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Conference Overview

The remarkable growth of vaccine biotechnology continues apace in basic science discovery, product development, market introduction, and adoption into immunization programs. New cytokines are identified, innate and induced immune regulatory pathways unraveled, novel adjuvants and antigen constructs prove effective, and recently-licensed products achieve high coverage, already yielding noticeable decreases in disease incidence. One can envision a growing number of challenging maladies – including chronic, non-infectious, and neoplastic – that may become vaccine-preventable or vaccine-treatable in the years ahead.

The Annual Conference on Vaccine Research (ACVR) aims to provide high-quality, up-to-date reports of such scientific progress in its unique mix of invited presentations by acknowledged international experts in symposia of topical interest, and its sessions and posters of peer-reviewed submitted abstracts. The ACVR encourages the participation of all the disparate fields of vaccinology in both its human and veterinary domains in order to facilitate valuable cross-fertilization of ideas and approaches among researchers often narrowly focused on their specific diseases or methods.

The Fourteenth ACVR promises to maintain its position as the largest scientific meeting devoted exclusively to research on vaccines and associated technologies for disease prevention and treatment through immunization. It is a premier venue for cutting-edge learning, effective data-sharing, and convenient networking for scientific collaboration.

The conference organizers and its volunteer committees enthusiastically invite registrants to participate in the audience discussions, poster presentations, meet-the-expert breakfast sessions, special luncheon lectures, evening receptions, and sponsored exhibits, and to provide the helpful feedback essential for further evolution and improvement. Welcome to the Fourteenth Annual Conference on Vaccine Research.

Conference Objectives

Overall Conference Objectives
At the conclusion of this conference, participants should be able to:
- Discuss recent scientific advances contributing to progress in the development of vaccines
- Identify research opportunities and scientific challenges associated with vaccine development, production, and distribution

Symposium Objectives
Keynote Address: One Health-One Medicine
- Review the science and organizational changes required to ensure that medical, veterinary, and ecological scientists work together to undertake research that will deliver the most effective options for managing infectious diseases risks and other health-related issues

Symposium 1: One Health Initiatives
- Discuss the nature of the emerging zoonotic Hendra virus and Nipah virus agents; identify the cause of human cases of infection, the pathology associated with infection by these viruses, and the animal models that are being used to study pathogenesis; review the antiviral countermeasure strategies that have been developed based on basic scientific research findings and how they are being applied in veterinary vaccine development and human immunotherapeutic approaches
- Identify the utility of viral vectors for development of a new generation of vaccines that stimulate both cellular and humoral immunity and the advantages of co-development of vaccines for some indications in parallel in humans and livestock
- Discuss factors that show aquatic birds of the world as the ultimate reservoir of all pandemic influenza viruses; discuss that the pig serves as the intermediate host between wild birds and humans and that prediction of future pandemics is the ultimate goal of influenza surveillance in lower animals and birds

Symposium 2: Advances and Challenges in the Development of Herpesvirus Vaccines
- Review the importance of congenital cytomegalovirus (CMV) infection as a cause of sensory, cognitive, and motor disability in children; identify the sources of maternal CMV infection and understand the difficulties inherent in preventing CMV exposure in women of child bearing age; analyze the evidence from observational studies and from randomized clinical trials which supports a role for active immunization in prevention of maternal and congenital CMV infection
Discuss the status of vaccines directed toward the prevention and treatment of herpes simplex virus (HSV) infections; analyze the use of genetically engineered HSV in gene therapy of cancer
Discuss the formulation of the varicella vaccine, the clinical experience with the vaccine pre- and post-licensure, and the current guidelines for its administration to children, adolescents, and adults and in high risk populations
Mary Lou Clements-Mann Memorial Lecture in Vaccine Sciences: Dynamic In Vivo Visualization of the Initiation and Effector Limbs of Adaptive Immune Response
Describe the role of structural and chemical cues that contribute to optimizing cell-cell interactions underlying adaptive immune responses in lymphoid tissues; identify the migratory activities of lymphocytes to their detection of antigen; review how different adhesion processes allow distinct cell-cell communication in the development of cell-mediated and humoral immunity
Symposium 3: Status of HIV Vaccines
Identify the key laboratory findings associated with the RV144 Thai HIV Vaccine trial; understand the basis for correlates of protection analysis; and describe the way forward for testing of the ALVAC vCP1521 prime + AIDSVAX B/E boost
Identify the findings in the RV144 vaccine and understand the measures currently underway to improve vaccine efficacy of the RV144 vaccine
Discuss pre-clinical and clinical advances with alternative serotype adenovirus vectors and novel HIV-1 vaccine immunogens
Symposium 4: Genomics
Explain the definition and importance of vaccinomics and how it informs the coming age of personalized vaccinology.
Analyze co-evolution of host and pathogen, as most populations of humans and livestock will have variable responses to pathogens and vaccines; discuss the variation likely to result from gene variants expressed in the immune system; identify the underlying genes suggesting new ways to improve the efficacy of vaccines that protect all individuals regardless of genotype
Summarize current approaches to investigation of causes of adverse events or immunogenicity using genetic and proteomic techniques; describe the use of state-of-the-art informatics to analyze data from vaccine trials
Symposium 5: Special Populations in Immunology
Describe the impact of various immunocompromised states on the response to various vaccines and the strategies used to improve these responses; with the advent of new vaccines for the prevention of nosocomial infections, analyze innovative approaches to their optimal use
Discuss the circumstances that would improve outcomes if vaccination in the neonatal period is desirable and understand when immunization can be achieved
Review age-related changes of the immune system, which contribute to reduced efficacy of vaccination in the elderly; explain official recommendations for vaccination of the elderly and recent improvements/ novel strategies to optimize vaccination for seniors
Symposium 6: Alternative Animal Models in Vaccine Discovery
Discuss the current status of veterinary tuberculosis (TB) vaccine research, opportunities afforded by use of cattle for TB research, and limitations of experimental approaches for TB vaccine discovery
Review current information on cognate respiratory virus infections as related to vaccine-development humans to broaden perspectives on available models
Describe the salient features of a piglet-pTTV-infection model; outline some of the intellectual challenges that the TTV's present to the research community
Acknowledgments (as of April 25, 2011)
This conference is supported, in part, through unrestricted educational grants from:
- Becton Dickinson
- CSL Biotherapies
- Dynavax Technologies
- Emergent BioSolutions Inc.
- Epivax, Inc.
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The National Foundation for Infectious Diseases is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The National Foundation for Infectious Diseases designates this educational activity for a maximum of 18.25 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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NFID is an approved provider of continuing nursing education by the Maryland Nurses Association, an accredited approver by the American Nurses Credentialing Center’s Commission on Accreditation. This educational activity has been approved for a maximum of 18.25 contact hours. To receive credit, each participant must attend the entire program, and complete a daily sign-in sheet and conference evaluation.

CONFERENCE EVALUATION
For CME and CNE credit, visit http://www.nfid.org/conferences/vaccine11/ to complete the conference evaluation and earn your continuing education credit.

If you need assistance with this process, please contact Kerry Bolton, NFID Education Coordinator, at kbolton@nfid.org.

GENERAL INFORMATION

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The Baltimore Marriott Waterfront Hotel is fully accessible to the public in accordance with the Americans with Disabilities Act guidelines. If you have any special meeting needs or requirements, please contact either Sharon Cooper-Kerr or a member of the hotel staff.

CONFERENCE INFORMATION DESK
The Conference Information Desk is located in the foyer area outside the Harborside Ballroom in the Baltimore Marriott Waterfront Hotel. NFID Conference staff will be available at the desk throughout the conference.

CONFERENCE LANGUAGE
The official language for the conference is English.

CONFERENCE LOCATION
All sessions of the conference will be held at:

Baltimore Marriott Waterfront Hotel
700 Aliceanna Street
Baltimore, MD 21202
1-410-385-3000

EXHIBIT HALL
Visit the Exhibit Hall in the Harborside Ballroom Salons A and B to meet with representatives from companies displaying the latest technologies in vaccine-related products and services. The exhibit hall hours are:

Monday, May 16 ...............5:00 pm–7:00 pm
Tuesday, May 17 ..............7:30 am–1:00 pm

A prize drawing will be held on Tuesday, May 17, at 1:15 pm. Be sure to get your exhibitor passport stamped by each of the exhibitors and return to the conference registration desk by 1:00 pm, Tuesday, May 17, to qualify for the drawing. Attendees must be present to win.
MESSAGES
All sleeping rooms in the hotel are equipped with a voice mail system. This system is accessible via the hotel operator using a house phone. In case of emergencies requiring immediate attention, your party should call the general hotel number listed above and instruct the switchboard to deliver a message to Sharon Cooper-Kerr at the NFID Conference Information Desk in the foyer area outside of the Harborside Ballroom.

NO SMOKING POLICY
The Baltimore Marriott Waterfront Hotel is a non-smoking facility. No smoking is allowed in any of the session rooms, coffee break area, in the foyer adjoining the session rooms, or sleeping rooms.

POSTER SESSIONS
Posters will be on display from 5:00 pm on Monday, May 16 until 12:00 pm on Wednesday, May 18 in the Harborside Ballroom Foyer. Presenters will be at their boards to answer questions and discuss their research during the poster reception scheduled for Monday, May 16, at 5:00 pm and during the official poster session on Tuesday, May 17, from 7:30–8:30 am.

PROGRAM AND ABSTRACTS
Each registered participant will receive one copy of the Program Agenda and Abstract Book included in the registration fee. Additional copies, if available, may be purchased for $25. Orders for additional copies will be taken at the Conference Information Desk beginning on Tuesday, May 17, 2011 and after the conference by e-mail to vaccine@nfid.org or fax to (301) 907-0878. PLEASE NOTE THAT NFID IS UNABLE TO REPLACE LOST OR STOLEN ABSTRACT BOOKS.

With the permission of each faculty member, the actual slides presented at the conference will be posted on the NFID website after the conference. Registered attendees will be notified by email when the slides are posted, and they will be available for one month. Please use this resource to find slides presented at the conference.

REGISTRATION FEES AND HOURS
The registration fee includes a program/abstract book, continental breakfast on each day of the conference, all scheduled coffee breaks, lunch presentation on Tuesday, and a reception on Monday. Accommodations and additional meals are not included.

Onsite registration will be available at the Conference Information Desk during registration hours as follows:

Sunday, May 15 .......... 6:00 pm–8:00 pm
Monday, May 16 ......... 7:00 am–5:00 pm
Tuesday, May 17 ......... 7:00 am–5:00 pm
Wednesday, May 18 ....... 7:00 am–12:00 pm

VERIFICATION OF ATTENDANCE
International attendees may obtain a letter of attendance verification from the NFID staff at the Conference Information Desk during registration hours.

