Vaccine Innovation Conference

2017

May 10, 2017
Hyatt Regency Hotel, Montréal, QC, Canada

Presented by:

Vaccine Industry Committee

Vaccine Industry Committee
Le comité de l'industrie du vaccin

Conference Chair:
Nathalie Charland, Medicago

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Kishna Kalicharran, Merck
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Andrew Potter, VIDO-InterVac
Brian Ward, McGill University

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VACCINE INNOVATION CONFERENCE PROGRAM

	Session
8:00-8:15	**Welcome** Nathalie Charland, Conference Chair
8:15-9:00	**Keynote Address: *High Efficacy Malaria Vaccines*** Adrian Hill, Nuffield Department of Medicine, Oxford University
9:00-10:15	**Emerging Diseases**
	Technologies for Improving Global Immunization Strategies Lorne Babiuk, University of Alberta (chair) ***Rapid Response to Protect Against Infectious Diseases of High Consequences*** Gary Kobinger, Laval University ***Animal Models for MERS: In Pursuit of Vaccines*** Darryl Falzarano, VIDO-Intervac ***Development of a Glycoconjugate Vaccine to Combat Disease Caused by Haemophilus influenzae type A*** Andrew Cox, National Research Council
10:15-10:30	**Break**
10:30-11:45	**Cancer Vaccines**
	The Resurgence of Cancer Vaccines John Bell, Ottawa Hospital Research Institute (chair) ***Rational Design Of Small Molecule Immune Checkpoints' Inhibitors: The PD-1 Challenge*** Khaled Barakat, University of Alberta ***Virus Synthesis as a Tool for Assembling Large Virus Vaccines*** David Evans, University of Alberta ***Driving Large T cell Responses with an Oncolytic Viral Vaccine*** Brian Lichty, McMaster University
11:45-12:30	**Lunch**

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12:30-1:15	**Keynote Address:** ***Advances in Understanding the Biology of Talimogene Laherparepvec (T-VEC)*** Howard Kaufman, Rutgers Cancer Institute of New Jersey
1:15-2:30	**Global Health Vaccines: Parasites and TB**
	Vaccines for Parasites? It's About Time! Brian Ward, McGill University (chair) ***Lung Mucosal Immunity & Mucosal TB Vaccination Strategies for Human Application*** Zhou Xing, McMaster University ***A Leishmaniasis Vaccine Breakthrough: Are we Almost There?*** Jude Uzonna, University of Manitoba ***Characterization of the Protection and Immune Response Elicited by the Immunization of Mice with Schistosoma mansoni Cathepsin B in the Presence of CpG Oligodeoxynucleotides or Montanide ISA 720 VG*** Momar Ndao, Montreal General Hospital
2:30-2:45	**Break**
2:45-3:45	**Vaccine Technologies**
	The Plant-based Proficia™ Technology, a Rapid and Efficient Platform for the Production of Influenza VLP Vaccines and Beyond Marc-André D'Aoust, Medicago (chair) ***DepoVax™: A Novel Delivery Formulation for Cancer Immunotherapy and Infectious Disease Vaccines*** Marianne Stanford, Immunovaccine ***Glycoprotein Enveloped Virus-Like Particle (eVLP) Delivery of an Optimized Form of Cytomegalovirus (CMV) Glycoprotein B (gB) Antigen for Prophylactic Vaccination Against Congenital CMV Infections*** Francisco Diaz-Mitoma, VBI Vaccines Inc.
3:45-4:45	**Panel Discussion:** ***Funding New Vaccine Development*** Kishna Kalicharran, Merck (chair) Cedric Bisson, Teralys Capital Inc. Isabelle Létourneau, Canadian Institutes of Health Research Bjørg Dystvold Nilsson, Coalition for Epidemic Preparedness Innovations (CEPI)
4:45	**Closing Remarks** Nathalie Charland, Conference Chair

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VACCINE TECHNOLOGIES

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FUNDING NEW VACCINE DEVELOPMENT

Chair: Kishna Kalicharran, Merck & Co.

PANELISTS:

Keynote Address:

Preventing Malaria Mortality: A Vaccine Solution

Adrian V.S. Hill, Director, The Jenner Institute, University of Oxford, UK

Malaria vaccine development has reached a remarkable turning point. One candidate vaccine has completed a >15,000 subject phase III trial with mixed results but is aiming for licensure. Another whole parasite approach has shown high level efficacy in the US but much lower efficacy in Africa, and the first four-stage malaria vaccine is approaching African trials.

Since 1984 the circumsporozoite protein has been a leading target for vaccine developers: GSK's RTS,S in the adjuvant AS01 induces remarkably potent antibodies to the conserved central repeat of this *P. falciparum* coat protein, with >50% efficacy in US controlled human malaria infection (CHMI) trials, but much lower efficacy in African infants. This reduced efficacy correlates with malaria-induced immunosuppression and waning of vaccine-induced antibodies with subsequent evidence of a rebound in susceptibility in children. A new better designed "R21" virus-like particle from Oxford in early stage trials shows high level efficacy pre-clinically with a less complex adjuvant and phase IIa CHMI trials will take place this year.

Liver-stage vaccines based on viral vectors and, more recently, whole sporozoites have reached African trials. Intravenously delivered irradiated sporozoites dissected from mosquitoes provide high level efficacy in US CHMI trials, but disappointingly low immunogenicity and efficacy in initial African field trials. In East African adults viral vectors have shown higher efficacy against infection. A new vectored "prime-target" immunisation strategy, based on targeting resident memory T cells to the liver, shows exceptional efficacy pre-clinically and in now entering clinical trials.

