

## MEETING REPORT

### **NEW CELLS FOR NEW VACCINES II: FOCUS ON Respiratory Virus Diseases**

William Egan, Ph.D.  
Member, International Program Committee  
New Cells for New Vaccines II

This International Scientific Workshop, held on September 17 – 19, 2007, at the Hotel duPont, Wilmington, Delaware, USA, was organized by the International Association for Biologicals (IABS), InB:Biotechnologies Inc., and the Fraunhofer USA Center for Molecular Biotechnology. The National Institute for Allergy and Infectious Diseases (NIAID), the International Society for Influenza and other Respiratory Virus Diseases (ISIRV), and Retroscreen Virology were co-sponsors. This year's Workshop follows, and builds on, the success of an IABS co-sponsored two-day Workshop on new cell substrates that was held last year, in September, in Coral Gables, Florida, USA.

Over 100 participants from 12 countries attended the current Workshop; the participants included scientists from industry, academia, public health, and regulatory agencies. The program focussed on recent developments in the use of new cell substrates – including mammalian, plant, and insect cells as well as duck and chick-embryo cell lines – for the manufacture of vaccines and therapeutic proteins, targeting primarily influenza and respiratory syncytial virus (RSV) disease. The three-day program included over 30 scientific presentations, panel discussions, poster sessions, and trade exhibits.

While the Workshop focused on the development of RSV and influenza vaccines and the use of new cell substrates in their development, it also addressed a number of the manufacturing and regulatory issues that attend the use of these cell substrates. An overview of manufacturers' and regulatory agencies' evolving perspective on cell substrates over the past 60 years opened the conference. During the conference, industry shared its view on both the advantages that accompany particular new cell substrates and the manufacturing and regulatory issues that arise with their use. These new cell substrates do engender a number of heretofore unfaced regulatory issues. To this end, the US and European regulatory perspectives, as well as the WHO perspective, on the issues associated with new cell lines were presented. Significantly, as was noted, several products manufactured with new cell substrates – an influenza vaccine manufactured in MDCK cells and an HPV vaccine manufactured in insect cells -- have recently been approved in Europe. Oncogenicity from DNA deriving from tumorigenic cell lines has been noted as a particular concern; in this regard, the need for both removing and degrading DNA has been emphasized. The quantitation of residual DNA in vaccines by various methods was reviewed during the conference, noting especially the dependence of analytical sensitivity on the size of the DNA being assayed; a sensitive qPCR-based method utilizing a fluorescence readout for DNA quantitation was presented.

Participants of the New Cells for New Vaccines II workshop heard of the significant progress that is being made in meeting the increased need and demand for pandemic and inter-pandemic influenza vaccines and the progress on developing immunologic correlates of protection against RSV disease and in the development of RSV vaccines. Of interest was the update on the variety of new approaches to influenza vaccines, including both the development of virus derived antigens and the development of rDNA-derived protein vaccines. Additionally, with regard to RSV vaccine development, an exciting update on the use of the cotton rat model as a predictor of vaccine efficacy was presented.

In addition to vaccine production and development, the meeting also provided several updates on the production of various recombinant proteins and monoclonal antibodies in plant and insect cells.

The Chairs of the workshop were: Thomas Monath, Yuri Gleba, Reinhard Glueck, Peter Collins, Jean-Louis Virelizier, David Fedson, and William Egan.

The International Program Committee for the Workshop were: Drs. Kathryn Zoon, Vidadi Yusibov, Jean-Louis Virelizier, Geoffrey Schild, John Petricciani, Reinhard Glueck, and William Egan.

Co-sponsors of the workshop, whose support is gratefully acknowledged, were: IABS, InB:Biotechnologies, Fraunhofer USA CMB, WHO, the US National Institute for Allergy and Infectious Diseases, Retroscreen Virology, and the International Society for Influenza & other Respiratory Viruses (ISIRV).

