2021 ISV Annual Virtual Congress

The 2021 Annual Virtual Congress featured three keynote lectures by Drs. Ian Lipkin (Columbia University), Peter Hotez (National School of Tropical Medicine, Baylor College of Medicine) and Albert Osterhaus (University of Veterinary Medicine, Hannover), fourteen invited lectures, six oral abstracts selected from 39 poster submissions, four master classes and five “meet the fellows” sessions discussing a broad range of vaccine development-related topics.

Approximately 530 people registered for the meeting, and about 11,000 webinar and poster clicks occurred during the actual meeting. Registrants were able to continue to access all conference materials until the end of December 2021. Thereafter, selected material was posted on ISV social media channels.

The general conference format was as follows: the day started with an overview by one of the conference chairs (theme of the day), followed by a keynote address and a combination of two prerecorded session tracks and subsequent interactive “live” Q&A sessions moderated by session chairs, intertwined with selected poster presentations, master classes, or meet the fellow sessions.

The four prerecorded master classes on T-cell immunity by Katherine Kedzierska (University of Melbourne), Innovation & Manufacturing of Covid vaccines by Barry Buckland (BiologicB), Vaccine Characterization and Analytics by Indresh Srivastava (Novavax) and The Concepts of GCP by Janet Rose Rea (Independent Consultant) were new this year. Also, new were the prerecorded meet the (ISV) fellows’ sessions featuring conversations between newly elected fellows and established fellows and one bonus session on “Everything you always wanted to know about ISV.”

This commentary provides highlights of the meeting and summarizes the recurring themes across various presentations.

Keynote lectures

In the first keynote address Dr. Ian Lipkin presented his vision for ending pandemics. After a brief introduction highlighting our vulnerability to pandemic risk and the urgency of addressing the challenges of climate change, food security, and the viral dissemination of misinformation, Dr. Lipkin focused on available tools to recognize threats to public health early. These tools include new molecular diagnostic platforms, investments in wildlife, domestic animal, and human microbial surveillance, and the advent of social media tools that mine the world wide web for clues to outbreaks of infectious disease. A global public health consortium composed of ministries of health and academic institutions has been established to better prepare for future pandemics. This program will focus on creating an infectious disease epidemiology network and has three main objectives: (1) develop a model rationalizing and extending the goals of the International Health Regulations established by the WHO in 2005 by providing inexpensive, rapid tools for diagnosis, discovery, and surveillance of infectious diseases, (2) identify and prioritize infectious agents based on pandemic risk, and (3) share data and build the infrastructure needed to produce, validate and implement drugs and vaccines to reduce morbidity and mortality. A commentary authored by Dr. Lipkin can be found in this issue.

The second keynote address was delivered by Dr. Peter Hotez, who recently authored a book on preventing the next pandemic with the subtitle vaccine diplomacy in a time of antiscience. Dr. Hotez highlighted drivers like war and conflict, poverty, urbanization, climate change, and a new troubling anti-science/anti-vaccination outlook that have resulted in a significant return of epidemic infectious diseases like polio and measles, culminating in COVID-19. He argued that we can—and must—rely on vaccine diplomacy to address this new world order in disease and global health. Tremendous progress made by vaccination of children around the world, for example, during the past two decades the number of children dying of a measles infection has been reduced from 500,000 to 70,000 per year. However, vaccine hesitancy is interfering with the success of vaccination campaigns. Dr Hotez became involved with the anti-vaccine/antisience world when he authored a book entitled: “vaccines did not cause Rachel’s autism or autism spectrum disorder” about his daughter who suffers from autism. The antivaccine movement started with the MMR vaccine and thimerosal being responsible for autism, and when science proved this theory wrong, alum and spacing of vaccines were substituted as being responsible for autism, followed by the theory that HPV vaccine caused infertility and autoimmunity or chronic illness. The health freedom movement in California resulted in a measles outbreak. In Texas alone over 70,000 children have non-medical vaccine exceptions (and that does not include the 200,000 children that are home schooled). Dr. Hotez concludes that the recent COVID outbreak has resulted in globalization of the antivaccine movement that will require an ambitious counteroffensive.