A new multi-stage programme, combining R21, viral vectors and also new subunit vaccines against the blood-stage and sexual stage of the life cycle, is currently in clinical trials with components being evaluated separately and in initial combinations. The blood-stage vaccine (Draper et al.), comprising the unusually conserved PfRH5 protein, induces cross-strain functional antibodies in phase I trials and is now in a phase IIa CHMI trial. Finally, a range of Pfs25-based candidate vaccines are in phase I testing, aiming to prevent transmission to mosquitoes; in particular a new heptamerised version in virla vectors (Biswas et al) has just reached clinical evaluation.

This remarkable progress leverages a diverse range of leading vaccine technologies and the capacity to measure efficacy in small numbers of volunteers, and suggests that a high efficacy deployable vaccine to prevent disease and death caused by *P. falciparum* should be feasible in the coming years.

Adrian Hill

Adrian V.S. Hill is Professor of Human Genetics and Director of the Jenner Institute at Oxford University. He leads research programmes in both the genetics of susceptibility to tropical infectious diseases and in vaccine development. The Jenner Institute links human vaccine research at the University of Oxford with veterinary vaccine development at The Pirbright Institute and the UK Animal and Plant Health Agency. The Institute is currently conducting Phase 1/2 trials for malaria, tuberculosis, pandemic influenza, meningitis, HCV, RSV and HIV.

His group has designed and developed candidate vaccines for malaria currently in field trials in endemic countries. His group have undertaken over fifty clinical trials to evaluate new vaccine technologies. In 2014 he led the Oxford-based trials of two candidate Ebola vaccines and rapidly demonstrated their safety and immunogenicity.

He has published about 500 research papers and is a Fellow of the UK Academy of Medical Sciences and of the Royal College of Physicians, a NIHR Senior Investigator and Wellcome Trust Senior Investigator.

Emerging Diseases

Chair: Lorne Babiuk, University of Alberta

Technologies for Improving Global Immunization Strategies

Lorne Babiuk, University of Alberta, Edmonton, AB, Canada

Vaccines have saved more lives than all other therapies for infectious diseases. This is especially true in today's environment where vaccines are having a major impact on the health of humans and animals as well as enhancing food security, especially in the developing world. New vaccine design, such as live recombinant vaccines and new formulations and delivery methods for killed or subunit vaccines will be described. For example, novel adjuvants based on their ability to modulate both the magnitude and quality (immune balance) of the immune response have been developed. These adjuvants can also act as delivery vehicles to provide mucosal immunity and eliminate the use of needles for delivery. These adjuvants are based on our understanding of the role of innate immunity and how innate immunity drives specific immune responses. Secondly, our ability to develop viral vectors that are thermostable and can carry genes from multiple pathogens provides an opportunity to control multiple diseases with a single immunization. These approaches are creating opportunity to reduce both economic losses and disease transmission between species, especially animal-human transmissions, will be described.

Lorne Babiuk
Dr. Lorne Babiuk is an internationally recognized leader in Canadian vaccine research who has devoted his career to Canadian-based research aimed at safeguarding the health of people and animals at home and abroad. The vaccines that he was involved in developing have had a significant impact on the economy as well as reduced mortality and morbidity caused by infectious diseases.

He specializes in immunology, pathogenesis, virology, molecular virology, and vaccinology, and is a world expert in infectious diseases and their control, specifically by vaccination. He has published over 500 manuscripts, awarded 42 patents, and trained over 100 PhD and post-doctoral fellows who have gone on to successful careers in academia, industry, and government.

Among his many honours, he is an Officer of the Order of Canada, a Fellow of the Infectious Disease Society of America, a Fellow of the Royal Society of Canada, and a Member of the European Academy of Sciences. Dr. Babiuk was also honoured to receive the Saskatchewan Order of Merit and to be inducted into the Saskatchewan Agricultural Hall of Fame. Dr. Babiuk was awarded the 2012 Canada Gairdner Wightman Award, the Killam Prize in health sciences in 2013, and the GCHERA World Agriculture Prize 2016.

Before taking up his position as Vice-President (Research) at the University of Alberta, Dr. Babiuk was the Director of the Vaccine and Infectious Disease Organization (VIDO). During his time at VIDO, Dr. Babiuk built the organization into an international powerhouse carrying out major research in immunology, pathogenesis, virology, molecular virology, and vaccinology.

Rapid Response to Protect Against Infectious Diseases of High Consequences

Gary Kobinger, Laval University, Québec City, Québec

Infections are one of the two leading causes of global mortality, killing twice as much as cancers. Less than 1,500 infectious diseases are known and therefore can be detected while it is estimated that approximately 320,000 pathogens remain to be discovered. This presentation will describe a rapid and innovative response structure to respond to emerging and re-emerging infectious diseases (EIDs) based on a multitude of expertise in basic, applied and clinical research. Ebola, MERS and Zika will serve as examples to highlights the needs and possibilities in regards to the development of vaccines and treatments to improve preparedness to protect populations against EIDs.

Gary Kobinger
Gary Kobinger is a professor in the Department of

Microbiology and Infectious Diseases and the Director of the Research Centre on Infectious Diseases, Faculty of Medicine at Université Laval. He is also an adjunct professor in the Department of Pathology and Laboratory Medicine at the University of Pennsylvania, and an associate professor in the Department of Medical Microbiology at the University of Manitoba. His work focuses on developing and testing new vaccine platforms and immune treatments against emerging and re-emerging viruses of high consequences to public health. Gary's goal as Director is to develop a research framework that can respond rapidly to emerging and re-emerging pathogens.