AFFILIATED EVENTS/MEETINGS
TUESDAY, MAY 17, 2011
Annual Conference on Vaccine Research Organizing and Scientific Program Committees Meeting (Closed meeting, by invitation only)
6:00 pm–9:00 pm, Essex A-C

THURSDAY, MAY 19–FRIDAY, MAY 20, 2011
IABS International Scientific Workshop Adventitious Agents, New Technology, and Risk Assessment
Baltimore Marriott Waterfront
Baltimore, MD
Conference Center Floor Plan
## PROGRAM AT-A-GLANCE

### Sunday, May 15
- 6:00 pm - 8:00 pm: Registration

### Monday, May 16
- 7:00 am - 5:00 pm: Registration
- 7:30 am: Poster Set-up
- 7:45 am: Continental Breakfast
- 8:15 am: Welcome and Introductions
- 8:30 am: Keynote Address
- 9:30 am: Coffee Break
- 9:45 am: Symposium 1: *One Health Initiatives*
- 11:45 am: Lunch (on your own)
- 1:00 pm: Symposium 2: *Advances and Challenges in the Development of Herpesvirus Vaccines*
- 3:00 pm: Coffee Break
- 3:30 pm: Concurrent Submitted Presentations 1A and 1B
- 5:00 pm: Adjournment/Exhibit and Poster Reception

### Tuesday, May 17
- 7:00 am - 5:00 pm: Registration
- 7:00 am: Meet the Experts Breakfast Session
- 7:30 am: Continental Breakfast/Exhibits/Poster Session
- 8:30 am: *Mary Lou Clements-Mann Memorial Lecture*
- 9:30 am: Coffee Break
- 9:45 am: Symposium 3: *Status of HIV Vaccines*
- 12:00 pm: Awards Luncheon: Robert Austrian Memorial Lecture/Charles Mérieux Award Presentation/Maurice R. Hilleman Early-Stage Career Investigator Award Presentation
- 1:30 pm: Symposium 4: *Genomics*
- 3:30 pm: Coffee Break
- 4:00 pm: Concurrent Submitted Presentations 2A and 2B
- 5:15 pm: Adjournment

### Wednesday, May 18
- 7:00 am - 12:00 pm: Registration
- 7:00 am: Meet the Experts Breakfast Session
- 7:30 am: Continental Breakfast
- 8:00 am: Concurrent Submitted Presentations 3A and 3B
- 9:30 am: Coffee Break
- 10:00 am: Symposium 5: *Special Populations in Immunology*
- 12:00 pm: Lunch (on your own)
- 1:15 pm: Symposium 6: *Alternative Animal Models in Vaccine Discovery*
- 3:15 pm: Adjournment
**On Vaccine Research**

**PROGRAM AGENDA**

**Sunday, May 15, 2011**

6:00 pm – 8:00 pm  **Registration**

**Monday, May 16, 2011**

7:00 am - 5:00 pm  **Registration**

7:30 am  **Poster Set-Up**

7:45 am  **Continental Breakfast**

8:15 am  **Welcome and Introductions**

Susan J. Rehm, MD  
*National Foundation for Infectious Diseases*  
*Bethesda, MD*

8:30 am  **Keynote Address**  
*Moderator: Cyril Gay, DVM*  
*U.S. Department of Agriculture*  
*Beltsville, MD*

8:45 am  **One Health – One Medicine**

Martyn Jeggo, PhD  
*Australian Animal Health Laboratory*  
*CSIRO Livestock Industries*  
*Geelong, Victoria, Australia*

9:15 am  **Questions and Answers**

9:30 am  **Coffee Break**

**Symposium 1: One Health Initiatives**  
*Moderator: Cyril G. Gay, DVM, PhD*  
*U.S. Department of Agriculture*  
*Beltsville, MD*

9:45 am  **Bridging Animal and Human Health in the Search for Countermeasures for Henipaviruses**

Christopher C. Broder, PhD  
*Uniformed Services University of the Health Sciences*  
*Bethesda, MD*
10:15 am  3  Co-development of Some Viral Vectored Vaccines for Livestock and Humans  
Adrian V.S. Hill, PhD  
The Jenner Institute  
Oxford, United Kingdom

10:45 am  4  From the Beach to the Bedside: Influenza’s Ability to Spread  
Robert G. Webster, PhD  
St. Jude’s Children Research Hospital  
Memphis, TN

11:15 am  Questions and Answers

11:45 am  Lunch (on your own)

Symposium 2:  Advances and Challenges in the Development of Herpesvirus Vaccines  
Harborside Ballroom, Salon C-E

Moderator:  Georges Peter, MD  
Warren Alpert Medical School of Brown University  
Brookline, MA

1:00 pm  5  Vaccine Prevention of Congenital CMV Infection: The Way Forward  
Robert F. Pass, MD  
University of Alabama at Birmingham  
Birmingham, AL

1:30 pm  6  Herpesvirus 1 & 2  
Richard J. Whitley, MD  
University of Alabama at Birmingham  
Birmingham, AL

2:00 pm  7  Varicella-Zoster Virus Vaccines  
Ann M. Arvin, MD  
Stanford University School of Medicine  
Stanford, CA

2:30 pm  Questions and Answers

3:00 pm  Coffee Break
Program Agenda

Submitted Presentations 1A: Influenza Vaccines (Concurrent Session)

Moderator: Susan J. Rehm, MD
National Foundation for Infectious Diseases
Bethesda, MD

3:30 pm
S1 Impact of Cross-Protective Vaccines on Epidemiological and Evolutionary Dynamics of Seasonal and Pandemic Influenza
N. Arinaminpathy¹, O. Ratmann², K. Koelle², S. Epstein³, G. Price³, C. Viboud⁴, M. Miller⁴, B. Grenfell¹
¹Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ,
²Duke University, Durham, NC, ³Center for Biologics Evaluation and Research, Food and Drug Administration, Rockville, MD, ⁴Fogarty International Center, National Institutes of Health, Bethesda, MD

3:45 pm
S2 Evidence from H1N1 Supporting Development of Broad-Spectrum Vaccines Against Influenza
A. S. De Groot¹, L. Moise¹, M. Ardito¹, E. McClaine¹, R. DuPont¹, R. Tassone¹, J. Haran², S. Suner², T. M. Ross³, W. Martin¹
¹EpiVax, Inc., Providence, RI, ²Rhode Island Hospital, Providence, RI, ³University of Pittsburgh Medical Center, Pittsburgh, PA

4:00 pm
S3 Antigenic Stability of H1N1 Pandemic Vaccines Correlates with Vaccine Strain
A. Farnsworth¹, T. D. Cyr¹, C. Li², J. Wang³, X. Li¹
¹Centre for Vaccine Evaluation, Health Canada, Ottawa, ON, Canada, ²National Institute for the Control of Pharmaceutical and Biological Products, The State Food and Drug Administration, Beijing, China

4:15 pm
S4 Aerosol Live-Attenuated Influenza Vaccine Protects Ferrets at a Reduced Dose
J. L. Humberd Smith¹, M. J. Papania², D. Knaus³, P. Brooks¹, D. Haas¹, R. Mair², J. J. Barry³, S. M. Tompkins¹, R. A. Tripp¹
¹College of Veterinary Medicine, University of Georgia, Athens, GA, ²National Center for Immunization and Respiratory Diseases, Centers for Disease Control, Atlanta, GA, ³Creare, Inc., Hanover, NH

4:30 pm
S5 Comparison of Live-Attenuated and Inactivated Influenza Vaccines: Domain-Specific Variation in T-Cell Immunity to Viral Hemagglutinin
S. Basha, S. Hazanfeld, R. Brady, R. Subbramanian
Division of Infectious Diseases, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH

4:45 pm
S6 Safety, Immunogenicity, and Productivity of a Recombinant Influenza A Vaccine Constructs for HA1 California/07, Novel H1N1 in Healthy Adults 18-49 and ≥ 65 Years of Age
D. N. Taylor¹, L. Tussey¹, J. Treanor², T. Fitzgerald², U. Kavita¹, L. Song¹, K. Ozer¹, A. Shaw¹, T. Hofstaetter¹
¹VaxInnate Corporation, Cranbury, NJ, ²Infectious Diseases, University of Rochester, Rochester, NY, ³Cytel, Cambridge, MA
### PROGRAM AGENDA

**Presentations 1B: New and Novel Vaccines**  
Concurrent Session  
**Moderator:** Bruce G. Weniger, MD  
Vaccine and Centers for Disease Control and Prevention  
Atlanta, GA

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| 3:30 pm | S7           | Phase 1, Randomized, Open-Label, Study to Assess the Safety and Immunogenicity of Serogroup B *Neisseria Meningitidis* (Mnb) Rlp2086 Vaccine in Healthy Adults | E. Sheldon¹, Q. Jiang², H. Schwartz³, P. Giardina³, J. Perez³  
¹Miami Research Associates, Miami, FL  
²Pfizer Vaccine Research Statistics, Collegeville, PA  
³Pfizer Vaccine Research, Pearl River, NY |
| 3:45 pm | S8           | Live, Attenuated, Tetravalent, CYD Dengue Vaccine in Healthy Adults and Children: Randomized Controlled Phase II Trial in Viet Nam | H. Tran Ngoc¹, T. Nguyen¹, A. Warte¹, R. Forrat¹, A. Bouckenoooghe², M. Saville³  
¹Pasteur Institute, Ho Chi Minh City, Vietnam  
²sanofi pasteur, Singapore  
³sanofi pasteur, Marcy l’Etoile, France |
| 4:00 pm | S9           | A Chimeric Vaccine Prevents Primary and Recurrent *Clostridium Difficile* Infection | H. Wang¹, X. Sun¹, Y. Zhang¹, L. Shi¹, W. Nie¹, S. Li¹, R. Kumar², T. Savidge³, S. Tzipori¹, J. Wang³, H. Feng¹  
¹Tufts University, North Grafton, MA  
²University of Texas Medical Branch, Galveston, TX  
³SCUT, Guangzhou, China |
| 4:15 pm | S10          | Treatment of Human Obesity by a Therapeutic Vaccination Approach       | K. N. Haffer  
Braasch Biotech LLC, Garretson, SD |
| 4:30 pm | S11          | Alternative Delivery Protocols of an Adenovirus Vector-Based Vaccine Against Foot-and-Mouth Disease Virus Enhances Protection of Swine | M. J. Grubman¹, C. C. A. Dias², F. San Segundo¹, M. P. Morales²  
¹Foreign Animal Disease Research Unit, Plum Island Animal Disease Center, USDA, ARS, Greenport, NY  
²Plum Island Animal Disease Center, USDA, ARS, Greenport, NY |
| 4:45 pm | S12          | Inoculation of Swine with Foot-and-Mouth Disease Virus SAP-Mutant Induces Early Protection Against Disease | T. de los Santos, F. Diaz-San Segundo, M. Weiss, E. Perez-Martin, C. C. Dias, M. J. Grubman  
Plum Island Animal Disease Center, NAA, ARS, USDA, Greenport, NY |
| 5:00 pm |              | Adjournment                                                           |
| 5:00 pm |              | Exhibits and Poster Reception                                         | Harborview Ballroom Foyer and Salon A-B |
Tuesday, May 17, 2011

7:00 am - 5:00 pm  Registration  Harborside Ballroom Foyer

7:00 am - 7:45 am  Meet the Experts Breakfast Session  Essex A & B

Gene Therapy of Glioblastoma Multiforme
Richard J. Whitley, MD
University of Alabama at Birmingham
Birmingham, AL

FMD New Generation Vaccines
Martyn Jeggo, PhD
Australian Animal Health Laboratory
CSIRO Livestock Industries
Geelong, Victoria, Australia

Will H5N1 Achieve its Potential in Humans?
Robert G. Webster, PhD, FRS
St. Jude’s Children Research Hospital
Memphis, TN

Publishing Your Results – Tips from a Journal Editor
Gregory A. Poland, MD
Mayo Clinic and Foundation
Rochester, MN

7:30 am  Continental Breakfast/Exhibits/Poster Session  Harborside Ballroom Foyer, Salon A-B

8:30 am  Mary Lou Clements-Mann Memorial Lecture in Vaccine Sciences  Harborside Ballroom, Salon C-E

Moderator: Hana Golding, PhD
U.S. Food and Drug Administration
Bethesda, MD

8  Dynamic In Vivo Visualization of the Initiation and Effector Limbs of Adaptive Immune Response
Ronald N. Germain, MD, PhD
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, MD

9:15 am  Questions and Answers

9:30 am  Coffee Break
Symposium 3: Status of HIV Vaccines

Moderator: Hana Golding, PhD
U.S. Food and Drug Administration
Bethesda, MD

9:45 am

9 Update on the Thai Phase III Trial: Sieve Analysis, Post-Infection Responses and Search for Correlates
Jerome H. Kim, MD
Walter Reed Army Institute of Research
Rockville, MD

10:15 am

10 Lessons from the Thai Trial RV144 and How to Improve Vaccine Induced Protective Antibodies
Barton F. Haynes, MD
Duke University
Durham, NC

10:45 am

11 Novel Vectors and Antigens for a Next Generation HIV-1 Vaccines
Dan H. Barouch, MD, PhD
Beth Israel Deaconess Medical Center
Boston, MA

11:15 am

12 Rational Design of Broadly Neutralizing HIV-1 Antibody Immunogens: Insights from Structure, Protein, and Vector Design
Gary J. Nabel, MD, PhD
National Institute of Allergy and Infectious Diseases
Bethesda, MD

11:45 am

Questions and Answers

12:00 pm

Luncheon*
Grand Ballroom Salon VI

Robert Austrian Memorial Lecture by Cynthia G. Whitney, MD, MPH
Chief, Respiratory Diseases Branch, Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention

Charles Mérieux Award Presentation to Robert B. Couch, MD
Distinguished Service Professor, Department of Molecular Virology & Microbiology, Baylor College of Medicine

Maurice R. Hilleman Early-Stage Career Investigator Award Presentation

*This session is supported by grants from Merck & Co., Inc. and sanofi pasteur
## PROGRAM AGENDA

### Symposium 4: Genomics (Concurrent Session)

**Moderator:** Cyril G. Gay, DVM, PhD  
*U.S. Department of Agriculture  
Beltsville, MD*

1:30 pm  
**13 Vaccinomics and Personalized Vaccinology**  
Gregory A. Poland, MD  
*Mayo Clinic and Foundation  
Rochester, MN*