The final keynote address by Dr. Albert Osterhaus focused on preparing for the next pandemic using a one health approach. Around the beginning of the past century
infectious diseases caused about fifty percent of human deaths in the western world. In the following decades, this decreased to less than a few percent, largely due to the implementation of sewage installment and development of clean drinking water systems but also because of the development of vaccines and antimicrobials. This success prompted policymakers and scientists to predict that infectious diseases of humankind and of their domestic animals would eventually be brought under control in the industrialized world. Paradoxically, the following decades confronted the world with an ever-increasing number of emerging or reemerging infectious diseases, some causing true human or animal pandemics. Pathogens spilling over from wildlife reservoirs, either directly or via intermediate hosts, were the basis of most of these epidemics and pandemics. Striking examples in humans started with the emergence of AIDS from chimpanzees, pandemic influenza from birds and pigs to be followed by Ebola, SARS, MERS, and, most recently, COVID-19 from bat reservoirs. As identified by other speakers a complex mix of predisposing factors in our globalizing world, linked to major changes in our societal environment and global ecology, collectively created opportunities for viruses to infect and adapt to new animal and/or human hosts. Understanding the underlying processes may eventually lead to better preparedness for outbreaks in humans and animals. Importantly, the increased emergence of viral infections is largely paralleled by medical, veterinary, technological, and scientific progress, continuously spurred by our never-ending drive to combat pathogens. The most recent example is the unprecedented speed with which COVID-19 vaccines were developed.

**Plenary sessions**

The first plenary session on new vaccines on the horizon featured three presentations and was chaired by David Weiner (The Wistar Institute) and Sanjay Phogat (GSK).

Jon Heinrichs presented Sanofi Pasteur’s (SP) and AstraZeneca’s (AZ) respiratory syncytial virus (RSV) immunization approaches for infants and children. RSV is the leading cause of bronchiolitis and hospitalization in infants and continues to be an important cause of visits to healthcare providers through a child’s first years of life. Despite more than half a century’s efforts, no vaccine has been licensed for prevention of RSV and no preventative options exist for all infants. SP and AZ have tested an antibody targeting the pre-fusion F protein (nirsevimab) with an increased half-life compared to the existing licensed monoclonal (Synagis). The goal is to provide protection for an entire RSV season for all infants entering their first RSV season, and for children with congenital heart disease or chronic lung disease entering their first and second RSV seasons. This antibody has now demonstrated its ability to protect infants from medically attended lower respiratory tract infection caused by RSV in two large late-stage clinical studies. To further protect all children for their second RSV season and beyond, SP is also evaluating an intranasally-delivered live-attenuated RSV vaccine (NS-2 deleted) in collaboration with the National Institute of Health. This vaccine has been demonstrated to be safe and well-tolerated and preliminary data suggest that this approach may be highly effective in prevention of serious RSV disease in children. These two approaches will, if successful, provide complementary methods to protect infants and children during their most vulnerable period of life. This issue includes a paper from Michelle Roberts et al, that describes the approach in greater detail.

Florian Krammer (Icahn School of Medicine at Mount Sinai) spoke about next-generation vaccines to prevent influenza based on the hemagglutinin (HA) stalk and neuraminidase (NA). Licensed influenza vaccines stimulate immune responses to the globular head domain of the HA protein. New vaccine formulations are required in most years because this domain is highly variable across strains. The proposed vaccine strategy induces immunity to the highly conserved stalk domain by using chimeric hemagglutinin constructs that express unique head and stalk combinations. These conserved stalk antibodies are not induced or boosted by the licensed vaccines. In addition, NA remains an insufficiently explored better conserved antigen that has a lot of potential to provide a more universal influenza vaccine. rNA constructs with tetramerized domains provided good protection in mouse and guinea pig models.