Animal Models for MERS: In Pursuit of Vaccines

Darryl Falzarano, PhD, Vaccine and Infectious Disease Organization – International Vaccine Centre (VIDO-InterVac), University of Saskatchewan, Saskatoon, SK

Nearly all camels sampled in the Middle East show serological evidence of exposure to Middle East respiratory syndrome coronavirus (MERS-CoV) and contact with camels is associated with many primary human cases in Saudi Arabia. As such, prevention of MERS-CoV in camels will be an important point of intervention to reduce and/or eliminate human cases. An infection model for MERS-CoV in camels has been described; however, this is an inconvenient and costly model for challenge studies, which require level 3–agricultural (CL3-Ag) containment. As a more practical alternative we have developed an alpaca (*Vicugna pacos*) model for MERS-CoV. To establish the model, alpacas were infected by the intranasal (n=3), intratracheal (n=3) or combined intranasal and intratracheal routes (n=4). Following inoculation, an increase in viral RNA was observed in nasal swabs with lower levels being detected in oral swabs. Infectious virus was subsequently isolated from nasal swabs from time points corresponding to high viral loads in all animals. No significant clinical disease or virus-associated gross pathology was observed; however, infiltration of inflammatory cells into nasal turbinates was observed in the animals euthanized on day 7 post-infection. All animals seroconverted and produced neutralizing antibodies by day 14 following infection. Animals infected by the combined inoculation route (n=3) were re-inoculated 60 days following the initial infection. Viral RNA was detected in nasal swabs only, approximately 4.5 logs lower than the initial infection, with no recovery of infectious virus. This suggests that the initial infection offers protection from subsequent infection, demonstrates the suitability of alpacas to be used as surrogates for camels and sets the bar for future vaccine studies.

Darryl Falzarano

Darryl Falzarano is a Research Scientist II at the Vaccine and Infectious Disease Organization – International Vaccine Centre (VIDO-InterVac) and an Adjunct Professor in the Department of Veterinary Microbiology at the Western College of Veterinary Medicine at the University of Saskatchewan in Saskatoon, Canada.

He received a Ph.D. from the Department of Medical Microbiology at the University of Manitoba in 2010 for determining the functional importance of post-translation modifications on Ebola virus glycoproteins. He then went on to complete a post-doctoral fellowship at Rocky Mountain Laboratories, part of the National Institute of Allergy and Infectious Disease, NIH in Hamilton, MT where he investigated antiviral and immunomodulatory strategies for Ebola and Middle East respiratory syndrome coronavirus (MERS-CoV). This included the development of a new animal model (common marmoset) and the first potential treatment for MERS-CoV. Dr. Falzarano has over 10 years of experience working in high containment (CL-3 and CL-4) laboratories with Ebola, Marburg, MERS-CoV and Lassa. While at the NIH he received the Norman P. Salzmann Memorial Award and Lecture in Virology and was the Kuan-Teh Jeang Scholar for Excellence in Virology.

Dr. Falzarano's lab is currently focused on using an alpaca model to design a vaccination strategy to prevent MERS-CoV transmission in camels.

Development of a Glycoconjugate Vaccine to Combat Disease Caused by Haemophilus Influenzae Type A

Andrew D. Cox, Vaccine Program, Human Health Therapeutics Portfolio, National Research Council, Ottawa, ON.

[Abstract and Bio not available].

Cancer Vaccines

Chair: John Bell, Ottawa Hospital Research Institute

The Resurgence of Cancer Vaccines

John Bell, Ottawa Hospital Research Institute, Ottawa, ON

There are a number of vaccination strategies that have been developed over the last several decades that are aimed at generating clinically effective anti-tumour immune responses. To date, these have been largely unsuccessful however novel technologies that both prime/boost anti-tumour immunity and reverse the immune suppressive tumour microenvironment have begun to show promise in the clinic. A summary of the promising strategies and recent clinical results will be presented.

John Bell
Dr. John Bell received his PhD from McMaster University in 1982. The three years that followed, he trained as a post-doctoral fellow at the University of Ottawa and then at the Medical Research Council in London, England. Dr. Bell began his independent research career at McGill University in 1986 and moved to the University of Ottawa, Department of Medicine, in 1989. He is a member of the Center for Cancer Therapeutics at The Ottawa Hospital Cancer Center, a Senior Scientist with the Ottawa Hospital Research Institute and Professor of Medicine at the University of Ottawa. He heads the Canadian Oncolytic Virus Consortium, a Terry Fox funded group from across Canada that is developing virus based cancer therapeutics and is the Director of the Biotherapeutics Program for the Ontario Institute for Cancer Research. He is the Scientific Director of the recently awarded BioCanRx Network Centres of Excellence for the development of Biotherapeutics for Cancer Therapy.

Rational Design of Small Molecule Immune Checkpoints' Inhibitors: The PD-1 Challenge

Khaled Barakat, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB

Blocking the PD-1/PD-L1 pathway recently emerged as a ‘game changer’ in cancer immunotherapy, leading to the selection of monoclonal-antibodies (MABs) targeting PD-1 as ‘drug of the year’ for 2013. Although these antibodies restored exhausted T cells’ function to recognize and kill tumor cells, these MABs have numerous disadvantages. These include their very high cost and very severe side effects. Our team has been focused on designing small molecule inhibitors for this pathway. Compared to available MAB therapies, our small molecules may offer a more affordable, more easily administered and better controlled treatment for a variety of cancers. Here, we demonstrate our efforts toward this goal and summarize preliminary data on one of our promising compounds, a small molecule inhibitor for the PD-1/PD-L1 pathway that binds to PD-1 and restores the polyfunctionality of exhausted T cells.

Khaled Barakat
Dr. Barakat is an Assistant Professor at the school of Pharmacy at the University of Alberta, Canada. He is currently the leader of a multidisciplinary world-class research team to develop novel immunotherapy drugs targeting the immune checkpoints' proteins. Dr. Barakat received his PhD in biophysics from the University of Alberta in 2012 followed by a postdoctoral fellowship in Professor Michael Houghton’s Lab for two years. His research stands at the multidisciplinary interface of physics, biology and computer science. Dr. Barakat’s major focus is on developing and applying state-of-the-art computational drug discovery tools to discover new antiviral and immunotherapeutic drugs. Dr. Barakat has made great contributions in understanding the nature and biophysical processes underlying protein–drug, protein–protein and drug off-target interactions and

predicting drug-mediated toxicity. He also received numerous awards including the CIHR and AIHS postdoctoral fellowships, the prestigious University of Alberta dissertation award and many distinction awards throughout his undergraduate and graduate studies. Dr. Barakat's lab is supported by different funding agencies including the Alberta Cancer Foundation, Li Ka Shing Applied Virology Institute, Natural Sciences and Engineering Research Council (NSERC), Li Ka Shing Institute of Virology and ICIMPACTS Centres of Excellence. He is also a member of many editorial boards including the Journal of Pharmaceutical Care & Health Systems and Austin Journal of Drug Discovery, Development and Delivery.

