effective. The institute also focuses on developing and implementing innovative and generic technologies applicable to a wide range of vaccines. Secondly, GVGH is actively engaged in the entire vaccine development process, from design to clinical proof-of-concept. This includes optimizing suitable antigens and formulations that generate robust immune responses while ensuring safety. Additionally, GVGH designs and implements manufacturing processes for pilot scale production, adhering to good documentation and manufacturing practices to comply with regulatory requirements for licensure. Special attention is given to sustainable technologies that are adaptable, affordable, and suitable for low-income settings, enabling the production of vaccines that are easy to deliver, store, and administer. Lastly, the institute transfers the vaccine candidates to industrial partners for further technical and clinical development, licensing, manufacturing, and distribution.

Notably, GVGH's Vi-CRM197, a conjugate vaccine against typhoid fever, obtained WHO prequalification a year after licensure in India, highlighting the success of the GVGH model. With support from GAVI, Nepal was the first country to launch a nationwide campaign to immunize all children between the ages of 15 months and 15 years and introducing TCV into the routine immunization program. Several other countries have licensed the vaccine and will conduct similar campaigns and introduction. This outcome validates the operating model and the institute will continue to develop vaccines for global health following a similar blueprint. Currently, the development pipeline includes new vaccine candidates in clinical development for Shigella, GAS, invasive non-typhoidal Salmonella (iNTS), new combination vaccines, and life cycle management of existing licensed products. The institute's expanded discovery pipeline also encompasses viral targets. At the conference, we will present an update on our clinical pipeline, focusing on the positive health impact we can have in LMICs.

Biography

Dr. Berlanda Scorza is Vice President for Global Health R&D Vaccines and GVGH Institute Director. GVGH is a key component of GSK's commitment to Global Health, dedicated to developing effective and affordable vaccines for neglected infectious diseases that affect communities in low- and middle-income countries.

Prior to joining GSK in 2020, Dr. Berlanda Scorza was a Senior Program Officer at the Bill and Melinda Gates Foundation and Senior Director for vaccine development at PATH, where he led programs to develop seasonal and pandemic influenza vaccines.

Previously, he was a senior scientist at Chiron and Novartis Vaccines, where he contributed to the development of a replicon RNA vaccine, a cell cultured influenza vaccine (Flucelvax) and a bacterial vaccine platform (GMMA). Dr. Berlanda Scorza received his Ph.D. from the University of Milano Bicocca and completed his post-doctoral studies at Imperial College London.

Accelerating recombinant protein vaccine development and manufacturing for disease X

Jian He (Jason)
CMC Head, WuXi Vaccines

As the world experienced the COVID-19 pandemic, we learned that manufacturing speed was one of the limiting factors in getting a vaccine product into the clinic and regulatory approved for mass production and global distribution. To prepare for the next potential pandemics, CEPI has set an aspirational 100-day mission to make a safe and effective vaccine against emerging viruses. While certain vaccine technology tends to be more favorable to react quickly, for example mRNA or viral vector vaccines, recombinant protein-based vaccines are relatively challenging due to lack of platform processes and complexity of each individual product. However, recombinant protein continues to be the major vaccine technology due to its several key advantages. WuXi Vaccines has developed several recombinant protein biologics/vaccines with accelerated timelines, several of which were used for prevention of SARS-CoV-2. This presentation is to demonstrate key enablers and strategy to streamline recombinant protein vaccine development to better prepare us, and our partners, in the fight against future disease X.

Biography

Jason He worked in WuXi Biologics started from Feb 2021 as CMC lead and took the role of WuXi Vaccines CMC Head on Mar 2023. Prior to working at WuXi Biologics, Jason had 14-year experience of product development in Merck, with growing leadership responsibilities in R&D and commercialization of recombinant proteins, conjugates, viral & virus like particle vaccines, and monoclonal antibodies.

Through Merck career, Jason's primary function was on development, qualification, transfer of analytical methods for large molecule release/stability and characterization. Jason has led assay development using a variety of LC/CE separation and spectroscopic techniques; He has led size and glycan (N-glycan and O-glycan) analytical groups to support Merck bio-venture projects covering mAbs or fusion proteins; He has also served as Analytical Lead of a VLP vaccine to set analytical strategy, to support process and formulation development, and to deliver the analytical commitments to external partner under research CRADA. In the last 6 years of Merck, Jason served as drug substance and drug product lead of a couple of vaccine products, governing the integrated process, analytical, and formulation teams on CMC activities through preclinical, clinical and BLA stages.

Jason received his Ph.D. in Biochemistry from University of Pennsylvania, and his B.S. in Chemistry from Peking University.

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Poster Presentations

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Poster Presentations

Title: **Neutralization of contemporary omicron subvariants after bivalent booster and XBB.1.5 breakthrough infections**
Ping Ren
University of Texas Medical Branch

Title: **Neoantigen adenoviral cancer vaccine generates improved CD8+ T-cell responses compared to conventional peptide vaccine**
Gabriel Dagotto
Harvard University

Title: **Advanced imaging techniques for pre-clinical differentiation of enabled vaccine formulations**
Michael McNevin
Merck and Co., Inc

Title: **Concurrent administration of COVID-19 and influenza vaccines enhances spike-specific antibody responses**
Susanna Barouch
Ragon Institute of MGH, MIT, and Harvard

Title: **A systems serology- and structural biology-based approach to identify humoral correlates of viral clearance**
Ryan P McNamara
Ragon Institute of MGH, MIT, and Harvard

Title: **Development of an anti-ang2 vaccine and characterization of its effects on AVMs in BMP9/10-deficient mice**
Sima Qutaina
Feinstein Institutes for Medical Research

Title: **C1 gene expression platform: Rapid, high yield, and lower cost way to develop and manufacture biologics**
Mark Emaflarb
Dyadic International Inc

Title: **Development of a novel *Shigella* quadrivalent conjugate vaccine using O-polysaccharide and IpaB carrier protein**
Shagndong Guo
Inventprise Inc

Title: **Compartmentalized vaccine responses in the intestine during murine norovirus infection**
Sanghyun Lee
Brown University

Neutralization of contemporary omicron subvariants after bivalent booster and XBB.1.5 breakthrough infections

Ping Ren[1], Jing Zou[2], Chaitanya Kurhade[2], Yanping Hu[2], Hope C. Chang[1], Debora K. Kim[1], Pei-Yong Shi[2] Xuping Xie[2]
[1]Department of Pathology, University of Texas Medical Branch, Galveston, Texas, USA
[2]Department of Biochemistry & Molecular Biology, University of Texas Medical Branch, Galveston, Texas, USA

The SARS-CoV-2 Omicron variants, which continue to evolve and emerge, have raised concerns about the efficacy of existing vaccines. This study aimed to investigate the neutralizing activities of three human serum panels collected from different groups: i) individuals who received 2-4 doses of the original mRNA vaccine and a BA.5-bivalent booster (parental-BA.5_booster); ii) individuals who received 2-4 doses of the original mRNA vaccine and had a previous SARS-CoV-2 infection, followed by a BA.5-bivalent-booster (parental-infection-BA.5_booster); iii) individuals who experienced a breakthrough infection with the XBB.1.5 variant after either original only or with bivalent mRNA vaccinations (vaccination-XBB.1.5_infection). The results of the study demonstrated a significant reduction in neutralizing activities against several variants, including XBB.1.5, DS.1, XBB.1.16, XBB.2.3, and CH.1.1, in all serum samples. The impact on neutralization was most pronounced against the CH.1.1 variant. Interestingly, individuals who received both vaccination and previous infection exhibited an enhanced magnitude and breadth of neutralizing response, indicating the presence of hybrid immunity that leads to increased neutralization. Furthermore, breakthrough infection with the XBB.1.5 variant resulted in elevated neutralizing activities against XBB sublineages and CH.1.1. This suggests that an updated vaccine that matches the sequence of the XBB subvariant may provide improved protection against contemporary XBB descendants. These findings have important implications for optimizing SARS-CoV-2 vaccine strategies and updating vaccines to address the evolving variants.

Biography

My research interests are diagnostic methods development and evaluation, pre-clinical and clinical trials on infectious diseases including new emergent, re-emergent infectious organisms such as SARS-CoV-2, Zika virus, Candida auris, measles virus, etc.

The second focus area is special investigations on infectious disease diagnoses such as bacterial, fungal, viral, and parasitical identifications using molecular methods and genotyping from formalin-fixed paraffin-embedded (FFPE) tissue blocks and other non-cultivable, non-viable specimens.

The third part is the drug combination susceptibility study on multi-drug resistant fungi. Besides the traditional microbroth dilution method for antifungal susceptibility testing, the new technology, Matrix-Assisted Laser Desorption/Ionization-Time Of Flight mass spectrometry (MALDI-TOF MS), has the potential to provide a rapid and reliable means of detecting emerging antibacterial and antifungal resistance and accelerating the initiation of appropriate antimicrobial treatment.

Neoantigen adenoviral cancer vaccine generates improved CD8+ T-cell responses compared to conventional peptide vaccine

Gabriel Dagotto, Alessandro Colarusso, Robert Patio, David Li, Tochi Anioke, Victoria Giffin, Malika Aid-Boudries, Dan Barouch
Harvard University, USA

Development of large, functional $CD8^+$ T cell responses is crucial for successful cancer vaccine therapeutics. Neoantigens have demonstrated their potential as cancer vaccine immunogens, but improvements in delivery method are still necessary. In this work, we characterized five candidate Adenovirus Serotype 26 (Ad26) cancer vaccines for prophylactic efficacy in the MC-38 cancer model. All five vaccines were immunogenic and generated varying degrees of protection against tumor growth. The best Ad26 vaccine candidates showed improved protection compared to long synthetic peptide vaccines containing the same immunogens, the current standard in the field. Ad26 expressing seven neoantigens conjugated to the Herpes Viral Protein 22 (VP22) (Ad26.VP227Epi) was found to be the most effective cancer vaccine. Ad26.VP227Epi was compared to peptide vaccination in immune recall post challenge studies, in both the spleen and the tumor. Both Ad26 and Peptide primarily recalled responses to the Adpgk neoantigen but only Ad26 induced responses to the Irgq neoantigen. The Ad26.VP227Epi vaccine demonstrated increased numbers of infiltrating $CD8^+$ T-cells, IFN^+ $CD8^+$ T-cells, and $CD107a^+$ $CD8^+$ T-cells, which all correlated with reduced tumor growth. To further investigate the differences between Ad26.VP227Epi and peptide, we used single cell RNA-seq (scRNA-seq) to characterize tumor infiltrating lymphocyte populations generated by the two platforms. We found that both Ad26 and Peptide induced higher numbers of infiltrating CD8+ T-cells within the tumor as compared to Sham. However, peptide vaccination induced $CD8^+$ T-cells showing increased upregulation of exhaustion pathways, identifying a potential mechanism explaining the difference in platform efficacy.

Biography

Gabriel Dagotto is a PhD Candidate in Dan Barouch's lab at Harvard University. Gabe received his BS in Chemistry at Duke University in 2018. Gabe's PhD research centers on viral vector research, in particular the usage of Adenoviral and Adeno-Associated viral vectors for vaccines, therapeutics, and gene therapy. Gabe's work on cancer vaccines aims to understand how different neoantigen delivery platforms impact the immune response both systemically and within the tumor microenvironment. In the future, he aims to continue expanding his work in cancer to generate more effective and efficient delivery methods for cancer vaccines.

Advanced imaging techniques for pre-clinical differentiation of enabled vaccine formulations

Michael McNevin[1], Leia Epstein[1], Jeremy Trausch[2], Helen Yarovoi[2], Akhilesh Bhambani[3], Donna Williams[3], & Craig McKelvey[3]
[1] Materials and Biophysical Characterization – Analytical R&D
[2] Cell Based Sciences – Analytical R&D
[3] Vaccine Drug Product Development – Pharmaceutical Sciences & Clinical Supply
DSCS – Merck Research Laboratories, Merck and Co., Inc.

Creation of long-acting formulations provides a differentiated pathway to gain adherence for therapeutics that require multiple doses to achieve optimal performance. The opportunity to reach a broader patient population in a more effective way would provide a significant advantage when inoculating the global patient population. Vaccines prevent infection, reducing the burden of diseases. Some vaccines have dosing regimens which include multiple injections spread over a period of months. Patients staying on and completing a course of treatment can present a major challenge for multidose biotherapeutics, with a significant drop in adherence rates between initial and subsequent administrations. Efforts to address this challenge leveraging administration of the initial and subsequent boost dose all during the first administration would alleviate the adherence challenge. Identifying an appropriate dosage form to control the release of the subsequent dose(s) is a difficult undertaking. The present work demonstrates the value of advanced imaging techniques combined with other analytical toolbox results to enable selection between formulations and compositions/processes in the preclinical space for assessment of viability for human administration.

Biography

After 15 highly successful years as a Team lead and eminent scientist at Merck, Michael's focus for the last 2 years has transitioned to organizational leadership and personal/professional development of Analytical R&D's best and brightest. His team studies vaccine virion/antigen/adjuvant morphology, enabled dosage forms and biophysical manifestations. Incorporating an extensive suite of fundamental and advanced physical and biophysical characterization tools, they are backed up by world-class expertise and drive to provide the finest patient solutions. Michael's focus is on building an opportunistic, high performing and strategically focused organization for rapid & robust CMC development of a wide variety of vaccine products.

Michael's research at Merck has enabled the development of dozens of therapeutic products including marketed and late development compounds Betrixaban, Suvorexant, Elbasvir, Ruzasvir, Uprifosbuvir, and Vaxneuvance. There is significant scientific experience within Merck Research Lab's preeminent solid-state and biophysical analytical development organizations which have now become Materials and Biophysical Characterization. The MBC team works across biotherapeutic modalities to study physical and biophysical properties of our biotherapeutics: process robustness, stability and formulation stability. This occurs both in early and late development. The work culminates with significant implications for patient well-being, impacts regulatory filing and is critical to IP protection.

Concurrent administration of COVID-19 and influenza vaccines enhances spike-specific antibody responses

Susanna Barouch
Ragon Institute of MGH, MIT, and Harvard

The bivalent COVID-19 mRNA boosters became available in fall 2022 and were recommended alongside the seasonal influenza vaccine. However, the immunogenicity of concurrent versus separate administration of these vaccines remains unclear. Here, we analyzed antibody responses in healthcare workers who received the bivalent COVID-19 booster and the influenza vaccine on the same day or different days. IgG1 responses to SARS-CoV-2 Spike were higher at peak immunogenicity and 6 months following concurrent administration compared with separate administration of the COVID-19 and influenza vaccines. These data suggest that concurrent administration of these vaccines may yield higher and more durable SARS-CoV-2 antibody responses.

Biography

Susanna Barouch is a student at Buckingham Browne & Nichols and works in the laboratory of Ryan McNamara at the Ragon Institute of MGH, MIT, and Harvard

A systems serology- and structural biology-based approach to identify humoral correlates of viral clearance

Ryan P McNamara[#1], Jenny S Maron[#1], Julie Boucau[1], Vicky Roy[1], Nicholas E Webb[1], Harry L Bertera[1], Amy K Barczak[1,2,3], The Positives Study Staff[2,4], Nicholas Franko[5], Jennifer K Logue[5], Megan Kemp[5], Jonathan Z Li[3,4], Ling Zhou[6], Ching-Lin Hsieh[6], Jason S McLellan[6], Mark J Siedner[2,3], Michael S Seaman[3,7], Jacob E Lemieux[2,3,8], Helen Y Chu[5], Galit Alter[1]

[1] Ragon Institute of MGH, MIT, and Harvard, Cambridge, Massachusetts, USA.
[2] Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA.
[3] Harvard Medical School, Boston, Massachusetts, USA.
[4] Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA.
[5] Division of Allergy and Infectious Diseases, University of Washington, Seattle, Washington, USA.
[6] Department of Molecular Biosciences, University of Texas at Austin, Austin, Texas, USA.
[7] Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA.
[8] The Broad Institute, Cambridge, Massachusetts, USA.

Structural determinants of immune responses are key in the development of next-generation vaccine design and antibody-based therapies. Anamnestic, or recall, responses to pathogens that individuals were previously vaccinated against can inform us how antibody responses are expanded to specific structural features of antigens. Moreover, applying a systems serology-based approach to this recognition can provide structural correlates of immunity at previously unrealized detail. Here, we show that anamnestic responses to SARS-CoV-2 Spike are disproportionately expanded to the highly conserved fusion peptide region. These responses are highly correlated with non-neutralizing functions such as antibody-dependent neutrophil phagocytosis and are inversely correlated with viral loads. This indicates that antibodies recognizing the fusion peptide in its exposed configuration act as key players in viral clearance and the mitigation of disease. We propose that targeting structurally conserved regions such as the fusion peptide of SARS-related coronaviruses can allow for the development of vaccines and antibody therapies that can elicit a greater breadth of protection. Moreover, the incorporation of structurally based antibody recognition into existing systems serology bioinformatics analyses can expand our knowledge of how the Fab and Fc regions of antibodies work in concert to blunt pathogen spread.

Biography

Ryan McNamara is the Director of the Systems Serology Laboratory at the Ragon Institute of MGH, MIT, and Harvard. The Systems Serology laboratory performs deep antibody profiling and functional correlates against an array of pathogens, malignancies, and inflammatory disorders. The laboratory is specifically interested in how antibody profiles change over time, and how temporal changes in humoral signatures are linked with protection from disease.

Development of an anti-ang2 vaccine and characterization of its effects on AVMs in BMP9/10-deficient mice

Sima Qutaina
Marambaud Lab
Feinstein Institutes for Medical Research – Zucker School of Medicine/Hofstra University

Angiopoietin-2 (Ang2) has been identified as a common upregulated secreted protein across different Hereditary Hemorrhagic Telangiectasia (HHT) models. In HHT mice, Ang2 neutralization reduces arteriovenous malformations (AVMs), a main abnormal vascular characteristic of HHT. Ang2 has thus emerged as a potential target in HHT treatment. Our laboratory has developed a method of selective peptide vaccine production that uses minimal peptidic epitopes coupled to the FDA-approved carrier CRM197. Here, we report the generation of an active CRM197 peptide vaccine that specifically targets Ang2 (Ang2-P3) and tested its efficacy at reducing retinal AVMs in mouse neonates injected with BMP9/10 blocking antibodies, a model of HHT. We injected adult female mice with the vaccine and measured their titers for Ang2 antibodies. 3 out of 5 vaccinated females had high titers and were chosen as the best responders. These females were then bred alongside other females that were not vaccinated. Litters from vaccinated females had comparable titers of Anti-Ang2 antibodies to their corresponding mothers demonstrating efficient immunization transfer to the pups during lactation. Administrating BMP9/10 immuno-blocking antibodies is an established model for HHT and results in the formation of AVMs in the pups' retinas by P6. To test the protective effect of the vaccine, all litters were treated with BMP9/10 i.b antibodies and collected at P6. The retinas were dissected and immunostained. There was a significant reduction in the AVMs number in the retinas of the pups that received Ang2 antibodies trans-mammary compared to those who did not. Additionally, AVMs surface area was diminished. These outcomes provide strong evidence that targeting Ang2 could ameliorate HHT pathology and strengthen the approach to target Ang2. Moreover, an active vaccine approach bypasses the disadvantage of antibody resistance that results from passive vaccines and provides a more clinically advantageous tool with less administration time and longer efficacy.

Biography

I received a B.Sc. degree in Genetic Engineering and Biotechnology from Jordan University of Science and Technology in 2018. I'm currently a 4th year PhD candidate in the Molecular Medicine PhD program at Zucker School of Medicine, Hofstra University/ Northwell Health. I'm conducting my research in Dr. Philippe Marambaud's lab at the Feinstein Institutes for Medical Research. I've worked and collaborated on multiple projects pertaining to Alzheimer's disease and Hereditary Hemorrhagic Telangiectasia.

C1 gene expression platform: rapid, high yield and lower cost way to develop & manufacture biologics

Joseph Hazelton[1], Ronen Tchelet[1], Noelia Valbuena[1], and Mark Emalfarb[1]
[1]Dyadic International Inc., USA

Dyadic's C1 protein production platform has been developed through more than 20 years of commercial genetic engineering. The thermophilic filamentous fungus Thermothelomyces heterothallica is a robust and versatile fungal gene expression system for the rapid development and manufacturing of proteins at very high yields for a wide variety of antigens and therapeutic proteins such as mAbs (24 g mAb/L in 7 days), Bispecific and Fc-Fusions and recombinant protein-based Vaccines such as ferritin nanoparticles (3.5 g/L in 5 days / human) and (10 g/l in 7 days / animal) antigens.

One of the major hurdles in fungal recombinant protein production is the abundance of host cell proteases. Our C1 protease characterization and protease gene deletion work has lead to creation of C1 production strains with 14-15 proteases deleted, allowing for the efficient development and production of a wide variety of stable antigens, monoclonal antibodies and other therapeutic proteins. These strains have been used to express more than a dozen antigens of different types including virus-like particles (VLPs), nanoparticles and individual antigens derived from viral surface proteins. In addition, C1 cells have been glycoengineered to produce various forms of N-glycosylated proteins, including monoclonal antibodies (mAbs) with human-like glycoprotein structures.

Over the last 6 years, the C1 protein production platform has been further improved to become a safe and efficient expression system with the prime objective of speeding up the development and production of commercial antigens and biotherapeutic products at larger quantities and lower cost under cGMP. Production can be scaled up in a more cost-effective manner using standard microbial E. coli fermenters. Unlike E.coli, insect (i.e. Baculovirus) and CHO cells there are no endotoxins or viruses in C1 cells that need to be removed in downstream processing. Unlike other filamentous fungal cells, C1 doesn't sporulate and has been used in cGMP manufacturing on different continents.

The C1 protein production platform has shown safety and efficacy in multiple animal studies including in a successful monoclonal antibody non-human primate study, a toxicology study, and in a clinical phase I human trial of the DYAI-100 RBD COVID-19 booster vaccine which has shown to be well tolerated with no serious adverse events or adverse events of special interest.

Biography

Mark A. Emalfarb is the founder of Dyadic. He has been a member of Dyadic's board of directors since October 2004 and has served as its Chairman as well as President and Chief Executive Officer from October 2004 until April 2007 and from June 2008 until the present.

Since founding Dyadic in 1979, Mr. Emalfarb has successfully led and managed the evolution of Dyadic from its origins as a pioneer and leader in providing ingredients used in the stone-washing of blue jeans to the discovery, development, manufacturing and commercialization of specialty enzymes used in various industrial applications and the development of an integrated technology platform based on Dyadic's patented and proprietary C1 fungal microorganism.

Mr. Emalfarb is an inventor of over 25 U.S. and foreign biotechnology patents and patent applications resulting from discoveries related to the Company's patented and proprietary C1 fungus, and has been the architect behind its formation of several strategic research and development, manufacturing and marketing relationships with U.S. and international partners.

Development of a novel *Shigella* quadrivalent conjugate vaccine using O polysaccharide and IpaB carrier protein

Shagndong Guo
Inventprise Inc

Development of a Novel *Shigella* Quadrivalent Conjugate Vaccine using O Polysaccharide and IpaB Carrier Protein Abstract *Shigella* induces shigellosis and is the world leading cause of diarrhea deaths. While there are multiple candidate vaccines under development and in clinical trials, no *Shigella* vaccine is currently available on the market. Glycoconjugate that consists of *Shigella* O-polysaccharide (O-PS) and a carrier protein has been considered a promising approach for developing *Shigella* vaccines1. *Shigella* bacteria contains four species that are *dysenteriae, flexneri, boydii*, and *sonnei. S.flexneri* has been recognized as the most prevalent species particularly in Low and Middle Income Countries (LMICs), and the top serotypes are *flexneri* 2a, 3a and 6. S.Sonnei has only one serotype but is a predominant cause of shigellosis in high income countries (HICs). For carrier proteins, tetanus toxoid (TT) or recombinant exoprotein A of *Pseudomonas aeruginosa* (rEPA) have been mostly selected1. In addition, IpaB protein has been recently reported as an immunogenic antigen for *Shigella* vaccines. IpaB is a critical virulence factor of *Shigella* type 3 secretion system (T3SS) that is extremely conserved across *Shigella* serotypes2. Studies have suggested adding IpaB as an antigen component will enhance the protection3. Inventprise platform technologies are designed to enable high valent vaccines inducing broad, robust, and durable protection against pathogenic strains of infectious diseases. The company is currently developing a *Shigella* quadrivalent conjugate vaccine that conjugates the O-PS of *flexneri 2a, 3a, 6, and Sonnei* to IpaB protein. Our preliminary animal studies indicated that *Shigella* O-PS-IpaB conjugate elicited strong immunogenicity against all four serotypes. The project is currently moving towards Pre-clinical/Phase I clinal trial.

Biography:

Dr. Shangdong Guo received his Ph.D. degree from pharmacology department of SUNY Upstate Medical University. He currently works as a Senior Scientist at Inventprise Inc. Inventprise platform technologies are designed to enable high valent vaccines to induce broad, robust, and durable protection against pathogenic strains of infectious diseases. Company is currently having multiple vaccine product pipelines under development. Shangdong is the project leader for Shigella Quadrivalent conjugate vaccine, actively participating in and supervising various project components, encompassing research and development, material manufacturing, and clinical trial planning.

Compartmentalized vaccine responses in the intestine during murine norovirus infection

Sanghyun Lee[1]
[1]Department of Molecular Microbiology and Immunology, Brown University, USA

Pathogenesis and immune control of human norovirus (HNoV) infection in humans is incompletely understood. HNoV infection in epithelial cells, myeloid cells, and B-cells is the expected cellular tropisms in the human intestine. We leverage current understanding of distinct cellular tropism of murine norovirus (MNoV) and differential immune controls of epithelial and myeloid cells. This study utilizes MNoV as a model pathogen to micro-dissect immune responses against noroviruses and provide an insight into a better vaccine for HNoVs. Non-overlapping, exclusive cellular tropisms of MNoV determine capsid-, or non-capsid based vaccine efficacy in epithelial cells and myeloid cells. This suggests that the most effective vaccine strategy may require a hybrid approach that targets the compartmentalized antiviral immune responses.