2:00 pm  
**14 Genetics of Good Responders to Cattle Vaccines**  
Elizabeth J. Glass, PhD, BSc  
*The Roslin Institute, Royal (Dick) School of Veterinary Studies  
University of Edinburgh  
Scotland, United Kingdom*

2:30 pm  
**15 Genetic and Proteomic Data Reveal Pathways Regulating Immunogenicity and Adverse Events Following Vaccination**  
James E. Crowe, Jr., MD  
*Vanderbilt University Medical Center  
Nashville, TN*

3:00 pm  
**Questions and Answers**

3:30 pm  
**Coffee Break**

### Submitted Presentations 2A: Vaccine Adjuvants (Concurrent Session)

**Moderator:** Hana Golding, PhD  
*U.S. Food and Drug Administration  
Bethesda, MD*

4:00 pm  
**S13 MF59 Adjuvant Enhances Antibody Specificity, Affinity Maturation, and Virus Neutralization Titers to Swine-Origin and Avian Influenza A Virus Vaccines**  
*CBER, FDA, Bethesda, MD, NIH, Bethesda, MD, Novartis Vaccines, Sienna, Italy*

4:15 pm  
**S14 Nanoemulsion (NE) Intranasal Adjuvant Facilitates Uptake of Antigen Loaded Epithelial Cells (EC) by Dendritic Cells (DC)**  
*Michigan Nanotechnology Institute for Medicine and Biological Sciences, University of Michigan, Ann Arbor, MI*
PROGRAM AGENDA

4:30 pm

S15 The Effects of Novel Adjuvant Complex on Host Immune Response to Recombinant Eimeria Profilin Vaccine

D. Kim¹, H. S. Lillehoj⁴, S. Lee¹, P. J. Dominowski², R. J. Yancey²
¹USDA, ARS, ANRI, APDL, Beltsville, MD, ²Pfizer Inc., Kalamazoo, MI

4:45 pm

S16 Development of New Adjuvants - A Role for the National Institute of Allergy and Infectious Diseases (NIAID/NIH)

N. Obiri, K. Bateman
NIAID/NIID, Bethesda, MD

Submitted Presentations 2B: Vaccine Safety (Concurrent Session)

Vaccine Safety CE Harborside Ballroom, Salon D-E

Moderator: Georges Peter, MD

Warren Alpert Medical School of Brown University
Brookline, MA

4:00 pm

S17 Rapid Pre-Season Trial of the Safety of 2010-2011 H1N1₂₀₀⁹-Containing Trivalent Inactivated Influenza Vaccine (TIV) in Young Children 12 to 59 Months of Age (YC) Who Received AS03-Adjuvanted H1N1₂₀₀⁹ Pandemic Vaccine; A PHAC/CIHR (PCIRN) Influenza Research Network Study

J. M. Langley¹, D. Scheifele², C. Quach³, O. Vanderkooi⁴, S. Dobson², B. Ward³, J. Kellner³, S. Kuhn³, T. Kollmann³, S. McNeil³, B. Smith³, D. MacKinnon-Cameron⁷, S. Halperin¹
¹Pediatrics, Dalhousie University, Halifax, NS, Canada, ²Pediatrics, University of British Columbia, Vancouver, BC, Canada, ³Pediatrics, McGill University, Montreal, QC, Canada, ⁴Pediatrics, University of Calgary, Calgary, AB, Canada, ⁵Medicine, Dalhousie University, Halifax, NS, Canada, ⁶Mathematics and Statistics, Dalhousie University, Halifax, NS, Canada, ⁷Canadian Center for Vaccinology, Dalhousie University, Halifax, NS, Canada

4:15 pm

S18 Safety and Immunogenicity of Re-vaccination with H1N1-Containing 2010-11 Seasonal Influenza Vaccine After Priming with 2009 Adjuvanted Pandemic Vaccine

D. W. Scheifele¹, M. Dionne⁸, B. Ward³, C. Cooper⁴, O. Vanderkooi⁵, S. Dobson¹, G. De Serres³, Y. Li⁸, B. Law⁸, S. A. Halperin⁸
¹Vaccine Evaluation Center, University of British Columbia, Vancouver, BC, Canada, ²Unité de Recherche en Santé Publique (CHUQ), Laval University, Québec City, QC, Canada, ³Vaccine Study Center, McGill University, Montreal, QC, Canada, ⁴University of Ottawa, Ottawa, ON, Canada, ⁵Alberta Children’s Hospital, University of Calgary, Calgary, AB, Canada, ⁶Virology Section, National Microbiology Laboratory, Winnipeg, MB, Canada, ⁷Vaccine Safety Section, Public Health Agency of Canada, Ottawa, ON, Canada, ⁸Canadian Center for Vaccinology, Dalhousie University, Halifax, NS, Canada
4:30 pm  
**S19** Randomized Controlled Trial of Dose-Response to Influenza Vaccine in Children 6-23 Months of Age  
D. M. Skowronski¹, T. S. Hottes¹, M. Chong³, G. De Serres³, D. W. Scheifele³, B. J. Ward⁴, S. A. Halperin⁵, N. Z. Janjua¹, T. Chan¹, S. Sabaiduc¹, M. Petric¹  
¹BC Centre for Disease Control, Vancouver, BC, Canada, ²Institut national de santé publique du Québec, Quebec City, QC, Canada, ³Vaccine Evaluation Centre, Child and Family Research Institute, Vancouver, BC, Canada, ⁴McGill University Health Centre (MUHC) Vaccine Research Unit, Montreal, QC, Canada, ⁵Canadian Center for Vaccinology, Halifax, NS, Canada

4:45 pm  
**S20** Case Definition, Data Collection Guidelines, and Yellow Fever Vaccine Causality Assessment for Viscerotropic Disease as an Adverse Event Following Immunization  
¹Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, Atlanta, GA, ²Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, CO, ³Department of Immunization, Vaccines, and Biologicals, World Health Organization, Geneva, Switzerland, ⁴Agence de Médecine Préventive, Paris, France, ⁵Escola Nacional de Saúde Pública, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil, ⁶Global Pharmacovigilance & Epidemiology, sanofi pasteur, Lyon, France, ⁷Center for Immunization Research, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, ⁸Hospital Clinic-University of Barcelona, Barcelona Centre for International Health Research (CRESIB), Barcelona, Spain, ⁹Division of Safety Monitoring and Risk Management for Pediatric and Travel Vaccines, sanofi pasteur MSD, Lyon, France, ¹⁰Barcelona Centre for International Health Research (CRESIB), Barcelona, Spain, ¹¹Global Pharmacovigilance and Epidemiology Department, sanofi pasteur Ltd, Toronto, ON, Canada, ¹²Bio-Manguinhos/Fiocruz, Rio de Janeiro, Brazil, ¹³Epidemiology Direction, Ministry of Health, Buenos Aires, Argentina, ¹⁴Pharmacovigilance Regional Center of Upper-Normandy, Rouen, France, ¹⁵Ministry of Health, Abuja, Nigeria, ¹⁶Robert Koch Institut, Berlin, Germany, ¹⁷Novartis Vaccines, Cambridge, MA, ¹⁸Department of Global Health and Population, Harvard School of Public Health, Boston, MA

5:00 pm  
**S21** Immunization of Women with Diphtheria and Tetanus Toxoids Combined with Acellular Pertussis Vaccine (Tdap) During the Late Third Trimester of Pregnancy: An Interim Analysis of Safety Outcomes  
B. A. Halperin¹, D. MacDougall¹, V. Allen³, S. McNeil³, J. Langley¹, P. MacIntyre¹, D. MacKinnon-Cameron¹, S. A. Halperin¹  
¹Pediatrics, Dalhousie University, Halifax, NS, Canada, ²Obstetrics and Gynecology, Dalhousie University, Halifax, NS, Canada, ³Medicine, Dalhousie University, Halifax, NS, Canada

5:15 pm  
Adjournment
Wednesday, May 18, 2011

7:00 am - 12:00 pm  Registration  Harborside Ballroom Foyer

7:00 am - 7:45 am  Meet the Experts Breakfast Session  Essex A & B

Broadly Cross-Reactive Antibodies to HIV and Influenza: Implications for Vaccine Design
James E. Crowe, Jr., MD
Vanderbilt University Medical Center
Nashville, TN

Strategies for HIV Vaccine Clinical Development
Jerome H. Kim, MD
Walter Reed Army Institute of Research
Rockville, MD

Strategies to Immunize Compromised Patient Populations
Alan S. Cross, MD
University of Maryland School of Medicine Center for Vaccine Development
Baltimore, MD

Hepatitis B Vaccination
Trudy V. Murphy, MD
Centers for Disease and Prevention
Atlanta, GA

7:30 am  Continental Breakfast  Harborside Ballroom Foyer

Submitted Presentations 3A (Concurrent Session)  The Impact of Vaccines on Public Health  Harborside Ballroom, Salon C

Moderator: Myron M. Levine, MD, DTPH
Center for Vaccine Development
University of Maryland School of Medicine
Baltimore, MD

8:00 am  S22  Pertussis Vaccine Effectiveness in the Setting of a 2010 California Pertussis Outbreak
J. Bartlett, A. Rowhani-Rahbar, B. Fireman, N. Klein, R. Baxter
Kaiser Permanente Vaccine Study Center, Oakland, CA

R. Baxter¹, P. Ray¹, T. Tran², P. Saddier²
¹Kaiser Permanente Vaccine Study Center, Oakland, CA, ²Epidemiology, Merck Research Laboratories, North Wales, PA
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| 8:30 am| S24         | Trends in U.S. Pediatric Influenza Vaccination from 2006 to 2011 Among Privately Insured Children | S. L. Toback¹, L. Edelman², J. Herley², C. S. Ambrose¹  
 ¹MedImmune, LLC, Gaithersburg, MD, ²SDI Health, LLC, Plymouth Meeting, PA |
| 8:45 am| S25         | Measles Vaccination in Presence of Maternal Measles Antibodies Confers Non-Specific Beneficial Effects on Child Survival | P. Aaby, C. S. Benn  
  Bandim Health Project, Bissau, Guinea-Bissau |
| 9:00 am| S26         | Early Impact of PCV13 on Nasopharyngeal Colonization among American Indian Children and Household Members of the Navajo and White Mountain Apache Communities | L. R. Grant¹, S. E. O'Brien¹, R. C. Weatherholtz¹, J. J. Campbell¹, S. Bajaksouzian², M. R. Jacobs², R. Reid¹, M. Santosham¹, K. L. O'Brien¹  
 ¹International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, ²Pathology, Case Western Reserve University and University Hospitals Case Medical, Cleveland, OH |
| 9:15 am| S27         | Projected Public Health Impact and Cost-Effectiveness of Adult Pneumococcal Conjugate Vaccination in 50-Year-Olds | K. J. Smith¹, M. P. Nowalk¹, M. Raymund¹, A. R. Wateska¹, P. Nuorti², R. K. Zimmerman¹  
 ¹University of Pittsburgh, Pittsburgh, PA, ²Centers for Disease Control and Prevention, Atlanta, GA |

Submitted Presentations 3B: Immune Response to Vaccines (Concurrent Session)  
Moderator: Edwin O. Nuzum, DVM, PhD  
National Institute of Allergy and Infectious Diseases  
Bethesda, MD

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| 8:00 am| S28         | Replication Study of Measles Vaccine-Specific Immune Responses and CD46, SLAM and CD209 Genes | I. G. Ovsyannikova¹, I. H. Haralambieva¹, R. A. Vierkant², M. M. O'Byrne², R. M. Jacobson¹, G. A. Poland¹  
 ¹Mayo Clinic Vaccine Research Group, Mayo Clinic, Rochester, MN, ²Health Science Research, Mayo Clinic, Rochester, MN |
  Pfizer, Pearl River, NY |
8:30 am  S30  Improved Antibody and CTL Immunogenicity of HIV-1 Envelope Antigen by consensus DNA Prime/Protein Boosting
1Dept. of Pathology and Lab. Medicine, University of Pennsylvania, Philadelphia, PA, 2Inovio Pharmaceuticals Inc., Blue Bell, PA, 3Dept. of Pathology and Lab. Medicine, Inovio Pharmaceuticals Inc., Blue Bell, PA