Virus Synthesis as a Tool for Assembling Large Virus Vaccines

David Evans, University of Alberta, Edmonton, AB

Advances in gene synthesis technology have revolutionized the way one might approach the production of complex biologicals. Moreover, when this is combined with reverse genetic systems, it provides a simple and rapid tool for producing infectious agents with novel genetic properties.

We have recently shown that these methods can also be used to manufacture Orthopoxvirus-based vaccines and as a proof of principle have assembled a 212kb synthetic horsepox virus (HPXV). To do this we designed and ordered 10 different DNA clones, encoding DNA fragments spanning the HPXV genome, and with each fragment sharing ~1kbp of overlapping sequence with neighbouring HPXV fragment(s). After adding the hairpin ends to fragments destined to become the telomeres, these DNAs were transfected into cells infected with rabbit fibroma virus, where they are recombined and reactivated by the “helper" virus. The new HPXV were then recovered by taking advantage of differences in host range and using a fluorescent selection strategy. These viruses replicated well in culture, infected mice, and engendered a vaccine response against a lethal vaccinia virus challenge.

This approach offers many advantages for researchers interested in innovative vaccines. In particular it provides a rapid and potentially automated route for assembling complex virus variants that could not be easily manufactured using traditional molecular genetic approaches..

David Evans

Dr. David Evans is a virologist with diverse interests in poxvirus biology as well as being an accomplished research administrator. His studies are supported by a network of collaborations and have been funded since 1987. Dr. Evans is considered a leader in the study of poxviruses with special expertise in virus recombination and replication

Dr. Evans has also demonstrated a longstanding commitment to research translation. His recombineering technology is licensed as InFusion® kits. More recently his research has focussed on developing oncolytic viruses for treating bladder cancer. He holds US patents relating to these technologies and is pursuing a Phase I clinical trial.

Dr. Evans is also a builder. In 2007 he was awarded $24.9 million to built and equip new facilities in Alberta. In 2010 the University was gifted with $25 million to support virus research, and Drs. Evans and Tyrrell merged several projects into the Li Ka-Shing Institute of Virology. Drs. Evans has also accumulated many years service on grant panels, reviews, and consults privately. He is a longstanding member of the WHO smallpox advisory committee. Most recently he conducted site visits for the FAO/OIE, and serves on the Canadian advisory committee on human pathogens and toxins.

Driving Large T cell Responses with an Oncolytic Viral Vaccine

Brian Lichty, McMaster University, Hamilton, ON

Recent clinical data has emphatically demonstrated the capacity of our immune systems to eradicate even advanced cancers. Oncolytic viruses (OVs) although originally designed to act as tumour lysing therapeutics have now been shown clinically to initiate systemic anti-tumour immune responses. Cell signalling pathways that are activated and promote the growth of tumour cells also favour the growth and replication of viruses within the cancer. The ability to engineer OVs to express immune stimulating cargo, their induction of immunogenic tumour cell death and the exquisite targeting of OVs to tumour beds argues that they are the ideal reagents to enhance anti-tumour immune responses. Coupling of OV therapy with tumour antigen vaccination, immune checkpoint inhibitors and

adoptive cell therapy appear ready to converge towards a new generation of multimodal therapeutics to improve outcomes for cancer patients.

Research Institute of the McGill University Health Centre/National Reference Centre for Parasitology/ Department of Medicine, Division of Infectious Diseases

Brian Lichty

Dr. Lichty did his undergraduate training at the University of Guelph and then received his PhD from the University of Toronto. He was subsequently a post-doctoral fellow in the laboratory of Dr. John Bell at the Ottawa Regional Cancer Centre and was involved in early studies to identify novel mechanisms directing viral oncolysis. He has been a professor in the Department of Pathology & Molecular Medicine and the McMaster Immunology Research Centre (MIRC) at McMaster University since 2004. His research program is focused on identifying strategies to use viruses to infect and destroy tumours while training the patient's own immune system to recognize and kill cancerous cells. By designing viruses to directly engage the adaptive immune system tumour-specific immunity is generated amenable to further enhancement through combination with other immunotherapies. He is also director of the Robert E. Fitzhenry vector lab at McMaster where clinical grade viral vaccines are manufactured for human clinical trials. The goal of this work is to use viruses to destroy tumours while vaccinating the patient against their cancer so their own immune system will prevent relapse.

Keynote Address:

Advances in Understanding the Biology of Talimogene Laherparepvec (T-VEC)

Howard Kaufman, Rutgers Cancer Institute of New Jersey

Talimogene laherparepvec (T-VEC) is the first oncolytic virus to be approved for the treatment of patients with advanced melanoma. The vector is an HSV-1 encoding human GM-CSF and is thought to mediate anti-tumor activity through both direct lysis of infected tumor cells and indirectly through induction of host anti-tumor immunity. The mechanism(s) proposed, however, have not been confirmed and may be important for identifying predictive biomarkers and for designing logical combination approaches. In this presentation, new data will be presented demonstrating that T-VEC enters most human melanoma cells, induces an immunogenic and apoptotic cell death releasing various danger-associated molecular pattern (DAMP) factors *in vitro*. In addition, melanoma cell lines with reduced levels of PKR, STING and interferon-related factors (IRF) 3 and 7 appear to be more permissive to T-VEC replication and lysis. Using a bilateral flank tumor model, we have also found that the T-VEC induces a rapid innate immune response and the early adaptive response appears to include HSV-specific CD8+ T cells that are recruited to both injected and un-injected tumors. These data provide support for the role of T-VEC in inducing tumor cell lysis through an immunogenic/apoptotic pathway and supports the early induction of anti-viral T cell immunity. In addition, STING and IRF expression may be potential biomarkers for identifying patients with tumors likely to be responsive to HSV-directed oncolytic therapy