Biography

Dr. Sanghyun Lee has focused his scientific career on dissecting virus-host interactions at molecular and physiological levels and understanding how these interactions contribute to viral pathogenesis and virulence. Dr. Lee received his Ph.D. at Seoul National University in South Korea, and worked on viral non-coding RNAs contributing virulence of Human cytomegalovirus. After he finished his Ph.D. training, he decided to pursue his postdoctoral fellowship in Skip Virgin's lab at Washington University in St Louis. During the postdoctoral training Dr. Lee focused on understanding the cellular tropism for norovirus and innate immune control in the intestine. He received the K99/R00 NIH Pathway to Independence Award. In 2020, Dr. Lee started his independent research program at Brown. His group is exploring novel host-virus interactions and seeking to develop vaccines and therapeutics for pathogenic viruses.

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Conjugate vaccine

Title: **Conjugation chemistry, carrier proteins and antigens: promoting conjugate vaccine development**
Andrew Lees
Fina Biosolutions

Title: **Glycoconjugate vaccines to prevent AMR pathogens**
Roberto Adamo
GSK

Title: **GA-VAX - Development of a conjugate vaccine targeting a genetic form of Amyotrophic Lateral Sclerosis (C9orf72)**
Robert van der Put
Intravacc.nl

Title: **Preparation of bacterial polysaccharide-protein conjugate vaccines**
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National Research Council of Canada

Title: **Conjugate vaccines for substance abuse adjuvanted with army liposome formulation and aluminum hydroxide**
Gary R. Matyas
US Military HIV Research Program, Walter Reed Army Institute of Research

Title: **Recent advancements in the glycoconjugate vaccines field**
Francesco Berti
GSK Vaccines

Title: **Conjugation increases the immunogenicity and efficacy of T-cell inducing Glycolipid-Peptide (GLP) vaccines**
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Victoria University Wellington

Title: **Peptide-glycolipid conjugate vaccines targeting Hepatitis B virus antigens**
Olivia Burn
Malaghan Institute of Medical Research

Title: **WISIT vaccines: Next generation vaccine platform leveraging skin immunity to treat chronic diseases**
Markus Mandler
Tridem Bioscience

Title: **Development of a pneumococcal conjugate vaccine and novel vaccines through research driven efforts in India**
Ramesh Matur
Biological E Ltd

Title: **Rational design of next-generation glycoconjugate vaccines inducing highly functional antibodies**
Giuseppe Stefanetti
Dipartimento di Scienze Biomolecolari, Universita degli Studi di Urbino Carlo Bo

Conjugation chemistry, carrier proteins, and antigens: promoting conjugate vaccine development

Andrew Lees, Ph. D
Fina Biosolutions LLC, USA

Chemists expend a great deal of effort to synthesize well-defined antigens. However, many antigens, such as glycans and peptides, are poorly immunogenic unless chemically linked to a carrier protein. The exquisite skills needed for synthesizing complex antigens do not necessarily overlap with the ones required for conjugation. Both the carrier protein and the conjugation chemistry can influence vaccine efficacy, but there is limited access to affordable, clinically relevant carrier proteins. Academic researchers have often used keyhole limpet hemocyanin (KLH) for conjugate development because the clinical-grade protein is relatively affordable, but its mollusk origin makes it generally unsuitable for commercial development. Indeed, only a few carrier proteins are used in licensed vaccines, including chemically detoxified diphtheria and tetanus toxins (DTxd, TTxd). These toxoids are made by extended incubation of the partially purified toxin with formaldehyde, resulting in heterogeneous products containing contaminating host cell proteins and media components. In contrast, recombinant carrier proteins are better defined and homogeneous. To improve accessibility to recombinant carrier proteins, we have assembled a collection of recombinant carrier proteins, and to simplify conjugate synthesis, we also provide these proteins already derivatized with reactive conjugation reagents. These proteins include CRM_{197} and 8MTT, genetically detoxified diphtheria and tetanus toxin, respectively, and TTHc (tetanus heavy chain fragment C). All three proteins are expressed using FinaBio's engineered *E. coli* platform, FinaXpress. The FinaXpress strains have an oxidative cytoplasm and are capable of expressing high levels of soluble, disulfide-bonded proteins in the E. coli cytoplasm without the need for refolding.

CRM_{197} has been successfully used in conjugate vaccines for several decades and is available for both research and clinical use. To further promote vaccine development, our clinical-grade CRM_{197} is priced below that of GMP KLH. We market our CRM_{197} as EcoCRM®. EcoCRM® is the carrier protein for several conjugate vaccines now in clinical trials. The tetanus fragment TTHc is of a comparable MW as CRM_{197} and contains pan T cell epitopes. 8MTT is a 150kDa protein and can be loaded with more hapten than the smaller proteins. We also provide Qb_{mutant} (a virus-like particle or VLP). Qb_{mutant} VLP are assembled from a mutant Qβ bacteriophage capsid to form a 28nm particle, much larger than the other carriers. Each capsid subunit is about 14kDa and contains ample amines and carboxyls for conjugation.

Each of these carrier proteins has unique properties and may give a better response with any given antigen. Their easy availability offers the opportunity to make reasonably well-defined conjugates and to determine the best carrier protein for an application. To further facilitate screening and the development of optimal vaccines, these carriers are also available in a ready-to-use format, labeled with a thiol linker (maleimide or bromoacetate) or a click reagent (azide). Here we provide examples of the synthesis of conjugates with these carrier proteins and the immune responses to conjugated synthetic glycans, polysaccharides, and peptides.

Biography

Dr. Andrew Lees, founder and Chief Scientific Officer of Fina Biosolutions, holds over 20 patents and is the author or co-author of more than 60 peer-reviewed papers. He holds a B.S. in Chemistry from Harvey Mudd College and a Ph.D. in Biophysics from The Johns Hopkins University. GlaxoSmithKline, the Serum Institute of India, the Chengdu Institute of Biological Products, and others all use conjugation chemistry (CDAP) developed by Dr. Lees in their S. pneumonia and meningococcal conjugate vaccines.

Dr. Lees is also an associate professor at the University of Maryland School of Medicine's Center for Vaccine Development, an affiliate at the University of Maryland Bioprocessing Scale-Up Facility, and an adjunct professor in the Department of Medicine at the Uniformed Services University. He teaches protein chromatography through the post-graduate level, and is a frequent speaker on conjugation chemistry and biotech entrepreneurship.

Glycoconjugate vaccines to prevent AMR pathogens

Roberto Adamo, Ph.D
GSK, Italy

Antimicrobial resistance (AMR) is responsible for the death of millions worldwide and stands as a major threat to our healthcare systems, which are heavily reliant on antibiotics to fight bacterial infections (1). The development of vaccines against the main pathogens involved is urgently required as prevention remains essential against the rise of AMR. Among AMR pathogens, six of them (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacteriacae* including *Escherichia coli*), known as ESKAPE, are considered as critical or high priority pathogens by the WHO and the CDC (2). Other such as Group A and B *Streptococcus*, represent major AMR threats too. Glycans constitute relevant virulence factors and have been used as antigens in several forms of conjugate vaccines to circumvent their inherent poor immunogenicity. Glycoconjugate vaccines have been successful in preventing meningitis and pneumoniae and there are high expectations that they will play a key role in fighting AMR (3-5). We will discuss on conjugate vaccine in clinical trials to target AMR pathogens, recent technological and preclinical advances, as well as on the challenges associated with the development of carbohydrate-based vaccines against leading AMR bacteria. Examples of approaches currently pursued by GSK will be presented.

Biography

Roberto Adamo has a long-standing experience in vaccine discovery. After post docs at the NIH and Utrecht University, in 2007 he joined Novartis, where he became Head of the Carbohydrate Chemistry Laboratory and Leader of the Conjugation & Synthesis platform. Following the company acquisition by GSK, he has covered the role of Conjugation Platform Leader and Discovery Project Leader. Currently he leads projects in early clinical phase as Vaccine Development Leader projects. His research interests vary from the synthesis of glycans, glycoconjugates and glyconanoparticles to structural glycobiology for the design of carbohydrate and protein-based therapeutics.

GA-VAX - Development of a conjugate vaccine targeting a genetic form of Amyotrophic Lateral Sclerosis (C9orf72)

Robert van der Put
Director Business Development, Intravacc

Amyotrophic lateral sclerosis (ALS) is a devastating disease with no existing disease-modifying treatments. Characteristic protein aggregates in brain and spinal cord, together with neuroinflammation, trigger the loss of motor neurons, leading to rapidly progressive paralysis and ultimately death from respiratory failure. In 5-10% of ALS cases, disease is caused by the pathogenic C9orf72 mutation [1, 2]. In these patients, unique poly-Glycine-Alanine (poly-GA) aggregates promote neuroinflammation and secondary TDP-43 pathology, which is a key trigger of neuron loss also in sporadic ALS [3, 4]. The therapeutic approach for development of a vaccine targeting C9orf72 ALS (GA-VAX [1]) is to reduce poly-GA pathology and downstream toxicity through vaccine-induced antibodies.

Currently, a peptide based conjugate vaccine targeting poly-GA is being developed and optimized towards preclinical proof-of-concept. Initial vaccine concepts already showed huge potential in reducing poly-GA aggregates, rescuing motor deficits, preventing neuroinflammation and attenuated neuroaxonal damage in a poly-GA mouse model [5].

Here, we present on the developments to overcome the previously observed aggregation propensity of the initially used peptide antigen, which pave the way towards successful future GMP manufacturing. This was done firstly by an *in-silico* screening of a large pool of different peptides deducted towards 10 favorable candidates. These candidates were evaluated for their susceptibility towards initial conjugation to the carrier protein. From these, 4 peptides continued into a deep evaluation, investigating reaction conditions towards optimization of the conjugation process, including immunological evaluation. The final peptide with an optimized peptide:carrier ratio is currently being evaluated in an *in vivo* efficacy study and scale-up of the production process has been initiated.

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4. Schludi, M.H., et al., *Spinal poly-GA inclusions in a C9orf72 mouse model trigger motor deficits and inflammation without neuron loss.* Acta Neuropathol, 2017. **134**(2): p. 241-254.
5. Zhou, Q., et al., *Active poly-GA vaccination prevents microglia activation and motor deficits in a C9orf72 mouse model.* EMBO Mol Med, 2020. **12**(2): p. e10919.

[1] *GA-VAX (https://www.dzne.de/forschung/projekte/ga-vax/welcome/). The GA-VAX project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101057649 in the context of the European Innovation Council (EIC).*

Biography

Robert van der Put 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. He has successfully facilitated the technology transfer of a Hib conjugate vaccine production process to several partners in Asia, and designed and delivered an international course on Hib conjugate QC tests in collaboration with WHO. Furthermore, he also contributed to the innovation and improvement of various vaccine production processes, such as Polio, N. meningitidis, Shigella flexneri 2a, and COVID-19. He has published multiple scientific papers and presented at several international conferences and workshops on vaccine-related topics. He is always eager to learn new skills, collaborate with diverse stakeholders, and create value for the vaccine community.

Preparation of bacterial polysaccharide-protein conjugate vaccines

Wei Zou
Human Health Therapeutic Research Centre, National Research Council of Canada, Canada

Glycoconjugates have been used as effective human vaccines against diseases caused by *Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae type b*, and *Salmonella typhi*. Their success is based on the fact that polysaccharides are the most conserved and accessible molecules on the bacterial surface, and their ability to raise boostable and protective antibodies in infants and young aged children. Although the immunogenicity of conjugates largely depends on the individual polysaccharides and the carrier proteins selected, there are evidences that the conjugation method can also be an important factor. The conjugation method should be simple, efficient and result in minimal disruption to the epitopes of polysaccharide. Among a few different approaches currently employed, we will present examples to recommend the improved reductive amination as the choice for glycoconjugation.

Biography

Wei Zou received his Ph. D. in Organic Chemistry from Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences in 1988. He then went to Queen's University at Kingston, Ontario, as a postdoctoral fellow before joining the Institute for Biological Sciences, National Research Council of Canada in 1993. Currently, he is a Senior Research Officer at Human Health Therapeutic Research Center, National Research Council of Canada.

His research interests include glycocojugate vaccine, carbohydrate synthesis, enzyme inhibitors, and targeted delivery of therapeutics.

Conjugate vaccines for substance abuse adjuvanted with army liposome formulation and aluminum hydroxide

Gary R. Matyas
U.S. Military HIV Research Program, Walter Reed Army Institute of Research, United States

Opioid use disorder (OUD) and fatal overdose due to intentional and unintentional consumption of fentanyl-laced heroin are emerging global concerns. Data from the US Centers for Disease Control and Prevention (CDC) show that in 2018, the number of reported opioid-related fatalities was 46,802, of which 67% (~31,350 cases) was related to synthetic opioids, mostly fentanyl and its analogues. Over the next few years, fatal cases steadily rose with increasing proportion due to synthetic opioids. The acceleration was even more pronounced during the COVID-19 pandemic, reaching > 72,000 synthetic opioid-related deaths at the end of 2022. The major barrier towards mitigation of opioid use disorder, particularly in the case of fentanyl-laced heroin remains the unavailability of effective treatment modalities. To date, there are only 3 pharmacotherapies approved to treat OUD including methadone, buprenorphine, and naltrexone or combinations of these therapeutics. Their efficacies are diminished by the availability of more potent fentanyl derivatives present in illicit drugs. 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/s conjugated to an immunogenic carrier protein. 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) with aluminum hydroxide were used as adjuvants for mouse and rat studies. The heroin vaccine protected mice 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 fentanyl vaccine protected mice from fentanyl challenge and induced antibodies that cross-reacted with other fentanyl analogs commonly found in confiscated opioids, but not the therapeutics. 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.

Recent advancements in the glycoconjugate vaccines field

Francesco Berti
GSK Vaccines, Italy

Glycoconjugate vaccines represent one of the keys for success of vaccination in children. They are a potent tool for prevention of life-threatening bacterial infectious diseases like meningitis and pneumonia.

The immunogenicity of these glycoconjugates is influenced by a series of interconnected parameters, some of which are related to the sugar carbohydrate antigen (length, non-end terminal residues, exposition of charged functional groups, number of sugar copies linked to the protein) and other to the conjugation chemistry to protein carrier (type of linker, length, etc.).

The complexity of randomly prepared glycoconjugates has not made possible to decipher the contribution of all the single parameters that underlay the overall immunological activity of the biomolecules. Recently, different methods for chemical or enzymatic assembly of defined oligosaccharides have rendered feasible the synthesis of complex carbohydrates. The modern methods for site selective conjugation could contribute to the production of a new generation of glycoconjugate vaccines with defined sugar and attachment site and to establish robust structure-immunogenicity relationship.

Biography

I earned my Bachelor (1998) and PhD's (2002) degrees in Physical Chemistry (1998) at the University of Siena (Italy). During my PhD course I worked on the physicochemical characterization of metal-peptide complexes by spectroscopic techniques (two years at Department of Chemistry - University of Siena) on the preparation and structural characterization of meningococcal ACWY polysaccharide-protein conjugate vaccines (one year at Chiron Vaccines - Siena, currently GSK Vaccines and formerly Novartis Vaccines). In 2002 I joined GSK Vaccines (formerly Novartis Vaccines; formerly Chiron Vaccines) as a young scientist and in the following 10 years was appointed Project Leader, Lab Head, Unit Head, Head of Vaccine Chemistry and Formulation Department and Head of Antigen Design Department. In September 2022 I have been appointed Senior Director – Bacterial Vaccines R&D, which is my current position. I served as a visiting scientist at the Institute of Biological Sciences (National Research Council) in Ottawa (Canada) in 2008 and at the Genomic Institute of Novartis Foundation (La Jolla, CA, US) in 2010. In the last 22 years, I have been working on research and development of several carbohydrate based vaccines, particularly focusing on carbohydrate- and protein-based antigens against bacterial (Neisseria meningitidis ACWYX, Streptococcus pneumoniae, group B Streptococcus, group A Streptococcus, Staphylococcus aureus, etc.), viral (HIV, RSV, CMV, etc.) and fungal (Candida albicans, etc.) infections. I have authored and co-authored of 108 published scientific papers and reviews and more than 20 patents.

Conjugation increases the immunogenicity and efficacy of T-cell inducing Glycolipid-Peptide (GLP) vaccines

Sarah Draper[1], Regan Anderson[1], Benjamin Compton[1], Taylor Cooney[1], Lauren Holz[2], Yu Cheng Chua[2], Kathryn Farrand[3], Olivia Burn[3], Ian Hermans[3], William Heath[2], Gavin Painter [1]

[1]Ferrier Research Institute, Victoria University of Wellington, Wellington, New Zealand,
[2]Peter Doherty Institute, University of Melbourne, Melbourne, Australia,
[3]Malaghan Institute of Medical Research, Wellington, New Zealand.

Whilst many vaccine approaches induce cellular immune responses, few have been optimised for the induction of specialised immune responses such as the generation of tissue **r**esident **m**emory **T** cells ($\mathbf{T_{RM}}$ cells). Tissue resident memory T cells are a sub-population of cytotoxic T cell lymphocytes (CTL) that remain resident within tissues rather than circulating through tissues as central and effector memory T cells do. T_{RM} have been implicated in many diseases including cancer, the clearance of chronic infection and protection against malaria.

We have developed a fully synthetic, CD1d-dependent, self-adjuvanting glycolipid-peptide (GLP) conjugate vaccine platform that generates substantial numbers of disease-specific T_{RM}[1] that is completely dependent on chemical conjugation. In this paper we will present the chemical and in vivo results of various conjugation and formulation strategies in the generation of T cell responses.

Biography

Professor Painter obtained his PhD in chemistry from the University of Otago in 1995 (synthetic methodology) which was followed by postdoctoral research at the University of Cambridge (the synthesis of inositol phospholipids for the elucidation of PI3K pathways). Since joining the Ferrier Research Institute in New Zealand his research laboratory has focussed on the synthesis of lipid-based materials including phosphatidyl inositol mannosides, glycolipids, glycolipid-peptide conjugates and novel lipid nano-delivery vehicles for encapsulation of various vaccine components including RNA, peptides, glycolipids and various immune stimulates.

Professor Painter has a strong interest in the immunological evaluation of vaccines and vaccine components. He holds a joint position with the Malaghan Institute of Medical Research Wellington New Zealand incorporating multiple national and international collaborations with immunologists.

Peptide-glycolipid conjugate vaccines targeting hepatitis B virus antigens

Olivia Burn[1], Anna H. Mooney[1], Sarah L. Draper[2], Regan J Anderson[2], Benjamin J. Compton[2], Chingwen Tang[1], Kathryn J. Farrand[1], Pietro Di Lucia[3,4], Micol Ravà[3,4], Valeria Fumagalli[3,4], Leonardo Giustini[3], Elisa Bono[3], Dale I. Godfrey[5,6], William R. Heath[5], Weiming Yuan[7], Francis V. Chisari[8], Luca G. Guidotti[3,4], Matteo Iannacone[3,4], John Sidney[9], Alessandro Sette[9], Shivali A. Gulab[2,10], Gavin F. Painter[2], Ian F. Hermans[1]

[1]Malaghan Institute of Medical Research, Wellington, New Zealand.
[2]Ferrier Research Institute, Victoria University of Wellington, Wellington, New Zealand.
[3]Division of Immunology, Transplantation and Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy.
[4]Vita-Salute San Raffaele University, Milan, Italy.
[5]Department of Microbiology & Immunology, Peter Doherty Institute for Infection and Immunity, University of Melbourne, Victoria, Australia.
[6]Australian Research Council Centre of Excellence in Advanced Molecular Imaging, University of Melbourne, Parkville, Australia.
[7]Department of Molecular Microbiology and Immunology, Keck School of Medicine, University of Southern California, Los Angeles, USA.
[8]Department of Immunology & Microbial Sciences, The Scripps Research Institute, La Jolla, California, USA.
[9]Center for Infectious Disease and Vaccine Research, La Jolla Institute for Immunology, La Jolla, California, USA.
[10]Avalia Immunotherapies Limited, Wellington, New Zealand.

As a major contributor to liver disease, chronic hepatitis B virus (HBV) infection is a significant cause of global morbidity and mortality. Therapeutic vaccines that trigger T cell responses capable of controlling the virus offer a potential long-term treatment approach. We evaluated a novel vaccine design that exploits the helper functions of type I natural killer T (NKT) cells to enhance virus-specific T cell responses. To generate vaccines, peptide epitopes from HBV antigens were conjugated to an NKT cell agonist with the aim of promoting co-delivery of NKT cell agonist and viral antigens to the same antigen-presenting cells *in vivo*. We show that in a model of chronic hepatitis B, where transfer of HBV core antigen (HBcAg)-specific transgenic $CD8^+$ T cells into mice expressing the complete HBV genome typically results in specific T cell dysfunction, vaccination with an HBcAg-specific vaccine was associated with T cell activation and antiviral activity. To advance this vaccine platform for future clinical use, stretches of sequence covering clusters of known HLA-restricted HBV epitopes were prepared as synthetic long peptides (SLPs) for conjugation, with immunogenicity of SLP-based vaccines then confirmed in HLA transgenic mice. Predictions of population coverage based on HLA distribution indicated that a combination of three SLP-based vaccines could give 91.9 % coverage in the worldwide population, with each individual recognizing an average of 3.38 epitopes. These novel vaccines therefore show promise for further clinical development as a treatment for chronic hepatitis B.

Biography

Dr Olivia Burn received her PhD in immunology from the University of Otago in 2020 and has since been a postdoctoral research fellow at the Malaghan Institute of Medical Research Wellington New Zealand. Olivia's research is centred around the phenotype of T cell responses in the setting of hepatotropic diseases, such as Hepatitis B. With Prof Gavin Painter and Prof Ian Hermans, Dr Burn investigates how vaccine design and the use of novel adjuvants can influence these T cell responses. Olivia is currently undergoing a fellowship at Icahn School of Medicine at Mt Sinai with Ass Prof Amaia Lujambio, an experienced liver cancer biologist who has developed state-of the-art animal models of liver cancer. Dr Burn is using these models to assess the influence of vaccine design on tumour-specific T cells and animal survival

WISIT vaccines: Next generation vaccine platform leveraging skin immunity to treat chronic diseases

Markus Mandler
Founder and CEO, of Tridem Bioscience

Tridem Bioscience is a Vienna based biotech company focusing on the discovery and development of innovative active immunotherapies based on our proprietary WISIT (WIn the Skin Immune system Trick) technology. It establishes a new vaccine format: β-glucan-based neoglucoconjugate vaccines specifically designed to target skin-derived dendritic cells (DCs) thereby avoiding the use of adjuvants required for vaccine efficacy.

WISIT constructs are unique as the vaccine backbone itself is the DC targeting/stimulating adjuvant (β-glucan), which is fused to variable, proprietary T helper and disease specific B cell peptide epitopes. WISIT vaccines are delivered directly into the skin, an organ rich in DC and other immune cell types. Through this intradermal (i.d.) application, the immunological potential of the skin, which is evolutionarily designed to initiate immune responses, can be maximally utilized.

We aim to realize this novel vaccine concept using Parkinson's disease (PD) as our first indication. PD is the major representative of synucleopathies, a group of neurodegenerative diseases with high-unmet medical need. Building on results obtained in our initial development program, we could already provide preclinical proof-of-concept for WISIT vaccines targeting human aSynuclein and demonstrated that these neoglucoconjugates are superior to conventional type PD conjugate vaccines in eliciting functional, protective immune responses in vitro and in vivo.

We are currently exploring other indications including other neurological disorders, type 1 allergies or pruritus.

Biography

Dr. Mandler is founder and CEO of Tridem Bioscience with over 15 years of collaborative research and management experience in academia and industry. Serving as Head of the Neurodegeneration Division of AFFiRiS AG he was developing new vaccination-based treatments for neurodegenerative diseases. Focusing on Alzheimer's disease and synucleinopathies such as Parkinson's disease and multisystem atrophy. Dr: Mandler – together with his Affiris team - was responsible for the selection of the first two peptide-based vaccines for Parkinson's disease and multisystem atrophy ever tested in humans. Before founding Tridem he served as CSO of Accanis Biotech where he was working on mRNA therapeutics in dermal applications. Dr. Mandler has authored numerous publications in high impact journals and holds several patents and patent applications. His work was awarded with multiple national as well as international research grants.

Development of a pneumococcal conjugate vaccine and novel vaccines through research driven efforts in India

Ramesh Matur
Sr Vice President and Head – Vaccines Research & Development, Biological E Ltd, India

Pneumococcal polysaccharide-protein conjugate vaccine is one of most complex vaccines, has been very efficacious in preventing the pneumococcal disease and infection in infants and children under 5 and adults above 55 years, with weak immune system. However, the largest population that need this vaccine and are most vulnerable to the infection, live in Asia, Africa and other LIC and LMIC. The access to this vaccine and affordability are both very low in these regions.

At Biological E we embarked in 2013 on the mission to develop a PCV and bring to the market with urgency. Pneumococcal serotypes composition, polysaccharide production, purification, technology development for carrier protein CRM_{197} manufacture, conjugation chemistry and conjugates characterization, formulation for drug product, developing several analytical methods and assays were all accomplished incrementally over few years. A fourteen valent conjugate vaccine (PCV14) (Serotypes 1,3,4,5,6B,7V ,9F,14,18C,19A,19F,22F,23F, and 33F) was developed and Preclinical animal safety studies were done and the vaccine was tested in Phase1 clinical study adults for safety. Subsequently a Phase2 clinical study with Prevnar13 as comparator in 120 toddlers was conducted for safety and immunogenicity. Based on the data a Phase3 clinical study was conducted for NI with Prevnar13 in 1290 infants under a 3+0 dose schedule. PCV14 was found to be safe and immunogenic in all three different age groups. The IgG GMC ratios for the all twelve serotypes common to both products were non inferior to those of Prevnar13. Few serotypes of PCV14 had better immune response than those in Prevnar13. Two serotypes 22F and 33F present only in PCV14 and not in Prevnar13, showed immune response with strong seroconversion. In addition, we found that serotype 6B present in PCV14 showed 70% seroconversion against serotype 6A, which is not present in PCV14. The PCV14 overall, showed seroprotection against 14 serotypes and for ST 6A a significant protection. BE received MAA in December 2022. This 9-year long journey was a good learning experience on how to overcome limitations to develop complex vaccines in a developing world like India. A next gen PCV24 development was also initiated.