Michael Princiotta (EpiVax Therapeutics) talked about personalized cancer vaccines. Rapid and accurate identification of non-synonymous mutations present in tumor cells, but not expressed by non-cancerous tissues, is now feasible thanks to advances in whole-exome sequencing. The main challenge to producing effective therapeutic neoantigen vaccines is the identification of peptides that will result in effector T cell responses able to control tumor growth. EpiVax Therapeutics selects tumor associated neoantigens by using a novel predictive algorithm called Ancer™. This algorithm selects neoantigens for recognition by both CD8+ and CD4+ T cells and removes potentially suppressive Treg and cross-reactive self-like epitopes. The presentation focused on how Ancer™ is being developed as an immunotherapy for the treatment of patients with cancer.

The second plenary session on new developments in technology was chaired by Lenny Moise (EpiVax) and Amy Espeseth (Merck) also included three presentations.

The first by Neil King (Institute for Protein Design, University of Washington) focused on the computational design of nanoparticle vaccines for influenza viruses, coronaviruses, and beyond. The speaker presented their two clinical-stage nanoparticle immunogens (for SARS-CoV-2 and influenza) as examples of the improved potency and breadth that can be elicited by computationally designed nanoparticle vaccines.

Colin Poutin’s (Monash University) presentation was on delivery of mRNA Vaccines. The COVID-19 pandemic has offered an ideal opportunity to test the potential of mRNA
vaccines. Lipid nanoparticle (LNP) technology has been a vital part of the success of the mRNA vaccines. An important aspect of mRNA vaccine design is how to best optimize the level and quality of innate immune responses that are necessary to stimulate adaptive immunity but can work against translation of the mRNA. The relative contributions of the RNA (whether native RNA or modified RNA) and the LNP, as a function of dose and lipid chemistry, are important topics for future research. Optimizing the biodistribution of the LNPs will also play a vital role in design of improved vaccines.

The third by Angus Forster (Vaxxas) was about the future of needle-free vaccination. Vaxxas’ High Density Micro-Projection Array Patch (HD-MAP) is a vaccine delivery technology that targets the abundant immune cells present in the top layers of the skin. The technology is based on a small patch, covered in a high-density of micro-projections which are coated with dried vaccine formulation. When applied to the skin using an integrated single-use applicator, the micro-projections penetrate the stratum corneum to deliver vaccine to the epidermis and upper dermis generating improved immune responses compared to needle and syringe in preclinical and recent clinical studies. Global pandemic vaccination efforts have highlighted the need for significantly improved approaches to vaccination; technologies that simplify vaccination, improve vaccine thermostability and provide alternative distribution channels. The talk covered the development status of Vaxxas’ HD-MAP technology, challenges – with a focus on manufacturing scale-up and opportunities especially in pandemic response. A commentary discussing the presented work is included in this issue.

The third plenary session on vaccine manufacturing and quality control was chaired by Linda Lua (Queensland University) and Indresh Srivastava.

Mireli Fino and her colleagues David McNally and Rashmi Prasad from Mass Biologics spoke about how they leverage vaccine manufacturing and quality control platforms for new modalities at Mass Biologics. The take home message from their presentation was that new modalities can benefit from the systems built in their organization to support legacy biologics. This can result in substantial time and cost savings for new products in development.

The talk by Sergio Valentinotti (Liomont) and Esteben Coreley (mAbxience) discussed challenges and opportunities of vaccine production in emerging economies. Briefly, mAbxience and Liomont are two Latin American pharmaceutical laboratories that are involved in the local production of the AstraZeneca Covid-19 vaccine. The speakers described how this consortium was created and the critical factors that were necessary to make this collaboration possible, including the active participation of AstraZeneca and support of the Carlos Slim foundation. The goal is to have a regional vaccine production program and some of the challenges that need to be overcome for this to become a reality were presented.

The fourth session was on regulation in times of pandemics & vaccine hesitancy chaired by Laura Palomares (National Autonomous University of Mexico) and Lars Frelin (Karolinska Institutet) and included a talk by Rogerio Gaspar (WHO, Director of Regulation and Prequalification) who discussed global regulation in challenging times. The emphasis during this talk was on the importance of global cooperation between regulators and the private sector, and regulatory science. Dr. Gaspar anticipates that two factors will become critical within the next few months: protein-based vaccines and an equitable distribution of the vaccine (example: booster doses without a clear basis of efficacy vs. providing vaccine to health care workers in developing world countries). The delivery technology for mRNA vaccines was new for use in humans; however, regulatory guidance documents were already available since 2008 and were used to enable an accelerated response to the pandemic. WHO recommends that only severe disease or death not infection or mild disease should be used to make decisions on whether new vaccines are needed to combat variant viruses.