Howard L. Kaufman, MD, FACS

Dr. Howard L. Kaufman has been a leading authority on tumor immunotherapy for the treatment of melanoma. He pioneered the development of recombinant viral vectors encoding eukaryotic tumor antigens and immune modulatory genes for cancer therapy and has conducted over 50 cancer vaccine and immunotherapy clinical trials. Dr. Kaufman has maintained an NIH-funded laboratory in tumor immunology for over 15 years. He was born in Chicago, Illinois and received his MD degree from Loyola University, did a residency in General Surgery at Boston University and completed fellowship training in Tumor Immunology and Surgical Oncology at the National Cancer Institute. He has previously held appointments as Chief of the Division of Surgical Oncology and Associate Director of the Herbert Irving Comprehensive Cancer Center at Columbia University in New York City. In 2009 he was recruited to be the first Director of the Rush University Cancer Center in Chicago and in 2014, he was recruited to New Jersey as the Chief Surgical Officer and Associate Director for Clinical Sciences at the Rutgers Cancer Institute of New Jersey. Dr. Kaufman has published over 400 peer-reviewed scientific papers, books, review articles and abstracts and serves on the editorial board of several biomedical journals. He is the Editor-In-Chief of the Journal of Targeted Therapies in Cancer and Targeted Therapy Oncology, and is a Senior Associate Editor at the Journal of Translational Medicine. He is a member of numerous professional societies and served as President of the Society for Immunotherapy of Cancer. Dr. Kaufman has chaired several NIH grant review study sections and has been appointed to the Board of Directors of several professional organizations, including the Melanoma Research Foundation, American Cancer Society-Eastern Division and the University of Illinois Chicago Board of Visitors. In 2016 he was accepted for a research sabbatical in the laboratory of Dr. Samuel Rabkin at Harvard University where he is studying the oncolytic properties of alpha-herpesviruses.

Global Health Vaccines: Parasites and TB

Chair: Brian Ward, McGill University

Vaccines for Parasites? It's About Time!

Brian Ward, McGill University, Montreal, QC

This brief presentation will review the history of parasite vaccine development efforts and argue that the tools now exist to produce candidate vaccines for a wide range of human and veterinary parasitoses.

Brian Ward
Dr. Ward received medical training at McGill, University of London and Johns Hopkins and research training at Oxford and Johns Hopkins. He returned to McGill in 1991 where he is a full professor. He is director of the McGill Vaccine Study Centre and medical director of the National Reference Centre for Parasitology. He serves on the CIHR Institutes Advisory Board for Health Promotion and Prevention and as interim chair of the Canadian Association for Immunization Research and Evaluation. Since 2010, he has served as Medical Officer for Medicago Inc. His research interests include nanoparticle vaccines, adjuvants & immunomodulators, micronutrient-virus interactions, and parasite diagnostics.

Lung Mucosal Immunity & Mucosal TB Vaccination Strategies for Human Application

Zhou Xing, MD, PhD, McMaster University, Hamilton, ON

Pulmonary TB caused by *M.tb* remains a leading infectious cause of global morbidity and mortality despite decades-long use of BCG vaccine and antibiotics. New vaccination strategies are needed to effectively control TB. However, the rational design of such strategies requires our expanded knowledge in anti-TB mucosal immunity. Since the natural immunity generated following pulmonary *M.tb* infection fails to effectively control TB, we believe any effective vaccination strategies ought to induce a state of sufficiently "un-natural" immunity. We have found the respiratory mucosal route of vaccination with viral-based vaccine to be adept at inducing such "un-natural" protective immunity in the lung. A viral-based TB vaccine has been evaluated in a wide range of animal models and in a phase 1 human trial via intramuscular route of delivery. Inhalational liquid-aerosol delivery technology has been developed for a phase 1 trial to evaluate the viral-based vaccine delivered to human lungs. Spray drying technology is used to produce vaccine powder with markedly increased thermostability for cold chain-free storage conditions.

Zhou Xing, MD, PhD
Professor, McMaster Immunology Research Centre & Department of Pathology and Molecular Medicine, McMaster University

Dr. Xing completed his training in Medicine in North Sichuan Medical College of China in 1981, and in Anatomic Pathology in Tongji Medical University of China in 1985. He then obtained his Ph.D in Immunology from the Department of Pathology of McMaster University in 1993. He has since worked at McMaster University as a faculty member since 1996.

Dr. Xing's research interest lies in two areas: dissecting the mucosal immune mechanisms of host defense against pulmonary infections by influenza virus, streptococcus, and tuberculous mycobacteria; and developing new tuberculosis (TB) vaccination strategies. He's an author of more than 165 peer reviewed publications.

A Leishmaniasis Vaccine Breakthrough: Are we Almost There?