Biography

Ramesh Matur has been heading Vaccines R&D Division since 2013 at Biological E Ltd, Hyderabad. Vaccines R&D Division comprises all scientific functions for vaccines development from ideation to proof of concept - bacterial, viral and subunit recombinant, manufacturing process development on different platforms-microbial and cell lines, analytical development, and animal studies for vaccine immunogenicity, and all the way to clinical Phase3 studies. Clinical Development function is part of R&D Division. He established a highly talented, vibrant, strong scientific team with cross functional expertise. He actively reviews potential technologies for novel products, opportunities for collaboration, technology-in licensing, and sponsored research in the USA, India and globally. The Pneumococcal Conjugate Vaccine PCV14 received regulatory and marketing approval in December 2022. The next gen version PCV24 was developed and completed the Phase1 safety study in adults. Created a strong product pipeline of vaccines such as Hepatitis A, Measles, Human Papilloma Virus vaccine (HPV), and a novel Human Polyoma Virus Vaccine (HPyV) at various stage of development. Recently he created a team to develop mRNA platform based vaccines for selected infectious diseases. Prior to joining BioE, Dr. Matur worked for Wyeth at Pearl River, NY (now Pfizer) in the USA, and led vaccines R&D at Indian Immunologicals Ltd. He also lead the Industrial Biotechnology R&D at DuPont Knowledge Centre, India. He has 28 research publications, filed 20 patents of which 8 were globally granted and other applications are under review in multiple countries. Dr. Matur has a Ph.D. in Biochemistry & M.Sc. in Microbiology. He pursued his postdoctoral research at Michigan State University, E Lansing, Michigan and at The Ohio State University Biotechnology Centre

Rational design of next-generation glycoconjugate vaccines inducing highly functional antibodies

G. Stefanetti[a], N.A. Okan[b], F. Avner[c] and D.L. Kasper[b]
[a]Department of Biomolecular Sciences, University of Urbino Carlo Bo, Urbino, Italy. E-mail: giuseppe.stefanetti@uniurb.it
[b]Department of Immunology, Blavatnik Institute, Harvard Medical School, Boston, MA, USA.
[c]Department Lautenberg Center for Immunology, The Hebrew University-Hadassah Medical School, Jerusalem, Israel.

Glycoconjugate vaccines have been a cornerstone of global health, but their efficacy in high-risk populations remains a persistent challenge. Traditionally, sugar antigens are conjugated to carrier proteins in an empirical manner, often overlooking key immune response variables. Emerging insights from two distinct studies have unveiled the potential for optimizing glycoconjugate vaccine efficacy.

The first study introduces a novel approach for rational glycopeptide vaccine construction, addressing factors such as polysaccharide chain length, peptide composition, and conjugation site. Previous finding suggested that carbohydrate presentation to T cells by antigen-presenting cells enhances antibody response efficacy[1,2,3], encouraging the use of peptides as carries in glycoconjugate vaccines as alternative to whole proteins. In this study, we compared the immune responses induced by optimized glycopeptide vaccines to conventional glycoprotein conjugate vaccines. Surprisingly, the glycopeptide conjugate vaccines outperformed standard glycoprotein conjugate vaccines in a mouse model of Group B Streptococcus infection, despite inducing significantly lower levels of anti-carbohydrate specific IgG antibodies. We also demonstrated the critical role of the peptide linker and the conjugation site in enhancing both the conjugation efficiency and the immune response to vaccines. This observation challenges the traditional belief in a direct correlation between IgG levels and conferred protection by glycoconjugate vaccines, emphasizing the need for more comprehensive assessments of humoral and cellular responses.

The second study focuses on *Francisella tularensis*, a highly infectious and lethal pathogen that presents unique vaccine development challenges. Despite previous efforts using O-antigen (OAg)-based glycoconjugate vaccines, protection against intranasal live vaccine strain (LVS) infection in mice has remained elusive. Notably, varying the OAg size in these glycoconjugates significantly impacted vaccine efficacy, with larger OAg sizes offering marked improvements in protection, despite the observed lower IgG titers induced compared to the glycoconjugates made with the smaller O-antigen sizes[4]. Further investigation into conformational antibodies against OAg epitopes will shed light on their role in controlling *F. tularensis* infection and their potential for enhancing glycoconjugate vaccines against intracellular pathogens.

These collective findings suggest that a paradigm shift in glycoconjugate vaccine design is warranted, highlighting the importance of optimizing carbohydrate presentation and considering factors beyond the induction of anti-carbohydrate specific IgG levels. This new approach offers the potential to develop glycoconjugate vaccines that provide enhanced efficacy and longer-lasting immunity, even against challenging pathogens.

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Biography

Dr. Giuseppe Stefanetti has been Assistant Professor at Urbino University since 2022, specializing in the interaction between microbes and the immune system, with a particular emphasis on developing new vaccines and exploring microbiome science.

Previously, Giuseppe worked at Harvard Medical School starting in 2015, first as a Principal Investigator on a Marie Curie grant fellowship in collaboration with the University of Milan, and then as an Instructor in Immunology. During his time at Harvard, he focused on studying the interaction of microbial carbohydrates with the immune system, aiming to develop innovative glycoconjugate vaccines.

In 2014, he successfully completed his Ph.D. in Molecular and Industrial Biotechnology at the Novartis Vaccine Institute for Global Health in Siena. His research there centered around investigating the impact of polysaccharide antigen structure and conjugation chemistry on Nontyphoidal *Salmonella* glycoconjugate vaccines. Subsequently, he worked as a postdoctoral fellow at the GSK Vaccine Institute for Global Health, where he focused on outer membrane vesicles as candidate vaccines.

Giuseppe earned a Master's degree in Chemical Science and pursued a Master's course in Polymer and Nanocomposites Science from the University of Perugia. He also holds an Executive MBA from Politecnico di Milano Business School.

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Coronavirus (COVID-19)

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Coronavirus (COVID-19)

Title: **MVA-vectored multi-antigen Covid-19 vaccines induce protective immunity against SARS-CoV-2 variants spanning Alpha to Omicron in preclinical animal models**
Mukesh Kumar
Georgia State University

Title: **Superior mucosal B- and T-cell responses against SARS-CoV-2 after heterologous intramuscular mRNA prime/intranasal protein boost vaccination with a combination adjuvant**
Michael Schotsaert
Icahn School of Medicine at Mount Sinai

Title: **Modular nanoarray vaccine for SARS-CoV-2**
Yuri Lyubchenko
University of Nebraska Medical Center

Title: **How to develop a long-lasting COVID-19 vaccine**
Gongyi Zhang
National Jewish Health

Title: **Comparative efficacy of antiviral strategies targeting different stages of the viral life cycle**
Barbara Jones
IBM Quantum

Title: **Intranasal Ad5 Omicron vaccine can build effective mucosal immunity wall against broad spectrum of SARS-CoV-2 variants**
Ling Chen
Guangzhou Laboratory, Guangzhou Medical University

Title: **Prevention of Covid-19 beyond the vaccine needle: Targeting transmission via development of a novel antiviral fusion peptide-based prophylactic nasal spray**
Shahin Gharakhanian
Decoy Therapeutics

Title: **Durable immunity to SARS-CoV-2 infection and vaccination**
Mehul Suthar
Emory University School of Medicine

Title: **Development of next generation vaccines against SARS-CoV-2 infection**
Tian Wang
University of Texas Medical Branch

Title: **Minimalistic pan-coronavirus vaccines with a safer LNP delivery system and devoid of adverse spike epitopes**
Janet K. Yamamoto
University of Florida

Title: **Selection for immune evasion in SARS-CoV-2 revealed by high-resolution epitope mapping and sequence analysis**
Jorg Hermann Fritz
McGill University

Title: **Design of a subunit precision vaccine against SARS-CoV-2**
M. Dahmani Fathallah
Arabian Gulf university

Title: **UB-612: A novel peptide/protein subunit COVID-19 vaccine booster stimulated broadly neutralizing and Fc-mediated effector antibodies in a head-to-head Phase 3 randomized clinical trial**
Alexander Rumyantsev
Vaxxinity

MVA-vectored multi-antigen Covid-19 vaccines induce protective immunity against SARS-CoV-2 variants spanning Alpha to Omicron in preclinical animal models4

***Mukesh Kumar, Shannon Stone, Amany Elsharkawy, Janhavi Natekar, Sreenivasa Rao Oruganti, Mary Hauser, Arban Domi, Pratima Kumari and Mark Newman**
*Georgia State University, Atlanta
GeoVax, Atlanta

Widespread and rapidly evolving SARS-CoV-2 posed an unprecedented challenge to vaccine developers. First generation vaccines based on the spike (S) protein induced neutralizing antibodies that provided significant levels of protection against the initial variants. However, vaccine efficacy was disrupted by emerging variants that contributed to neutralizing antibody evasion. In response, efforts were implemented to develop updated vaccines that specifically target these variants or target multiple antigens in SARS-CoV-2 to effectively broaden immunity and mitigate the impact of variants spread. GeoVax has designed a multiantigen SARS-CoV-2 vaccine that expresses S, membrane (M), and envelope antigen (E)s, designated GEO-CM02, which was tested in hACE2 transgenic mice. CM02 vaccine efficacy studies in the lethal hACE2 mouse model demonstrated complete protection with a single dose against the original Wuhan strain and BA.1 Omicron variant. Animals were fully protected prior to the detection of neutralizing antibodies, the widely accepted as the correlation of protection, likely indicating a critical T-cell contribution. Two-dose CM02 vaccination elicited high levels of neutralizing antibodies, effectively controlled lung viral burden, reduced viral load in the lung, brain, and olfactory bulb and reduced inflammatory cytokines and chemokines in the lungs. In addition, CM02 conferred 80% protection against lethal challenge with the B.1.351 Beta variant. These data indicate that immunization with the multi-antigen GEO-CM02 vaccine can protect against severe disease and death induced by SARS-CoV-2 and its variants in a highly relevant pre-clinical model.

Biography

Dr. Mukesh Kumar is an Associate Professor in the Department of Biology at Georgia State University. He is a virologist and immunologist with expertise in the studies of RNA virus/host interactions. Kumar's major area of research interest is to identify novel therapeutic targets and diagnostic biomarkers for emerging infectious diseases, which include COVID-19, West Nile virus encephalitis and Zika virus-associated neurological disease. His lab is studying the pathogenic mechanisms underlying the development of brain dysfunction during neurotropic virus infection.

Superior mucosal B- and T-cell responses against SARS-CoV-2 after heterologous intramuscular mRNA prime/intranasal protein boost vaccination with a combination adjuvant

Nandini Arya[*], Gabriel Laghlali[*], Dilara Karadag, Jeffrey J. Landers, Jessica J. O'Konek, Katarzyna W. Janczak, Prajakta Warang, Gagandeep Singh, Mohammad Farazuddin, James R. Baker, Jr., Pamela T. Wong[#] and Michael Schotsaert[#]
Icahn School of Medicine at Mount Sinai

Background: In countries with access to COVID-19 vaccines, many have received two or more vaccine doses, often mRNA vaccines. mRNA vaccines are typically administered via the intramuscular (IM) route and are efficient at inducing protective B and T cell responses in the periphery. However, mucosal vaccination can be an efficient way to induce immune protection at the portal entry site for respiratory viruses like SARS-CoV-2. There has been strong interest in rerouting humoral and cellular responses induced in the periphery by IM vaccination to mucosal sites.

Methods: We have used a novel combination adjuvant that consists of a mixture of a nano-emulstion (NE) and a RIG-I agonist (in vitro transcribed Sendai virus defective interfering RNA, IVT) for which have shown in the past it is able to induce potent systemic and mucosal immune responses when used to adjuvant protein-based SARS-CoV-2 vaccine or inactivated influenza virus vaccine administered as a prime/boost vaccination via the intranasal (IN) route. In this work we investigated in mice if IM mRNA vaccine priming followed by IN boosting with protein vaccine formulated in NE/IVT can promote strong mucosal humoral and cellular immune responses and correlated these vaccine responses with protection during infection with Beta and Omicron SARS-CoV-2 variants of concern that were antigenically different from the ancestral spike antigen used in the vaccine.

Results: mRNA prime/boost vaccination resulted in high cross-reactive antibody and T cell responses in serum and spleen, comparable to NE/IVT prime/boost or hybrid mRNA NE/IVT prime/boost vaccination. However, mucosal boosting with NE/IVT of mRNA primed animals resulted in superior mucosal IgA antibody levels combined with superior T cell responses in mucosa-draining lymph nodes. T cell responses resulting from mucosal vaccination are characterized by a balanced Th1/Th17 signature based on cytokine profiling. All prime/boost regimens tested resulted in control of lung virus replication after Beta or Omicron BA5 replication, but mucosal NE/IVT vaccination, either as prime/boost or as IN boost after IM mRNA prime was required to fully control virus replication in nasal turbinates of experimentally infected mice.

Conclusions: Our data shows there is benefit in hybrid immunization regimens whereby strong humoral and cellular immune responses are induced in the periphery after IM vaccination that can then be rerouted to mucosal sites by mucosal adjuvanted vaccines like the NE/IVT platform to provide optimal protection from respiratory pathogens like SARS-CoV-2 and influenza viruses. Similar experiments with hybrid prime/boost strategies are currently performed using preclinical influenza vaccination models.

Biography

Dr. Schotsaert obtained a master's degree in bio-engineering (2003), a master's degree in molecular medical biotechnology (2004) and a PhD in molecular biotechnology (2011) from Ghent University (Belgium). In 2013 he joined the lab of Dr. Adolfo García-Sastre for postdoctoral work as an immunologist and vaccinologist and has since established different vaccination and infection models (BSL2, BSL3 and BSL3+). Dr. Schotsaert's work focuses on influenza, ZIKA and SARS-CoV-2 viruses and he has over fifteen years of experience with studying host-pathogen interactions in preclinical infection models to immunologically characterize and validate candidate vaccines, adjuvants and antiviral treatments. From an immunological point of view, his research focuses on the interplay and cross-talk between innate and adaptive immune responses during virus infection. Since January 2020, the Schotsaert laboratory is established in the Department of Microbiology and the Global Health and Emerging Pathogens Institute at the Icahn School of Medicine at Mount Sinai in New York, and together with his team he continues to study host-immune responses to infection and vaccination in the context of comorbidities like obesity, diabetes and advanced age.

Modular nanoarray vaccine for SARS-CoV-2

Karen Zagorski[1a], Kabita Pandey[2,3a], Rajesh Rajaiah[2], Omalla A. Olwenyi[2,3], Aditya N. Bade[2], Arpan Acharya[2], Morgan Johnston[2], Shaun Filliaux[1], Siddappa N. Byrareddy[2] and Yuri L. Lyubchenko[1*]

[1] Department of Pharmaceutical Sciences, University of Nebraska Medical Center, USA

[2] Department of Pharmacology and Experimental Neuroscience, University of Nebraska Medical Center, USA

Background: The current vaccine development strategies for the COVID-19 pandemic utilize whole inactive or attenuated viruses, virus-like particles, recombinant proteins, and antigen-coding DNA and mRNA with various delivery strategies. While highly effective, these vaccine development strategies are time-consuming and often do not provide reliable protection for immunocompromised individuals, young children, pregnant women, and elderly people with neurodegenerative diseases.

Aim/Purpose of the research: We propose a novel modular vaccine platform by using nano assembly approach with the use of chemically synthesized peptides – epitopes of the spike protein of SARS-CoV-2 viral particles.

Methods: The vaccine is based on the rational design of an immunogen containing two defined B-cell epitopes from the spike glycoprotein of SARS-CoV-2 and the universal T- helper epitope PADRE. The epitopes were conjugated to short DNA probes and assembled on a complementary DNA scaffold strand due to the sequence-specific self-assembly. The immunogens terminated with thiol groups were chemically conjugation to gold nanoparticles using three different approaches. Gel electrophoresis was used to evaluate the coating of gold nanoparticles with the immunogen. BALB/C mice were immunized with each formulation, and the IgG immune responses and virus neutralizing titers were measured and compared with each formulation.

Results: The immunogen was obtained by annealing the long DNA template with a mixture of DNA-peptide conjugates. The results demonstrate that this assembly is immunogenic in vivo and generated immune response and neutralizing antibodies against SARS-CoV-2 wild type and its variants of concerns (VOCs). Since the immunogen is modular, epitopes or immunomodulatory ligands can be quickly introduced to tailor the vaccine to the recipient. This also allows the already developed vaccine to be modified rapidly according to the identified mutations of the virus.

Biography

Dr. Yuri L. Lyubchenko is Professor of Pharmaceutical Sciences University of Nebraska Medical Center, Omaha, NE. His research spans a broad range of biomedical problems aimed at unraveling molecular mechanisms of such diseases as cancer, Alzheimer's and Parkinson's diseases. He has authored 320 research articles/book chapters. He was named UNMC distinguished scientist (2008). He is an Academic Editor for Nature-Scientific Reports, associate editor for New Journal of Science, Frontiers in Bioscience, Journal of Molecular Pharmaceutics and Precision Nanomedicine and serves as editorial member of a number of reputed journals. He also serves on NIH and NSF grant proposal review panels.

How to develop a long-lasting COVID-19 vaccine

Gongyi Zhang
Department of Immunology and Genomic Medicine, National Jewish Health, and Department of Immunology and Microbiology, School of Medicine, University of Colorado, USA
NB Life Laboratory LLC, 10490 E Aberdeen Ave, Englewood, USA; Competing Interest: G.Z. holds equity at NB Life Laboratory LLC.

Re-infection after a previous infection of SARS-CoV-2 or infection after vaccinations even with multiple boosts is 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 pathogens. It seems impossible to generate herd immunity with either a higher rate of infection or universal vaccination of populations, emerging variants of SARS-CoV-2 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 difficulties 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 three successful examples regarding SARS-CoV-2, Influenza A, and Influenza B. We may have potentially resolved this long-standing 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 granted 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 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 University of Colorado Anschutz Medical Campus. He set up a company, NB Life Laboratory, to develop long-lasting vaccines against pathogens such as influenza, SARS-CoV-2, and others in 2018.

Comparative efficacy of antiviral strategies targeting different stages of the viral life cycle

Barbara Jones[1], Mo Das[2] and Pancy Lwin[3]
[1]IBM Quantum
[2]Rochester Institute of Technology

While the COVID-19 pandemic continues to impact public health worldwide significantly, the use of antivirals has dramatically reduced the instances of severe disease and death. Antivirals also provide hope for preventing similar viral outbreaks in the future. Here we ask: What are the comparative impacts of antivirals targeting different stages of the viral lifecycle? How do antivirals impact the viral population in the blood stream (viral load) in high and low-immunity individuals? We use a viral quasispecies dynamics model to study the efficacy of antiviral strategies targeting three critical aspects of the viral life cycle, fecundity, reproduction rate, or infection rate. We find a linear relationship of the viral load with the change in fecundity and a power law with the change in the reproduction rate of the virus, with the viral load decreasing as the fecundity and the reproduction rates are decreased. Interestingly, however, for antivirals targeting the infection rate, the viral load changes non-monotonically with the change in infection rate; it initially increases and then decreases as the infection rate is decreased. The initial increase is especially pronounced for low-immunity individuals. By examining the virus population inside cells for such cases, we found that the therapeutics are only effective in such individuals if they stop the infection process entirely. Our results predict the effectiveness of different antiviral strategies for COVID-19 and similar viral diseases and provide insights into the susceptibility of individuals with low immunity to effects. We also discuss the applicability of this work for quantum computing, and in general the use of quantum computing for epidemiology.

Biography

Dr. Barbara Jones is currently a Senior Research Scientist in IBM Quantum, Quantum Applications group, at IBM Research Almaden in San Jose, California. Over the years at IBM she has been a manager of both experimental and theoretical groups, working on a number of areas both fundamental and more applied. She has also been a Consulting Professor at Stanford University in Physics and Applied Physics Departments. Her long-term interests have involved theories of quantum interactions in molecular and atomic-scale magnetic systems, as well as physics applied to biological systems such as host/microbe interactions and cells, modeling viral evolution and mutation including the effects of viral therapeutics.

Dr. Jones is a Fellow of the American Physical Society (APS) and of the American Association for the Advancement of Science (AAAS). She is a recipient of a TWIN Award (Tribute to Women in Industry). She is Chair of the Physics Section of the AAAS and has served on the Council of AAAS also. She is Past Chair of the APS Forum on Industrial Applications of Physics, at the time the largest unit of APS, and of the Division of Condensed Matter Physics, the current largest. Committee on National Academy of Science Decadal Survey of Materials 2019, past Chair NAS Board on Physics and Astronomy, Honorary Member Aspen Center for Physics, past PRX and PRB editorial boards and Buckley Prize Committee Chair, current chair of many university advisory committees. She was a member of the committee who wrote the most recent National Academy of Sciences Decadal Survey of Materials, appearing in March 2019, as well as a recent Chair of the Board on Physics and Astronomy of the National Academy of Science. She is in addition an Honorary Member of the Aspen Center for Physics, has served on the editorial boards of PRX and PRB and in addition is on many university science advisory committees, and is organizer of international conferences in the U.S. and Europe.

Intranasal Ad5 Omicron vaccine can build effective mucosal immunity barieer against infection of broad spectrum of SARS-CoV-2 variants

Ling CHEN
State Key Laboratory of Respiratory Disease, The First Affiliated Hospital of Guangzhou Medical University; Guangzhou Laboratory; Guangzhou nBiomed Ltd. Guangzhou, China

The highly contagious SARS-CoV-2 Omicron subvariants severely attenuated the effectiveness of intramuscularly injected SARS-CoV-2 vaccines. We designed a replication-incompetent recombinant adenovirus type 5 vectored Omicron vaccine (NB2155) and evaluated in an IIT to test intranasal Ad5-S-Omicron as a heterologous booster in people previously injected with ancestral inactivated vaccine. Nasal mucosal lining fluids collected after intranasal booster showed dramatic elevation of secretary IgA that can bind to at least 10 spike proteins of variants. Instillation of nasal lavage fluids into mouse nostril conferred protection against Omicron challenge. Nasal secretary IgA showed potent neutralizing activities against multiple Omicron subvariants including BA.1, BA.5, BF.7, BQ.1.1, and XBB, as well as pre-Omicron strains. Taken together, intranasal booster using NB2155 on the basis of ancestral vaccines can establish an effective immunity barrier against Omicron subvariants and multiple SARS-CoV-2 variants. This candidate vaccine warrants further development as a safe, effective, and user-friendly infection- and transmission-blocking pan-Omicron vaccine.

Biography:

Dr. Chen has been a Professor in State Key Lab of Respiratory Disease, Guangzhou Medical University since 2013. Dr. Chen received a medical degree from Shanghai Medical College in 1984. He obtained a Ph.D. in Biochemistry and Molecular Biology from Indiana University School of Medicine. Dr. Chen completed his postdoctoral training at Dana-Farber Cancer Institute, Harvard Medical School. From 1997-2001, Dr. Chen served as a Senior Research Fellow at Merck Research Laboratories, where he was the first inventor on Merck's MRK Ad5 based AIDS vaccine that entered clinical trial worldwide. Dr. Chen served as Vice Presidents of R&D for GlaxoSmithKline in 2009-2011 and as Vice President at Sanofi Pasteur in 2012. Dr. Chen has over 200 publications in infectious diseases, vaccine research, and cancer research. His current research is focused on vaccine and antibody research on adenovirus, influenza virus, and emerging viruses. Since 2020, Dr. Chen has been working on developing a user-friendly intranasal vaccine to induce mucosal immunity. In a recent study, this intranasal vaccine showed promising result in inducing nasal secretory IgA and efficacy in preventing Omicron infection.

Prevention of Covid-19 beyond the vaccine needle: Targeting transmission via development of a novel antiviral fusion peptide-based prophylactic nasal spray

Barbara Hibner[1], Jodi Cooper[1], Peter Marschel[1], Michael Lipp[1], Bradly Pentelute[1, 2], Frederick E. Pierce II[1], Shahin Gharakhanian[1]
[1]Decoy Therapeutics, Cambridge Innovation Center,
[2]Pentelute Lab., Department of Chemistry, Massachusetts Institute of Technology, both in Cambridge MA, USA.

Introduction: Unmet Public Health Needs: Sars-CoV2 is mainly transmitted by respiratory droplets. Contact tracing supports infection following inhalation up to 2 m (6 ft.) from the source. Asymptomatic and symptomatic subjects can transmit. SARS-CoV-2 has become endemic to humans, and recent projections indicate the fifth endemic seasonal coronavirus, alongside four other human coronaviruses. It is therefore essential to develop novel and adapted public health strategies to contain endemicity and protect fragile populations (1). A literature search was conducted on PubMed, and Google using search terms "COVID-19", "challenges", "prevention", and "control" in different combinations. COVID-19 prevention and control challenges are related to health-system, vaccines, administration, and society culture (2). The pandemic revealed the complexities of global infection control involving age-driven infection patterns, levels of awareness, high viral variations, changes to vaccine immune response over time, social media, the heterogeneity of social responses and medical co-morbidities. A "one-size-fits-all" approach has proven insufficient. Vaccines are the backbone, but gap analysis points to the need for additional agents (3). Here, we report Decoy Therapeutic's R&D program developing a broad antiviral bioconjugate platform. Our lead candidate is a novel antiviral fusion peptide-based prophylactic nasal spray Peptide conjugates are intricately engineered molecules pre-emptively target a conserved region of viral spike proteins, disrupting the fusion process that underpins infection at its initial juncture.

