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Meeting Report

The Sir Mark Oliphant Conferences

International frontiers of science and technology

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The Vaccines and Immunotherapy Technologies Conference was organized by Professor Ian Frazer FAA, FTSE (Chair)(Centre for Immunology and Cancer Research, University of Queensland), Professor Peter Gray FTSE (Australian Institute for Bioengineering and Nanotechnology, University of Queensland), Professor Ian Gust FTSE, (Department of Microbiology and Immunology, University of Melbourne), Professor Graham Mitchell FAA, (Foursight Associates Pty Ltd), Professor Ian Ramshaw (John Curtin School of Medical Research, Australian National University) and held at The Shine Dome in Canberra, 9–11 April. The conference was funded by the Australian Department of Innovation, Industry, Science and Research.

In a unique alliance, the Australian Academy of Sciences and Australian Academy of Technological Sciences and Engineering combined energies to bring together eminent scientists from around the world to discuss approaches to the global war on infection. They presented insights to the most recent cutting edge technologies and basic science concepts in vaccine and immunotherapy research.

Professor Ian Frazer (Diamantina Institute for Cancer, University of Queensland, Australia), the developer of GARDASIL, the world's first cervical cancer vaccine, introduced the conference in his plenary address. Although tremendous progress has been made recently with the development of two vaccines that help prevent cancer—against Hepatitis B, which causes liver cancer, and against the human papilloma virus, which causes cervical cancer and genital warts, he emphasized that we still have a considerable way to go in dealing with the challenges of such diseases. More than 20% of cancers are caused by viruses and more vaccines that target these viruses are under development. In addition to understanding how to make effective vaccines that amplify positive immune responses against cancers, we also need to understand how to turn off the signals that cancers give to the immune system that endeavor to stop an active defence response. Progress is now being made in new cytokine-inhibiting approaches that can switch off this defence mechanism.

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Tackling Issues Globally

Sir Gustav Nossal (Department of Pathology, The University of Melbourne and consultant for the World Health Organization and the Bill and Melinda Gates Foundation) touched on several aspects of worldwide efforts to halt tomorrow's killers and the enormous efforts to boost vaccination programs, particularly outside the wealthy G8 countries. He emphasized how the effort of The Global Alliance for Vaccines and Immunization (GAVI) Fund (headed by Dr. Julian Lob-Levyt), synergized with an innovative partnership with the Bill and Melinda Gates Foundation, provides a compelling successful strategy for moving progress in vaccine development and delivery forward. Dr. Julian Lob-Levyt expanded on the work of GAVI, highlighting their role in saving children's lives and protecting people's health by increasing access to poor countries. This is achieved by bringing together new and established markets, identifying sources of funding and building the partnerships necessary to achieve these goals. He highlighted that even in the privileged world in which we live, still 9.7 million children under five die every year, and most of these are in the poorest countries in the world. GAVI is tackling distribution of vaccines for *Haemophilus influenzae* type b, tetanus, hepatitis B, diptheria and pertussis all in one (Hib vaccine), rotavirus and pneumococcal infections. While we often focus on diseases such as AIDS, malaria and measles, pneumonia is the single biggest killer of the young, proving fatal to 2 million children per year. The Hib vaccine has been an enormous success in Uganda, and the first children in Papua New Guinea will begin receiving the vaccine in April. The new pneumococcal vaccine is expected to save an estimated 5.4 million lives by 2030. To clarify just how important the effort to tackle infectious disease and vaccination is, Bill and Melinda Gates have said that "childhood immunization is undoubtedly the best investment we have ever made."

New Solutions to Old Problems

Diseases such as tuberculosis, malaria, HIV, Epstein-Barr virus, influenza, herpes simplex and hepatitis C virus are the major infectious diseases that cause the morbidity and mortality worldwide. Despite knowing much about the immune response to pathogens, developing effective vaccine strategies, particularly against persistent infections, remains one of our greatest challenges.

Professor Warwick Britton (Centenary Institute of Cancer Medicine and Cell Biology, Sydney, Australia) described recent work using recombinant BCG overexpressing host cytokines.

In a mouse model, immunization with a rBCG expressing the cytokine GM-CSF enhanced T cells secretion of interferons, offering a first lead in potential protection against *M. tuberculosis* infection and halting dissemination of the bacterium from the lung to other organs of the body. Combination approaches that optimize this vaccine strategy for human populations are under way.

Dr. Louis Schofield, Head, Laboratory of Malaria Immunology, The Walter and Eliza Hall Institute of Medical Research (WEHI), described an innovative approach to malaria prophylaxis. Noting that the 2 million fatalities annually are thought to result in part from inflammatory cascades initiated by a malaria toxin, he described an approach that focused on reducing malaria toxicity. His laboratory has developed and tested chemically synthetic glycosylphosphatidylinositol (GPI) conjugated to protein carrier and shown that immunization with GPI glycan substantially reduced severe pathology, cerebral malaria and fatalities in mice.