The fifth session “One World; One Health Veterinary Vaccines” was chaired by Alejandro Gil (Sinergium) and Randy Albrecht (Icahn School of Medicine at Mount Sinai) and included three speakers.

Cyril Gay (USDA ARS) gave a nice overview of the research and development of veterinary vaccines from a biodefense and one health perspective. He provided two examples of important veterinary vaccines Foot and Mouth Disease (FMD) and African Swine Fever for which there is no vaccine available at this time. Veterinary vaccines are important for biodefense and there is a need to establish animal health research laboratories dedicated to delivering medical countermeasures to address emerging infectious diseases. Scientific discovery is delivering promising new vaccine candidates, tools and technologies to tackle infectious diseases.

Madhaven Nallani (ACM Biolabs) discussed a next-generation vaccine platform with polymersomes as stable nanocarriers for a highly immunogenic and durable SARS-CoV-2 spike protein subunit vaccine. ACM is working on developing subunit vaccines based on the spike protein of Porcine Epidemic Diarrhea Virus, a coronavirus that affects swine, causing diarrhea and vomiting, and death of 50–100% of infected piglets and applied the lessons learned for developing a SARS-CoV-2 vaccine. Polymersomes have an ability compartmentalize antigens and adjuvants in the aqueous compartment and serve as antigen delivery vehicles that are efficiently taken up by DC1 and DC2, the key initiators of the adaptive immune response. The immunological effect of ACM polymersomes on different SARS-CoV-2 spike proteins, namely the ectodomain of the spike protein, the S2 domain only, and a trimeric spike protein demonstrated strong immunogenicity and robust and durable humoral and cellular immunity against SARS-CoV-2 in C57BL/6 mice that persist for at least 40 days.
This session concluded with a presentation by Andres Wigdorovitz (INTA -CONICET- Bioinnova SA) who provided two examples of innovation in veterinary vaccines: virus like particles FMD and a targeted vaccine for Bovine diarrhea virus (BVD). FMD is a highly contagious viral disease of cloven-hoofed animals, which causes severe economic losses and has global importance. A novel vaccine against FMDV is desirable considering primarily the costs and regulatory concerns associated with the high biosecurity facilities required for production of the inactivated vaccine. Their FMD vaccine candidate is based on transient gene expression in 293-6E cells. The resulting FMD virus-like particles (VLPs) induce immunity in mice, cattle and pigs. BDV is also an important cause of economic loss within bovine herds worldwide. Vedevax Bock is the first subunit recombinant vaccine approved against BVD virus, a disease that affects a large part of cattle herds. It is made using a different approach than traditional vaccines: it combines the E2 glycoprotein of the virus with the APCH antibody that has an affinity for the immune system. This mechanism greatly increases its effectiveness. Trials were carried out with more than 7,000 dairy cattle breeding in different establishments with different sanitary conditions. In conclusion, the Vedevax Block vaccine was highly immunogenic under field conditions, making it a useful tool to reduce the productive and reproductive losses associated with infection by the BVD virus.

The sixth and final plenary session on Global Health & Vaccine Development chaired by Linda Klavinskis (King’s College London) and Nathalie Garcon (BioAster) featured two speakers.

Subhash Kapre (Inventprise) described his case study of setting up a research unit, the efforts of converting the unit into a manufacturing company, and the challenges faced. Dr. Kapre founded Inventprise in 2012 with the goal of improving global health by focusing on developing efficacious, affordable vaccines for global populations most in need. The company received substantial financial support from the Bill & Melinda Gates Foundation that funded development of a cost-effective pneumococcal vaccine. Over the years, the company has grown from a small R&D lab, operating out of a start-up accelerator in South Lake Union, Seattle, to a clinical-stage biotech organization with multiple production locations with a goal of commercializing the novel vaccine candidates. A paper authored by Dr. Kapre is included in this special edition.