Research & Development Program: DCOY101+ consists of peptides from the highly conserved S2 heptad repeat region of b coronaviruses conjugated to PK extending lipids ("lipopeptides") that inhibit viral fusion and entry by preventing proper viral fusion structure assembly. In addition, **fre**e virions are directly inhibited by lipopeptide insertion in the viral membrane, rendering expelled virus inactive. This combined dual action prevents infection *and* transmission. DCOY101+ has low nanomolar potency across all the SARS-CoV-2 variants of concern and is active against all the human infecting coronaviruses tested including SARS-CoV-1, MERS, OC43, NL63 and 229E in live virus assays. Once-a-day intranasal DCOY101+ has demonstrated inhibition of viral infection in a Syrian hamster PrEP model with dosing before viral challenge and in the hamster PEP/therapeutic model with dosing beginning at 2, 12, 24 or 36 hours after viral challenge. Pharmacokinetic (PK) levels were well above in vitro IC50/IC90 in the nasal cavity and lungs for 8 hrs, (at this point the longest time point measured)(4).

Concluding Perspectives: DECOY 101+ is a pan-coronavirus inhibitor for Pre-Exposure and Post Exposure Prophylaxis with potential for (early) therapeutic use. This non-systemic once-a-day nasal spray is temperature stable, requires no cold chain, and demonstrates high safety window with no potential for drug interaction, all in an easily carried personal device for self-administration. Complementing vaccination, DECOY 101 + is thus a core component to a "public health toolbox" approach including multiple prophylactic and population-friendly customized approaches in order to control coronaviruses globally.

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Biography

Shahin Gharakhanian, MD, DTM&H, DPH, is Chair, Scientific Advisory Board of Cambridge MA-based DECOY Therapeutics & the Chief Medical Officer. He is a Physician-Executive with expertise in Pharmaceutical Medicine, Leadership/Management, and an international track record both in Clinical Medicine and Pharmaceutical Medicine Including Vice-President of Vertex Pharmaceuticals Inc. in Boston/Cambridge MA, USA, Global R&D group and Corporate Operating Council Member. Overall, clinically developed/launched four novel treatments including a first-in-class Direct Acting Antiviral in chronic Hepatitis C (HCV). His biopharmaceutical R&D or academic research includes Antibiotics, Malaria, Microbiomes, Tuberculosis, Viral infections [AIDS/HIV infection, HBV, HCV, Influenza, RSV]. Dr Gharakhanian is a member of the IAS: International AIDS Society, IDSA: Infectious Diseases Society of America, & SPILF: French-language Infectious Diseases Society. Shahin Gharakhanian's medical education has been at Paris-Sorbonne University Medical Schools & Hospitals and at Harvard Medical School CME Programs.

Durable immunity to SARS-CoV-2 infection and vaccination

Mehul S. Suthar
Associate Professor, Department of Pediatrics-Infectious Disease, Emory University School of Medicine

Infection with SARS-CoV-2 in humans has caused a pandemic of unprecedented proportions. The development and deployment of effective SARS-CoV-2 vaccines are one of the most successful countermeasure efforts in history. While the correlates of protection are not yet fully defined, antibody (Ab) and T cell responses to the spike protein, the principal antigenic target of SARS-CoV-2 vaccines, are linked to vaccine efficacy. However, the emergence of variants with mutations in the spike protein jeopardizes the effectiveness of SARS-CoV-2 vaccines. Omicron variants, with more than 30 mutations in the spike protein, have caused significant vaccine breakthrough and re-infection cases. My group uses animal models and human samples to study the impact of emerging variants on the immunological response to infection and vaccination.

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. 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

Development of next generation vaccines against SARS-CoV-2 infection

Tian Wang[1,2]
[1]Department of Microbiology & Immunology,
[2]Sealy Institute for Vaccine Sciences, University of Texas Medical Branch, Galveston, USA.

The recent coronavirus disease 2019 (COVID-19) pandemic had made a serious impact on global public health for more than three years. Four vaccines have been granted emergency use authorization (EUA) by the FDA. Although these vaccines are highly effective against severe disease, their efficiency has been challenged by the increasing rates of variants of concern that are characterized by increased viral transmissibility and immune evasion. Continuous work is needed to optimize existing vaccine platforms and to develop more effective novel vaccines. Multiple COVID-19 vaccine platforms have been tested with collaborative efforts in our studies, including a multigenic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine based on an MVA vector expressing both viral nucleocapsid (N) and spike (S) proteins (MVA-S + N), a modified porous silicon microparticle (mPSM)-adjuvant to SARS-CoV-2 receptorbinding domain (RBD) vaccine, and an attenuated SARS-CoV-2 virus with modified viral transcriptional regulatory sequences and deletion of open-reading frames 3, 6, 7 and 8 (Δ3678). While all three vaccine candidates induced protective immunity against SARS-CoV-2; mPSM-based RBD subunit vaccine and Δ3678 generated potent and/or durable SARS-CoV-2- specific humoral and type 1 helper T (Th) cell- mediated systemic and mucosal immune responses and protected host against SARS-CoV-2 and variants infection in animal models. Overall, these vaccines are important for prevention and control of COVID-19 morbidity and mortality following SARS-CoV-2 and variants infection. They can also serve as attractive mucosal vaccine candidate to boost pulmonary immunity against SARS-CoV-2.

Biography

Dr. Tian Wang is a Professor of Department of Microbiology & Immunology at the University of Texas Medical Branch (UTMB) at Galveston. She received her Ph.D. degree in Immunology from UTMB and completed a Postdoctoral training in Infectious Disease at Yale University. Over the past two decades, Dr. Wang's research has mainly focused on vaccine development and understanding of the disease mechanisms of emerging and re-emerging RNA viruses

Minimalistic pan-coronavirus vaccines with a safer LNP delivery system and devoid of adverse spike epitopes

Bikash Sahay[1,2], John G. Morris Jr [3], Subhashnie Kariyawasam[2,4], and Janet K. Yamamoto[2,4,*]
[1]Department of Infectious Diseases and Immunology, College of Veterinary Medicine, University of Florida, Gainesville, FL 32610
[2]Laboratories of Comparative Immunology & Virology for Companion Animals, CDPM, College of Veterinary Medicine, University of Florida, Gainesville, FL 32610
[3]Emerging Pathogens Institute, University of Florida, Gainesville, FL 32610
[4]Department of Comparative, Diagnostic, and Population Medicine (CDPM), College of Veterinary Medicine, University of Florida, Gainesville, FL 32610

The three major problems of the current COVID-19 vaccines in the U.S. are the adverse epitopes on SARS-CoV-2 (SCoV2) spike glycoprotein for mRNA and the inflammatory nature of the lipid nanoparticle (LNP) used for mRNA-LNP delivery in humans. The third problem extends to all COVID-19 vaccines worldwide: none prevents SCoV2 infection; however, they decrease the incidence of hospitalization and death. Since SCoV2 RBD glycoprotein is hyper-stimulatory, other adverse epitopes on spike need to be eliminated to reduce the inflammatory responses, and other reported adverse effects. The most well-described adverse epitopes on the SCoV2 spike are the superantigen, ICAM-1, bullous pemphigus, and neurotoxin motifs. Our multivalent B-cell constructs (RBD-HR1-SH-HR2-TM-cCT) are devoid of such adverse epitopes while retaining the receptor binding domain (RBD) for major neutralizing antibody (NAb) epitopes against SCoV2 and stem helix (SH) as broadly NAb epitopes against β-coronaviruses (βCoVs). Since the SCoV2 spike has a minimal number of conserved cytotoxic T lymphocyte (CTL) epitopes, CTL epitopes for T-cell/CTL epitopes were derived from SCoV2s' and αCoVs' RdRp polymerases and M-proteases, which are highly evolutionarily conserved viral enzymes, with least mutations among the majority of SCoV2 variants. The ionizing cationic lipid needed for the LNP has been improved and differs from those used by the best U.S. COVID-19 vaccines. The minimalistic pan-CoV vaccine for cats was derived from SCoV2 Wuhan, feline coronavirus serotype 1 (FCoV1-UCD1), and FCoV2-79-1146 B-cell constructs and T-cell/CTL epitope chains of pDNA/mRNA in an LNP delivery system (PCT/US23/72907). Remarkable serological and T-cell cross-reactivities reside on SCoV2, human αCoVs, and FCoV1 RBDs. The pilot pan-CoV vaccine for cats has been safely vaccinated at high doses intramuscularly in laboratory cats with no adverse reactions. The minimalistic pan-CoV vaccine for humans consists of B-cell constructs and T-cell/CTL epitope chains in pDNA/mRNA of SCoV2 Wuhan, SCoV2 variant, and two human αCoVs in a LNP delivery system (U.S. Patent Application 63/508,697). Our team is using the domestic cat model of SCoV2 infection because domestic cats are highly susceptible to natural SCoV2 infection from their SCoV2-infected owners and readily infected in laboratory cats by intranasal inoculation with SCoV2. Our laboratory cat lineages also recognize human HLA-A2 and HLA-B27 for CTL epitopes, the common HLAs in the U.S. population. Furthermore, the feline pan-CoV vaccine will protect against fatal feline infectious peritonitis virus infection and, at the same time, prevent pet cats from becoming a reservoir for human transmission of new SCoV2 variants. Combining the B-cell and T-cell epitopes in the pan-CoV vaccine, such bimodal immune mechanisms should generate potent sterilizing immunity to prevent SCoV2 infection in humans and cats, with minimal to no adverse effects.

Biography

Dr. Janet K. Yamamoto is a professor of viral immunology in the University of Florida College of Veterinary Medicine's Department of Comparative Diagnostic, and Population Medicine. In 1984, she established the HIV/AIDS BSL3 laboratory under the joint directive of the Schools of Medicine and Veterinary Medicine at the University of California-Davis (UCD), which became the Center for AIDS Research. She is the first to demonstrate, together with Nobel laureate Dr. Francoise Barré-Sinoussi, that interferon-gamma will not protect against HIV-1, and she has served as the consultant of the second FDA-approved HIV-1 Western blot for HIV-1 confirmatory test. Yamamoto co-discovered the feline immunodeficiency virus, FIV, the feline counterpart of HIV. She also invented the first commercial FIV vaccine sold by Pfizer-Zoetis and Boehringer. Her current research focus is on the development of a combined therapy for FIV and HIV-1 cure, and the development of minimalized pan-coronavirus vaccine for cats, dogs, and humans. The veterinary drug, diagnostic, and vaccine developments, and the establishment of Comparative Immunology and Virology Program for Companion Animals (LCIV-CA) and the CVM Cat Breeding Program are funded by her personal patent royalty/licensing income and retirement fund donated by her to this veterinary research and academic mission. She and her colleagues recently discovered that sera from FCoV-infected cats cross-reacts strongly with SARS-CoV2 receptor binding domain (RBD). This discovery has been reported to UF Innovate and Tech Licensing, and LCIV-CA program has received an U.S. Provisional Patent No. 63/373,474 for the FCoV and SARS-CoV-2 immunoblot diagnostics and minimalized pan-CoV vaccines for human and companion animals (cats, dogs, and hamsters).

Selection for immune evasion in SARS-CoV-2 revealed by high-resolution epitope mapping and sequence analysis

Jorg Hermann Fritz
McGill University, Canada

Here, we exploit a deep serological profiling strategy coupled with an integrated, computational framework for the analysis of SARS-CoV-2 humoral immune responses. Applying a high-density peptide array (HDPA) spanning the entire proteomes of SARS-CoV-2 and endemic human coronaviruses allowed identification of B cell epitopes and relate them to their evolutionary and structural properties. We identify hotspots of pre-existing immunity and identify cross-reactive epitopes that contribute to increasing the overall humoral immune response to SARS-CoV-2. Using a public dataset of over 38,000 viral genomes from the early phase of the pandemic, capturing both inter- and within-host genetic viral diversity, we determined the evolutionary profile of epitopes and the differences across proteins, waves, and SARS-CoV-2 variants. Lastly, we show that mutations in spike and nucleocapsid epitopes are under stronger selection between than within patients, suggesting that most of the selective pressure for immune evasion occurs upon transmission between hosts.

Biography

Dr. Jörg Hermann Fritz graduated from the University of Vienna, Austria, where he received his Ph.D. in Immunology in cooperation with the biotech start-up Intercell (now Valneva). There he developed the vaccine adjuvant IC31, which is currently in Phase 2 and Phase 3 clinical trials for novel vaccine candidates.

Following two postdoctoral training periods at the Institute Pasteur Paris and the University of Toronto he joined the Department of Microbiology and Immunology at McGill University in Montreal, Quebec, Canada in 2010.

Since summer 2022 Jörg is the Director of the McGill Research Center on Complex Traits (MRCCT) and member of the the recently formed Dahdaleh Institute of Genomic Medicine (DIgM).

Jörg's research interests are focused on how innate immunity shapes antigen-specific memory and contributes to chronic inflammatory diseases. His research in the field of cellular and molecular immunology was awarded several project grants by the Canadian Institutes of Health Research (CIHR) and the New Frontiers Research Fund (NFRF) of the Canadian government.

Design of a subunit precision vaccine against SARS-CoV-2

M. Dahmani Fathallah*, Khaled Trabelsi, Noureddine Ben Khalaf and Ahmed R. Ramadan
Health Biotechnology Program, Dept of Life Sciences, Arabian Gulf university, Manama, Bahrain

The high genetic variability of the new coronavirus SARS-CoV-2 that caused the ongoing severe acute respiratory syndrome related coronavirus 2 disease (COVID19) pandemic, is urging the development of precision vaccines. We herein, present the development of vaccine subunits that mimic the natural protective immunity elicited by structural regions of the virus associated with infective power. We have first identified using rational and computational approaches 14 potential epitopes located in a region involved in SAR-CoV-2 high infectivity. Hence, we engineered a series of polypeptides containing these epitopes. We developed an indirect ELISA assay and used it to show that the antibody response, to two polypeptides is highly associated to the asymptomatic and mild forms of the disease in a patients-centered study using a cohort of 500 SARS-CoV-2 COVID19 patients [$p<0.001$]. Furthermore, immunization of BALBc mice with these polypeptides, using various adjuvant, elicited strong humoral immune response. Upon these findings, we engineered different multivalent subunits from the sequences found to elicit a protective immune response. We showed that these engineered antigens elicit B and T cell immunity in patients with COVID19. Computational analysis tools showed that these subunits were structurally stable, antigenic and non-allergenic, thus suitable for human precision vaccination. Immunization of BALBc mice with recombinant forms of the engineered subunits using various adjuvants yielded a strong long lasting humoral. The approach we used to design a precision vaccine to SARS-CoV-2 can be applied to a number of highly pathogenic human viruses that can cause pandemics.

Biography

MDF is King Fahd chair Professor of Medical Biotechnology and expert in Biotechnology and Bioproducts development. He is a Certified Innovation Strategist and International Consultant in Medical Biotechnology & Technology Transfer strategies. He is also a UN expert in Innovation and Science and technology He received his degrees and training in Molecular Biology, Molecular Genetics and Immunology from the University of Paul Sabatier, Toulouse, France, Oxford University, UK and Harvard University, Boston, MA, USA. In addition, he holds an MBA in Health biotech. He is the former dean of the College of Graduate studies at the Arabian Gulf University Manama-Bahrain. He is currently the Chairman of the Biotechnology PhD program. He founded ArabOmiX a Biotech & Technology Transfer consulting office for the development of startups and SME in the fields of high tech. He is a former senior investigator at the Institute Pasteur of Tunis (Head of the Medical Biotechnology Group) and the CSO of Jeddah Biocity Inc and CEO/Founder of RethabBiotech Inc a startup in the engineering and development of recombinant antibodies. He holds nine International patents for the development of five biopharmaceutical [Biosimilar & Innovative] products]. He authored over 150 international scientific papers, three books [One book on *Transfer of Technology in the Pharmaceutical & Medical fields*.] and several general papers on Bio-economy, Transfer of Biotechnologies and Education policies. He is the founder and president of the Harvard Alumni of Tunisia and the co-founder of the Arab Policy Institute. MDF received several international awards.

UB-612: A novel peptide/protein subunit COVID-19 vaccine booster stimulated broadly neutralizing and Fc-mediated effector antibodies in a head-to-head Phase 3 randomized clinical trial

Alexander Rumyantsev
Therapeutic Area Head, Infectious Diseases
Vaxxinity

- Vaxxinity's peptide/protein subunit COVID-19 vaccine, UB-612, was tested in a pivotal Phase 3 international multisite RCT head-to-head with mRNA (Pfizer), adenovirus (AstraZeneca), and inactivated virus (Sinopharm) active comparators delivered as boosters.
- Primary objectives were met with UB-612 boosting non-inferior neutralizing antibodies against Wuhan and Omicron BA.5 compared to all tested vaccine platforms.
- UB-612 also demonstrated significantly higher neutralizing antibodies than the adenovirus and inactivated boosters.
- The antibodies stimulated by UB-612 demonstrated broad functionality, including neutralization of the emerging XBB1.5 variant and Fc-mediated effector activity in antibody-dependent cellular phagocytosis.
- Immunity following administration of the UB-612 booster was long-living compared to that following the inactivated and adenovirus boosters.
- UB-612 was generally safe and well tolerated throughout the trial.
- UB-612 is under review for conditional/provisional market authorization as a COVID-19 booster with stringent health agencies in the UK and Australia.

Biography

Alexander (Sasha) Rumyantsev, MD, PhD, MBA has over 20 years of experience of developing vaccines in the private and government sectors. Currently, he is a Therapeutic Area Head, Infectious Diseases at Vaxxinity, with its novel COVID-19 vaccine at the regulatory submission stage. Previously, he led preclinical and strategic efforts across a broad range of vaccine platforms and target programs at Sanofi and Acambis

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New Vaccine Development

Title: **Vaccines and monoclonal antibodies for treatment and prevention of opioid use disorders and opioid-related overdoses**
Marco Pravetoni
University of Washington School of Medicine

Title: **Robust immunogenicity and protection with PlaCCine: A novel DNA vaccine delivered with a functionalized polymeric delivery system**
Jean D Boyer
Imunon

Title: **Safety profile and analytical assessment of a cross-platform trivalent combination vaccine against invasive nontyphoidal salmonellosis and typhoid fever**
Francesco Citiulo
GSK Vaccines Institute for Global Health

Title: **Development of a broadly cross-reactive vaccine against rhinoviruses**
Sebastian L. Johnston
Imperial College London

Title: **Interrogation of human monoclonal antibodies induced by meningococcus B vaccination to identify cross-protective antigens against gonococcus**
Oretta Finco
GSK (Bacterial Vaccines Unit)

Title: **SERA- universal serology enabling high-throughput, antigen agnostic studies of adaptive immune responses**
John Shon
Serimmune

Title: **The respiratory syncytial virus G protein enhances the immune responses to the RSV F protein in an enveloped virus-like particle vaccine candidate**
Trudy Morrison
University of Massachusetts Chan Medical School

Title: **Correlative outcomes of maternal immunization against RSV in cotton rats**
Jorge C. Blanco
Sigmovir Biosystems Inc.

Title: **CD40 ligand (CD40L)-based, dendritic cell-targeted vaccine ("FortiVac") as a platform technology for high-level CD8+ T cell responses**
Richard Kornbluth
Multimeric Biotherapeutics, Inc.

Title: **Development of a pan-species/pan-disease T cell vaccine platform to address one health zoonotic risks**
Thomas Tillett
MBF Therapeutics

Title: **mRNA vaccines against Lassa virus**
Alexander Bukreyev
University of Texas Medical Branch

Title: **Nanoparticle-based antigen favors high level of humoral immune responses and increases antigenicity of highly glycosylated protein**
Yi Yang
Hunan Agricultural University

Title: **Development of a Marburgvirus subunit vaccine adjuvanted with a novel TLR7/TLR8 Agonist**
Shweta Kailasan
Abvacc

Title: ***ultra*IPVTM: An improved polio vaccine**
Stephen J. Dollery
Biological Mimetics, Inc

Vaccines and monoclonal antibodies for treatment and prevention of opioid use disorders and opioid-related overdoses

Marco Pravetoni
Professor of Psychiatry and Behavioral Sciences, University of Washington School of Medicine. Director, Center for Medication Development for Substance Use Disorders and Overdose

The incidence of fatal drug overdoses has dramatically increased due to the widespread availability of fentanyl and its analogs, often found in street drug mixtures or in counterfeit prescription pills. In United States, more than 100,000 fatal drug overdoses occur each year. Current medications are not sufficient to curb the opioid overdose epidemic. To provide a complementary and alternative strategy, our team has developed a series of vaccines and monoclonal antibodies (mAb) against a variety of opioids of public health interest. Anti-drug antibodies selectively sequester the target drug from circulation, thus preventing opioid-induced respiratory depression and bradycardia, as well as the rewarding properties of opioids. Our team advanced a candidate oxycodone vaccine to Phase I clinical trials, and other leads are being readied for clinical evaluation. Monovalent and multivalent vaccine formulations may offer protection in different clinical scenarios. Additionally, high affinity anti-drug mAb effectively reverse the effects of fentanyl and other target opioids post-exposure and synergize with naloxone. Compared to opioid receptor antagonists, vaccines and mAbs offer longer-lasting protection against toxicity associated with overdose. Translation of vaccines and mAbs will benefit individuals with opioid or substance use disorders as well as those at risk of accidental or deliberate overdoses.

Biography

Marco Pravetoni is the Rick L. Seaver Endowed Professor of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, and Director of a Center for Medication Development for Substance Use Disorders and Overdose. Prior to joining the University of Washington, Marco was a Tenured Associate Professor of Pharmacology at the University of Minnesota Medical School in Minneapolis, MN. He earned a PhD in Pharmacology from the University of Minnesota in 2008. His NIH-funded research program focuses on the pre-clinical and clinical development of vaccines, monoclonal antibodies, and small molecules to treat opioid use disorders and reduce fatal overdoses. Other interests include biologics targeting chemical and biological threats.

Robust immunogenicity and protection with PlaCCine: A novel DNA vaccine delivered with a functionalized polymeric delivery system

Jean D Boyer
VP Preclinical RD, Imunon

PlaCCine is a DNA-based vaccine modality that includes a proprietary pDNA backbone and novel synthetic functionalized polymers. PlaCCine increases transfection and protein expression by 5-15-fold in murine skeletal muscle compared to naked DNA. Studies using a PlaCCine SARS-CoV-2 DNA vaccine expressing spike proteins in mice and primates demonstrated induction of spike-specific neutralizing antibody responses and CD8 and CD4 spike-specific cellular responses. The induced immune responses in vaccinated mice were maintained for up to 14 months after vaccination. Further, following viral challenge, in the case of both primates and mice the induced immune responses resulted in decreased lung viral loads by greater than 90% along with improved clinical score when compared to placebo controls. In mouse studies robust immune responses were observed following a single IM needle injection of either PlaCCine SARS-CoV-2 DNA vaccine or a novel PlaCCine Lassa Virus DNA vaccine. Importantly, PlaCCine DNA vaccines demonstrate stability over at least 12 months at 4C and for one month at 25C. As such, PlaCCine vaccines could be easily deployed and delivered to contain outbreaks such as with Lassa fever, EBOLA or Marburg. PlaCCine is an important vaccine advancement that can have a positive impact on global health.

Biography

Dr. Boyer leads a team of scientists at Imunon in vaccine development for novel DNA based vaccines in preclinical research focusing on both infectious disease and cancer targets. The scientific team is a multidisciplinary group that is responsible for characterization of immunological profiles and analytical assays. Further, Dr. Boyer has led immunology and analytical programs for Phase I through Phase III clinical trials for infectious diseases and oncology at Inovio Pharmaceuticals.

Prior to joining the Biotechnology Industry, Dr. Boyer lead a research team as an Associate Research Professor at the University of Pennsylvania from 1996 to 2018 in the Department of Pathology and Laboratory Medicine. In conducting original research Dr. Boyer had over 100 publications. She also served as Director of the Human Immunology Core within Pathology and Laboratory Medicine. Dr. Boyer led cutting edge immunology for clinical development, collaborating with scientists and physicians across multiple departments and scientific areas at the University of Pennsylvania Hospital and the Abramson Cancer Center.

In addition, at the University of Pennsylvania, Dr. Boyer was Director of the Post Baccalaureate Research Education Program with the goal of developing a diverse pool of scientists focused on PhD and MD/PhD programs.

Dr. Boyer received her BS and PhD from Rutgers University, NJ. Her PhD degree was in Biochemical Engineering where she focused on developing a mathematical model to predict plasmid concentration during the fermentation of recombinant bacteria.

Safety profile and analytical assessment of a cross-platform trivalent combination vaccine against invasive nontyphoidal salmonellosis and typhoid fever

Francesco Citiulo*[1], Francesca Necchi[1]
Antonia De Felice[1], Federico Pippi[1], Alessandra Acquaviva[1], Maria Grazia Aruta[1], Emilia Cappelletti[1], Vittoria Marchetti[1],Filomena De Luca[1], Angela Daniele[1], Caroline Vipond [2], Carlo Giannelli[1], Daniele De Simone[1], Claudia G. Vitali[3], Omar Rossi[1], Francesco B. Scorza[1], Anna M. Colucci[1], Rocio Canals[1]
[1] GSK Vaccines Institute for Global Health (GVGH)*, Siena, Italy
[2] National Institute for Biological Standards and Control (NIBSC), UK
[3] GSK Vaccines, Siena, Italy
* GVGH is an affiliation of GlaxoSmithKline Biologicals SA

GSK Vaccines Institute for Global Health (GVGH) is developing a trivalent *Salmonella* vaccine to prevent invasive nontyphoidal salmonellosis (iNTS) and typhoid fever, especially aimed for sub-Saharan Africa to impact disease burden and to reduce antimicrobial resistance spread. While there are licensed vaccines for prevention of typhoid fever, the only current intervention for iNTS is treatment with antibiotics with no available vaccine.