8:45 am  S31  DNA Prime-Protein Boost Approach Was Effective in Eliciting Neutralizing Antibody Responses Against a High Percentage of Subtype BC HIV-1 Viruses Circulating in China
M. Zhang1, L. Zhang1, C. Zhang1, X. Hong2, Y. Shao2, Z. Huang1, S. Wang3, S. Lu3
1US-China Vaccine Research Center, First Affiliated Hospital of Nanjing Medical School, Nanjing, China, 2Center of AIDS and STD, China CDC, Beijing, China, 3Department of Medicine, Univ. of Massachusetts Medical School, Worcester, MA

9:00 am  S32  Circulating Cytokine Levels and Responses to Influenza Vaccine
H. Talbot1, K. Crimin2, M. T. Rock2, Y. Zhu2, D. Shay4, M. Griffin5
1Infectious Diseases, Vanderbilt University Medical Center, Nashville, TN, 2Biostatistics, Vanderbilt University Medical Center, Nashville, TN, 3Pediatric Infectious Diseases, Vanderbilt University Medical Center, Nashville, TN, 4Centers for Disease Control and Prevention, Atlanta, GA, 5Medicine and Preventive Medicine, Vanderbilt University Medical Center, Nashville, TN

9:15 am  S33  Trivalent Inactivated Vaccine Containing Influenza B/Victoria Induces Strong Recall of B/Yamagata but Inadequate B/Victoria Antibody Responses in Children Primed With Two Doses of B/Yamagata
D. M. Skowronski1, T. S. Hottes1, G. De Serres2, B. J. Ward3, N. Z. Janjua1, T. Chan1, S. Sabaiduc1, M. Petric1
1BC Centre for Disease Control, Vancouver, BC, Canada, 2Institut national de santé publique du Québec, Québec, QC, Canada, 3McGill University Health Centre (MUHC) Vaccine Research Unit, Montreal, QC, Canada

9:30 am  Coffee Break  Harborside Ballroom Foyer

Symposium 5:  Special Populations in Immunology  CE  Harborside Ballroom, Salon C-E
Moderator: Myron M. Levine, MD, DTPH
Center for Vaccine Development
University of Maryland School of Medicine
Baltimore, MD

10:00 am  16  Vaccination of Immunocompromised Patients
Alan S. Cross, MD
Center for Vaccine Development
Baltimore, MD
10:30 am  17 Vaccination of Neonates
Trudy V. Murphy, MD
Centers for Disease Control and Prevention
Atlanta, GA

11:00 am  18 Vaccination of Seniors
Birgit Weinberger, PhD
Institute for Biomedical Aging Research of the Austrian Academy of Science
Innsbruck, Austria

11:30 am  Questions and Answers

12:00 pm  Lunch (on your own)

Symposium 6:  Alternative Animal Models in Vaccine Discovery  
Harborside Ballroom, Salon C-E

1:15 pm  19 Cattle as a Model to Evaluate New Vaccine Strategies for Tuberculosis
W. Ray Waters, DVM, PhD
United States Department of Agriculture
Agricultural Research Service
Ames, IA

1:45 pm  20 Bovine Paramyxoviruses, BRSV and BPIV-3, as Models for HRSV and HPIV-3
John A. Ellis, DVM, PhD
Western College of Veterinary Medicine
University of Saskatchewan
Saskatoon, Canada

2:15 pm  21 Swine Model for Torque Teno Virus
Steven Krakowka, DVM, PhD
Department of Veterinary Biosciences, College of Veterinary Medicine
The Ohio State University
Columbus, OH

2:45 pm  Questions and Answers

3:15 pm  Adjournment
POSTER SESSION
GENERAL POSTERS (P1-P28)

P1  Characterization of the Mechanism of Protection Mediated by CS-D7, a Monoclonal Antibody to Staphylococcus Aureus Iron Regulated Surface Determinant B (Isdb), with Functional Activity In Vitro and Invivo
G. Pancari
Microbial Vaccine Research, Merck & Co., West Point, PA

P2  Genomic Sequence of Live, Attenuated Salmonella Typhi Vaccine Strain Ty21--Towards an Understanding of Attenuation
D. Xu1, J. Cisar3, F. Poly3, J. Albanese1, S. Porwollik4, M. McClelland4, P. Kopecko4, M. Dharmasena1, T. Wai1, D. J. Kopecko1
1Enteric and STDs, FDA-CBER, Bethesda, MD, 2NIDCR, Bethesda, MD, 3Enteric Diseases, Naval Medical Center, Silver Spring, MD, 4Vaccine Research Institute, San Diego, CA, 5The Vaccine Institute, San Diego, CA, 6Enteric Diseases, Naval Medical Research Center, Silver Spring, MD

P3  Safety and Immunogenicity of a DNA Vaccine Expressing H5 Hemagglutinin Delivered by Intramuscular or Intradermal Route in Healthy Adults
1Vaccine Research Center /NIAID/NIH, Bethesda, MD, 2Clinical Trials Core, Vaccine Research Center/NIAID/NIH, Bethesda, MD, 3Branch of Biostatistics Research, NIAID/NIH, Bethesda, MD

P4  Lack of Protective Efficacy of an Adenovirus-vectored P. falciparum Malaria Vaccine in the Absence of DNA Priming
C. Tamminga1, M. Sedegah1, I. Chuang1, M. Spring1, S. Maiolatesi1, C. Fedders1, S. Reyes1, A. Reyes1, K. Limbach1, N. B. Patterson1, E. Abot1, J. Murphy1, J. Komisar1, H. Ganeshan1, G. Banania1, M. Belmonte1, C. Park1, J. Huang1, D. Litlil1, J. T. Bruder1, L. Soisson3, C. Digg1, C. Ockenhouse1, J. E. Epstein1, T. L. Richie1
1US Military Malaria Vaccine Program, Naval Medical Research Center/Walter Reed Army Institute of Research, Silver Spring, MD, 2GenVec Inc., Gaithersburg, MD, 3USAID, Washington, DC

P5  Efficacy of Pentavalent Human-Bovine Reassortant Rotavirus Vaccine Among American Indian Children
International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

P6  Barriers and Drivers to Introduction of New TB Vaccines in High Burden Countries: A Market Research Study
L. F. Barker
Medical Affairs, Aeras Global TB Vaccine Foundation, Rockville, MD

P7  Pediatric Compliance to Iraqi’s Immunization Guideline
O. Q. B. Al-lela1, M. B. Bahari1, M. G. Al-abbassi1, A. Y. Bashier1
1Pharmaceutical School-Clinical Pharmacy, Universiti Sains Malaysia (USM), Pinang, Malaysia, 2Pharmacy College, Almustansaria University, Baghdad, Iraq, 3Advance Medical and Dental Institute, Universiti Sains Malaysia (USM), Pinang, Malaysia

P8  Research Roadblocks: Attempts to Measure the Influence of Adverse Events Following Immunization on Parental Immunization Behaviors
J. A. Bettinger1, S. Dobson1, J. Buxton2, G. Ogilvie2
1Pediatrics, University of British Columbia, Vancouver, BC, Canada, 2BC Centre for Disease Control, University of British Columbia, Vancouver, BC, Canada
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<td>Oxford Outcomes, Bethesda, MD, MedImmune, LLC, Gaithersburg, MD, Kentucky Pediatric Research, Bardstown, KY, Marshfield Clinic, Marshfield, WI</td>
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<td>Microbiology, Nigerian Institute of Medical Research, Lagos, Nigeria, Clinical Sciences, Nigerian Institute of Medical Research, Lagos, Nigeria</td>
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<td>Rapid, Non-Invasive Imaging of Encephalitic Viruses: Reducing Animal Numbers and Morbidity to Identify Efficacy of Potential Vaccines and Anti-Virals</td>
<td>M. Patterson, A. Seregin, A. Poussard, K. Taylor, B. Peng, S. Paessler</td>
<td>University of Texas Medical Branch, Galveston, TX</td>
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<td>Albert B. Sabin Vaccine Institute, Washington, DC, Department of Microbiology, Immunology and Tropical Medicine, George Washington University, Washington, DC, Fundação Oswaldo Cruz, Instituto René Rachou, Belo Horizonte, Minas Gerais, Brazil</td>
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<td>RMIT University, Bundoora, Australia, CSL Limited, Parkville, Australia, Burnet Institute, Melbourne, Australia</td>
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<td>A. S. Reslow, D. Aguirre, L. Cousens, B. Martin, C. Weber, W. Martin, A. S. De Groot, L. Moise</td>
<td>Institute for Immunology and Informatics, University of Rhode Island, Providence, RI, EpiVax, Inc., Providence, RI, University of Freiburg, Freiburg, Germany</td>
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<td>E. A. Gustafson, L. Moise, M. Ardito, G. Tejada, J. Desrosiers, W. Martin, A. S. De Groot</td>
<td>Institute for Immunology and Informatics, University of Rhode Island, Providence, RI, EpiVax, Providence, RI</td>
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| P19          | Vaccine Potential of Nipah Virus-Like Particles                                                                                       | P. Walpita¹, J. Barr², M. Sherman³, C. Basler⁴, L. Wang⁵  
¹Microbiology and Immunology, University of Texas Medical Branch, Galveston, TX, ²ACSIRO Australian Animal Health Laboratory, Geelong, Australia, ³Biochemistry and Structural Biology, University of Texas Medical Branch, Galveston, TX, ⁴Microbiology, Mount Sinai School of Medicine, New York, NY, ⁵ACSIRO Australian Animal Health Laboratory, Geelong, Australia |
| P20          | Alphavirus Vaccines: A Novel Inactivation Approach Towards Better Vaccine Development                                                  | A. Sharma¹, P. Gupta¹, S. P. Honnold¹, Y. Raviv², M. Viard², R. Blumethal³, M. Parker⁴, P. J. Glass⁴, R. K. Maheshwari¹  
¹Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD, ²National Cancer Research Institute and SAIC, Frederick, MD, ³National Cancer Research Institute, Frederick, MD, ⁴US Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD |
| P21          | NSs-Mediated PKR Degradation is Required for Efficient Induction of Neutralizing Antibodies by the Rift Valley Fever Virus MP-12 Vaccine Strain | B. K. Kalveram¹, O. Lihoradova¹, T. E. Hill², C. K. Tseng², T. Ikekami²  
¹Department of Pathology, University of Texas Medical Branch, Galveston, TX, ²Department of Microbiology and Immunology, University of Texas Medical Branch, Galveston, TX |
| P22          | Salmonella Enteritidis Core-O Polysaccharide (COPS) Conjugated to Enteritidis Flagellin (H:g,m) as a Candidate Vaccine for Protection Against Salmonella Enteritidis Infection | R. Simon¹, S. Tennant¹, J. Y. Wang¹, A. Lees², J. E. Galen¹, M. M. Levine¹, R.K. Ernst¹, M. Pasetti⁴  
¹Center for Vaccine Development, University of Maryland, Baltimore, Baltimore, MD, ²Fina Biosolutions, Rockville, MD, ³Department of Microbial Pathogenesis, University of Maryland Dental School, Baltimore, MD, ⁴Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD |
| P23          | Dengue Tetravalent Consensus DNA Vaccine Induces Antibodies Against All Four Serotypes of Dengue Virus                                   | P. Pankhong¹, J. Yan², T. Shin², R. Toporovski³, A. S. Khan³, N. Y. Sardesai³, D. B. Weiner³  
¹Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA, ²Inovio Pharmaceuticals Inc., Blue Bell, PA |
| P24          | Induction of False-Positive PTT Elevations by Investigational Adenoviral Vector Vaccines                                              | M. E. Enama¹, L. Novik, C. S. Hendel, R. Sheets, J. E. Ledgerwood, B. S. Graham  
VRC, NIAID, NIH, Bethesda, MD |
| P25          | The Unintended Consequences of Vaccine Delivery Devices Used to Eradicate Smallpox: Lessons for Evaluating Future Vaccination Methods | B. G. Weniger¹, T. S. Jones², R. T. Chen³  
¹Associate Editor, Vaccine, CAPT, USPHS (ret.), Atlanta, GA, ²CAPT, USPHS (ret.), Florence, MA, ³National Center HIV/AIDS, Viral Hepatitis, STD, & TB, Centers for Disease Control and Prevention, Atlanta, GA |
| P26          | Serological Cross-Reactivity of the 2009 Pandemic H1N1 Virus with Current Swine Influenza Viruses and Implications for Protection with a Commercial Vaccine | S. Ramamoorthy¹, S. Block², K. Bosenberg², X. Lin², J. Johnson³, A. Vincent³  
¹Department of Infectious Diseases, University of Georgia, Tifton, GA, ²Veterinary Diagnostic and Production Animal Medicine, Iowa State University, Ames, IA, ³Virus and Prion Diseases of Livestock Research Unit, National Animal Disease Center, Ames, IA |
P27 A Cytopathic Effect Reduction Assay for Measuring Anti-Foot and Mouth Disease Virus (FMDV) Activity of Bovine Interferons
P. Ramanathan, L. L. Rodriguez, M. J. Grubman, J. J. Zhu
USDA, Agriculture Research Service, Plum Island Animal Disease Center, Orient Point, NY