Peter Dull (Bill & Melinda Gates Foundation) presented on Correlates of Protection for COVID-19: What We’ve Learned So Far. The identification of correlate of protection for COVID-19 is critically important for product development, regulatory authorities and policy makers as it would accelerate licensure of new vaccines and provide guidance for better use of the existing vaccines. It has been shown that both binding and neutralizing antibodies are relevant biomarkers for protection. However, new results from preclinical, natural history and vaccine efficacy studies are being generated continuously. The talk summarized the information collected, highlighted gaps that necessitate cautious interpretations of where we stand and provide a look forward to where additional studies might provide more clarity.

**Oral abstracts**

Selected poster presentations included two talks on vaccines against SARS-CoV-2: the first by Kevin Liaw (The Wistar Institute) was on DNA delivery of a SARS-CoV-2 nanoparticle vaccine driving a rapid and potent immunogenicity and achieving single-dose protection and the second by H. Christian Hong (EyeGene, INC.) was about their mRNA vaccine – a polyethylene glycol-free, liposome-based vaccine candidate EG-COVID – that induced high neutralizing antibody levels.

Naomi Pompa (University of Santo Tomas) presented on the perception of vaccination of Filipino mothers in the NCR area Post-Dengvaxia.

One selected paper focused on a new drug candidate: Jihae Choi (The Wistar Institute) showed improved protection against multidrug Pseudomonas Aeruginosa following administration of an Fc engineered DNA-encoded monoclonal antibody (DMAB).

Andrez Gutierrez (Epivax) presented T Cell Epitope content comparison (EpiCC) Analysis between PCV2 vaccines and field strains and Lauren Hook (University of Pennsylvania) presented a high throughput biosensor method to establish dosing frequency and concentration for an mRNA-LNP Genital Herpes vaccine.

**Meet the fellows**

The meet the fellow sessions provided insights in the careers of the 2020 newly elected ISV fellows through spontaneous conversations with veteran ISV fellows. David Weiner (Elected ISV Fellow 2014 & ISV Officer [The Wistar Institute] spoke with Sarah Gilbert (University of Oxford); Linda Klavinskis (Elected ISV Fellow 2017 & ISV Secretary [King’s College London]) with Xavier Saelens (Ghent University); Margaret Liu (Elected ISV Fellow 2014 & Chairman of the ISV Board [ProTherImmune] with Gary Kobinger (Laval University) and Annie de Groot (Elected ISV Fellow 2014 [Epivax]) with Tonya Villafana (AstraZeneca). The new fellows described their motivation to become scientists, how they became interested in vaccines, why they made various careers choices, and what challenges they faced along the way. In addition, fellows spoke about their “most important accomplishment, what they still want to do before they retire and shared some fun-facts. Background information on each fellow can be found on the ISV website (https://isv-online.org/isv_fellows_of_year).

The special fellow session on “everything about ISV” was moderated by Manon Cox (Elected ISV Fellow 2015 [NextWaveBio]), who interviewed ISV Officers Ted Ross (Elected ISV Fellow 2013 & President [University of
Georgia]), Denise Doolan (Elected ISV Fellow 2017 & incoming President [James Cook University]), and Shan Lu (Elected ISV Fellow 2013 & Officer [UMAS]). Each of whom introduced themselves and described their role within the ISV organization. The officers talked about how they became involved in the organization, the history of ISV, its mission and the organization, and the goals for the future. They introduced how one can get more involved in the organization, what you need to do to become a member of the organization or an elected member of the Board of Directors, how you can become a fellow, and the volunteer opportunities existing within the organization. A summary of this final session is included in this special issue. Conversations will be posted on ISV social media.

**ISV congress 2022**

The 2022 ISV congress will be held in Quebec, Canada from September 18–20, and is chaired by Joon Rhee (Elected ISV Fellow 2017 [Chonnam National University]) and co-chaired by Gary Kobinger (Elected ISV Fellow 2020 [Texas University]) and Manon Cox (Elected ISV Fellow 2015 [NextWaveBio]). This congress will likely have a hybrid format due to continued COVID uncertainty.

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