Jude E. Uzonna, Departments of Immunology and Medical Microbiology, Rady College of Medicine, University of Manitoba, Winnipeg, MB

Parasitic diseases are among one of the major causes of mortality and morbidity around the world, particularly in developing countries. Human leishmaniasis are a complex spectrum of diseases affecting over 12 million people with an estimated 350 million people at risk of becoming infected globally. Manifestations of the disease range from small self-healing skin ulcers and lesions to large

disfiguring scars or even death, depending on the species of *Leishmania* involved. Despite this significant health and societal burden, there is currently no effective vaccine against the disease. Worse still, the existing treatments either cause major side effects or are only effective in specific circumstances. The lack of effective vaccine is mostly attributed to lack of understanding of factors that regulate the development, maintenance and loss of secondary immunity. Interestingly, humans and animals that recover from infection remain immune for life, suggesting that memory cells able to protect against secondary infection develop following recovery from primary infection. Using reverse immunology and proteomics techniques, we identified a highly conserved protein that provides striking protection in vaccinated mice. With the help of collaborators around the globe, we demonstrated this protein also induces strong immune response in human patients. These studies subsequently led to the development of first *Leishmania*-specific reagent called tetramers, which is capable of identifying *Leishmania*-specific T cells at single cell level over an entire course of infection. It also helped to show that majority of the immune response is directed towards this protein. This unique reagent helped us to generate transgenic mice whose T cells all express receptor for this particular protein. We are now poised to use these animals to address fundamental questions regarding the factors that regulate antigen-specific memory response in leishmaniasis. Understanding these factors is critical for developing effective vaccine and vaccination strategies against leishmaniasis.

Jude E. Uzonna

Dr. Uzonna is a Professor in the Departments of Immunology and Medical Microbiology at the University of Manitoba. He obtained a Doctor of Veterinary Medicine (DVM) degree with distinction from the University of Nigeria and Ph.D. Immunology from the University of Saskatchewan where he studied host-parasite interactions, focusing on African trypanosomiasis. He did his postdoctoral fellowship training at the University of Pennsylvania under the guidance of Professor Phillip Scott. The research program in Dr. Uzonna's laboratory focuses on understanding the cellular and molecular mechanisms that regulate induction, maintenance and loss of protective immunity against parasitic infections. The goal is to exploit the knowledge gained from these studies to develop effective vaccines and/or vaccination strategies against these infections. In addition, he is interested in understanding immunomodulatory mechanisms that regulate the pathophysiology of sepsis and septic shock. Dr. Uzonna is Associate Head of Department of Immunology and holds the Research Manitoba Chair Professor in Infectious Immunology. He was a recipient of The Canadian Society for Immunology Investigator Award, CIHR New Investigator Award and Research Manitoba Chair in Infectious Immunology. He has also received numerous community, teaching, academic and research awards, the most recent includes The Ken Hughes Award for Outstanding Achievement in Biomedical Research and The Manitoba Black Community Award for Outstanding Achievement in Mentoring and Education. He has published over 85 articles (> 35 articles in the last 5 years) in several excellent and high impact journals. His important contributions include elucidation of the role of central and effector memory CD4+ T cells in anti-*Leishmania* immunity, the importance of persistent antigen in maintenance of infection-induced immunity and identification of broadly conserved and highly immunodominant protective CD4+ T cell epitope in *Leishmania*. Research in the Uzonna laboratory is funded by the Canadian Institutes for Health Research, Natural Sciences and Engineering Research Council of Canada, and Research Manitoba.

Characterization of the Protection and Immune Response Elicited by the Immunization of Mice with Schistosoma mansoni Cathepsin B in the Presence of CpG oligodeoxynucleotides or Montanide ISA 720 VG

Momar Ndao, Research Institute of the McGill University Health Centre/ National Reference Centre for Parasitology/ Department of Medicine, Division of Infectious Diseases, Montreal General Hospital, Montreal, QC

Schistosomiasis is the most important human helminth infection due to its impact on public health. The clinical manifestations are chronic and significantly decrease an individual's quality of life. Infected individuals suffer from long-term organ pathologies including fibrosis which eventually leads to organ failure. The development of a vaccine against this parasitic disease has the potential to contribute a long-lasting decrease in disease spectrum and transmission. Our group has chosen to

target Schistosoma mansoni Cathepsin B (Sm-CB) as a vaccine candidate. Immunizations with Sm-CB adjuvanted with CpG oligodeoxynucleotides conferred a 59% decrease in worm burden. Hepatic and intestinal egg burdens were decreased by 56% and 54% respectively compared to control groups. Sm-CB formulated with Montanide ISA 720 VG decreased worm, hepatic egg, and intestinal egg burdens by 60%, 62%, and 56% respectively compared to control groups. Antibody production was significantly augmented in the vaccinated mice; both formulations elicited Sm-CB specific total IgG endpoint titers > 120,000. Furthermore, analysis of cytokine secretion levels revealed that immunization with Sm-CB+CpG resulted in a Th1 biased response (IFN-γ and TNF-α) whereas immunization with Sm-CB+Montanide led to a mixed Th1/Th2 response (IFN-γ, TNF-α, IL-5). Our results highlight the potential of Sm-CB as a strong vaccine candidate against schistosomiasis.

Momar Ndao

Following veterinary studies in Senegal, Dr. Momar Ndao completed his MSc and PhD in international health & tropical diseases at the Institute of Tropical Medicine in Antwerp. He is currently Associate Professor at McGill University, Montreal, and has served as Director of the Canadian National Reference Centre for Parasitology (NRCP) Laboratory since 2002. Selected as member of the Expert Review Committee for the Canadian Biosafety Standards & Guidelines, and Co-chair of the Food and Environmental Parasitology Network (Health Canada) among others, he was nominated member of the prestigious Executive committee of the World Federation of Parasitologists in 2014.

His laboratory has interests in diagnosis of parasitic diseases, study of host-parasite interactions, screening drugs to be used as therapies for protozoan parasitic disease, developing vaccines to prevent parasitic diseases, and applying proteomic technology to discover infectious disease biomarkers for diagnostic and drug treatment efficacy assessment.