The iNTS-TCV formulation was generated by combining two different technologies: GMMA for the iNTS components, *S.* Typhimurium (STm) and *S.* Enteritidis (SEn); and the Vi-CRM197 glycoconjugate, a typhoid conjugate vaccine (TCV) originally developed by GVGH and WHO prequalified as TYPHIBEV by Biological E Ltd (Hyderabad, India). This is a first example of successfully combining the GMMA technology with a glycoconjugate.

The iNTS-TCV vaccine was well tolerated in a GLP repeated dose-toxicology study and induced a spectrum of non-adverse changes consistent with the expected physiological reaction following immune stimulation in response to an adjuvanted vaccine. In addition as part of safety assessment, a Monocyte Activation Test (MAT) was developed to monitor the intrinsic pyrogenicity of the GMMA componets in the vaccine. Overall, we demonstrated the preclinical safety profile of this cross-platforms vaccine.

The complex matrix may pose challenges in the analytical assessment of this vaccine, thus a set of analytical methods were developed to support the release and characterization of an iNTS-TCV vaccine lot manufactured to be used in a Phase 1 clinical study. Content determination of key active ingredients has been achieved through the development of antigen-specific methodologies. O-antigen of iNTS components is quantified by a competitive ELISA-based method that uses antigen-specific monoclonal antibodies (Formulated Alhydrogel competitive ELISA assay (FAcE)). Vi polysaccharide is instead quantified by HPAEC-PAD method. To characterize the immunogenicity of the vaccine lot, an *in vivo* potency assay that compares the immune response of the vaccine in mice with the immune response elicited by freshly formulated material was set up for release and real-time stability assessment. Significant antibody responses to each of the active ingredients of the iNTS-TCV vaccine candidate were observed in the immunogenicity studies. These data supported further clinical development and a Phase 1 clinical trial in healthy adults to evaluate safety and immunogenicity is currently ongoing.

Overall, the combination of iNTS-GMMA and Vi-CRM197 could rapidly result in an effective and affordable vaccine, iNTS-TCV, as a viable option for a sustainable iNTS vaccine to be delivered to populations at risk in sub-Saharan Africa.

Biography:

Francesco Citiulo, Senior Scientist, with research and development skills in vaccinology.

I am involved in generating the evidence package for the immuno-potency and preclinical safety (toxicology studies) of the vaccines currently under development at the GSK Vaccines Institute for Global Health, Siena, Italy.

My research during the PhD at Trinity College Dublin, Ireland and during the post doc at the Leibniz Institute Jena, Germany, focussed in the host phatongen interaction dissecting the pathways that human fungal and bacterial pathogens use to sequester micronutrients, and in particular zinc, from the host.

Development of a broadly cross-reactive vaccine against rhinoviruses

Sebastian L. Johnston*[1, 2], Chloe Pyle[2], Neeta Patel[2], Ziyin Wang[1], John Tregoning[1], Paul Hamblin[3], Richard Butt[3], Michael Edwards[1, 2], Stephen Shaw[3].
[1]Imperial College London
[2]Virtus Respiratory Research Ltd
[3]Apollo Therapeutics Ltd

Rationale: Rhinoviruses (RV) are responsible for most common colds, the majority of asthma, COPD and chronic lung disease exacerbations and acute respiratory infections in hospitalised infants. Despite the great medical need there are no licensed therapies to protect against RV infection. The enormous antigenic diversity among the ~180 identified RV strains has hampered efforts toward vaccine development. We have identified a candidate vaccine that generates T cell-mediated immunity to strains from all three RV species and demonstrated its efficacy using both adjuvanted protein subunit and mRNA platforms.

Methods: Bioinformatic analysis was used to identify VP0 protein sequences from A, B and C RV strains likely to provide heterotypic immunity. Mice were immunised with adjuvanted VP0 protein subunit or mRNA using a standard prime and boost model. The immune response to vaccination and its ability to generate type I immunity against heterotypic RV strains was examined in mice and non-human primates. The response to heterotypic infection was also examined in mice.

Results: Vaccination with VP0 protein increased T_{FH} and germinal centre B cell populations in the draining lymph nodes and drove B cell class-switching, production of plasma cells, and high levels of serum VP0-specific IgG. In addition, splenocyte IFN-γ ELISpot analysis demonstrated that vaccination evoked cellular immunity to homotypic RV strain VP0 peptide pools, as well as cross-reactive immunity to multiple (n=16) heterotypic RV strain VP0 peptide pools, representative of all 3 RV species. Infection of VP0 protein subunit vaccinated mice with a live heterotypic strain of RV accelerated and enhanced the production of neutralizing antibodies to the heterotypic RV strain and boosted IFN-γ ELISpot responses to heterotypic VP0 peptide pools in spleen and lung. Vaccinated mice cleared the RV infection from the lungs more rapidly than control mice. In cynomolgus monkeys, vaccination with VP0 protein subunit generated VP0-specific antibodies and cellular immunity that cross-reacted with heterotypic peptide pools from all 3 species of RV.

Vaccination of mice with VP0 mRNA also generated VP0-specifc antibody titres and IFN-γ ELISpot analysis demonstrated the expansion of splenocytes that cross-reacted with heterotypic VP0 peptide pools. Infection of mRNA vaccinated mice with live heterotypic RV evoked rapid expansion of effector and tissue-resident memory T cells in the airways and lungs that was associated enhanced virus clearance. Intracellular cytokine staining demonstrated that mRNA vaccine primed T cells in the lungs were cross-reactive with heterotypic VP0 peptide pools. VP0 mRNA vaccination of cynomolgus monkeys evoked production of VP0-specific antibodies and cellular immunity that cross-reacted with heterotypic peptide pools.

Conclusions: We have identified a RV VP0 vaccine that generates cross-reactive cellular immunity to multiple strains of RV representative all 3 RV species and have validated its efficacy using both adjuvanted protein subunit and mRNA platforms. The vaccine will be entering clinical development in the near future.

Biography

Sebastian L Johnston: is Professor of Respiratory Medicine & Allergy and Head of Airway Disease at the National Heart and Lung Institute, Imperial College London, UK. He has been working in respiratory virus research for more than 30 years and is widely regarded as a leading global expert in respiratory viral infections. He developed the world's first mouse model of rhinovirus infection and has used this model extensively in his work towards a rhinovirus vaccine. He also performs human experimental rhinovirus infection studies in healthy subjects, and in patients with asthma and chronic obstructive pulmonary disease (COPD), both academically, and commercially at his CRO Virtus Respiratory Research Ltd https://virtus-rr.com/.

Background

He was the Director of the Medical Research Council & Asthma UK Centre in Allergic Mechanisms of Asthma and the Asthma UK Clinical Professor, both from 2010-2021. He is a former and current European Research Council Advanced Grant holder. He is Emeritus Senior Investigator at the National Institute of Health Research, UK.

He became a Professor at Imperial in 1999. He became a Fellow of the Royal College of Physicians, London in 2000, of the Royal Society of Biology in 2011, of the Academy of Medical Sciences and the European Respiratory Society in 2014, of the European Academy of Allergy & Clinical Immunology in 2020 and of the Association of Physicians in 2021.

He won the Paul Ehrlich Award for his research in Allergy & Clinical Immunology in 2018, the BMJ research paper of the year in 2018 and the European Respiratory Society Gold Medal for his asthma research in 2020.

He edited The International Respiratory Journal "Thorax" from 2002-2010. He has published >520 scholarly manuscripts in peer reviewed journals and has 18 patents. He has an h-index of 120, and more than 68,000 lifetime citations.

Interrogation of human monoclonal antibodies induced by meningococcus B vaccination to identify cross-protective antigens against gonococcus

Oretta Finco
GSK, Siena, Italy

No vaccine is currently available for *Neisseria gonorrhoeae*a (Ng), an high priority pathogen responsible for more than 80 million cases of infection annually and showing the emergence of anti-microbial resistant strains. Ng is therefore an urgent public health threat for which the development of an effective vaccine represents a medical need. Recent retrospective studies conducted in different countries have reported about 30% reduction of gonococcal infections in individuals vaccinated with the licensed meningococcus B OMV-based vaccines (4CMenB), providing a very useful hint for gonococcal vaccine research. To profile the antibodies induced by the OMV component of the 4CMenB vaccine that could contribute to the cross-recognition of Ng, the Reverse Vaccinology 2.0 approach has been applied, that by the isolation of human monoclonal antibodies (HumAbs) induced in response to vaccination or infection, allows an in depth-profiling of the key antigens that contribute to the functional immune response against diverse gonococcal and meningococcal strains. By dissecting the antigen recognition profile of cross-reacting HumAbs we revealed that a number of OMV components are targeted, with PorB being the most recognized antigen. This finding provides a mechanistic explanation of the cross-protection observed in clinical trials and offers the basis for the design of widely protective vaccines and development of new therapeutics against antimicrobial resistant Ng.

Biography

Oretta holds a master's degree in Biological Sciences and a PhD in Immunology and Microbiology from the University of Pavia. She completed her PhD and Post-doc at Harvard Medical School before joining the pharmaceutical sector in 1993. In her career she developed a strong scientific expertise in vaccines immunology contributing to several projects (MenB, Flu, RSV, new Adjuvants). Since 2016 she is leading a team of immunologists to provide evidence and understanding on the mode of action of new vaccine candidates in preclinical models or in early clinical studies. She contributed to the growth of capabilities in the analysis of human B cell response and profiling of the antibody repertoire that led to the creation of the B cell CoE.

SERA- universal serology enabling high-throughput, antigen agnostic studies of adaptive immune responses

John Shon
Serimmune

Individuals are exposed to a wide variety of environmental, infectious, vaccines and therapeutic agents stimulating humoral immune response. Serum Epitope Repertoire Analysis enables the analysis of an unlimited number of exposures in a single assay, enabling comparative immunomics. Whether studying longitudinal samples, multiple formulations of vaccines or boosters, pre-clinical vs. clinical, or vaccine vs. natural infection, SERA enables comparative, high-throughput, high-resolution analysis of epitopes to enable precision immunology, all in one assay. We will review how SERA has been applied in multiple studies to gain insight into humoral response in individuals and cohorts.

Biography

John Shon, MD, MS, is the Chief Technology Officer of Serimmune where he leads the development of machine learning algorithms for the identification of humoral epitopes in individuals and populations. Dr. Shon was previously VP of Bioinformatics and Data Sciences at Illumina, where he led teams focused on deep learning for the interpretation of whole genomes in rare disease and cancer in the 100.000 genomics project. Prior to Illumina, Dr. Shon spent more than a decade in pharma as VP of Informatics, Research IT and External Innovation at Janssen, and Roche, where he led teams in translational informatics. He earned his A.B. in Biochemistry from Harvard and an MD from Stanford. He completed his residency in Internal Medicine at the University of Chicago and his postdoc at Stanford University School of Medicine as an NLM fellow in informatics.

The respiratory syncytial virus G protein enhances the immune responses to the RSV F protein in an enveloped virus-like particle vaccine candidate

Trudy G. Morrison [1] *, Lori McGinnes Cullen[1], Bin Luo[2], Zhiyun Wen[3], Lan Zhang[3], Eberhard Durr[3]
[1]Department of Microbiology and Physiological Systems, Program in Immunology and Microbiology, University of Massachusetts Chan Medical School, Worcester, MA, USA
[2]Pharmacology, Merck & Co., Inc., West Point, PA, USA
[3]Infectious Diseases and Vaccines Discovery, Merck &Co., Inc., West Point, PA, USA

Respiratory syncytial virus (RSV) is a serious human respiratory pathogen. Many, if not most, RSV vaccine candidates are focused on targeting the viral F protein since the F protein is more conserved than the viral G protein across RSV serotypes, genotypes, and strains, thus the F protein is thought more likely to induce a broader range of protection from infection. However, it is the G protein that binds the likely receptor, CX3CR1 in lung ciliated epithelial cells, raising the question of the importance of the G protein in vaccine candidates. We have been developing virus-like particle vaccine candidates for RSV with the goal of presenting glycoprotein antigens in a virus-sized particulate form. Using these virus-like particle (VLP) vaccine candidates, we have directly compared VLPs containing only the pre-fusion F protein, only the G protein, or both glycoproteins. We found that VLPs containing both glycoproteins bind to anti-F protein specific monoclonal antibodies differently than VLPs containing only the pre-fusion F protein. In RSV naïve cotton rats, VLPs assembled only with the pre-F protein stimulated extremely weak neutralizing antibody (NAb) titers as did VLPs assembled with only G protein. However, VLPs assembled with both glycoproteins stimulated quite robust neutralizing antibody titers, induced improved protection of the animals from RSV challenge compared to pre-F VLPs, and induced significantly higher levels of antibodies specific for F protein antigenic sites 0, site III, and AM14 binding site compared with VLPs containing only the pre-F protein. These results indicate that assembly of pre-F protein with G protein in VLPs altered the conformation of the F protein increasing the induction of protective antibodies. Our results suggest that inclusion of both F and G protein in vaccine candidates will result in higher titers of NAbs and likely improved protection from RSV infections. Formulation of vaccine candidates for different populations, RSV experienced-adults vs RSV naïve infants and young children, should consider the importance of G protein in those candidates relative to its efficacy taking into consideration any contribution to lung pathology upon RSV challenge.

Biography

Dr. Morrison has a BA from Wellesley college and obtained her Ph. D from the Department of Molecular Biology and Microbiology at Tufts University Medical School. She was a postdoctoral fellow in the Department of Biology at the Massachusetts Institute of Technology and is currently a Professor in the Department of Microbiology and Physiological Systems of the University of Massachusetts Medical School. She was elected a fellow of the American Association for the Advancement of Sciences (AAAS) and fellow of the American Academy for Microbiology. She is an Associate Editor for Science Advances, the online version of Science Magazine, and a member of the editorial board of the Journal of Virology. She has served as the Program Chair for the American Society for Virology, the Chair of the Microbiology Test Committee for the National Board of Medical Examiners, the Chair of Division T of the American Society for Microbiology, and a member of numerous study sections of the National Institutes of health. She has over 100 publications concerning RNA virus entry and assembly as well as vaccine development.

Correlative outcomes of maternal immunization against RSV in cotton rats

Jorge C.G. Blanco[a]*, Lori M. Cullen[b], Arash Kamali[a], Fatoumata Y. D. Sylla[a], Zenab Chinmoun[a], Marina S. Boukhvalova[a], Trudy G. Morrison[b]*
[a]Sigmovir Biosystems Inc.USA;
[b]University of Massachusetts Chan Medical School, USA

Maternal anti-respiratory syncytial virus (RSV) antibodies protect neonates from RSV disease throughout first weeks of life. Previous studies of maternal immunization in cotton rats showed that a single immunization during pregnancy of RSV-primed dams with virus-like particles (VLPs) assembled with pre-fusion F protein and the wild type G protein boosted their RSV serum antibody concentration and protected pups early in life against RSV challenge. We extended these findings by evaluating responses to RSV infection in litters from two consecutive pregnancies of immunized dams. Using an RSV-primed population of VLP-vaccinated and unvaccinated dams, we defined correlations between dams' and litters' RSV neutralizing antibodies (NA); between litters' NA and protection; and between litter's NA and their lung expression of selected cytokines, of a first or of a second pregnancy. Lung pathology was also evaluated. We found positive correlation between the NA titers in the dams at delivery and the NA in their first and second litters and negative correlations between the litters' NA and protection from RSV challenge. Vaccination of dams modulated the mRNA expression for IFNγ and IL-6 and lung pathology in the first and in the second litter at different times after birth, even in the absence of detectable NA. Thus, maternal RSV vaccination enhanced the levels of antibodies transferred to offspring and their protection from challenge. However, maternal vaccination also impacted the immunological and inflammatory response of the offspring's lungs well into maturity, and after the antiviral effect of maternally transferred NA wane or was no longer detectable.

Biography

Dr. Blanco obtained his Ph.D. in Molecular Biology from the University of Buenos Aires, Argentina. He pursued his studies in infectious diseases and the host response to infection, first, in a postdoctoral position at NICHD, NIH, and then as a Senior Scientist at USUHS, MD. In 2010, Dr. Blanco co-founded Sigmovir Biosystems Inc. (SBI), a Maryland biotech company focused on the study of viral infections, with emphasis on human respiratory viral infections. Since the beginning of his career, and as independent investigator, he published > 100 peer-reviewed articles in the field of infectious diseases and secured many NIH research grants including RO1s, R21s, SBIRs, and STTRs. Dr. Blanco's laboratory has particularly interest in studies on viruses that produce the largest impact on human health throughout life: respiratory syncytial virus (RSV), influenza, rhinovirus, and SARS-CoV2. Using the cotton rat model (Sigmodon sp.) due to its permissiveness to non-adapted strains of all these viruses, Dr. Blanco's laboratory studies innate and adaptive response, explores different inflammatory pathways affecting infection, determines specific pathological outcomes in different populations (different ages, immunological status, or e.g., during pregnancy or immune suppression), and tests vaccines and therapeutics

CD40 ligand (CD40L)-based, dendritic cell-targeted vaccine ("FortiVac") as a platform technology for high-level CD8+ T cell responses

Richard S., Kornbluth[1], Christopher Adase[1], Victoria Hamilton[1], and Geoffrey W. Stone[2]
[1]Multimeric Biotherapeutics, Inc., USA,
[2]University of Miami, USA

Dendritic cells (DCs) can take up antigen via a number of routes. Of these, several studies have shown that antigen uptake via the CD40 receptor generates some of the strongest CD8+ T cell responses. At the same time, stimulation through CD40 activates DCs for cross-presentation and T cell activation. Consequently, it is desirable to combine the CD40 targeting of antigen and a CD40 stimulant into a single vaccine formulation. When the CD40 stimulant is CD40 ligand (CD40L, CD154), it is important to use a multi-trimer complex that clusters CD40 in the DC membrane, thereby engaging downstream signaling pathways. Such a multi-trimer form of CD40L can be provided by genetically fusing the extracellular domain of CD40L with the body of surfactant protein D (SPD), a soluble self-assembling 12-chain molecule with 4 trimeric "arms." When an antigen sequence is included within the SPD arms, the entire protein complex is referred to as "FortiVac". Studies in mice have shown that the FortiVac design elicits very high levels of antigen-specific CD8+ T cells with high TCR avidity and functional activity. FortiVac can be effectively delivered as a DNA vaccine i.m. and even more effectively using an adenoviral (Ad5) vector. For FortiVac encoding HIV-1 Gag, vaccination with Ad5-FortiVac-Gag led to complete protection ("sterilizing immunity") from Vaccinia-Gag challenge (i.e., 7 log reduction of tissue viral load). A FortiVac vaccine against the gp100 melanoma antigen had antitumor effects against B16 melanoma. Other FortiVac formulations have been made for tumor-specific neoantigens, hepatitis B virus (HBV), malaria, and HIV-1 Gag. In all of these cases, there may be a clinical benefit for a vaccine that elicits very strong CD8+ T cell responses.

Biography

Richard S. Kornbluth, MD, PhD is the founder, president, and chief scientific officer of Multimeric Biotherapeutics, Inc. which is a vaccine and cancer immunotherapy company located in San Diego, CA. He trained at Harvard, Mount Sinai School of Medicine, Columbia, and Scripps Research. Prior to founding Multimeric Biotherapeutics, he was a Professor of Medicine at UC San Diego. He is currently a Professor at the Vaccine Research Institute of San Diego. His main research interests are the TNF SuperFamily (TNFSF) of ligands, especially CD40 ligand (CD40L) and 4-1BB ligand (4-1BBL). He also studies MAVS and STING as vaccine adjuvants and immuno-oncology agents. He is an inventor on several vaccine patents and is the co-inventor of the company's lead technology, FortiVac. He has authored >60 papers and has been the principal investigator on numerous grants from the NIH and CDC. He currently serves on the Scientific Advisory Committee of amfAR, The Foundation for AIDS Research.

Richard S. Kornbluth, MD, PhD trained as a medical doctor and also received research training at Harvard Medical School, Columbia University, and The Scripps Research Institute. He was a professor at University of California, San Diego and then founded Multimeric Biotherapeutics, Inc. which is a biotech based in La Jolla, CA. His research is focused on CD40 ligand (CD40L) and other TNF SuperFamily ligands and their activating effects on DCs, macrophages, and B cells.

Development of a pan-species/pan-disease T cell vaccine platform to address one health zoonotic risks

Thomas Tillett
MBF Therapeutics

MBFT Brief:

MBF Therapeutics has developed an innovative and promising T-Max Precision™ DNA vaccine platform with the potential to revolutionize the field of animal health and vaccine development. Our focus on mucosal delivery and the induction of robust T cell-mediated immune responses addresses significant limitations of traditional vaccine technologies and offers numerous advantages in terms of safety, effectiveness, ease of administration, manufacturing, and storage.

Here are some key takeaways:

1. T-Max Precision™ DNA Vaccine Platform: This innovative platform aims to deliver vaccines mucosally, stimulating durable and potent T cell-mediated immune responses. These responses rapidly clear viruses at the site of infection, preventing their spread throughout the body and blocking transmission to other animals.

2. Advantages of T-Max Technology:

- Safe and Effective: The T-Max platform offers safe and efficacious vaccines without the need for live viruses.
- Cross-Protection: T-Max vaccines have the potential to provide broad cross-protection against multiple strains of pathogens.
- Flexible Administration: The vaccines can be administered by injection intramuscularly, subcutaneously, or using needle-free methods like intranasally, orally or intravaginally.
- Scalable Manufacturing: The DNA-based platform allows for straightforward and cost-effective vaccine production.
- Environmental Stability: T-Max vaccines are stable at room temperature and do not require refrigeration, facilitating global distribution.

Summary:

MBF Therapeutics' innovative T-Max Precision™ DNA vaccine platform approach to vaccine development, its potential impact on the state of the art in veterinary vaccinology, and the path forward for further research, development, and commercialization will lead to better solutions for many of the challenging diseases in animal health. The T-Max Precision™ DNA vaccine platform has the potential to address critical challenges in disease prevention and control, and its unique features make it a promising candidate for disrupting the animal health vaccine market.

Biography

Thomas Tillett – Cofounder and CEO of MBF Therapeutics, an immunotherapeutics company that has developed and patented an innovative, proprietary T-Max™ DNA vaccine platform to deliver commercial protective vaccines that provide safe, durable, heterologous protection against endemic, emerging and re-emerging diseases of global concern to livestock and companion animals, with significant translational opportunities in human health. Tom is the founder and Executive Director of Sustained Acts, a Christian non-profit focusing on sustainable projects in Africa and serves on the Friends of Kijabe Hospital Board of Directors. Mr. Tillett was founder, and CEO of RHeoGene. As RheoGene CEO, he and his team created the RheoSwitch® Therapeutic System (RTS) that led to the first human clinical trial of a small molecule-induced gene regulation system. In 2007, he successfully completed the merger of RheoGene Inc. with Intrexon Corporation who has continued the development of RTS through a various clinical trials for cancer and other important therapeutic indications. In April, 2019 the FDA announced that the RheoSwitch Therapeutic System for glioma blastoma was approved for Fast Track designation. Mr. Tillett has served on the board of numerous non-profits including; University of North Carolina General Alumni Association, Impact Thrift Stores, Chelten Church Elder Board, and the American School of Paris. He was also elected to the Hatboro-Horsham Hall of Fame in 2017.

mRNA vaccines against Lassa virus

Alexander Bukreyev
Departments of Pathology and Microbiology & Immunology, Galveston National Laboratory, University of Texas Medical Branch, Galveston, USA

Lassa virus is a member of the *Arenaviridae* family, which causes human infections ranging from asymptomatic to severe hemorrhagic disease with a high case fatality rate. We have designed and generated lipid nanoparticle encapsulated, modified mRNA vaccines that encode for the wild type Lassa virus strain Josiah glycoprotein compex or the prefusion stabilized conformation of Lassa virus glycoprotein complex. Hartley guinea pigs were vaccinated with two 10 µg doses, 28 days apart, of either construct. Vaccination induced strong binding antibody responses, specific to the prefusion conformation of glycoprotein complex, which were significantly higher in the prefusion stabilized gylycoprotein complex construct group and displayed strong Fc-mediated effects. However, Lassa virus neutralizing antibody activity was detected in some but not all animals. Following challenge with a lethal dose of Lassa virus, all vaccinated animals were protected from death and severe disease. Although definitive mechanism of protection is still unknown, and assessment of the cell-mediated immune response was not investigated in this study, these data demonstrate the promise of mRNA as a vaccine platform against Lassa virus and that protection against Lassa virus can be achieved in the absence of virus-neutralizing antibodies.

Biography

Dr. Alex Bukreyev worked at the Laboratory of Infectious Diseases, NIAID, NIH, in 1995 – 2010. In 2010 he accepted a position of Professor at the University of Texas Medical Branch at Galveston in connection with the launch of the Galveston National Laboratory. Dr. Bukreyev expertise includes molecular virology, emerging viral infections, viral immunology, vaccinology.