P28 Surface Display of Immunogenic Epitopes of FMDV in E. coli
S. H. Khodadad, Sr., M. Karbalayi Ali, A. Mohabati Mobare
1Microbiology, Tonekabon Islamic Azad University, Tehran, Iran, 2Bacteriology, Tarbiat Modares University, Tehran, Iran

TRAVEL GRANT RECIPIENTS (TG1-TG10)

TG1 Local Development of Safe and Effective Recombinant Hepatitis B Vaccine at the WHO GMP Standard Plant in Myanmar
W. Aung, Sr.
Department of Medical Research (Lower Myanmar), Ministry of Health, Yangon City, Myanmar

TG2 Evaluating Accessibility of Children Under Two Years to Measles Vaccination at Health Districts with Challenges of Vaccine Preservation
A. A. Adeiga, J. Onyewuche, S. Ahmad
1Nigeria Institute of Medical Research, Yaba, Lagos, Nigeria, 2Sokoto State Ministry of Health, Sokoto, Nigeria

TG3 Cytokine Signatures of Innate and Adaptive Immunity in 17DD Yellow Fever Vaccinated Children and its Association with the Level of Neutralizing Antibody
1Centro de Pesquisas René Rachou - Fiocruz, Belo Horizonte MG, Brazil, 2Universidade Federal de Ouro Preto, Ouro Preto MG, Brazil, 3Escola Nacional de Saúde Pública - Fiocruz, Rio de Janeiro RJ, Brazil, 4Instituto de Tecnologia em Imunobiológicos-Biomanguinhos, Fiocruz, Rio de Janeiro RJ, Brazil, 5Secretaria de Estado de Saúde de Minas Gerais, Belo Horizonte MG, Brazil, 6Faculdade de Medicina - Universidade Federal de Minas Gerais, Belo Horizonte MG, Brazil

TG4 Positive Selection on the Member of Plasmodium falciparum SURFIN
M. K. M. Kombo, II
National Institute of Biomedical Research, Kinshasa, Democratic Republic of the Congo

TG5 Leishmania Donovani Vaccine Candidate Arrest in Intracellular Replication Induces Th1 Specific Immune Response Towards Lasting Protection Against Experimental Leishmaniasis
A. Selvapandiyam, R. Dey, S. Nylen, R. Duncan, S. David, H. Nakhasi
1Institute of Molecular Medicine, New Delhi, India, 2Division of Emerging Transfusion and Transmitted Diseases, FDA, Bethesda, MD, 3Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, MD

TG6 Challenges of Retaining the Fisher Folk in an HIV Vaccine Preparatory Cohort Study
A. N. N. NANVUBYA
UVRI/IAVI HIV Vaccine Program, Entebbe, Uganda
**TG7**  
Survey of Human Papilloma Virus Vaccine Awareness and Vaccination History in Relation to the Presence of HPV Antibodies in Patients Attending STI Clinics in Lagos and Ibadan, Nigeria  
A. O. Faneye  
_Institute of Medical Research, Yaba, Lagos, Lagos, Nigeria_

**TG8**  
Avidity of IgG Antibodies Against Meningococcal Serogroup A Polysaccharide and Correlation with Bactericidal Activity in Sera of Meningitis Patients and Controls from Ethiopia  
M. M. Gebreselassie  
_AHRI, Addis Ababa, Ethiopia_

**TG9**  
Immunization Cost Among Iraqi Pediatric Practice Younger Than 2 Years  
O. Q. B. Al-lela¹, M. B. Bahari¹, M. G. Al-abbassi², A. Y. Basher²  
¹Pharmaceutical School, Universiti Sains Malaysia (USM), Pinang, Malaysia, ²Pharmacy College, Al-Mustansaria University, Baghdad, Iraq  
³Advance Medical and Dental Institute, Universiti Sains Malaysia (USM), Pinang, Malaysia

**TG10**  
Qualitative and Quantitative Analysis of Rubella IgG Antibody Among Pregnant Women in Ibadan, Nigeria  
O. M. Adewumi, B. R. Olusanya, A. B. Oladunjoye, A. J. Adeniji  
_University of Ibadan, Ibadan, Nigeria_
INVITED SPEAKER BIOGRAPHIES
Ann M. Arvin, MD
Dr. Arvin is the Lucile Packard Professor in pediatrics, microbiology, and immunology at Stanford University School of Medicine. Dr. Arvin’s basic laboratory research interest is in molecular mechanisms of pathogenesis and the host response to the human herpes virus, varicella zoster virus (VZV). Dr. Arvin has had a long-term commitment to clinical research related to viral vaccines, including measles and influenza, age-related maturation of antiviral immune responses and herpes simplex virus type 2, VZV, and human cytomegalovirus infections.

She has received numerous honors and awards and served on many national advisory boards. She recently chaired the committee that prepared the Institute of Medicine 2009 Report on the Scientific Uses of Variola Virus. Other recent national service includes service on the President’s Council of Advisors on Science and Technology working groups on U.S. Preparations for 2009-H1N1 influenza and on Influenza Vaccines, the NAS/NRC Board on Life Sciences, and the Director’s Advisory Council of the National Institute of Allergy and Infectious Diseases.

Dr. Arvin is an elected member of the Association of American Physicians, the American Association for the Advancement of Science, and the Institute of Medicine of the National Academy of Sciences. She has served as the vice provost and dean of research at Stanford University since 2006.

Dan H. Barouch, MD, PhD
Dr. Barouch received his PhD from Oxford University in 1995 and his medical degree from Harvard Medical School in 1999. He currently serves as the chief of the Division of Vaccine Research, Department of Medicine, Beth Israel Deaconess Medical Center. His laboratory focuses on studying the immunology and virology of HIV-1 infection, developing novel vaccine strategies, and is a key part of the Bill & Melinda Gates Foundation Collaboration for AIDS Vaccine Discovery (CAVD), the NIH Center for HIV/AIDS Vaccine Immunology (CHAVI), and the Ragon Institute of MGH, MIT, and Harvard.

Christopher C. Broder, PhD
Dr. Broder received his BS (1983) and MS (1985) degrees from Florida Tech, and his PhD (1989) from the University of Florida. His thesis work was the discovery and characterization of a specific receptor for human plasmin on Group A Streptococci, forming a molecular-pathogenic model for the “flesh-eating streptococci.” He joined the Laboratory of Viral Diseases, NIAID, NIH, as a National Research Council Research Associate in 1989, where he focused on the membrane fusion and entry mechanisms of HIV-1 and formulated the model of distinct membrane fusion accessory factors as the basis for HIV-1 cell-type tropism in 1993, which led to the discoveries of the CXCR4 and CCR5 HIV-1 coreceptors, for which he received The Fellows Award for Research Excellence from the NIH Office of Science Education and was co-recipient of the AAAS, Newcomb Cleveland Prize in 1997. Dr. Broder also developed the first full-length, soluble, oligomeric HIV-1 envelope glycoprotein known as gp140 as a potential subunit vaccine for HIV.

Dr. Broder shares inventorship on several US patents including the CXCR4, CCR5, and gp140 developments. He joined the Department of Microbiology and Immunology of the Uniformed Services University (USU) in Bethesda, Maryland in 1996, as an assistant professor, participating in a variety of teaching activities in both the graduate and medical schools. His current research programs, in collaboration with other national and international research groups, focus on virus-host cell interactions with an emphasis on vaccine and therapeutics development for HIV and important emerging viral agents including Nipah and Hendra viruses, Ebola and Marburg viruses, and Australian Bat Lyssavirus.

Recent research findings include the discovery of the receptor proteins (ephrin-B2 and -B3) employed by Nipah and Hendra for infection, and the development of an effective recombinant subunit vaccine and antiviral human monoclonal antibodies against Nipah and Hendra virus. His laboratory of postdoctoral fellows, research associates, graduate students, and technicians is supported by NIH funding. He has served as a member of numerous national and international review panels, committees and editorial boards, and has co-authored over 100 scientific articles and book chapters. He is now a professor and also director, of the Emerging Infectious Diseases Graduate Program at USU.

Alan S. Cross, MD
A graduate of Harvard College and the University of Pennsylvania School of Medicine, Dr. Cross is currently professor of Medicine at the University of Maryland School of Medicine and associate director for Adjuvant Biology Research at the Center for Vaccine Development at the University of Maryland School of Medicine. Following fellowships in infectious diseases at the University of Rochester and the Walter Reed Army Institute of Research.
James E. Crowe, Jr., MD

Dr. Crowe is an immunologist and board-certified pediatric infectious diseases specialist. He is professor of Pediatrics, Microbiology, and Immunology, Ingram professor of Cancer Research, and director of the Vanderbilt Vaccine Center. His laboratory has a broad portfolio of work in the area of viral immunology and cell biology, with an aim to discovery of mechanisms important to development of new vaccines.

Dr. Crowe received his medical degree from the University of North Carolina at Chapel Hill, where he also did his pediatrics residency. Following his clinical training, he received five years of postdoctoral training in the Laboratory of Infectious Diseases at NIH. He completed infectious diseases fellowship training in 1996 at Vanderbilt. He has run an independent laboratory at Vanderbilt since that time. In addition, he directs two institutional core laboratories, the Human Immunology Core and the Flow Cytometry and Cell Sorting Core. His work has been published in over 150 publications including Nature, Science, Nature Medicine, Proceedings of the National Academy of Sciences USA, the New England Journal of Medicine, and JAMA.

He has been the recipient of investigator awards from the March of Dimes, American Society for Microbiology, Pediatric Infectious Diseases Society, and Society for Pediatric Research. He has been awarded the Judson Daland Prize of the American Philosophical Society, the Oswald Avery Award of the Infectious Disease Society of America, the E. Mead Johnson Award for Excellence in Pediatrics, the 2007 Outstanding Investigator Award of the American Federation for Medical Research, and the 2010 Norman J. Siegel Award of the American Pediatric Society. He is an elected Fellow of AAM, AAAS, ASCI and AAP, IDSA, APS, and others.

John A. Ellis, DVM, PhD

Dr. Ellis received his DVM from the University of Illinois in 1979 and a subsequent PhD in comparative pathology from Colorado State University in 1984. After graduation from veterinary school, he worked as a staff veterinarian and instructor in animal science at the Navajo Community College in Arizona and a Research Associate in Peru for the US Agency for International Development. Additionally, Dr. Ellis was previously on the faculty of Veterinary Science at the University of Wyoming, and was a postdoctoral fellow and subsequently visiting Scientist at the International Laboratory for Research on Animal Disease in Nairobi, Kenya, where he worked on bovine cellular immunology.

Since 1992, Dr. Ellis has served on the faculty of the Western College of Veterinary Medicine at the University of Saskatchewan in Saskatoon, Saskatchewan, Canada. He is a Diplomate of the American College of Veterinary Pathologists and the American College of Veterinary Microbiology (Immunology, Virology). Dr. Ellis is extensively published, having written or co-authored more than 150 peer-reviewed articles and textbook chapters, as well as numerous papers and lectures published in conference proceedings. Science Watch recently reported that Dr. Ellis was the number 2 most cited author in the veterinary literature from 1995-2005. He has given over 200 invited lectures in various scientific forums. His research interests are varied, and focus on vaccine efficacy and safety in livestock and companion animal species.

Ronald N. Germain, MD, PhD

Dr. Germain received his MD and PhD in 1976 from Harvard University, the latter for research with B. Benacerraf, recipient of the 1980 Nobel Prize in Physiology and Medicine. Since that time, he has investigated basic T-cell immunobiology, first on the faculty of Harvard Medical School and, since 1982, as the Chief, Lymphocyte Biology Section in the Laboratory of Immunology at the National Institute of Allergy and Infectious Diseases, National Institutes of Health. Over the years, he and his colleagues have made key contributions to our understanding of Major Histocompatibility Complex (MHC) class II molecule structure–function relationships, the cell biology of antigen processing, and the molecular basis of T cell recognition, especially the role of self-recognition and the organization of signaling networks involved in ligand discrimination. More recently, his laboratory has been focused on the details of T cell-antigen presenting cell interactions and the relationship between immune tissue organization and
control of adaptive immunity at both the initiation and effector stages.