Vaccine Technologies

Chair: Marc-André D'Aoust, Medicago

The Plant-based Proficia™ Technology, a Rapid and Efficient Platform for the Production of Influenza VLP Vaccines and Beyond

Marc-André D'Aoust, Medicago, Québec City, QC

There is a need for influenza vaccine production platform that can deliver efficient vaccines faster. Our Proficia™ technology uses transient expression in plants and can produce a first lot of influenza VLP within 19 days after the identification of a given circulating strain. Combined to the capacity of plant-made influenza VLP product to trigger a balanced, cross-reactive and long lasting immune response, this technology has the potential to provide a rapid riposte to international emergencies and pandemic but also, a better response to epidemics of seasonal influenza. The capacity of the platform to produce other VLP vaccines will also be discussed.

Marc-André D'Aoust
Dr. D'Aoust joined Medicago in July 1999 as Team Leader, Research and Development. He was successively Project Leader, Product Development, and Director, Research and Innovation, prior to his appointment as Vice-President, Research and Innovation. He was closely involved in development of the Medicago technological platform as well as the capacity to produce virus-like particles and bio-therapeutics in alfalfa and Nicotiana benthamiana. He is co-inventor on more than 330 patents or patent applications related to the technological platform or the company's products. Mr. D'Aoust holds a bachelor's degree in biology and a PhD in plant biochemistry and molecular biology.

DepoVax™: A Novel Delivery Formulation for Cancer Immunotherapy and Infectious Disease Vaccines

Marianne Stanford, Immunovaccine, Halifax, NS

Immunovaccine develops T cell activating cancer immunotherapies and infectious disease vaccines based on DepoVax™, a patented platform that provides controlled and prolonged exposure of antigens and adjuvant to the immune system. DPX-Survivac, a cancer immunotherapeutic vaccines is in a Phase 1b study in combination with Incyte's IDO1 inhibitor epacadostat in ovarian cancer as well as a Phase 2 study in combination with Merck approved anti-PD-1 drug, Keytruda. The Company is also exploring additional applications of DepoVax™, including DPX-RSV, an innovative vaccine candidate for respiratory syncytial virus (RSV), which has recently completed a Phase 1 clinical trial. An overview of the mechanism of action of this unique delivery formulation and its application in multiple clinical indications will be presented.

Marianne Stanford
Dr. Stanford oversees all preclinical research activities in cancer immunotherapies and infectious disease vaccines. She also serves as adjunct professor in Microbiology and Immunology at Dalhousie University; as a member of the Vaccine Discovery group of the Canadian Centre for Vaccinology, and as an Associate Member of the Beatrice Hunter Cancer Research Institute. Before joining the company in 2010, Dr. Stanford conducted her postdoctoral training at the Robarts Research Institute and at the Ottawa Hospital Research Institute, focusing her research on the use of viruses in the development of novel cancer treatments. While at the OHRI, she worked with Jennerex Biotherapeutics (now SillaJen) in the development of Pexa-Vec for human clinical trials. She received her BSc and MSc from Memorial University of Newfoundland and her PhD from Dalhousie University. In her spare time, Dr. Stanford is involved in science outreach and policy.

Enveloped Virus-Like Particle (eVLP) Delivery of an Optimized Form of Cytomegalovirus (CMV) Glycoprotein B (gB) Antigen for Prophylactic Vaccination Against Congenital CMV Infections

Francisco Diaz-Mitoma, M Kirchmeier, C Soare, T Ahmed, A Diress, B Ontsouka, J, Bozic, A-C Fluckiger, and DE Anderson. Variation Biotechnologies (VBI) Vaccines, Ottawa, ON

Introduction: An efficacious prophylactic vaccine to prevent congenital transmission of human cytomegalovirus (HCMV) would prevent one of the most frequent causes of birth defects in the Western World.

Methods: We have used enveloped virus-like-particles (eVLPs), in which particles are produced in HEK 293 cells after transient expression of murine leukemia virus (MLV) viral matrix protein Gag to express the full extracellular domain of CMV gB fused with the transmembrane and cytoplasmic domains from vesicular stomatitis virus (VSV) G protein (gB-G eVLPs). Proof of concept experiment were conducted in mice and rabbits. A phase one clinical trial in humans is in progress.

Results: Cryo electron microscopy analysis of eVLPs expressing native gB as well as the gB-G form of antigen demonstrates different structures, and expression of the gB-G form is associated with a 5-fold improvement in neutralizing titers relative to native gB. Immunization of rabbits demonstrates that two doses of gB-G eVLPs adsorbed to alum induce neutralizing antibody titers that exceed naturally acquired levels of immunity. Analytical testing of toxicology and clinical batches demonstrates manufacturing consistency and purity that met Health Canada regulatory guidelines. The vaccine was formulated with Alum hydroxide. The vaccine phase one trial is fully enrolled and subjects have received the full series of vaccinations at 0, 2 and six months.

Discussion: eVLP expression of an optimized form of gB antigen absorbed to alum represents a novel approach to developing a potentially efficacious and safe prophylactic CMV vaccine. Clinical evaluation of this candidate in a phase one study started in 2016. This double-blind trial finished enrolment of 129 subjects in five arms: placebo, non-adjuvanted vaccine and three arms/dose levels of adjuvanted vaccine. Results of CMV serology markers of protection and follow up of safety data will be available later this year.

Francisco Diaz-Mitoma, MD, PhD, FRCPC

Dr. Diaz-Mitoma is a physician scientist and a co-founder of VBI Vaccines. Currently, he serves as its Chief Medical Officer. His portfolio includes the global phase 3 clinical program for Sci-B-Vac, a third-generation hepatitis B vaccine that contains the pre-S1, pre-S2 and S Hepatitis B surface proteins; the clinical development of a prophylactic vaccine for CMV and an anti-cancer vaccine for glioblastoma. These last two programs are in phase one clinical development. He has authored and co-authored more than 140 peer reviewed publications in infectious diseases as well as several patents. He began his medical professional career in academia as a practicing microbiologist and infectious disease specialist. From 1989 to 2010, Dr. Diaz-Mitoma held several hospital appointments, including roles as Physician Consultant in Infectious Diseases at the Children's Hospital of Eastern Ontario (CHEO) and the Ottawa Hospital. From 2011-2015, Dr. Diaz-Mitoma was the founding Chief Executive Officer of The Advanced Medical Institute of Canada (AMRIC), now the Health Sciences North Research Institute in Sudbury, Ontario. Dr. Diaz-Mitoma also has served as a board member of The Northern Ontario Cancer Foundation, Ashbury College, Folia, Biogenix and Bowhead Health, Inc. Dr. Diaz-Mitoma received his M.D. degree from the University of Guadalajara in Mexico, a Ph.D. degree from the University of Alberta and is a Fellow of The Royal College of Physicians and Surgeons of Canada.