Dr. Bukreyev served as a member of the NIH Vaccine against Microbial Diseases study section from 2017 to 2021

Nanoparticle-based antigen favors high level of humoral immune responses and increases antigenicity of highly glycosylated protein

Yawen Zou and Yi Yang
Hunan Agricultural University

Nanoparticles (NPs) have shown great potential as advanced vaccines and immunotherapy platforms for stimulating immune responses owing to their size and polyvalent epitopes. However, the impact of particle size and surface physicochemical characteristics on the immune response remains to be determined. In this study, we designed three protein-based NPs derived from Ferritin, porcine circovirus type 2 (PCV2) capsid protein, and AP205 coat protein, based on distinct diameters and valences. Two viral enveloped proteins were conjugated with different degrees of glycosylation onto the three NP surfaces, respectively, using SpyTag/SpyCatcher. Immunoassays demonstrated that these NPs rapidly induced high levels of antigen-specific IgG, suggesting that they are more effective than the monomeric subunits in eliciting humoral immune responses. This effect was particularly pronounced when the highly glycosylated viral antigen CD2v was presented on these NP surfaces. Notably, all NPs substantially promoted the production of the IgG2a subtype, indicating that these NPs may dictate T-cell differentiation into Th1 cells and enhance their effectiveness against intracellular pathogens. Furthermore, PCV2 NP reached the mouse popliteal lymph node (PLN) as early as 5 min after injection. Importantly, NP persisted in the PLN for at least 21 days and interacted extensively with B cells, thus laying the molecular basis for rapidly producing high-titer antibodies. Overall, these findings provide evidence and deep insights into using NP as powerful carriers for enhancing the immunogenicity of various antigens, particularly highly glycosylated antigens. Highly effective vaccination and immunotherapy strategies can be developed by selecting appropriate NP with specific physicochemical characteristics.

Biography

Yi Yang is the Scientific Director of Research Center of Reverse Vaccinology (RCRV) and Laboratory of Functional Proteomics (LFP) in Hunan Agricultural University (HUNAU). He is also a distinguished professor at the College of Veterinary Medicine, HUNAU. He earned his PhD in Biochemistry at China Agricultural University, Beijing, China and was a postdoctoral fellow and research fellow in National Institutes of Health (NIH), USA. He received rewards of “2016 The First Prize of Vaccine Study, China (Boehringer Ingelheim), “2009 Outstanding Award on Biomedical Research (NIH)” and so on. He has published more than 50 research papers in peer-reviewed journals.

He has employed multiple disciplines (immunoinformatics, molecular dynamics and protein structure) to development the new generation vaccines against various animal infectious diseases, such as PCV2, PEDV, TGEV, etc. Particularly, he has developed various protein-based nanoparticles (NPs) to display foreign antigen(s) multivalently on their surfaces. These NPs exhibit excellent capacities of eliciting humoral and cell-mediated immunities against infections with the highest biosafety.

Development of a Marburgvirus subunit vaccine adjuvanted with a novel TLR7/TLR8 Agonist

Shweta Kailasan
Director, Discovery & Preclinical Research, Abvacc

Ebola (EBOV) and Marburg (MARV) viruses are highly lethal hemorrhagic fever viruses with case-fatality rates as high as 90%. The number of filovirus disease outbreaks has been rising in the past two decades. Outbreaks of Marburg virus (MARV) disease (MVD) have occurred several times since 1967, most recently in in Equatorial Guinea (Feb 2023) and Tanzania (Mar 2023). These filovirus outbreaks threaten human life, the world economy, and the healthcare system, therefore the need for a highly effective and safe vaccine against Marburg Virus Disease (MVD) is paramount. Currently there are no approved vaccines or therapeutics for MVD and very few in clinical development. Here we developed a vaccine against MVD comprised of an engineered Marburg glycoprotein component in combination with a safe and novel adjuvant that has shown excellent safety in millions of people during COVID-19 pandemic. We have rationally designed an immunogen based on MARV glycoprotein (GP) by excluding domains known to trigger non-neutralizing antibodies allowing exposure of key neutralizing epitopes capable of generating a strong immune response and introducing trimer-stabilizing point mutations. Combined with a novel TLR7/8 agonist adjuvant, Alhydroxyquim-II (AhQ-II), our rationally designed MARV vaccine induces broadly neutralizing antibodies against isolates Angola, CI67, and Musoke strains of MARV as well as the phylogenetically more distant RAVV and showed 100% protection against lethal challenge in small animals. Mice immunized with this MARV vaccine with two or three doses compared to unadjuvanted antigen showed robust antigen-specific binding and neutralizing titers against all four MARV strains demonstrated by ELISA and pseudovirus neutralization assays. In the guinea pig model of MARV infection which shows all hallmarks of filovirus disease, the vaccine provided 100% protection against lethal challenge with no detectable viremia, suggesting that the vaccine is likely inducing sterilizing immunity. We have also demonstrated immunogenicity in an ongoing filovirus gold standard nonhuman primate model. Four cynomolgus macaques were immunized four times, ~45 days apart. Antigen-specific neutralizing titers against MARV strains were seen after the third vaccination. Latest developments to further develop this subunit vaccine as a highly efficacious and safe candidate for protection against a large Marburg outbreak will be presented.

Biography

Dr. Kailasan is a structural virologist and immunologist.She oversees discovery and pre-clinical research projects that encompass structure-based design, protein production, assay development, and in vitro & in vivo characterization of vaccine and novel antibody therapeutic candidates for infectious disease targets. She received her PhD in Biomedical Sciences in the lab of renowned structural virologist & biochemist, Dr. Mavis Agbandje-McKenna, from University of Florida in 2015. Dr. Kailasan used a combination of X-ray crystallography and high-resolution cryo-EM to solve 3D structures of several viral capsid and capsid-antibody complexes of infectious ssDNA viruses (Human bocavirus1-4, Bovine parvovirus, Gorilla bocavirus and Human parvovirus 4) that cause respiratory and gastrointestinal infections. Using molecular biology to complement her structural observations, she worked toward elucidating mechanisms of host pathogen interactions such as receptor binding and antigenicity. She has also contributed to projects focused on novel gene therapy vector design and bacteriophage structures. During her post-doc training at the National Institute of Health, she worked on the structure of a CRISPR-Cas like enzyme to reveal a unique mechanism of DNA target site insertion. At IBT, as a Principal Investigator (SBIR-funded program) and/or Scientific Lead, she has been working on several vaccine and/or monoclonal antibody development projects related to Ebola virus, Marburg virus, Nipah virus and Multi-drug Resistant Staphylococcus aureus infections.

*ultra*IPV™: An Improved Polio Vaccine

Stephen J. Dollery*[1], John K. Tobin[1], Ruth V. Bushnell[1], Taralyn J. Wiggins[1], David A. MacLeod[1], Michael J. Daly[2], and Gregory J. Tobin[1]
[1]Biological Mimetics, Inc., Frederick, MD USA
[2]Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda MD, USA

Since their introduction in the 1950s, polio vaccines have performed a remarkable service in reducing the incidence of infection and disease. In the past 10 years alone, an estimated 8.5 million cases of poliomyelitis have been averted. Global eradication efforts have succeeded in eliminating wild-type strains of PV2 and PV3 and only 13 cases of wtPV1 were reported in 2022. Eradication efforts have been complicated by reversion of Sabin strains used in the oral polio vaccine (OPV) from attenuated to neuropathogenic phenotypes during replication in the intestinal tract. The reverted viruses can cause circulating vaccine-derived polioviruses which resulted in over 450 cases of poliomyelitis in a total of 47 countries in 2022. Efforts to genetically engineer reversion-resistant strains have reduced, but not eliminated the reversion problem. The majority of high- and middle-income countries phased out the use of OPV in favor of inactivated polio vaccines (IPV). IPVs cannot revert, but are considerably more expensive than OPVs. Conventional IPVs are manufactured from wild-type, neuropathogenic strains which leads to increasingly serious biosafety and biosecurity problems.

To address the need for new polio vaccine technologies, we have derived the novel inactivated vaccine candidate, *ultra*IPV™. The new vaccine candidate is produced by ultraviolet-C (UVC) exposure of attenuated strains in the presence of MDP, a powerful Mn^{2+} antioxidant complex adapted from the radio-resistant bacteria *Deinococcus radiodurans*. The inactivation method is quick (1 minute compared to 2-4 weeks for formalin inactivation) and results in many more doses of vaccine per milligram of starting virus due to the protection of epitopes by the MDP complex. In this presentation, we will review supporting data on ultraIPV™ and provide updates on the developmental pathways.

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.

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Day 3: November 15, 2023

Infectious & Non-Infectious Diseases

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Infectious & Non-Infectious Diseases

Title: **SchistoShield®, Sm-p80-based schistosomiasis vaccine: Human clinical trials in USA and Africa**
Afzal A. Siddiqui
Texas Tech University Health Sciences Center

Title: **Development of an effective nontoxigenic *Clostridioides difficile*–based oral vaccine against *C. difficile* infection**
Xingmin Sun
University of South Florida

Title: ***Ex vivo* antigen-loading of dendritic cells as a platform for personal cancer and infectious disease vaccines**
Robert O. Dillman
AIVITA Biomedical, Inc

Title: **An ecosystem for the rapid generation of biological reagents against infectious diseases**
Sumana Sundarmurthy
Sino Biological

Title: **DNA-based delivery of antiviral antibodies for infectious disease prevention**
Rachel A. Liberatore
RenBio

Title: **Immune monitoring read outs when vector-based vaccines are used: including ELISPOT assays**
Magdalena Tary-Lehmann
Cellular Technology Limited

Title: **The underlying genetic architecture of the immune system responsible for immunodominance**
Stephen J Elledge
Harvard Medical School

Title: **How advances in artificial intelligence are optimizing the deployment and utilization of life-saving infectious disease countermeasures to high-consequence epidemics**
Kamran Khan
BlueDot

SchistoShield®, Sm-p80-based schistosomiasis vaccine: Human clinical trials in USA and Africa

Afzal A. Siddiqui
Department of Immunology & Molecular Microbiology; Center for Tropical Medicine and Infectious Diseases, Texas Tech University Health Sciences Center, USA

Schistosomiasis is endemic in 79 countries including countries in sub-Saharan Africa, the Middle East, South America (primarily Brazil), the West Indies and Asia (primarily China and the Philippines). World Health Organization estimates that over 200 million people are currently infected and additional 800 million at risk of acquiring the infection. Schistosomiasis carries pronounced mortality (~200,000 deaths per year) and high morbidity (3.3 million annual DALYs). Existing infection control measures have been suboptimal in reducing parasite transmission, morbidity and disease burden. Currently, there is no vaccine available for human use to prevent or treat schistosomiasis. Science has highlighted schistosomiasis vaccine in Unfilled Vials feature as one of the ten Top Shots that needed to be urgently developed.

Over the last three decades, our team has followed a systematic and methodical approach to develop a Sm-p80-based vaccine as a viable and effective schistosomiasis vaccine for humans, called SchistoShield®. Phase 1 human clinical trials of SchistoShield® in USA conducted through NIAID's Infectious Diseases Clinical Research Consortium have just been completed. Interim data shows no safety signals and seroconversion of all vaccinated individuals with pronounced vaccine-mediated humoral responses. Phase 1b/2 trials in Africa (Madagascar, Burkina Faso) are starting in the fall of 2023. SchistoShield® is concurrently optimized in schistosome human challenge infection model in Europe (The Netherlands) and Africa (Uganda). Deployment of SchistoShield®, a first anti-helminth vaccine, could potentially benefit hundreds of millions of people in geographical areas ranging all across sub-Saharan Africa and parts of Asia/South America where schistosomiasis is endemic. (This project is supported by grants from NIAID/NIH, Bill and Melinda Gates Foundation, RIGHT Foundation, EU/Horizon 2020, and Wellcome Trust)

Biography

Dr. Afzal A. Siddiqui holds the highest academic rank of Grover E. Murray Professor that Texas Tech University Health Sciences Center (TTUHSC) bestows on its faculty. He is the Chair of the Department of Immunology & Molecular Microbiology at the TTUHSC-School of Medicine. He has earned his B.Sc. (Hons), M.Sc. and M. Phil. degrees from the Aligarh Muslim University in India and his Ph.D. degree from the University of Western Ontario in Canada. His professional training is from the Centers for Disease Control and Prevention, Morehouse College, University of Illinois College of Medicine, and Harvard University School of Public Health. He is a recipient of Fulbright Research and Teaching Scholarship for Southeast Asia.

Dr. Siddiqui has authored over 100 research papers, book chapters/reviews and articles. He serves on several Editorial Boards of scientific journals and has served as peer-reviewer for over 100 international journals. He has served on numerous NIAID and NIH study sections. He serves as a consultant to US FDA. He has reviewed grants for Ministry of Labor, Health and Social Policies, Republic of Italy; Romanian National Council for Scientific Research; Medical Research Council, Australia; Czech Science Foundation; and Netherlands Organization for Scientific Research.

Dr. Siddiqui has developed a vaccine against schistosomiasis, called SchistoShield® which has received patents in the USA and internationally. Schistosomiasis is a debilitating disease with which 252 million people are currently infected and an additional 779 million are at risk of acquiring the infection in 79 countries.

Phase 1 human clinical trials of SchistoShield® in USA have just been completed at the Kaiser Permanente Washington Health Research Institute (NIAID's Infectious Diseases Clinical Research Consortium). Phase 1b/2a trials in Africa (Madagascar, Burkina Faso) starting in the fall of 2023 are funded through Bill & Melinda Gates Foundation, European Union/Horizon 2020 and RIGHT Foundations grants. SchistoShield® is concurrently optimized in schistosome human challenge infection model (Funded by Wellcome Trust) in Europe (The Netherlands) and Africa (Uganda).

Development of an effective nontoxigenic *Clostridioides difficile*–based oral vaccine against *C. difficile* infection

Shaohui Wang, Duolong Zhu, Xingmin Sun*
Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa, Florida, USA

The symptoms of *Clostridioides difficile* infection (CDI) are largely attributed to two *C. difficile* toxins, TcdA and TcdB. Significant efforts have been devoted to developing vaccines targeting both toxins through parenteral immunization routes. Recently, we generated a novel chimeric protein (designated Tcd169), comprised of the glucosyltransferase domain (GT), the cysteine protease domain (CPD), and the receptor binding domain (RBD) of TcdB, and the RBD of TcdA. Parenteral immunizations with Tcd169 provide mice effective protection against infection with a ribotype (RT) 027 *C. difficile* strain. In this study, we expressed Tcd169 in a nontoxigenic C. *difficile* CCUG37785 strain (designated NTCD), resulting in strain NTCD_Tcd169 to develop an oral vaccine that can target both *C. difficile* toxins and colonization/adhesion factors. Oral immunizations with NTCD_Tcd169 spores induced systematic and mucosal antibody responses against, not only both toxins, but also *C. difficile* flagellins (FliC/FliD). Intriguingly yet importantly, anti-Tcd169 sera raised against Tcd169 protein were significantly cross-reactive with FliC/FliD and two surface layer proteins (SlpA and Cwp2). Oral immunizations with NTCD_Tcd169 spores provided mice effective protection against infection with a hypervirulent RT027 *C.difficile* strain R20291and significantly reduced R20291spore numbers in feces compared with NTCD or PBS immunized mice. These results imply that the genetically modified, nontoxigenic *C. difficile* strain expressing Tcd169 may represent a novel mucosal vaccine candidate against CDI.

Biography

Dr. Sun is an Associate 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 Degree in Veterinary Microbiology and Immunology from the 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 Tufts Institute for Innovation Inaugural Award in 2014. In 2018, he was awarded “Faculty Outstanding Research Achievement Award” at USF. In 2019, he was awarded “Excellence in Innovation Award” at USF. He chaired the Research Committee of College of Medicine at USF from 2019 to 2020. Currently, he serves as the President for the USF Chapter, National Academy of Inventors, USA.

Ex vivo antigen-loading of dendritic cells as a platform for personal cancer and infectious disease vaccines

Robert O. Dillman, M.D.
AIVITA Biomedical, Inc., University of California Irvine

Ex vivo loading of antigens into autologous dendritic cells (DC) provides a personalized approach to vaccines, and the direct loading of DC with relevant antigen may offer advantages over other vaccine methods that rely on uptake of antigen *in vivo* by endogenous DC to initiate an adaptive immune response. Peripheral blood mononuclear cells are differentiated into dendritic cells (DC) *in vitro*, then incubated with the antigens of interest. Personal therapeutic dendritic cell-autologous tumor antigen (DC-ATA) cancer vaccines have been manufactured using lysates of irradiated tumor cells from short term cultures enriched for self-renewing tumor initiating cells. This has been tested in human trials in renal cell, hepatocellular, and ovarian cancer as well as melanoma and glioblastoma in which feasibility, safety, induction/enhancement of immune responses, and suggestion of efficacy have been demonstrated. A similar approach has been used to make personal vaccines to the spike protein of the SARS-CoV-2 virus. Human trials confirmed induction/enhancement of antigen-specific humoral and cellular immune responses and high efficacy in preventing symptomatic Covid infection. In this presentation, the methods for manufacturing these personal DC vaccines and available clinical and immune response data will be reviewed.

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.

An ecosystem for the rapid generation of biological reagents against infectious diseases

Sumana Sundarmurthy
Technical Account Manager, Sino Biological

Biological reagents, in the form of recombinant proteins, antibodies…, are key materials for virology research. They are heavily used in the studies of pathogens that cause various infectious diseases. These reagents are developed in highly specialized manufacturing facilities. They have played a major role in the development of vaccines and serological tests during the early pandemic stage and continue to facilitate the discovery of new tools for virus mutant variant tracking and anti-viral therapy. Here we present a closed-loop ecosystem for the rapid development of high-quality biological reagents using multiple platforms, from recombinant protein expression to antibody discovery and assay kit assembly. Integration of conventional techniques with next-generation high-throughput methods allows a sustainable supply of reagents that closely follow the rapid mutation of viruses such as SARS COV-2, RSV, influenza... and also provides a one-stop solution for the generation of reagents for other emerging infectious diseases.

Biography

Sumana Sundaramurthy is the Technical Account Manager at Sino Biological where she supports R&D projects for industry and academic clients. Sumana completed her PhD in Cell Biology from SUNY Upstate Medical University. Dr. Sundaramurthy's expertise lies in cytoskeleton, oncology and immunology.

In addition to her academic pursuits, Sumana held various leadership positions at Upstate and other professional organizations. She has also worked for a preclinical CRO and a few notable research groups at Loyola University, the University of Chicago, and Sanofi Pasteur

DNA-based delivery of antiviral antibodies for infectious disease prevention

Rachel A. Liberatore
RenBio

The importance of vaccines for public health can hardly be overstated, and yet there are two areas of infectious disease prevention that remain sources of vulnerability for vaccine use and effectiveness: rapid responses to emerging infectious diseases and protection of immunocompromised populations.

Though vaccines are an invaluable tool for the prevention of infectious diseases, there are barriers to their rapid development and deployment in the event of an outbreak of a novel pathogen. The COVID-19 pandemic revealed the possibilities for rapid vaccine development where preexisting research on SARS provided a head start for vaccine design (and previously unproven technologies yielded excellent clinical results), but there will almost certainly be future pathogens for which that scenario doesn't exist. The successful development of a vaccine often takes many years, a timeframe incompatible with quickly halting a novel infectious disease outbreak. In contrast, the identification and characterization of antiviral antibodies, primarily from patient sera, is a field that has made significant advances in recent years, enabling programs like the DARPA-funded Pandemic Prevention Platform to boast multiple groups capable of screening and down selecting to potential clinical candidate molecules in a matter of weeks. The rapid deployment of such antibodies could serve as a firebreak while vaccine development is underway. A method for further improving the speed of such a response could be to deliver such antibodies not as traditional recombinant proteins, but via antibody-encoding DNA. Just as plasmid DNA would typically be used as the starting material for manufacturing antibodies, it can be administered directly to patients using intramuscular electroporation, where an individual's own muscle cells act as a bioreactor, durably delivering the encoded antibody to systemic circulation.

In the case of infectious diseases for which effective vaccines already exist, there remain a substantial number of people whose compromised immune systems prevent them from fully benefitting from vaccine-induced protective immunity. For these patients, the acquisition of passive immunity in the form of antiviral antibodies could be lifesaving. Indeed, the anti-SARS-CoV-2 antibody cocktail, Evusheld, was authorized by the US FDA for both treatment and prevention of COVID-19. In order to provide the most durable protection, however, the delivery of antiviral antibodies in DNA form has the potential to transform months-long protection of recombinant protein into protection for a year or more from a single administration.

Vaccines have been, and undoubtedly will continue to be, one of the most valuable tools for protecting public health. There are, however, gaps in their timing and widespread coverage in the settings of rapid responses to novel viral outbreaks and robust protection of immunocompromised populations. In these areas, DNA-based delivery of antiviral antibodies has the potential to be enormously impactful.

Biography

Rachel Liberatore is the President and Chief Scientific Officer at RenBio, a biotechnology company in New York City developing a platform technology for the DNA-based delivery of monoclonal antibodies and therapeutic proteins for the prevention of infectious diseases and the treatment of chronic diseases. RenBio's MYO Technology™ platform uses intramuscular electroporation of plasmid DNA to deliver sustained levels of antibodies and other therapeutic proteins. Current programs include the development of a monoclonal antibody for the prevention of Zika virus disease and a therapeutic protein for chronic neutropenia treatment.

Previously, as a postdoctoral fellow at the Aaron Diamond AIDS Research Center, she used genetic techniques to understand how intrinsic cellular defenses restrict the spreading of retroviruses, including murine leukemia viruses and HIV-1. She also studied the elicitation of antiviral antibodies directed at viral envelope proteins using recombinant viruses.

Dr. Liberatore received her bachelor's degree in Molecular Biology from Princeton University and her Ph.D. in Cellular, Molecular, and Biomedical Studies from Columbia University.

Immune monitoring read outs when vector-based vaccines are used: including ELISPOT assays

Magdalena Tary-Lehmann
Chief Scientific Officer, Cellular Technology Limited

Assessing immunogenicity of antigen specific responses is a challenge in the biopharmaceutical industry, as an increasing number of drugs/vaccines/ gene therapy trials aim to elicit a response from the cellular components (e.g., T, B cells) of the immune system in both the preclinical and clinical phases. Measurements of antibodies in bodily fluids (e.g., by ELISA) have provided robust and reproducible results for decades, and such assays have been validated for monitoring of B-cell immunity. In contrast, measuring T-cell immunity has proven to be more of a challenge, due to the need to test live cells in functional assays ex vivo. While T cells play a critical role reliable measurements of antigen-specific T cell responses ex-vivo remain seemingly problematic, as typically, T cells occur in very low frequencies in test samples, such as peripheral blood. Therefore, monitoring antigen-specific T cells and their effector functions is critical for the assessments of the efficacies of specific immune therapies. For this reason, assays such as ELISA and others should be complemented with a single cell assay such as ELISPOT. ELISPOT assays can be run in a reproducible fashion and be employed in a regulated environment using fresh or cryopreserved PBMC's from patients.

We CTL specialize in cell mediated immune monitoring (using ELISPOT, ELISA, micro-neutralization assays, etc.), standardization of procedures including separation and cryopreservation of functional PBMC from whole blood, instrumentation and materials. Our extensive contract laboratory services support many pharmaceutical studies (clinical and preclinical) from custom development to validation, and testing. Examples of such successful T and B cell monitoring will be presented.

Biography

Dr. Magdalena Tary-Lehmann is Co-Founding Scientist and Chief Scientific Officer for Cellular Technology Limited (CTL). Dr. Tary-Lehmann received her M.D. and Ph.D., both from the University of Tübingen, Germany. Her postdoctoral training in Immunology was at the University of California, Los Angeles. She moved thereafter to Case Western Reserve University, where she was awarded tenure and appointed as Associate Professor in the Department of Pathology. As CEO for the contract laboratory, she oversees the performance of immunology assays in CTL's GCP, GLP- and CLIA certified contract laboratory for various pharmaceutical and biotechnology clients and serves as CSO for CTL.

The underlying genetic architecture of the immune system responsible for immunodominance

Ellen L. Shrock[1,2,3], Richard T. Timms[4,†], Tomasz Kula[1,2,3,5,†], Elijah L. Mena[1,2], Anthony P. West, Jr.[6], Rui Guo[7,8,9], I-Hsiu Lee[10], Alexander A. Cohen[6], Lindsay G. A. McKay[11], Caihong Bi[12,13], Keerti[12,13], Yumei Leng[1,2], Eric Fujimura[1,2], Felix Horns[14], Mamie Li[1,2], Duane R. Wesemann[9,12,13,15], Anthony Griffiths[11], Benjamin E. Gewurz[7,8,9,16], Pamela J. Bjorkman[6], Stephen J. Elledge[1,2,*]

[1] Department of Genetics, Harvard Medical School, USA.
[2] Division of Genetics, Department of Medicine, Howard Hughes Medical Institute, Brigham and Women's Hospital, USA.
[3] Program in Biological and Biomedical Sciences, Harvard University, USA.
[4] Cambridge Institute of Therapeutic Immunology and Infectious Disease, Jeffrey Cheah Biomedical Centre, Cambridge Biomedical Campus, University of Cambridge, Cambridge, UK.
[5] Society of Fellows, Harvard University, USA.
[6] Division of Biology and Biological Engineering, California Institute of Technology, USA.
[7] Division of Infectious Disease, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, USA.
[8] Department of Microbiology, Harvard Medical School, USA.
[9] Broad Institute of Harvard and MIT, USA.
[10] Center for Systems Biology, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, USA.
[11] Emerging Infectious Diseases Laboratories, Boston University School of Medicine, Boston University, USA.
[12] Division of Allergy and Immunology, Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, USA.
[13] Massachusetts Consortium on Pathogen Readiness, USA.
[14] Department of Bioengineering, Department of Applied Physics, Chan Zuckerberg Biohub and Stanford University, USA.
[15] Ragon Institute of MGH, MIT, and Harvard, USA.
[16] Graduate Program in Virology, Division of Medical Sciences, Harvard Medical School, USA.

Despite the vast diversity of the antibody repertoire, infected individuals often mount antibody responses to precisely the same epitopes within antigens. The immunological mechanisms underpinning this phenomenon remain unknown. By mapping 376 immunodominant "public epitopes" at high resolution and characterizing several of their cognate antibodies, we conclude that germline-encoded sequences in antibodies drive recurrent recognition and the process of immunodominance. Systematic analysis of antibody–antigen structures uncovered 18 human and 21 partially overlapping mouse germline-encoded amino acid-binding (GRAB) motifs within heavy and light V gene segments that, in case studies, are critical for public epitope recognition. GRAB motifs represent a fundamental component of the immune system's architecture that ensures antibody recognition of pathogens and promotes species-specific reproducible responses that can exert selective pressure on pathogens. We are exploring the extent of immunodominance in SARS-CoV-2 immune responses and find extensive immunodominance on the humoral response to SPIKE. We think the principles uncovered for B cell immunodominance also play a role in T cell immunodominance.