## **Presentations**

- Historic Overview of New Substrates for Vaccine Development and Production, Rebecca Sheets, National Institute of Allergy and Infectious Diseases (USA)
- Advantages and Challenges of Plant-based Vaccine Development, Theodore F. Tsai, Novartis Vaccines and Diagnostics (USA)
- Advantages and Challenges of Plant-based Vaccine Development, Vidadi Yusibov, Fraunhofer USA Center for Molecular Biotechnology (USA)
- Advantages and Challenges of Vaccine Development in Insect Cells, Gale Smith, Novavax, Inc. (USA)
- Overview of Safety, Immunogenicity, and Efficacy of GSK's Cervical Cancer Vaccine Candidate Manufactured with Baculovirus Expression Vector System (BEVS), Marguerite Deschamps, GlaxoSmithKline Biologicals (Belgium)
- Development of a Novel Recombinant Influenza Vaccine in Insect Cells, Clifton McPherson, Protein Sciences Corporation (USA)
- Plant Expressed Influenza Hemagglutinin Characterization and Preliminary Efficacy Against Highly Pathogenic Isolates, Stephen R. Webb, Dow AgroSciences (USA)
- Vero Cell Derived Pandemic Vaccine Production at Industrial Scale – Preclinical and Clinical Evaluation, Otfried Kistner, Baxter (Austria)
- Rapid and Robust Transient Expression Technology for the Production, in Plants, of Influenza Vaccine Antigens, Louis-P. Vezina, Medicago (Canada)
- Avian Influenza Vaccines, Kristi Moore Dorsey, Ceva Biomune (USA)
- Safety Evaluation of Cell Substrates: WHO Approach, Ivana Knezevic, World Health Organization (Switzerland)
- Efficient Production of Recombinant Proteins in Plants Using Magniffection, Yuri Gleba, Icon Genetics (Germany)
- Learning to Express Mammalian Proteins, James Hartley, National Cancer Institute (USA)
- Production of Influenza Virus-Like Particles in Baculovirus, James Robinson, Novavax (USA)
- Efficient Production of Therapeutic Proteins in the LEX System, Kevin M. Cox, Biolex Therapeutics (USA)
- The Duck Cell Line AGE1cr – A New Substrate Designed to Produce Vaccines, Volker Sandig, ProBioGen (Germany)

- Successful Commercialization of Recombinant Proteins Produced in Plants: Case Studies, Ronald Bassuner, Sigma-Aldrich (USA)
- Basic Vaccine Research, Preclinical and Clinical Studies: An Investigator's View, Lars R. Haaheim, University of Bergen (Norway)
- RSV Vaccine Development, Peter L. Collins, National Institute of Allergy and Infectious Diseases (USA)
- The Cotton Rat as a Model to Study Respiratory Syncytial Virus (RSV) Pathogenesis and Immunity, Marina S. Boukhvalova, Virion Systems, Inc. (USA)
- Adenoviral Vector-Based H5N1 Influenza Vaccines, Suresh K. Mittal, Purdue University (USA)
- Influenza N1 Neuraminidase-Specific Monoclonal Antibody, Gene A. Palmer, Fraunhofer USA Center for Molecular Biotechnology (USA)
- Antibody Expression in Microalgae, Peter Heifetz, Rincon Pharmaceuticals, Inc. (USA)
- Neutralizing Human Monoclonal Antibodies Against H5 HA are Effective in Prevention and Treatment of H5N1 Infection in Mice, Amorsolo Suguitan, National Institute of Allergy and Infectious Diseases (USA)
- Plant-Produced anti-HIV Antibodies, Rainer Fischer, Fraunhofer Institute for Molecular Biology and Applied Ecology (Germany)
- U.S. Regulatory Perspective on New Cell Substrates for Manufacture of Viral Vaccines, Arifa S. Khan, Food and Drug Administration (USA)
- Regulatory View from the European Medicines Agency, Michael Pfeleiderer, Paul Ehrlich Institute (Germany)
- In Vivo Models to Evaluate the Oncogenic Risk of DNA Derived from Vaccine Cell Substrates, Keith Peden, Food and Drug Administration (USA)
- New Analytical Methods for Host Cell Residual DNA Testing, Laurent Mallet, sanofi pasteur (France)
- Challenges of Meeting Global Demand for Pandemic Flu Vaccine, David S. Fedson (France)
- Therapeutic and Preventive Strategies against Pandemic Influenza: Challenges and Opportunities, Suryaprakash Sambhara, Centers for Disease Control and Prevention (USA)
- Opportunities for Vaccine Development and Production Using Novel Cell Substrates, François Arcand, ERA Biotech (Spain)