Experiments at the whole cell, tissue, and organism level are being used to build a more complete picture of the operation of the adaptive immune system, including those utilizing novel dynamic in situ microscopic live animal imaging methods that his laboratory helped pioneer. Efforts are also underway to create computer models of T-cell signaling and activation based on these studies. The aim of this work is to create a detailed understanding of how immunity develops and to develop new tools for prediction of how the immune system will respond if perturbed, for example, by a candidate vaccine. The latter studies are being pursued in a new Program in Systems Immunology and Infectious Disease Modeling (PSIIM) that is working on creating and applying the next generation of computer software and research tools for quantitative modeling and simulation of complex biological systems.

Dr. Germain has published more than 300 scholarly research papers and reviews. Among numerous honors, he was elected as an Associate (foreign) member of EMBO (2008), awarded the Landsteiner Medal of the Austrian Society for Allerology and Immunology (2008), selected as a Distinguished Lecturer, American Association of Immunologists (2006), and given numerous named lectureships at major academic institutions in the US and abroad. He serves as an associate or advisory editor of the J Exp Med, Immunity, Current Biology, Mol Systems Biol, Int Immunol, and BMC Biology and has previously served as Deputy Editor of J Immunol and Editor, Immunity. He helped co-founded the Immunology Interest Group and Systems Biology Interest Group at NIH and he serves as Associate Director for the trans-NIH Center for Human Immunology. The Lymphocyte Biology Section he directs in the Laboratory of Immunology has trained dozens of postdoctoral fellows, many of whom now occupy senior academic posts at universities and medical schools around the world and who are internationally recognized investigators in their own right.

Elizabeth J. Glass, PhD, BSc
Dr. Glass is chair of Veterinary Immunogenetics at The Roslin Institute. She leads a group exploiting the recent advances in genetics and genomics for farm animals to identify significant variation in chromosomal loci and genes that control vaccine responsiveness and disease resistance in livestock species. Her research will aid both vaccine development as well as markers for improved disease resistance in livestock and is supported by both industry and research councils. She is interested in how comparative genomics can shed light on the evolutionary selection of host disease resistance phenotypes and is particularly focused on the early host-pathogen interactions involving intracellular pathogens that target macrophages.

Barton F. Haynes, MD
Barton Haynes received his MD from Baylor College of Medicine in 1973. After completing infectious diseases and allergy and immunology training at NIH, he came to Duke University in 1980. At Duke, he is Director of the Human Vaccine Institute, where teams of investigators are working on vaccines for emerging infections including HIV-1, TB, and pandemic influenza. He currently is the leader of the Center for HIV/AIDS Vaccine Immunology (CHAVI) funded by NIH and Collaboration for AIDS Vaccine Discovery Center funded by the Bill and Melinda Gates Foundation. Dr. Haynes is a member of the Institute of Medicine of the National Academy of Sciences and a Fellow of the American Academy of Arts and Sciences.

Adrian V.S. Hill, PhD
Dr. Hill trained at Trinity College Dublin and Oxford is now professor of Human Genetics and director of the Jenner Institute at Oxford University. He leads research programs in genetic susceptibility to tropical infectious diseases and in vaccine design and development. His group identified heterologous prime-boost immunization using non-replicating vectors as an exceptionally potent approach for inducing protective T cell responses in murine malaria and undertook the first clinical trials of this vaccination strategy.

In 2005, he was appointed director of the Jenner Institute, a new initiative aimed at accelerating public sector vaccine development for a variety of human and livestock infectious diseases. The Institute aims to fill the gap between pre-clinical vaccine design and large-scale field efficacy trials particularly for infections that pose great disease burdens in developing countries. He currently also chairs the Centre for Clinical Vaccinology and Tropical Medicine and the Clinical Biomanufacturing Facility in Oxford. He has published over 350 research papers. He is a fellow of the UK Academy of Medical Sciences and the Royal College of Physicians and a NIHR Senior Investigator.

Martyn Jeggo, PhD
Dr. Jeggo is director of the Australian Animal Health Laboratory (AAHL), a global leader in research into and diagnosis of major diseases affecting livestock throughout
the world. The Laboratory is a frontline defense, helping to protect Australia from the threat of exotic and emerging animal diseases. Dr. Jeggo holds a Bachelor of Veterinary Medicine from the Royal Veterinary College, London, UK, a master of Tropical Veterinary Science from the Centre for Tropical Veterinary Medicine, Edinburgh University, UK, and a Doctor of Philosophy from Surrey University, UK.

From 1996–2002, he was the head of the Animal Production and Health Science Section of the Joint Food and Agricultural Organisation/ International Atomic Energy Agency (FAO/IAEA) Division of Agriculture, in Vienna, Austria. In that role, he managed a range of FAO/IAEA Coordinated Research Programs involving more than 200 research contracts relating to animal production and health. These were operational in some 130 countries. Among other international activities, Dr. Jeggo also developed an international external quality-assurance program for veterinary laboratories.

**COL Jerome H. Kim, MD**

Col. Jerome H. Kim, MD, is currently Deputy Director (Science) and Chief, Department of Molecular Virology and Pathogenesis, Division of Retrovirology, Walter Reed Army Institute of Research (WRAIR) (U.S. Military HIV Research Program), a multidimensional, international research program encompassing vaccine research and development, HIV prevention research, and clinical research. He also serves as the HIV Vaccines Project Manager, U.S. Army Medical Materiel Development Activity, Fort Detrick, MD. Dr. Kim's current research interests include HIV molecular epidemiology, host genetics, and HIV vaccine development.

Prior to serving as Deputy Director (Science), Dr. Kim was the Thai Phase III Trial Sponsor Liaison and Chief, Department of Retrovirology, U.S. Army Medical Component, Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand (2004-2008). Dr. Kim is an Associate Professor of Medicine, Uniformed Services University of the Health Sciences and a Clinical Associate Professor of Medicine at the John A. Burns School of Medicine, University of Hawaii. He is a Fellow of both the American College of Physicians and the Infectious Diseases Society of America. Dr. Kim graduated with highest honors in Biology and high honors in History from the University of Hawaii, Manoa in 1980. He graduated from the Yale University School of Medicine in 1984. Dr. Kim completed his training in Internal Medicine (1987) and fellowship in Infectious Diseases (1990) at Duke University Medical Center.

**Steven Krakowka, DVM, PhD**

Dr. Krakowka received his DVM in 1971 from Washington State University, College of Veterinary Medicine in Pullman, WA. He received his PhD in 1974 from College of Veterinary Medicine, Department of Veterinary Pathobiology (now Veterinary Biosciences), The Ohio State University, Columbus, OH. Since 1998, he has been a professor in the Department of Veterinary Pathobiology (Biosciences) at The Ohio State University’s College of Veterinary Medicine and adjunct professor, Department of Veterinary Microbiology, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Canada.

He has co-authored three books on veterinary immunology and viral infectious diseases, over 290 peer-reviewed papers and book chapters, and has received numerous extramural grants and contracts throughout his professional career in the Department of Veterinary Biosciences, College of Veterinary Medicine, The Ohio State University. His research programs have been supported by NIH grants for all or portions of four decades. His greatest funding accomplishment has been to provide continuous and uninterrupted financial support of The Gnotobiotic Life Laboratory since 1974.

**Trudy V. Murphy, MD**

Dr. Murphy completed her undergraduate studies at the University of California, Berkeley and earned her Doctor of Medicine degree at the University of California at Los Angeles. She completed a fellowship in Pediatric Infectious Diseases at the University of Texas Southwestern Medical School in Dallas, TX. She is Board Certified in Pediatrics and Pediatric Infectious Diseases. Dr. Murphy joined the Centers for Disease Control and Prevention (CDC) after 15 years on the pediatric and infectious disease faculty at the University of Texas Southwestern Medical School in Dallas. Her initial research was in vaccine immunology, surveillance, and epidemiology of *Haemophilus influenzae* type b, and 4 other invasive bacterial pathogens that were potential candidates for new vaccines.

Dr. Murphy joined the CDC in September 1998, as Chief of the Infant Immunization Activity, and later had positions as Associate Director for Science and Team Leader for the Diphtheria, Tetanus, Pertussis, and Hib Team. She currently is the Vaccine Research and Policy Team Leader in the Division of Viral Hepatitis of the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP). She has worked on the development of vaccine policy for a wide range of vaccines to prevent bacterial and viral
Gary J. Nabel, MD, PhD

Dr. Nabel is well known as a molecular virologist and immunologist for his work in the fields of HIV, cancer, and Ebola virus research. His laboratory has studied mechanisms by which cells coordinateely regulate the expression of genes during viral infection and development. He undertook the position of Director of the Vaccine Research Center in 1999 to develop a vaccine against AIDS. At his prior institution, University of Michigan in Ann Arbor, he was the Henry Sewall Professor of Internal Medicine, professor of biological chemistry, and Howard Hughes Medical Institute investigator.

His early work defined the key cellular protein that acts as a switch to stimulate the HIV virus to start copying itself during activation of immune system cells. These studies defined one of the important determinants of whether the virus lies quietly in the cells or starts reproducing. Since then, his laboratory has examined this regulatory pathway in much more detail, identifying several other regulators and their roles and showing that activation of the key regulator is linked to cell cycle control.

Dr. Nabel graduated magna cum laude from Harvard College in 1975, then entered the university’s MD-PhD program, completing his PhD in 1980 and his MD 2 years later. He then served as a postdoctoral fellow in the laboratory of David Baltimore at MIT’s Whitehead Institute. In 1987, Dr. Nabel became an assistant professor of internal medicine and assistant professor of biological chemistry at University of Michigan in Ann Arbor. In addition to his faculty positions, Dr. Nabel was the director of the Center for Gene Therapy and co-director of the Center for Molecular Medicine at the university.

In recognition of his expertise at the forefront of virology, immunology, gene therapy, and molecular biology, Dr. Nabel was elected a member of the Institute of Medicine of the National Academy of Sciences in 1998. Another of his honors is the American Society for Biochemistry and Molecular Biology-Amgen Scientific Achievement Award in 1996. He was an associate editor of *Journal of Virology* and serves on the editorial boards of several other journals. He has participated on numerous NIH advisory committees, including the National Institute for Allergy and Infectious Diseases AIDS Research Advisory Committee, which he chaired from 1996-97.

Robert F. Pass, MD

Dr. Pass is a professor of Pediatrics and Microbiology at the University of Alabama at Birmingham. He has studied human CMV infection for over 30 years, including the epidemiology of maternal and congenital infection, disability due to the congenital infection, cell mediated immune response to CMV in infected infants, routes of vertical and horizontal transmission, and molecular epidemiology of CMV infections in children and families. Dr. Pass’ current research involves clinical trials of CMV vaccines with the goal of advancing the effort toward a vaccine for prevention of congenital CMV infection.

Gregory A. Poland, MD

Dr. Poland is the director of Mayo Clinic’s Vaccine Research Group – a state-of-the-art research group and laboratory that investigates issues surrounding vaccine response and novel vaccines important to public health. He is a professor of Medicine and Infectious Diseases, the director of the Immunization Clinic, and director of the Program in Translational Immunovirology and Biodefense at the Mayo Clinic. He is the Editor-in-Chief for the journal *Vaccine*.

Dr. Poland was awarded the Secretary of Defense Award for Excellence in December 2008. In 2008, he was named a Master of the American College of Physicians. Dr. Poland received the Hsu prize in International Infectious Disease Epidemiology in 2007, and the Charles Mérieux Lifetime Achievement Award in Vaccinology from NFID in May 2006. In December 2006, Dr. Poland was elected President of the Defense Health Board, serving two terms, and currently serves as the Vice-President and advisor on pandemic influenza issues to the Secretary of Defense. In 2005 he was awarded an honorary Doctor of Humane Letters by Illinois Wesleyan University, his alma mater. He was appointed as the Mary Lowell Leary Professor in Medicine (the highest academic distinction for a faculty member) by Mayo Clinic’s Board of Trustees in 2004. In May 2003, he was awarded the Secretary of Defense Award for Outstanding Public Service. Since 2004, Dr. Poland has served on the Infectious Diseases Society of America Taskforce on Pandemic Influenza, and chaired the American College of Physician’s Adult Immunization Advisory Board. Dr. Poland received the inaugural Gold Medal from the Spanish Vaccinology...
Society in 2001. In 1998, he received a joint award from the CDC and the Health Care Financing Administration for his contribution to increasing adult immunization rates in the U.S., which was awarded by the Surgeon General of the United States. In 1997, he was honored as the “Outstanding Clinical Investigator of the Year” by Mayo Clinic.