Dr. Wayne Koff (International AIDS Vaccine Initiative, USA) and Professor Stephen Kent (Department of Microbiology and Immunology, University of Melbourne, Australia) tackled two different approaches to development of an HIV vaccine. Dr. Koff set out the issues of how antibody might be used to develop a safe vaccine while Professor Kent showed that a simplistic approach to stimulating T cells by immunization with autologous peptide-pulsed fresh blood was an effective immunotherapy. Deborah Fuller, who heads a collaborative team of investigators from the University of Pittsburgh, Albany Medical College, and GlaxoSmithKline described her preclinical studies of therapeutic HIV vaccination. Ballistic delivery of a DNA vaccine, in a reduction of viral load in 65 per cent of the vaccinated animals. Administration of the vaccine with a mucosal adjuvant increased the immune response to 86 per cent in the DNA + LT group contained viral rebound. The DNA + LT group also had substantially lower virus in the gut, suggesting the vaccine targeted and reduced the mucosal viral reservoir.

New Adjuvants and New Vaccine Approaches

Dr. Annie De Groot, CEO of EpiVax and Research Professor at the University of Rhode Island, described her laboratory's progress with epitope driven vaccines for a range of pathogens (smallpox, tularaemia, tuberculosis, *H. pylori* and HIV). Epitope derived from the genomes of these pathogens can be optimized using computational tools that configure epitope spacing and alignment for enhanced processing, modify the sequence for improved expression, and introduce pathway-targeting sequences. She described how her team focuses on the essential elements for disease protection, and suggested that computer-driven vaccine design may have a significant advantage over conventional approaches, as careful design may diminish unexpected adverse side effects, such as have been observed with whole pathogen and subunit vaccines.

Continuing along the theme of multi-epitope targeting, Associate Professor Rajiv Khanna (Queensland Institute of Medical Research, Australia) outlined how multiple short peptide sequences that encode the minimal determinants for $CD4^+$ and $CD8^+$ T cells as a string can be developed into a single artificial construct that can be used as an effective immunogen against Epstein Barr Virus. To enhance the efficacy of such constructs, they can be also be linked to targeting signals or viral sequences.

Professor Lawrence Stanberry (College of Physicians and Surgeons of Columbia University, New York, USA) described efforts to develop effective vaccines towards herpes simplex virus (HSV). While success has been gained in progressing a vaccine for HSV-2, unexpectedly it appears to be protective only for a very small target group. This still leaves open the necessity to develop a more broadly protective HSV vaccine targeting HSV-1 and 2.

Adjuvants—Driving Adaptive and Innate Immunity

Adjuvants and carriers of immunogenic material are key to effective immune responses. Associate Professor David Jackson (Department of Microbiology and Immunology, University of Melbourne, Australia) has developed a simple synthetic lipid structure (lipopeptide) that can be exploited to carry peptides to dendritic cells to provide a self-adjuvanting solution to vaccine delivery. This technology has been exploited to test vaccine approaches against influenza and immunocontraceptives. In novel use of this technology, Professor Eric Gowans (Macfarlane Burnet Institute for Medical Research and Public Health, Melbourne, Australia) described the efforts at conditioning human monocyte-derived dendritic cells with lipopeptides encompassing peptides to $CD4^+$ and $CD8^+$ T cells against hepatitis C virus and the additional steps that may be necessary to optimize this vaccine strategy. In a different approach to adjuvant technology, Associate Professor Eugene Maraskovsky (CSL Limited, Melbourne, Australia) described the intricacies of the ISCOMATRIX® adjuvant for both prophylactic and therapeutic vaccines. It is now appreciated that while ISCOMATRIX® is a potent adjuvant for delivery of proteins or peptides, it acts much more broadly to stimulate the innate arm of immunity which may jump-start the immune response.

Back to Basics

Dr. Gabrielle Belz (The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia) and Professor Jonathan Sprent (Garvan Institute of Medical Research, Sydney, Australia) outlined recently defined rules that govern the formation and recruitment of memory T cells in the context of pathogen infection or autoimmune disease. Recently Professor Sprent uncovered a novel and unexpected role for interleukin-2 (IL-2) complexed to IL-2 monoclonal antibodies in preferentially stimulating memory T cells and NK cells. In an extension of this work, regulatory T cells also appear to be preferentially stimulated permitting resistance to autoimmune encephalomyelitis and long-term acceptance of allografts. Dr. Belz expanded on how T cells develop, highlighting how our understanding of the rules governing naïve and memory T cells have changed in recent years and how the timing and type of antigen presenting cells involved in the response shape the outcome for viral and vaccine challenge.

Public, Government and Perceptions

Dr. Norman Swan from the Australian Broadcasting Corporation Radio National provided a provocative and entertaining perspective of how we might view the future of Australian Science. He emphasized the responsibility of scientists to develop a language about their research with which the public can identify and to motivate governments to prioritize health and research.

Note

Conference proceedings will be available from www.oliphant.org.au/april2008.html