Biography

Stephen Elledge is the Gregor Mendel Professor of Genetics and Medicine at Harvard Medical School and the Brigham and Women's Hospital. He received his B.S. in chemistry from the University of Illinois and his Ph.D. in biology from MIT. He is a member of the National Academies of Sciences and of Medicine. His awards include the Gairdner Award, Albert Lasker Basic Medical Research Award, the Breakthrough Prize, and the Gruber Prize in Genetics.

His interests center on genetic approaches to biological problems including the DNA damage response, cell cycle, cancer evolution and immunity. With Wade Harper he uncovered the two largest families of E3 ubiquitin ligases: the CRLs and the RING ligases. He has also worked in unraveling the role of cancer drivers in the evolution of cancer and how tumor suppressors allow cancers to evade the immune system. Dr. Elledge has developed a suite of immunological methods, such as T-Scan, VirScan and EpiScan, that allows the genome-wide identification of epitopes recognized by B and T cells to investigate the role of viruses in human disease.

How advances in artificial intelligence are optimizing the deployment and utilization of life-saving infectious disease countermeasures to high-consequence epidemics

Kamran Khan
BlueDot

Explosive international epidemics arising from emerging pathogens are increasing in frequency. At the same time, the global epidemiological landscape of many other infectious diseases is shifting due to factors such as climate change, humanitarian crises, and eroding public health systems. In a highly interconnected world, emerging and reemerging pathogens can spread and disrupt distant populations with remarkable efficiency and speed. Getting ahead of local epidemics and preventing or attenuating their global health, economic, and societal impacts requires smarter, faster, and better coordinated public health actions.

Recent advances in artificial intelligence, notably large language models (LLMs), are augmenting our ability to detect global infectious disease threats at their earliest stages, characterize these threats to determine which are anomalous and demand further assessment, and better anticipate their local and global trajectory and impacts. These advanced analytical capabilities are foundational to informing the production and deployment of essential infectious disease countermeasures such as vaccines, therapeutics, diagnostics, disinfectants, and personal protective equipment. Moreover, generative artificial intelligence (GenAI) models offer new opportunities to efficiently articulate and communicate timely, actionable insights about infectious disease threats at scale to a diverse set of audiences from government decision-makers, to manufacturers and distributors of infectious disease countermeasures, to frontline healthcare providers, and even healthcare consumers.

This presentation will contrast the growing global threat posed by emerging and reemerging infectious diseases with recent advances in artificial intelligence, and its potential when coupled with human intelligence, to inform and empower timely, coordinated, cross-sectoral actions that protect the health of global populations.

Biography

Dr. Kamran Khan is an infectious disease physician-scientist and a Professor of Medicine and Public Health at the University of Toronto. Motivated by his experiences as a frontline healthcare worker during the 2003 Toronto SARS outbreak, Dr. Khan has been studying outbreaks of emerging and reemerging diseases for over a decade to lay the scientific foundation for a global early warning system. He founded BlueDot in 2013, a global infectious disease intelligence company that uses big data, human and artificial intelligence, and information technologies to help governments and pharmaceutical companies build readiness and respond to emerging global infectious disease threats.

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Cancer Vaccines & Immunotherapy

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Cancer Vaccines & Immunotherapy

Title: **Preclinical proof of concept studies of a novel human HER-2 virus like particle as a vaccine candidate for human breast cancers**

Farshad Guirakhoo
ExpreS2ion Biotechnology

Title: **Exploring T-Cell pathways to enhance immunotherapies in cancer and infection**

Christopher E. Rudd
Universite de Montreal

Title: **Stimulation of anti-tumor responses with small molecules that induce Z-DNA**

Alan Herbert
InsideOutBio, Inc

Title: **Development of an enhanced IL-12-containing in situ vaccine for the treatment of solid tumor patients, refractory to anti-PD(L1) agents**

Robert Hamilton Pierce
Attivare Therapeutics

Preclinical proof of concept studies of a novel human HER-2 virus like particle as a vaccine candidate for human breast cancers

Farshad Guirakhoo*, Francesca Ruzzi, Stine Clemmensen, Anette Strøbæk, Klaas Buijs, Tanja Domeyer, Jerzy Dorosz, Vladislav Soroka, Christina Jo Rasmussen, Ida Busch Nielsen, Max Soegaard, Mette Thorn, Mattis Flyvholm Ranthe, Maria Sofia Semprini, Laura Scalambra, Stefania Angelicola, and Pier-Luigi Lollini
*ExpreS2ion Biotechnology

In 20-30 % of human breast cancer tumors, HER-2 is overexpressed, which is associated with a more aggressive disease, higher recurrence rate, and increased mortality. Current therapies with anti-HER-2 monoclonal antibodies, like trastuzumab and pertuzumab, have resulted in significant improvement in patients‘- survival rates. ─However high costs, recognition of a single epitope on HER-2 protein and tumor resistance have hindered their broad applications.

A vaccine including the extracellular domain (ECD) of a HER-2 protein could potentially be safe, cost effective and produce a polyclonal antibody response targeting multiple epitopes overcoming the tumor resistance. We have developed a human HER-2 vaccine candidate based on a proprietary virus-like particle (VLP) platform which allows the assembly of ~50 molecules of HER-2 extracellular domain (ECD) on the surface of each particle. The HER-2-VLP vaccine showed promising therapeutic and prophylactic activity in human HER-2 transgenic mouse models where animals were cured and remain tumor free for their entire lives. After completion of GLP (Good Laboratory Practice) toxicology safety studies in rats and monkeys, and favorable response from Denish Medicine Agency (DMA), vaccine candidate is ready to be partnered to support funding needed for clinical trials in breast cancer patients in 2024.

Biography

Dr. Guirakhoo has 30+years of broad translational research experience in the vaccine development field. Dr. Guirakhoo was named as no. 22 in The Most Influential People in Vaccines. He is the co-inventor of the ChimeriVax™-technology platform, the world’s first recombinant viral vector platform that was approved for any human vaccine. Dr. Guirakhoo has broad experience in the application of genetics, gene expression technologies and molecular virology for the construction and production of recombinant proteins, human antibodies and attenuated viral vectored vaccines for prevention and treatment of infectious diseases and cancers. He is the author of over 100 peer-reviewed publications, including book chapters and holds dozens of issued patents. Dr. Guirakhoo holds a PhD in Virology from the Medical University of Vienna, Austria.

Exploring T-cell pathways to enhance immunotherapies in cancer and infection

Christopher E. Rudd[1-3]
[1] Département de Medicine, Université de Montréal, Canada
[2] Division of Immunology-Oncology, CR-HMR, Canada
[3] ImmunAb Research, Montreal, Canada

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 therapeutic strategies in the realm of infection and tumor immunity.

Biography

He previously held professorial positions at the Harvard Medical School, the Dana-Farber Cancer Institute (Boston) and Cambridge University (UK). He has received awards from the Wellcome Trust (UK), Cancer Research Institute (New York) and the Leukemia/Lymphoma Society (USA) and is an elected Fellow of the Royal College of Pathologists (2002), the Academy of Medical Sciences (2002) and the Royal Society of Canada (2021). Professor Rudd's research focus is on uncovering T-cell receptors and signaling mechanisms in immunotherapy and the therapeutic feasibility of novel small molecules in anti-tumor immunity.

Stimulation of anti-tumor responses with small molecules that induce Z-DNA

Alan Herbert
President and Founder
InsideOutBio

Genetic and cellular studies evidence Z-DNA and Z-RNA regulate innate immune responses through recognition of these conformations by the proteins ADAR1, an RNA editing enzyme, and ZBP1, an inducer of cell death. I will discuss how small molecules such as CBL0137 can modulate these responses to induce anti-tumor immunity and regressions of lesions refractory to checkpoint inhibitor therapy.

Key Words: Z-RNA; Aicardi Goutières Syndrome; Interferonopathy; flipons; Zα ;ADAR1; ZBP1

Biography

Alan Herbert is leading the team at InsideOut Bio to develop cancer therapeutics based on his pioneering work that has unraveled the role played by left-handed Z-DNA and Z-RNA in the regulation of innate immune responses to viruses and cancers

Development of an enhanced IL-12-containing in situ vaccine for the treatment of solid tumor patients, refractory to anti-PD(L1) agents

Robert Hamilton Pierce
Chief Scientific Officer, Attivare Therapeutics

IL-12 is a potent pro-inflammatory cytokine, expressed mainly by innate immune cells upon encountering immunologic "danger signals" (i.e. PAMPS/DAMPs). It represents a critical "signal three" in the immune synapse where it helps to drive a Th1/Type I immune response, characterized by interferon-gamma (IFNγ) production, activation of NK cells and cytotoxic T cells. Unfortunately, systemic delivery of recombinant IL-12 leads to severe cytokine-mediated toxicity, which limited its clinical utility. Attivare Therapeutics, Inc is developing a novel, mesoporous silica rod-based biomaterial drug delivery technology for controlled, sustained delivery of immune activating molecules (AttImmune™). ATT-02 delivers IL-12 directly into the tumor microenvironment (TME), driving significant pro-inflammatory changes in the TME. ATT-02 functions as a potent "in situ vaccine" by leveraging tumor cells themselves as the antigen source, generating systemic anti-tumor immune responses and causing tumor growth inhibition of treated tumors as well distant, untreated tumors (i.e. "abscopal effect"). In this presentation, the mechanism underlying IL-12's ability to convert an immunosuppressive tumor microenvironment into an inflamed immunogenic state will be discussed as well as the potential to impact patients, who are refractory to or relapse after anti-PD(L)-1 therapy.

Biography

Robert H. Pierce is currently Chief Scientific Officer (CSO) of Attivare Tx, a new immunotherapy company developing novel biomaterial-based immune-activating technology from the Wyss Institute at Harvard. Dr. Pierce is an anatomic pathologist who brings more than two decades of scientific leadership and experience managing large teams dedicated to translational medicine and immune-oncology drug development in both academia and industry. His research has focused on the mechanisms of tumor-induced immune tolerance and he has longstanding expertise in the development of biomarkers to predict responses to immuno-oncology treatments. While at Merck, Dr. Pierce led a team focused on the development of tissue-based biomarker approaches for Merck's anti-PD1 therapeutic antibody (pembrolizumab; KEYTRUDA®) to define response and non-response phenotypes to anti-PD1 blockade, including the 22C3 PD-L1 companion diagnostic IHC assay. He was also the medical lead responsible for the early clinical development of pembrolizumab in Merkel cell carcinoma and cutaneous T cell lymphoma. He also previously served as the CMO and, later, CSO of OncoSec Medical, Director of Immunopathology at the Fred Hutchinson Cancer Research Center and Chief R&D Officer at Sensei Biotherapeutics. Dr. Pierce has a B.A. from Yale University, was awarded a Fulbright scholarship to study philosophy at the Albert-Ludgwig University in Freiburg, Germany and the went on to receive an M.D. from Brown University School of Medicine, where he currently serves as an adjunct professor. Following graduation from medical school, he completed a residency program in Anatomic Pathology and a post-doctoral research fellowship at the University of Washington in Seattle.

SCIENTIA MEETINGS

VACCINES 2023

Day 3: November 15, 2023

Influenza Vaccines

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Influenza Vaccines

Title: **Approaches to enhance the generation of broadly reactive influenza-specific antibodies in newborns**

Martha Alexander-Miller
Wake Forest University School of Medicine

Title: **Rapid development and flexible scale of complex recombinant proteins and antigens including ferritin nanoparticles for infectious diseases including COVID-19 and seasonal and pandemic influenza**

Mark Emaflarb
Dyadic International Inc

Title: **Liposome-display of antigens: A powerful approach for vaccine development**

Jonathan Lovell
University at Buffalo

Approaches to enhance the generation of broadly reactive influenza-specific antibodies in newborns

Martha A. Alexander-Miller
Dolores G. Evans PhD Chair in Microbiology and Immunology
Professor and Chair, Dept. of Microbiology and Immunology
Director Center for Vaccines at the Extremes of Aging
Wake Forest University School of Medicine

Newborns are at significantly increased risk for development of severe disease following infection with influenza virus. This is the collective result of their naïve status and altered immune responsiveness. At present, we lack of an effective vaccine for infants less than 6 months of age. Thus, a significant challenge for protecting this at risk population lies in increasing the immunogenicity of influenza vaccine approaches. In addition, a highly sought after goal is the ability to elicit antibodies that are broadly protective that can provide multi-season protection. Antibodies directed to the conserved stem region of hemagglutinin (HA) have been shown to meet this criterion. We are exploring vaccine approaches that can target stem-specific responses, evaluating antibody production, cellular responses, and protective capacity in the newborn. Our laboratory uses a newborn nonhuman primate model to probe these questions because of the strong advantages it provides: 1) similarity to humans in immune system development and 2) a prolonged period of infancy. This work will provide critical insights into the ability to target stem-specific responses as an approach to elicit protection in newborns.

Biography

Dr. Alexander-Miller is Professor and Chair of the Department of Microbiology and Immunology at Wake Forest University School of Medicine (WFUSM). In addition, she serves as Director of the WFUSM Center for Vaccines at the Extremes of Aging and is the Director of an NIH-funded T32 pre-doctoral training grant. She holds the Dolores G. Evans, PhD endowed chair in Microbiology and Immunology.

As departmental chair, Dr. Alexander-Miller oversees a group of highly interactive faculty working on host-pathogen interactions. Dr. Alexander-Miller joined the faculty of WFUSM in 1997 after completing a postdoctoral fellowship at the National Institutes of Health. She obtained her doctorate at Washington University School of Medicine in St. Louis.

Dr. Alexander-Miller's career has been dedicated to understanding regulation of the immune response following pathogen infection. She was the first to report the T cell attribute of functional avidity as a critical determinant of the effectiveness of these cells for viral clearance. Based on her seminal work, this is now a routine measure of cellular function. Her current area of focus is the development of influenza vaccines that are effective in young infants. Her passion around this goal led to the establishment of the WFUSM Center for Vaccines at the Extremes of Aging. In addition to facilitating basic and clinical research in this area, the center is committed to public outreach and education, including delivering seminars for teachers across North Carolina.

Dr. Alexander-Miller has been the recipient of the Mid-Career Investigator Award and the Innovator Award. She has served on numerous NIH study sections. Currently, Dr. Alexander-Miller is an Associate Editor for the journal *Frontiers in Immunology* and a member of the editorial board for *Vaccines*. She is the senior representative to the Council of Faculty and Academic Societies for the Association of American Medical Colleges, a national organization that serves as a voice for medical school faculty within AAMC's leadership and governance structures. In this role she serves as a member of the Program Committee and Vice-Chair for the Biomedical Research and Training Committee. She has served in a number of faculty-elected positions at WFUSM, including representative to the Wake Forest Graduate Council and Faculty Senate and as the Director of the Molecular and Cellular Biosciences Graduate Program.

Rapid development and flexible scale of complex recombinant proteins and antigens including ferritin nanoparticles for infectious diseases including COVID-19 and seasonal and pandemic influenza

[1] Ronen Tchelet, [2] Marika Vitikainen; [1] Noelia Valbuena ; [2] Anne Huuskonen; [3] Abraham Nyska; [2] Markku Saloheimo and [1] *Mark Emalfarb.
[1] Dyadic International Inc
[2] VTT Technical Research Centre of Finland Ltd
[3] Tel Aviv University, Tel Aviv, Israel

C1 protein production platform has been developed through more than 20 years of commercial genetically engineering. The thermophilic fungus *Thermothelomyces heterothallica* is a robust and versatile fungal expression system for the rapid production of proteins at very high levels. In the last 6 years, the C1 protein production platform has been further improved to become a safe and efficient expression system with the prime objective of speeding up the development and production of commercial scale human and animal vaccines, monoclonal antibodies, biosimilars, as well as other therapeutic proteins at larger quantities and lower cost.

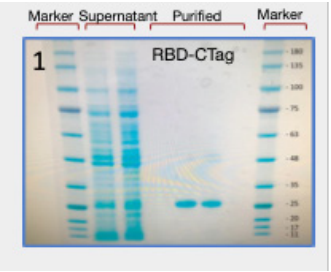
C1 is a very efficient platform to produce antigens, even to generate multicomponent vaccines. The production levels of engineered C1 strains are similar in terms of yield and purity, reaching in some cases more than 2.5 g/L (in 4-5 days). In contrast to other vaccine platforms, C1 has a higher safety profile, and production can be scaled up in a more cost-effective manner using standard microbial *E. coli* fermenters. Stable cell lines have been developed to produce different antigens as influenza, neuraminidase, west Nile, rabies, rift valley fever..etc.

Here we present the production of Dyadic´s DYAI-100 vaccine candidate against the Covid-19 pandemic, based on the ~25 kilodalton-large Receptor Binding Domain (RBD) within the S1 subunit that was identified as the most effective SARS-CoV-2 neutralizing antibodies described to date. The use of C1 as vaccine production platform against the SARS-CoV-2 offers several advantages as follows:

(i) The C1 platform can support the global immunization strategies that are needed against emerging new SARS-Covid-2 variants. In 7 weeks, new RBD variant's genes can be inserted into the same C1 cell line (same genotype) to develop stable cell lines which can be used to produce antigens at the same production levels (1-2 g/L) in 4-5 days. So far, the following variants were successfully produced; Alpha (UK), Beta (SA) Gamma (BR) Delta (Ind) and Omicron (B.1.1.529) at levels and qualities that are similar to the Wuhan RBD – DYAI-100.

(ii) Safety and Persistence - the results show that DYAI-100 elicits safe, effective, and protective immune responses in several successful mice studies including challenge study with hACE2-transgenic C57BL/6J mice that demonstrated full protection without adverse events. Importantly, a rabbit toxicology study demonstrated that the C1-SARS-CoV-2 RBD vaccine candidate is safe and has the potential to be an effective vaccine with a safety and tolerability profile suitable for evaluation in humans. In addition, the study suggested a major beneficial effect of the vaccination demonstrating continued, and not declining antigenic stimulation, for relatively long duration, without any local or systemic adverse effect.

This DYAI-100 vaccine candidate has been produced under GMP standards (99% purity) and proposed for further testing in safety and efficacy clinical trials.



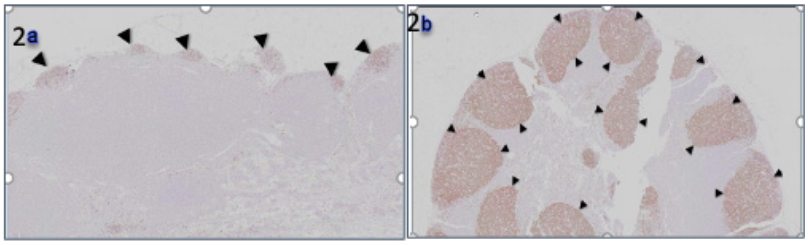


Figure 1: C1 RBD strain was run in 5L scale fermentation. The RBD was purified through CaptureSelectTM Ctag column rendering 98% purity, 70% recovery. Figure 2: (2a) The iliac lymph nodes from an animal injected with the Alhydrogel®'85' (Placebo) and (2a) and with C1-RBD Vaccine (2b) after sacrificed 42 days post first dosing (Recovery phase). Note, arrowheads in 2a- no evidence of germinal centers. The lesions (arrowhead in 2b) consist of mild germinal centers increased lymphocytic cellularity (i.e., follicular hyperplasia).

Key Words: Next generation platform / vaccine / mAbs / Biotherapeutics / SARS-CoV-2

Biography

Mark A. Emalfarb is the founder of Dyadic. He has been a member of Dyadic's board of directors since October 2004 and has served as its Chairman as well as President and Chief Executive Officer from October 2004 until April 2007 and from June 2008 until the present.

Since founding Dyadic in 1979, Mr. Emalfarb has successfully led and managed the evolution of Dyadic from its origins as a pioneer and leader in providing ingredients used in the stone-washing of blue jeans to the discovery, development, manufacturing and commercialization of specialty enzymes used in various industrial applications and the development of an integrated technology platform based on Dyadic's patented and proprietary C1 fungal microorganism.

Mr. Emalfarb is an inventor of over 25 U.S. and foreign biotechnology patents and patent applications resulting from discoveries related to the Company's patented and proprietary C1 fungus, and has been the architect behind its formation of several strategic research and development, manufacturing and marketing relationships with U.S. and international partners.

Liposome-display of antigens: A powerful approach for vaccine development

Jonathan Lovell
University at Buffalo

Display of protein-based antigens in nanoparticle format has attracted interest for improving vaccine immunogenicty. We have developed cobalt-porphyrin-phospholipid (CoPoP) as a lipid-like excipient that enables the rapid and biostable anchoring of his-tagged peptides and proteins with simple admixture of proteins and liposomes. His-tagged antigens stably interact with cobalt within the lipid bilayer. Numerous antigens exhibit orders-of-magnitude stronger humoral and cellular responses with this approach. Improved delivery to antigen presenting cells in the draining lymph node is typically observed. This approach has recently completed Ph3 testing in the EuCorVac-19 COVID-19 vaccine. Recent findings on this approach for rapid nanoparticle-based vaccine prototyping and emerging vaccine candidates using this technology will be discussed.

Biography

Jonathan F. Lovell is an Empire Innovation Professor of Biomedical Engineering at the State University of New York at Buffalo. He received his PhD in Biomedical Engineering from the University of Toronto in 2012 and started as a UB faculty in the same year. Dr. Lovell's work has been recognized with awards including the NIH Early Independence Award, the Biomedical Engineering Society Young Investigator Award, the NSF CAREER award, and the Porphyrin Society Young Investigator Award. He is a fellow of the American Institute for Medical and Biological Engineering. Dr. Lovell has co-authored over 200 peer reviewed manuscripts.

SCIENTIA MEETINGS

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Vaccine adjuvants

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Vaccine adjuvants

Title: **Immunomodulators identified via high-throughput screening enhance control of vaccine adjuvanticity**
Matthew Rosenberger
University of Chicago

Title: **Adjuvantation with mRNA encoding IL-12 overcomes mRNA vaccine limitations**
Byron Brook
Boston Children's Hospital

Title: **Harnessing sustained release technologies to produce robust, durable, and high-quality immunity**
Eric Andrew Appel
Stanford University

Title: **mRNA vaccine against malaria tailored for liver-resident memory T cells**
Gavin Painter
Victoria University Wellington

Title: **Development of saponin-based adjuvant IA-05 for subunit-vaccines**
Pi-Hui Liang
Professor, School of Pharmacy, National Taiwan University, Founder and CEO of ImmunAdd, Inc. Taipei, Taiwan

Immunomodulators identified via high-throughput screening enhance control of vaccine adjuvanticity

Matthew Rosenberger
University of Chicago, USA

Stimulation of the innate immune system is crucial in both vaccinations and immunotherapies. This is often achieved through adjuvants, molecules that usually activate pattern recognition receptors (PRRs) and stimulate two innate immune signaling pathways: the nuclear factor kappa-light-chain-enhancer of activated B-cells pathway (NF-κB) and the interferon regulatory factors pathway (IRF). Engineering the immune response via fine control of these pathways, however, is quite difficult. We demonstrate the ability to alter and improve adjuvant activity via the addition of small molecule "immunomodulators" to existing PRR agonists. By modulating signaling activity instead of receptor binding, these molecules allow the customization of select innate responses. We demonstrate both inhibition and enhancement of the products of the NF-κB and IRF pathways by several orders of magnitude. Some modulators apply generally across many receptors, while others focus specifically on individual receptors. Modulators boosted correlates of protection and reduced correlates of reactogenicity in an inactivated flu vaccine. These modulators have a range of applications: from adjuvanticity in prophylactics to enhancement of immunotherapy. This approach to adjuvanticity offers greater control over early immune activation and provides researchers with a new tool to tailor end immune responses.

Biography:

Matt Rosenberger is a fifth year PhD candidate from the University of Chicago in Professor Aaron Esser-Kahn's lab. He received a bachelor's degree in Biomedical Engineering from the University of Texas at Austin where he studied T cell immunology in the lab of Prof George Georgiou. Currently, his research is focused on vaccine adjuvants and their activation of the innate immune system. Matt is exploring modulating adjuvant activity via small molecule inhibitors to improve the immune response. Altered innate signaling improves vaccines by decreasing systemic inflammation while increasing antigen-specific antibodies. These small molecules were identified through a series of high throughput screens and are now being explored in influenza vaccine and challenge studies.

Adjuvantation with mRNA encoding IL-12 overcomes mRNA vaccine limitations

Byron Brook[1], Soumik Barman[1], Cali Sweitzer[1], Manisha Menon[1], Lauren Speciner[2], Asad Khanmohammed[2], Etsuro Nanishi[1], Ofer Levy[1,3,4], Thomas Vancott[2], Valerie Duval[2,†], Romain Micol[2,†], David J. Dowling[1,†,*]

[1]Precision Vaccines Program, Division of Infectious Diseases, Boston Children's Hospital, Boston, MA, USA.
[2] Combined Therapeutics, Incorporated, Boston, MA, USA.
[3] Department of Pediatrics, Harvard Medical School, Boston, MA, USA.
[4] Broad Institute of MIT & Harvard, Cambridge, MA, USA.

mRNA vaccines have been critical in combatting SARS-CoV-2, yet there are platform limitations. Previous vaccine development focused on antigen delivery and minimizing immune activation to vaccine components. We describe a novel molecular biological adjuvantation system, constituting a single chain mRNA encoding an IL-12p70 heterodimer (scIL-12) which had TH1 polarizing bioactivity, inducing IFNg in human samples. Admixing a pharmacy grade mRNA vaccine encoding SARS-CoV-2 Spike antigen with mRNA encoding scIL-12p70 amplified humoral immunity with antigen dose sparing and induction of TH1-polarized immunity. Aged mouse models (>10 months old), modeling elder immunity, could be adjuvanted to restore humoral immunity to young-adult or greater levels. Incorporation of a multi-organ protection (MOP) system into the mRNA enabled restriction of transcript expression to only the injection site, reducing expression in distal organs. MOP inclusion in mRNA encoding spike antigen conferred protection in a hamster live viral challenge model. Adjuvantation with IL-12-MOP amplified aged animal cell mediated immunity and extended murine humoral immune durability over 1-year postimmunization. IL-12 biological adjuvantation enabled antigen dose-sparing, amplification of humoral and cellular immunity, and induction of more durable immunity, each overcoming mRNA vaccine limitations. IL-12 restoration of elder immunogenicity to young adult levels is a solution for an immunologically distinct population that suffers the greatest disease burden from SARS-CoV-2.