He is the immediate past President of the International Society for Vaccines, and is the current president and co-founder of the Edward Jenner Society. Dr. Poland participates on many national and academic review committees and actively peer-reviews journal articles for over 26 different publications including The Lancet, Annals of Internal Medicine, and New England Journal of Medicine. A prolific writer, Dr. Poland has published over 350 peer-reviewed scientific articles and book chapters.

**W. Ray Waters, DVM**

Dr. Waters received a BS degree in Biological Sciences and Doctor of Veterinary Medicine degree from Auburn University in 1985 and 1988, respectively, and a Doctor of Philosophy in Immunobiology from Iowa State University in 1996. Currently, he is lead scientist of the Tuberculosis Research Project at the National Animal Disease Center (NADC), Agricultural Research Service, Ames, IA and Collaborator/Assistant Professor with the Veterinary Microbiology and Preventive Medicine Department at Iowa State University, Ames, IA. Past work experience includes 5 years of small animal veterinary practice; research associate at the NADC; Microbiologist at Plum Island Animal Disease Center, Greenport, NY; and Associate Scientist at Iowa State University.

The current focus of Dr. Waters’ research is evaluation of the immune response of cattle and various wildlife hosts to *Mycobacterium bovis* infection. Dr. Waters has authored and/or co-authored more than 130 research papers and book chapters on veterinary immunology and tuberculosis research topics, is an editor for Clinical and Vaccine Immunology, and a member of several professional societies.

**Robert G. Webster, PhD**

Dr. Webster is professor in the Division of Virology; Department of Infectious Diseases at St. Jude Children’s Research Hospital and holds the Rose Marie Thomas Chair. A native of New Zealand, Dr. Webster received his BS and MS in Microbiology from Otago University in New Zealand. In 1962, he earned his PhD from the Australian National University and spent the next two years as a Fulbright Scholar working on influenza in the Department of Epidemiology at the University of Michigan, Ann Arbor. Dr. Webster’s interests include the emergence and control of influenza viruses, viral immunology, the structure and function of influenza virus proteins, and the development of new vaccines and antivirals. Together with Graeme Laver, he developed one of the first subunit vaccines for influenza that is still being produced in Australia.

The major focus of his research is the importance of influenza viruses in wild aquatic birds as a major reservoir of influenza viruses and their role in the evolution of new pandemic strains for humans and lower animals. His *curriculum vitae* contains over 500 original articles and reviews on influenza viruses. He has trained many scientists who now contribute to our understanding of the evolution and pathogenesis of influenza. He continues to work in the Center of Excellence for Influenza Research and Surveillance (CEIRS) which he initiated at St. Jude Children's Research Hospital.

**Brigit Weinberger, PhD**

Dr. Weinberger is a senior post-doctoral member at the internationally renowned Institute for Biomedical Aging Research in Innsbruck, Austria. She focuses on biogerontology studying aging processes at the cellular/molecular level. The Immunology Division, where Dr. Weinberger is a senior post-doctoral member, focuses on immunosenescence, particularly within the T-cell compartment. Besides several basic research projects, the optimization of vaccinations for the elderly is a central interest of the department. The Immunology Division addresses this issue in several research projects analyzing immune responses to vaccination in the elderly.

Dr. Weinberger studied biology in Regensburg, Germany and Boulder, CO, focusing on Genetics, Developmental Biology, and Medical Microbiology. She holds a PhD from the Institute for Medical Microbiology and Hygiene of the University of Regensburg, where she worked on the role of Epstein-Barr virus in transplant recipients. Dr. Weinberger is a member of the German Society for Virology, the Austrian Society for Allergology and Immunology, and the American Aging Association.

**Richard Whitley, MD**

Dr. Richard Whitley is a UAB Distinguished Professor of Pediatrics, Microbiology, Medicine, and Neurosurgery, as well as the Loeb Scholar in Pediatrics. He directs the Division of Pediatric Infectious Diseases and is also the Vice-
Chair of the Department of Pediatrics. He co-directs the merged UAB Center for Emerging Infections and Emergency Preparedness (CEIEP) and is heavily involved in activities that create awareness of and develop strategies for dealing with pandemic influenza. Dr. Whitley is responsible for the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group (CASG) whose role is to perform clinical trials of antiviral therapies directed against medically important viral diseases of children and adults. Dr. Whitley’s other research interest is in the translation of molecular biology to clinical application, particularly in the development of human monoclonal antibodies for therapy and engineering of herpes simplex virus for gene therapy.

He is a past President of the International Society of Antiviral Research. He is the current Past President of the Infectious Diseases Society of America, and is also a member of the American Society of Microbiology, American Society of Clinical Investigation, and Association of American Physicians. At UAB Commencement on May 3, 2007, he received the UAB President’s Medal for his accomplishments and many years of dedicated service to the University.

His research focuses on three areas. First, he directs studies of antiviral agents for unmet medical needs, including herpes simplex encephalitis, neonatal herpes simplex virus infection, congenital cytomegalovirus infection, West Nile Virus encephalitis, and influenza in infants, among others. Each clinical trial incorporates natural history of disease, diagnosis, and risk factors. Second, he is responsible for the development of antiviral drugs to treat orthopox virus infections. These studies involve coordinating the team efforts of crystallographers, in vitro and in vivo antiviral testing, and iterative medicinal chemistry. Lastly, he is the principal investigator on a program project grant that engineers herpes simplex virus to treat brain tumors.

He received his BA in chemistry from Duke University and his MD from the George Washington University. He subsequently completed an internship in pediatrics and a fellowship in infectious diseases/virology at the University of Alabama at Birmingham. He has published over 334 articles. He chairs the CDC’s Coordinating Center for Infectious Diseases Board of Scientific Counselors and participates in numerous Data Safety and Monitoring Boards for ongoing clinical studies. He currently is serving a four year term on the NIH National Allergy and Infectious Diseases Advisory Council, ending in 2012. In June of 2009, he was tapped to serve as a member of the Novel H1N1 Influenza Working Group of the President’s Council of Advisors on Science and Technology (PCAST).
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1

**One Health-One Medicine**
Martyn Jeggo, PhD
Australian Animal Health Laboratory
Geelong, Australia

**Objective:** Review the science and organizational changes that are required to ensure that medical, veterinary, and ecological scientists work together to undertake research that will deliver the most effective options for managing infectious diseases risks and other health-related issues.

The first international Congress on One Health was held in Melbourne, Australia on February 14–16, 2011. Approximately 650 participants attended including doctors, veterinarians, agriculturists, and ecologists working on a range of issues dealing with the risks of infectious diseases to humans, animals and the environment. Equally important, the meeting was attended by representatives from key international organizations (WHO, OIE, FAO, EU, WB) as well as national governments that will utilize this science and the research outcomes to drive policy and reform in the One Health space. This marriage of research workers and policy makers provided an ideal platform to debate many of the key issues around One Health-One Medicine. Not only was it possible to gain a current insight into the science underpinning disease emergence, food safety and food security but it put in context the required policy changes needed to have real impact in this area. We will explore both the science undertaken as well as policy and organizational reforms needed.

**Reference:**

2

**Bridging Animal and Human Health in the Search for Countermeasures for Henipaviruses**
Christopher C. Broder, PhD
Uniformed Services University of the Health Sciences
Bethesda, MD

**Objectives:** Discuss the nature of the emerging zoonotic Hendra virus and Nipah virus agents; identify the cause of human cases of infection and the pathology associated with infection by these viruses and the animal models that are being used to study pathogenesis; review the antiviral countermeasure strategies that have been developed based on basic scientific research findings and how they are being applied in veterinary vaccine development and human immunotherapeutic approaches.

Hendra and Nipah virus are highly pathogenic zoonotic agents that cause severe and often fatal neurologic and respiratory disease in a wide variety of mammals including humans. Together they comprise the genus *Henipavirus*, within the *Paramyxoviridae* family. Henipaviruses are classified as BSL4 agents and there is currently no licensed antiviral therapies or vaccines available. Initial studies focused on henipavirus entry and uncovered many details of the attachment and membrane fusion steps of virus infection including the identification of the receptor proteins employed by the viruses. Structural studies on the henipavirus attachment G glycoproteins have provided important details on both receptor binding and antibody based neutralization mechanisms. Stemming from these studies has been the development of therapeutics and vaccine candidates, and animal models for antiviral testing. Two new models of henipavirus pathogenesis are the ferret and African green monkey, each offering an accurate and consistent representation of the pathogenesis seen in human infections. Among several antiviral strategies tested in animals to date, two have shown significant promise; passive immunization with a cross-reactive and neutralizing human monoclonal antibody (m102.4) targeting the henipavirus G glycoprotein receptor binding site, and a soluble form of G (sG) as a subunit vaccine. Together, these countermeasures offer viable countermeasures against Hendra and Nipah virus infection that are applicable to either livestock or humans.
References:


3 Co-Development of Some Viral Vectored Vaccines for Livestock and Humans
Adrian V.S. Hill, PhD
The Jenner Institute
Oxford, United Kingdom

Objectives: Identify the utility of viral vectors for development of a new generation of vaccines that stimulate both cellular and humoral immunity and the advantages of co-development of vaccines for some indications in parallel in humans and livestock.

Despite considerable progress in understanding innate immune pathways and the requirements for protective cellular and humoral immunity, there are many viral, bacterial, and parasitic infections of both humans and livestock for which we have no useful vaccines. It is proposed here that the utilization of particular non-replicating recombinant adenoviral and poxviral vectors provide a useful platform for the generation of a new range of viral vectored vaccines that will allow cost partly generic manufacturing processes. I will discuss examples of how similar or identical vaccines are being developed to tackle related diseases in human and livestock with examples from viral (influenza), bacterial (tuberculosis), and parasitic (apicomplexan) diseases.

Reference:

4 From Beach to the Bedside: Influenza's Ability to Spread
Robert G. Webster, PhD
St. Jude's Children Research Hospital
Memphis, TN

Objectives: Discuss factors that show aquatic birds of the world as the ultimate reservoir of all pandemic influenza viruses; discuss that the pig serves as the intermediate host between wild birds and humans and that prediction of future pandemics is the ultimate goal of influenza surveillance in lower animals and birds.

The aquatic birds of the world are recognized as the natural reservoirs of all influenza A viruses; they replicate predominantly in the intestinal tract and are spread mainly via fecal/oral transmission through the water. The pandemics of influenza in humans that occur at irregular intervals originate from the influenza viruses in the aquatic bird reservoir. Surveillance for influenza viruses at the wild aquatic bird/domestic animal/human interface and molecular analysis of the isolated viruses was used to establish the genesis and emergence of pandemic influenza viruses. The 16 hemagglutinin and 9 neuraminidase subtypes of influenza A viruses are largely benign in their natural hosts and cause no apparent disease. The segmented nature of the influenza genome together with the co-circulation of multiple different subtypes permits ongoing reassortment in nature.

The successful transmission of avian influenza viruses to mammals involves changes in the site of replication (intestinal tract versus respiratory tract replication), the optimal temperature of replication (42°C versus 37°C) and receptor specificity (SA a 2-3 versus SA a 2-6 sialic acid). Intermediate hosts including pigs and turkeys are involved in transmission to mammalian species including humans. The genesis and evolution of both the highly pathogenic H5N1 and the 2009 H1N1 pandemic...
influenza viruses are examples of influenza viruses that originated from the aquatic bird reservoir of influenza viruses.

It has not been possible to predict which influenza subtype will cause the next pandemic. Detailed analysis of the genomics of influenza in wild birds and surveillance in pigs globally will provide much needed information.

Reference:

Vaccine Prevention of Congenital CMV Infection: The Way Forward
Robert F. Pass, MD
University of Alabama at Birmingham
Birmingham, AL

Objectives: Review the importance of congenital cytomegalovirus (CMV) infection as a cause of sensory, cognitive, and motor disability in children; identify the sources of maternal CMV infection and understand the difficulties inherent in preventing CMV exposure in women of child bearing age; analyze the evidence from observational studies and from randomized clinical trials which supports a role for active immunization in prevention of maternal and congenital CMV infection.

Congenital CMV infection is probably the leading infectious cause of central nervous system damage in children in developed countries; it can lead to sensorineural hearing loss, mental retardation, cerebral palsy, and impaired vision. CMV infections are almost always clinically silent in children and adults but virus is shed in body fluids for months to years. The source of maternal infection during pregnancy is often within the family usually a child or intimate contact which makes prevention of exposure very difficult. Economic analysis of the burden of CMV disease and cost of vaccine development suggests that a vaccine that could prevent congenital CMV infection would be very valuable to society both in terms of healthcare dollars saved and in improvement in health and well-being. Results from studies of the effect of immunity from infection and from randomized clinical trials of investigational vaccines indicate that vaccine prevention of maternal and congenital CMV infection is a biologically achievable goal.