Panel Discussion

Funding New Vaccine Development

Chair: Kishna Kalicharran, Merck & Co.

PANELISTS:

Kishna Kalicharran, PhD, MSc, MBA, Merck & Co., North Wales, PA

Kishna is currently Executive Director, Global Vaccines Strategy & Alliances at Merck & Co., Inc. He brings a strong track record with over seventeen years of experience in the healthcare industry, combining a unique blend of corporate strategy, business development, R&D, operations, commercial, investment management, IP, portfolio management and entrepreneurship expertise in US and Canada.

Kishna completed a BSc., in Biology at Acadia University, MSc., in Virology at University of Ottawa, PhD in Virology at Western University, MBA at Johns Hopkins University and a Postdoctoral Fellowship at Johns Hopkins University School of Medicine. He is Registered US Patent Agent.

Cedric Bisson, MD, JD, Partner, Teralys Capital Inc., Montreal, QC

Cedric Bisson has extensive experience across Canada, Europe and the USA creating, building and advising businesses in biopharmaceuticals, healthcare and the innovation sector in general. He is passionate about growing Canada as a premier environment for innovation, and during his career has structured over $3 B in transactions in funds and companies.

Mr. Bisson is currently partner at Teralys Capital where he focuses on healthcare and life sciences investments, as well as growth opportunities. Teralys Capital (www.teralyscapital.com) is Canada's largest innovation-focused investor, financing private funds in IT, life sciences, and clean or industrial innovations, from early stage start-ups to expansion, growth and technology buy-outs.

He was previously managing partner for life sciences at iNovia Capital (www.inovia.vc) in Montreal, Calgary and the USA, a private venture capital firm aimed at entrepreneurship and company building, during which he also created MSBi Valorisation (now Allgo, www.aligo.ca/en/), a seed technology transfer and investor firm focused principally on McGill University. Prior to this, he spent close to a decade internationally as associate principal at McKinsey & Company (www.mckinsey.com), a management consulting firm, where he was a leader in the biopharma, healthcare and innovation practices in New York City, Paris, Montreal, and Toronto.

Mr. Bisson obtained a M.D. degree from McGill University and a J.D. (law) degree from Universite de Montreal. He still actively engages globally with various government and private entities on innovation and related public policy matters, most notably Grand Challenges Canada (www.grandchallenges.ca), a Toronto organization dedicated to supporting bold ideas with big impact in global health, as well as Vancouver-based Accel-Rx (http://www.accel-rx.com), Canada's national health sciences accelerator.

In his community time, Mr. Bisson serves as chairman of the board of the Biennale de Montréal (contemporary visual arts: www.bnlmtl.org/en/) and chairman of the board of Procure (non-profit charity against prostate cancer: www.procure.ca).

Isabelle Létourneau, PhD, Associate, Strategic Initiatives, CIHR – Institute of Infection and Immunity, Quebec City, QC

Dr. Létourneau completed a Bachelor's degree in Microbiology and Immunology from McGill University and then pursued a Ph.D. in Pharmacology and Toxicology at Queen's University. She completed two post-doctoral fellows; one, at the St. Jude Children's Research Hospital (Memphis, TN), studying the Multidrug Resistance Protein 4 (MRP4) and a second at the *Institut du Cancer de Montréal*, part of the Research

Centre of the *Centre Hospitalier de l'Université de Montréal* (CRCHUM) looking at prognostic markers in ovarian cancer.

After one year in a knowledge transfer company as a biology-toxicology scientist, Isabelle joined the CIHR-Institute of Infection and Immunity (III) in 2014 as in the position of associate for strategic initiatives. She was responsible for the antimicrobial resistance (AMR) initiatives from 2014-2015, during which time she participated in the elaboration of the Federal Framework and Action Plan on AMR, and has represented CIHR-III at the Joint Programing Initiative on Antimicrobial Resistance (JPIAMR) meetings held in Europe. Isabelle is now working on initiatives in human immunology; inflammation; vaccines; HIV; and, Hepatitis C; and is responsible for various communication activities for the CIHR-Institute of Infection and Immunity. Dr. Létourneau is also working closely with the Public Health Agency of Canada on different files and on the design of several funding opportunities.

Bjørg Dystvold Nilsson, Coalition for Epidemic Preparedness Innovations (CEPI), Oslo, Norway

Bjørg Dystvold Nilsson is the acting team lead for advocacy and communications in CEPI – Coalition for Epidemic Preparedness Innovations. She was the project coordinator from the Norwegian side for the phase III trial of the Ebola vaccine in Guinea during the 2014-2015 outbreak. The trial was led from the Norwegian Institute of Public Health in close collaboration with WHO, MSF and the government of Guinea. The trial managed, for the first time, to document effective protection by a vaccine against Ebola Virus Disease.

Nilsson has extensive experience from policy affairs and communication in Norway and internationally. She was head of communications at Sanofi Pasteur MSD during the introduction of the HPV vaccine in Norway, worked at the IHR department in WHO and at Sanofi Pasteur MSD head office in Lyon, France.

Nilsson holds a BA in history, Spanish and Scandinavian languages in addition to studies in journalism and public health.