Biography

Dr. Byron Brook earned his Ph.D. in Experimental Medicine from the University of British Columbia and has since been a postdoctoral research fellow in the *Precision Vaccines Program* (PVP) at Boston Children's Hospital, with secondary appointment in the Department of Pediatrics at Harvard Medical School, working with Dr. Ofer Levy and Dr. David Dowling.

Dr. Brook's interests are centered around maximizing vaccine benefits, via application of existing and novel adjuvantation technologies to maximize immunogenicity, permitting dose sparing to extend vaccine reach, reduce reactogenicity, and enable multivalent immunization, or from evaluation and application of BCG nonspecific effect mechanisms able to protect vulnerable populations. He has published on a variety of applications including adjuvantation, challenge model development, elucidation of BCG-induced emergency granulopoiesis sufficient and required for protection, AI-modeling to predict subsequent outcome, and SARS-CoV-2 related research of vulnerable populations. Recently, he has investigated ontogeny-specific immunity identifying contributors to distinct immunity in the elderly and has adjuvanted mRNA vaccines through admixing lipid nanoparticles encapsulating mRNA encoding IL-12p70 with BNT162b2 to subsequently amplify SARS-CoV-2 specific immunity.

Harnessing sustained release technologies to produce robust, durable, and high-quality immunity

Eric A. Appel
Department of Materials Science & Engineering, Stanford University

Vaccines have dramatically reduced the occurrence and spread of infectious disease, but key barriers exist that complicate the development of potent, durable, and broadly protective vaccines for pathogens such as Influenza, HIV, SARS-CoV-2, and Malaria. To induce persistent, high-affinity, and broad antibody responses, vaccines must drive the formation of long-lived germinal centers in lymphoid organs, which in turn promotes the selection-driven process of somatic hypermutation and antibody affinity maturation. Conventional vaccines often fail to elicit robust and broad immune responses against rapidly mutating pathogens such as those listed above due to inadequate spatiotemporal control over the presentation of vaccine components to the immune system. As the immune system evolved to respond to extended pathogen exposure during natural infections, the prolonged exposure to vaccine components is essential to developing potent and durable immunity. To address this shortcoming, we have endeavored to develop injectable hydrogel depot technologies exhibiting unique cargo delivery characteristics whereby physicochemically distinct compounds can be co-delivered over tunable timeframes extending upwards of months. These materials can be easily administered with standard syringes and needles, and form robust depots upon administration in the body that slowly dissolve over tunable timeframes. We have found that prolonged co-exposure of protein antigens and adjuvants improve the magnitude and durability of germinal center reactions and result in a 1000-fold improvement in affinity maturation compared to the same vaccine delivered in a standard bolus. Recently we have shown that sustained delivery of various subunit vaccines against HIV, SARS-CoV-2, and influenza with our hydrogel technology elicited more potent, durable, high-affinity, and broadly protective humoral immunity compared to traditional administration of the same vaccines. Overall, this presentation will discuss the design of a biomaterial technology affording unique opportunities in the formulation and controlled release of vaccines, thereby constituting simple and highly effective controlled delivery platform for vaccines against numerous targets.

Biography

Eric A. Appel is an Associate Professor of Materials Science & Engineering at Stanford University. He received his BS in Chemistry and MS in Polymer Science from California Polytechnic State University in San Luis Obispo, CA. Eric performed his MS thesis research with Dr Jim Hedrick and Dr Robert Miller on the synthesis of polymers for drug delivery applications at the IBM Almaden Research Center in San Jose, CA. He then obtained his PhD in Chemistry with Prof. Oren A. Scherman at the University of Cambridge. For his PhD work, Eric was the recipient of the Jon Weaver PhD prize from the Royal Society of Chemistry and a Graduate Student Award from the Materials Research Society. Upon graduating from Cambridge, he was awarded a National Research Service Award from the NIBIB and a Wellcome Trust Postdoctoral Fellowship to work with Prof. Robert Langer at MIT. Eric's research at Stanford focuses on the development of biomimetic polymeric materials that can be used as tools to better understand fundamental biological processes and to engineer advanced healthcare solutions. His research has led to more than one hundred publications and 35 patents. He has been awarded young faculty awards from the Hellman Foundation, American Diabetes Association, American Cancer Society, and PhRMA Foundation. Eric received the IUPAC Hanwha-TotalEnergies Young Polymer Scientist Award in 2022 and the Society for Biomaterials Young Investigator Award in 2023.

mRNA vaccine against malaria tailored for liver-resident memory T cells

Gavin F. Painter[*1, 2], Mitch Ganley[1,2], Lauren E. Holz[3], Jordan J. Minnell[4], Sarah L. Draper[1], Olivia K. Burn[4], Regan J. Anderson[1], Benjamin J. Compton[1], Andrew J. Marshall[1], David F. Ackerley[2,5], Ian F. Hermans[2, 4], William R. Heath

[1]Ferrier Research Institute, Victoria University of Wellington, Lower Hutt, New Zealand.
[2]Maurice Wilkins Centre for Molecular Biodiscovery, Auckland, New Zealand.
[3]Department of Microbiology and Immunology, The Doherty Institute for Infection and Immunity, The University of Melbourne, Australia.
[4]Malaghan Institute of Medical Research, Wellington, New Zealand.
[5]School of Biological Sciences, Victoria University of Wellington, Wellington, New Zealand.

With the advent of the COVID-19 pandemic, vaccines based on mRNA have made a major impact on the prevention of human death and suffering. In contrast, malaria has increased its contribution to human morbidity and mortality, with various intervention strategies negatively impacted by the pandemic. Development of a highly effective malaria vaccine is still a major goal. With the recent identification of liver tissue-resident memory T (Trm) cells as crucial effectors for the control of liver stage Plasmodium infections we embarked on a strategy to develop an mRNA-based vaccine to prevent malaria. Here, we show that while a standard mRNA vaccine could effectively induce circulating T cells, this approach was unable to generate liver Trm cells and failed to protect against challenge with Plasmodium sporozoites in mice. However, addition of an agonist for type I Natural Killer T (NKT) cells, modified to effectively recruit NKT cell help under mRNA-vaccination conditions, showed efficient induction of liver Trm cells and was highly protective against parasite challenge in mice. Protection could be mediated by vaccination with both model and authentic parasite antigens and was dependent on liver Trm cells. Moreover, while prior exposure to blood-stage infection (as occurs in malaria-endemic regions) impaired traditional liver-stage vaccines, mRNA vaccination was unaffected. We therefore describe a rational mRNA-based approach for potent induction of liver Trm cells and the prevention of malaria, with potential for application to malaria-endemic regions.

Biography

Professor Painter obtained his PhD in chemistry from the University of Otago in 1995 (synthetic methodology) which was followed by postdoctoral research at the University of Cambridge (the synthesis of inositol phospholipids for the elucidation of PI3K pathways). Since joining the Ferrier Research Institute in New Zealand his research laboratory has focussed on the synthesis of lipid-based materials including phosphatidyl inositol mannosides, glycolipids, glycolipid-peptide conjugates and novel lipid nano-delivery vehicles for encapsulation of various vaccine components including RNA, peptides, glycolipids and various immune stimulates.

Professor Painter has a strong interest in the immunological evaluation of vaccines and vaccine components. He holds a joint position with the Malaghan Institute of Medical Research Wellington New Zealand incorporating multiple national and international collaborations with immunologists.

Development of saponin-based adjuvant IA-05 for subunit-vaccines

Pi-Hui Liang[1,2]
[1]Professor, School of Pharmacy, National Taiwan University
[2]Founder and CEO of ImmunAdd, Inc. Taipei, Taiwan

Saponin adjuvants are potent immune stimulators and important essential components of clinically-advanced infectious disease vaccines, including those against shingles, malaria, COVID-19, influenza, and cancer, combined sales of billions of dollars. Existing saponin adjuvants are limited by inefficient manufacturing. They are unsustainably sourced from the inner lining of the bark of the *Quillaja Saponaria* tree, which grows only in parts of South America. IA-05 is a fully synthetic, rationally designed, saponin-based small molecule vaccine adjuvant which that has demonstrated improved tolerability and elicited improved enhanced immune responses compared with QS-21 in influenza, HBV, and anti-cancer vaccines. In addition, IA-05 is stable and can work without complicated formulation and low toxicity in animals. Our novel saponin-based adjuvant IA-05 can provide a high-demand key ingredient used in vaccine manufacturing.

Biography

Dr.-Hui Liang obtained her Ph.D. in Pharmacy from National Taiwan University (NTU), Taiwan. After a short stay in Formosa Lab as a research chemist and pharmacist, she joined Prof. Chi-Huey Wong's laboratory as a postdoctoral fellow at The Genomics Research Center and the Scripps Research Institute. She started her independent career as an Assistant Professor of Pharmacy at NTU in August 2008. The major interest of her lab is new drug discovery. In the past 15 years, her group focus on developing chemical and enzymatic methods to create various saponin libraries as anticancer/antivirus agents/immune-modulating agents. She published more than 100 peer review articles and patents.

Dr. Liang has received multiple awards-including National Innovation Awards, Award of industry-academia collaboration from the National Science and Technology Council (NSTC) in Taiwan, Wu Ho-Su Medical Award from Taiwan Bio Development Foundation, Future Tech Break-Through Award from NSTC, Young Scholar Award from NSTC and several excellent teaching/mentoring awards from NTU. Dr. Liang has been the advisory committee of New Drug Evaluation/Orphan Drug Evaluation of Taiwan FDA for 4 years.

For the development of saponin-based vaccine adjuvant, she found ImmunAdd Inc. in 2022 and then be the CEO of ImmunAdd in Oct. 2023.

SCIENTIA MEETINGS

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HIV Vaccine

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HIV Vaccine

Title: **Induction of CD4-mimicking HIV-1 broadly neutralizing antibody precursors in macaques with protein and mRNA vaccination**
Kevin O. Saunders
Duke Human Vaccine Institute

Title: **HIV clade C vaccine adjuvanted with NE/AS01B in SHIV-challenged macaques**
Siddappa N. Byrareddy
University of Nebraska Medical Center

Title: **Vaccination with immune complexes modulates the elicitation of functional antibodies against HIV-1**
Catarina Hioe
Icahn School of Medicine at Mount Sinai

Title: **Antiviral vaccine route and form potently impact immunogenicity and efficacy**
Mark Connors
NIAID/LIR

Title: **Synergy between tissue resident memory CD8 T cells and antibody for protection against HIV**
Rama Rao Amara
Emory National Primate Research Center

Induction of CD4-mimicking HIV-1 broadly neutralizing antibody precursors in macaques with protein and mRNA vaccination

Kevin O. Saunders
Duke Human Vaccine Institute, Duke University School of Medicine, USA
Department of Surgery, Duke University School of Medicine, USA
Department of Immunology, Duke University School of Medicine, USA
Department of Molecular Genetics and Microbiology, Duke University School of Medicine.

The CD4 binding site (CD4bs) is a conserved epitope on HIV-1 envelope (Env) that can be targeted by protective broadly neutralizing antibodies (bnAbs). HIV-1 vaccines have not elicited CD4bs bnAbs for many reasons, including the CD4bs is occluded by glycans, immunogen expansion of appropriate naïve B cells, and selection of functional antibody mutations. The first step in the process of eliciting HIV-1 bnAbs is the engagement of antibody precursors with correct epitope specificity and structural elements to cross-react with diverse HIV-1 envelopes. Here, we demonstrate immunization of macaques with a CD4bs-targeting immunogen elicits neutralizing bnAb precursors with structural and genetic features of CD4-mimicking bnAbs. Structures of the CD4bs nAbs bound to HIV-1 Env demonstrated binding angles similar to human bnAbs and heavy chain second complementarity determining region-dependent binding characteristic of all known human CD4-mimicking bnAbs. Macaque nAbs were derived from variable and joining gene segments orthologous to the genes of human V_H1-46-class bnAbs. Stabilization of the HIV envelope immunogen enabled translation into a lipid nanoparticle encapsulated nucleoside modified mRNA vaccine (mRNA-LNP). The mRNA-LNP technology was used to express either transmembrane envelope or envelope trimer nanoparticles. Immunization of humanized immunoglobulin knock-in mice and macaques with the mRNA-LNP HIV-1 envelope vaccine initiated CD4bs bnAbs precursors and serum neutralizing antibodies. This vaccine study initiated the B cells from which derive CD4bs bnAbs in primates with protein or mRNA-LNP vaccination, accomplishing the key first step in development of an effective HIV-1 vaccine.

Biography

Dr. Kevin O. Saunders graduated from Davidson College in 2005 with a Bachelor of Science in Biology. At Davidson College, he trained in the laboratory of Dr. Karen Hales identifying the genetic basis of infertility. Dr. Saunders completed his doctoral research on CD8+ T cell immunity against HIV-1 infection with Dr. Georgia Tomaras at Duke University in 2010. He subsequently trained as a postdoctoral fellow in the laboratories of Drs. Gary Nabel and John Mascola at the National Institutes of Health NIAID Vaccine Research Center. In 2014, Dr. Saunders joined the faculty at the Duke Human Vaccine Institute and is currently an Associate Professor with Tenure in the Department of Surgery. He was subsequently appointed as the Duke Human Vaccine Institute Director of the Laboratory of Protein Expression and Associate Director of the Duke Human Vaccine Institute. Dr. Saunders has given invited lectures at international conferences such as HIVR4P and the Keystone Symposia for HIV Vaccines. He has authored book chapters and numerous journal articles, and holds patents on vaccine design concepts and antiviral antibodies. His current research interests include vaccine and antibody development to combat viral infections.

HIV clade C vaccine adjuvanted with NE/AS01B in SHIV-challenged macaques

Michellie Thurman[1], Viswanathan Chokkavelu[2], Samuel D Johnson[1,3], Omalla A Olwenyi[1,3], Morgan Johnston[1], Kabita Pandey[1,3], Jianshi Yu[4], Samson Adeniji[5], Kai Ying Hong[5], Hongmei Gao[6], David Montefiori[7], Pam Wong[8], James R. Baker, Jr[8]. Francois Villinger[9], Mohamed Abdel-Mohsen[5], Maureen Kane[4], Siddappa N. Byrareddy[*1,6,]

[1]Department of Pharmacology and Experimental Neuroscience, University of Nebraska Medical Center, USA
[2]Clinical Infectious Unit, Fort Myers, Florida, USA
[3]Department of Pathology and Microbiology, University of Nebraska Medical Center, USA
[4]Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, USA
[5]The Wistar Institute, USA
[6]Department of Genetics, Cell Biology and Anatomy, University of Nebraska Medical Center, USA
[7]Department of Surgery, Duke University, Duke University, Durham, NC, USA
[8]Michigan Nanotechnology Institute, for Medicine and the Biological Sciences, USA
[9]New Iberia Research Center, University of Louisiana at Lafayette, USA

Background: HIV is primarily transmitted through the mucosal route, and advancements in antiretroviral therapy have rendered the infection manageable, though not without co-morbidities and accelerated aging. Here, we tested the hypothesis that combining gut homing cell-mediated immunity with nanoemulsion (NE) adjuvant and humoral immunity with AS01B would elicit robust immune responses and protect against SHIV infection.

Methods: Four RMs were initially immunized with clade C HIV gp140 envelope glycoprotein and SIVmac239 P55 Gag and Nef antigens delivered in 3x Pure Soybean oil-nano emulsion and AS01B mucosal adjuvants intranasally and subsequently boosted IM and subQ. Both vaccinated and naïve control macaques (n=3) were challenged intrarectally with repeated low-dose SHIV.

Results: Vaccinated macaques developed potent gag-specific lymph node CD107a+ responses in CD4+ (all $P>0.05$ but <0.07) and PBMC CD8+ T cells ($P=0.057$), as well as robust CD8+ gag IFNγ responses within axillary and inguinal lymph nodes ($P<0.05$), and CD8+ gag TNF α+ responses within inguinal lymph nodes ($P<0.05$). We did not observe robust neutralizing antibodies, but significant ADCD and ADCP-induced responses were observed ($P<0.01$). Next, increased mucosal but not plasma retinoic acid signaling was observed in vaccinees. Additionally, control monkeys experienced acute SHIV infection-associated dysbiosis not seen in vaccinated monkeys. Immunization did not protect completely against SHIV infection; however, vaccinated animals had significantly reduced viral loads in the plasma ($P=0.003$), CSF ($P=0.001$), and reduced levels in the gut.

Conclusions: Our studies demonstrate that the gut-homing properties of the NE adjuvant may serve as a valuable mucosal adjuvant strategy in future HIV vaccine design.

Biography

Our laboratory focuses on understanding host-virus dynamics using molecular biology, virology, immunology, systems biology, and genomic tools to develop prevention strategies for HIV/AIDS and other infectious diseases such as SARS-CoV-2 and Zika virus. We use non-human primate models most often for *in vivo* studies, while also using small animal models. Our long-term goal is to set up well-controlled clinical cohorts in tandem for testing the disease outcomes in relevant animal models as a synergistic platform for preclinical development of vaccines/therapeutics.

Vaccination with immune complexes modulates the elicitation of functional antibodies against HIV-1

Catarina E. Hioe[*1,2], Xiaomei Liu[1], Andrew N. Banin[1], Daniel W. Heindel[1], Jéromine Klingler[1], Priyanka G. Rao[1], Christina C. Luo[3], Xunqing Jiang[3], Shilpi Pandey[4], Tracy Ordonez[4], Philip Barnette[4], Maxim Totrov[5], Jiang Zhu[6], Arthur Nádas[7], Susan Zolla-Pazner[1], Chitra Upadhyay[1], Xiaoying Shen[8], Xiang-Peng Kong[3], Ann J. Hessell[4]

[1]Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, USA
[2]James J. Peters VA Medical Center, USA
[3]Department of Biochemistry and Molecular Pharmacology, New York University Grossman School of Medicine, USA
[4]Division of Pathobiology and Immunology, Oregon National Primate Research Center, Oregon Health and Science University, USA
[5]Molsoft L.L.C., USA
[6]Department of Integrative Structural and Computational Biology and Department of Immunology and Microbiology, The Scripps Research Institute, USA
[7]Department of Environment Medicine, New York University Grossman School of Medicine, USA
[8]Division of Surgical Sciences, Department of Surgery, Duke University School of Medicine, USA

Neutralizing antibodies (Abs) are one of the immune components required to protect against viral infections. However, developing vaccines capable of eliciting neutralizing Abs effective against a broad array of HIV-1 isolates has been an arduous challenge. This study sought to test vaccines aimed to induce Abs against neutralizing epitopes at the V1V2 apex of HIV-1 envelope (Env). Four groups of rabbits received a DNA vaccine expressing a trimeric V1V2-scaffold along with a protein vaccine consisting of a re-engineered gp140 Env trimer or a V1V2-scaffold protein, and their respective immune complexes (ICs). These IC vaccines were made using a V1V2-specific monoclonal antibody, which induces steric and allosteric changes on V1V2. Rabbit groups immunized with the DNA vaccine and uncomplexed or complexed gp140 proteins (DNA/gp140-UC or IC) displayed similar profiles of Env- and V1V2-binding Abs, but differed from the rabbits receiving the DNA vaccine and uncomplexed or complexed V1V2-scaffold proteins (DNA/V1V2-UC or IC), which generated more cross-reactive V1V2 Abs without detectable binding to gp120 or gp140 Env. Notably, the DNA/gp140-UC vaccine elicited neutralizing Abs against some heterologous tier 1 and tier 2 viruses from different clades, albeit at low titers and only in a fraction of animals, whereas the DNA/V1V2-UC or IC vaccines did not. In comparison with the DNA/gp140-UC group, the DNA/gp140-IC group showed a trend of higher neutralization against the V1V2 apex and a greater potency of V1V2-specific antibody-dependent cellular phagocytosis (ADCP) but failed to neutralize heterologous viruses. These data demonstrate the capacity of DNA/gp140, but not DNA/V1V2, vaccines to elicit homologous and heterologous neutralizing activities in rabbits. The elicitation of such activities was modulated by the delivery of ICs, indicating the modulatory effects of ICs on the generation of functional antibodies against HIV-1.

Biography

Catarina E. Hioe, PhD, has been a principal investigator since 1998. She initiated her independent research at the Manhattan VA and New York University Medical Center. She is now Professor of Medicine/Infectious Diseases at Mount Sinai School of Medicine and a research career scientist at the Bronx VA. Dr. Hioe has established a basic and translational research program in the field of viral immunology. Her current research focuses on studying the molecular and functional properties of antibodies against HIV-1 and SARS-CoV-2. Dr. Hioe's laboratory has received continuous supports from VA Merit Review Awards, VA Research Career Scientist Awards, NIH grants, and non-federal funding sources.

Antiviral vaccine route and form potently impact immunogenicity and efficacy

Mark Connors
Chief, HIV-Specific Immunity Section
NIAID/LIR

There are a number of reasons that replication-competent viral vaccines are commonly more immunogenic than replication-incompetent vectors in humans. First, there is the potential for greater total antigen dose. In addition, they provide prolonged protein expression, which is likely critical to the development of effective cellular or humoral immunity. Importantly, this expression persists until it is terminated by an effective immune response. Live vectors also induce proinflammatory cytokines and costimulatory molecules that function as adjuvants to improve immunogenicity. In some cases they replicate in the epithelium of the upper respiratory tract or gut, offering the potential to induce cellular and humoral mucosal immune responses. Our laboratory is using virus-like particle immunization of animals to understand the features of a live virus infection (eg. dose, conformation, valency, adjuvants, TLR agonists) that contribute the most to immunogenicity and durability to vaccines for influenza virus, HIV, and SARS-CoV-2. These results will be discussed in the context of results from 5 clinical trials of replicating adenoviral vectors in humans.

Biography

Dr. Connors received his M.D. from Temple University and was trained in pediatrics at Tufts New England Medical Center. He joined the NIAID Laboratory of Infectious Diseases in 1989 to study the immune response to respiratory syncytial virus. He was trained in infectious diseases at the National Institutes of Health Clinical Center and at the Children's Hospital of Philadelphia. He joined the Laboratory of Immunoregulation in 1994 to study the human immune response to HIV. Dr. Connors has published a series of discoveries that have laid the framework for current understanding of immunologic control of HIV in some rare patients and loss of immunologic control in the majority of infected patients.

Synergy between tissue resident memory CD8 T cells and antibody for protection against HIV

Rama Rao Amara
Emory National Primate Research Center, Emory University, USA

We recently demonstrated that an intravenous heterologous viral vector (HVV) vaccination consisting of sequential immunization with VSV, vaccinia and Ad5 viral vectors that is designed to induce strong T-RMs against SIV Gag markedly enhances the durability of protection against intravaginal SHIV challenges mediated by a protein vaccination. In this study we compared the T-RMs induced by DMC Gag vaccine (DNA, modified vaccinia Ankara and chimpanzee adenovirus) with HVV Gag vaccine in Mamu A*01 positive macaques. The DNA was delivered via IM and viral vectors were delivered via either IM (DMC-IM) or IV (DMC-IV) routes.

The Gag-specific CD8 T cells were measured using Gag CM9 tetramer in blood, rectum and vagina longitudinally after each vaccination, and were phenotyped for expression of markers associated with proliferation, cytolytic function, tissue migration and memory differentiation.

All three vaccination regimens induced strong Gag specific CD8 T cells in blood, rectum and vagina. However, the HVV vaccination induced 5-10-fold higher frequency in tissue, and these cells showed better persistence (less than 2-fold decline over 3 months) compared to DMC vaccination. The HVV vaccine induced CD8 T cells also showed higher cytolytic potential. The CD8 T cells induced by IV vaccination showed higher CXCR3 and CD69 expression at mucosal tissues compared to cells induced by IM vaccination.

HVV vaccination induces CD8 T-RM that are distinct from T-RM induced by DMC vaccination, and the route of vaccination significantly influences the functional quality of T-RM.

Biography

Dr. Amara is a Charles Howard Candler Professor in the Department of Microbiology and Immunology, Emory Vaccine Center, Emory National Primate Research Center of Emory University. He received his Ph.D. from the Indian Institute of Sciences, Bangalore, India and did his postdoctoral fellowship at Emory University. His research is focused on the development of vaccines for infectious diseases such as HIV, SARS-CoV-2 (COVID-19), HCV and Tuberculosis. Amara's lab has pioneered the heterologous prime/boost vaccination approaches using DNA, modified vaccinia Ankara (MVA) and novel protein immunogens for vaccine delivery. A HIV vaccine based on these vectors was shown to be safe in healthy human volunteers and completed phase 2 studies in humans. Newer versions of this vaccine are under development and showed promise in the macaque model. More recently, Amara's laboratory developed MVA and RBD-trimer based vaccines for COVID-19 and these vaccines showed promise in the NHP model. The MVA-COVID-19 vaccine is being manufactured in India for human testing. In addition, Amara's lab is developing novel vaccination strategies to induce a strong mucosal antibody response and tissue resident memory CD8 T cells. Amara's lab is also developing novel therapies for HIV by targeting the PD-1 co-inhibitory pathway combined with therapeutic vaccination. He published more than 130 peer-reviewed manuscripts and received multiple grants from NIH.

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