References:

The Development of Vaccines for Herpes Simplex Virus Infections
Richard Whitley, MD
University of Alabama at Birmingham
Birmingham, AL

Objectives: Discuss the status of vaccines directed toward the prevention and treatment of herpes simplex virus (HSV) infections; analyze the use of genetically engineered HSV in gene therapy of cancer.

Herpes simplex virus (HSV) infections have been identified since ancient Greek times. These viruses have the unique propensity to establish latency in sensory ganglia and recur in spite of both humoral and cell mediated immune responses. Over the last century significant efforts have been devoted to vaccine HSV development, including ultraviolet light
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inactivation and serial passage, but without evidence of efficacy and, in some cases, toxicity. More recently, glycoprotein vaccines have been assessed. The two immunodominant glycoproteins (g), B and D, have been used alone and in combination with selected adjuvants. After promising Phase II results with one construct, gD, a Phase III study failed to support efficacy. Other approaches include the genetic engineering of HSV. Such viruses have been administered to humans as gene therapy of glioblastoma multiforme without evidence of toxicity and suggestions of a beneficial effect.

Reference:

7 Varicella-Zoster Virus Vaccines
Ann M. Arvin, MD
Stanford University School of Medicine
Stanford, CA

Objective: Discuss the formulation of the varicella vaccine, the clinical experience with the vaccine pre- and post-licensure, and the current guidelines for its administration to children, adolescents, and adults and in high risk populations.

Varicella-zoster virus is a medically important human herpesvirus that causes varicella as the primary infection in susceptible children and adults. The varicella vaccine is the first live attenuated human herpesvirus vaccine that is licensed for clinical use in several countries. The vaccine virus was derived from a clinical isolate of VZV, the Oka strain (1). Tissue culture propagation attenuated the virus so that vaccine containing as much as 17,000 pfu per dose of infectious virus induces VZV immunity but rarely produces clinical symptoms. Introduction of the varicella vaccine as a routine early childhood vaccine in 1995 has dramatically reduced the risk of life threatening infections in otherwise healthy children. Since this time, based on the observations of breakthrough varicella in young children who had received a single dose, the varicella vaccine regimen is now two doses for susceptible individuals of all ages. Recent studies also indicate that the administration of varicella vaccine as the first dose in a combined measles-mumps-rubella-varicella (MMRV) vaccine was associated with an incremental risk of fever and febrile seizures compared to MMR and varicella vaccines given at separate sites. Whether the original cohort of varicella vaccine recipients will require booster doses of varicella vaccine at a later age requires continued surveillance.

References:
3. Klein NP, Fireman B, Yih WK, et al.; Vaccine Safety Datalink. Measles-mumps-rubella-varicella (MMRV) vaccine was associated with an incremental risk of fever and febrile seizures compared to MMR and varicella vaccines given at separate sites. Whether the original cohort of varicella vaccine recipients will require booster doses of varicella vaccine at a later age requires continued surveillance.

8 Dynamic In Vivo Visualization of the Initiation and Effector Limbs of Adaptive Immune Response
Ronald N. Germain, MD, PhD
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, MD

Objectives: Describe the role of structural and chemical cues that contribute to optimizing cell-cell interactions underlying adaptive immune responses in lymphoid tissues; identify the migratory activities of lymphocytes to their detection of
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antigen; review how different adhesion processes allow distinct cell-cell communication in the development of cell-mediated and humoral immunity.

Immune responses involve multiple cell-cell interactions within lymphoid tissues, the trafficking of activated cells to sites of effector function, and the migration/function of such effector cells within peripheral tissues. Individual cell behavior depends on the interpretation of exogenous signals by receptors, the activation of signaling pathways, and the modulation of cytoskeletal function and gene transcription. To gain a more detailed appreciation of both the details of these biochemical processes and the macroscale dynamics of immune cell behavior, we have used a combination of cell biological tools and intravital multiphoton microscopy to analyze the interactions of antigen (Ag)-specific T and B cells with each other and with Ag-bearing dendritic cells (DCs).

Our data show that T and B cells follow stromal pathways during their migration in LNs. In the fibroblastic reticular cell (FRC)-defined T zone, this constrained trafficking enhances interactions with DCs attached to the same FRC network. Additional guidance cues facilitate interactions among rare antigen-presenting and antigen-recognizing cells. Naïve CD8 T cells are actively attracted to DCs that present antigen to CD4 T cells based on a cascade of inflammatory signals. Adhesive interactions regulating the duration of cell-cell association are also critical to for adaptive immune responses. The absence of the small adapter SAP in T cells leads to a defect in humoral immunity and in the development of germinal centers. The primary effect of this genetic deficiency (equivalent to the human immunodeficiency X-linked lymphoproliferative disease) is to prevent stable adhesion between antigen-specific T and antigen-bearing B cells, which interferes with effective delivery of 'help' to the B cells in both the early interfollicular and late germinal center phases of the B cell response.

These findings help provide a new level of understanding of how adaptive immune responses are orchestrated and controlled within complex lymphoid tissues in response to infections or vaccines.

Reference:

9 Update on the Thai Phase III Trial: Sieve Analysis, Post-infection Responses, and Search for Correlates
Jerome H. Kim, MD
Walter Reed Army Institute of Research
Rockville, MD

Objectives: Identify the key laboratory findings associated with the RV144 Thai HIV Vaccine trial; understand the basis for correlates of protection analysis; and describe the way forward for testing of the ALVAC vCP1521 prime + AIDSVAX B/E boost.

The Thai Prime Boost HIV Vaccine trial was the first human efficacy study to show that a combination HIV vaccine could reduce the risk of HIV-1 acquisition. Intensive laboratory analysis of archived specimens from the trial have revealed new insight into the antigenicity of both the prime and the boost, and surprising immune responses. Humoral responses shows a broad range of induced antibody, of particular interest are antibodies targeting the V2 loop, and in particular a region of V2 that contains the α4β7 integrin binding site. There are a number of cellular (largely CD4 responses) that appear to be cytolytic, polyfunctional and also target V2. Sieve analysis is similarly beginning to show differences between breakthrough viruses in vaccine and placebo recipients. A formal case control correlates analysis was initiated in March 2011.

Reference:
Lessons from the Thai RV144 Trial and How to Improve Vaccine Induced Protective Antibodies

Barton Haynes, MD
Duke University
Durham, NC

Objective: Identify the findings in the RV144 vaccine and understand the measures currently underway to improve vaccine efficacy of the RV144 vaccine.

The RV144 vaccine showed 31% vaccine efficacy, which showed proof of concept of prevention of HIV acquisition, but did not protect sufficiently for deployment of the current vaccine. New studies suggest that the Envs used in the trial expressed potentially protective antibody epitopes. Data will be presented that define the types of antibodies that were induced in RV144, and plans will be reviewed for strategies for improvement on the vaccine in order to achieve greater vaccine efficacy in subsequent protection trials.

Reference:

Novel Vectors and Antigens for a Next Generation HIV-1 Vaccine

Dan H. Barouch, MD, PhD
Beth Israel Deaconess Medical Center
Boston, MA

Objective: Discuss pre-clinical and clinical advances with alternative serotype adenovirus vectors and novel HIV-1 vaccine immunogens.

Alternative serotype Ad vectors such as rAd26 and rAd35 are biologically substantially different than rAd5 vectors. We have evaluated rAd26 and rAd35 vectors expressing SIV antigens in immunogenicity and challenge studies in rhesus monkeys, and we have shown that rAd35/rAd26 as well as rAd26/MVA prime-boost regimens afford partial protection against both acquisitions of infection as well as virologic control following fully heterologous, intrarectal SIVmac251 challenges. We have also advanced prototype rAd26 and rAd35 vectors expressing HIV-1 Env into phase 1 clinical trial. These vectors have proven safe and immunogenic in humans at doses of $10^9$ vp, $10^{10}$ vp, and $10^{11}$ vp. In addition, we have demonstrated that computationally optimized “mosaic” HIV-1 Gag/Pol/Env antigens substantially expand cellular immune breadth and depth and induce noninferior antibody responses as compared with consensus or natural sequence antigens in rhesus monkeys. Taken together, these data suggest that a rAd35/rAd26 prime-boost vector regimen expressing mosaic HIV-1 antigens should be evaluated in clinical studies.

Reference:

Rational Design of Broadly Neutralizing HIV-1 Antibody Immunogens: Insights from Structure, Protein, and Vector Design

Gary J. Nabel, MD, PhD
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, MD

Objective: Describe the most recent advances in the design of HIV vaccines.
Advances in our basic scientific understanding of the immune system and mechanisms of HIV pathogenesis have provided the tools to rationally design an effective vaccine for AIDS. Cross-reactive neutralizing antibodies (NAb) are found in the sera of many HIV-1 infected subjects, but the virologic basis of their neutralization remains poorly understood. We have used knowledge of HIV-1 Envelope (Env) structure to develop antigenically resurfaced glycoproteins specific for the structurally conserved site of CD4 receptor binding. These probes identified sera with such NAbs from infected donors and enabled the isolation of B cells that recognized the CD4-binding site (CD4bs).

By expressing immunoglobulin genes from individual B cells, we identified three monoclonal antibodies, including a pair of somatic variants that neutralized over 90% of circulating HIV-1 isolates. Exceptionally broad HIV-1 neutralization can be achieved with individual antibodies targeted to the functionally conserved CD4bs of gp120, an insight critical to the development of an AIDS vaccine. The status of the rational immunogen design, strategies related to targets of other broadly neutralizing abs, and novel therapeutic interventions that prevent HIV infection will be discussed.

References:

Objective: Explain the definition and importance of vaccinomics and how it informs the coming age of personalized vaccinology.

By necessity, vaccinology is moving away from its historical paradigm of empiric vaccine development ("Isolate – Inactivate – Inject") and broad use across gender, age, and race; and toward an era of vaccinomics and personalized vaccinology whereby new vaccines are developed, and genetic-driven decisions made regarding use and dose of vaccines to administer or forego. The rationale and examples of vaccinomics and personalized vaccinology will be given.

References:

Objectives: Analyze co-evolution of host and pathogen, most populations of humans and livestock will have variable responses to pathogens and vaccines; discuss the variation likely to result from gene variants expressed in the immune system; identify the underlying genes suggesting new ways to improve the efficacy of vaccines that protect all individuals regardless of genotype.
Humans and livestock remain at risk of endemic, exotic, and newly emerging pathogens. Vaccination is often promoted as the best possible solution, and yet for many pathogens, either there are no appropriate vaccines or those that are available are far from ideal. A complementary approach to disease control may be to identify genes and chromosomal regions that underlie genetic variation in response to vaccination. These genes may pinpoint the pivotal pathways that determine whether a vaccine induces protection or allows infection to prevail. However, identification of the causal polymorphisms is not straightforward as it generally requires large numbers of animals with linked phenotypes and genotypes. Investigation of genes underlying complex traits such as response to vaccines can take complementary approaches: candidate genes deduced from prior knowledge or unbiased whole genome scans using markers spread across the genome.

To explore the contribution of the host genome to variation in vaccine response, a large cattle cross herd was vaccinated against viral pathogens involved in bovine respiratory disease and genotyped with a variety of markers, some of which were in candidate loci. Several distinct loci have been identified that contribute to the observed variation in vaccine response, highlighting novel regions of the bovine genome as well as specific ligand binding domains of MHC class II and toll-like receptors (TLRs). The data to be presented suggests that vaccines with a minimal number of epitopes that are recognized by most cattle and vaccine adjuvants that are better tailored to livestock species could be designed. In addition, a genetic approach to vaccination may identify individuals that make good responses to vaccines. With the advent of livestock genome sequences and availability of high density SNP arrays, it should ultimately be possible to identify causal genes with major impact on vaccine responses, leading to new ways to improve vaccine efficacy.

Reference:

15 Genetic and Proteomic Data Reveal Pathways Regulating Immunogenicity and Adverse Events Following Vaccination
James E. Crowe, Jr., MD
Vanderbilt University Medical Center
Nashville, TN

Objectives: Summarize current approaches to investigation of causes of adverse events or immunogenicity using genetic and proteomic techniques; describe how state-of-the-art informatics approaches are being used to analyze data from vaccine trials.

Despite the amazing success of vaccine programs against infectious diseases, the molecular and cellular basis for the effect of vaccines in humans is often poorly understood. Typically, early vaccine trials focus on the measurement of safety parameters (lack of adverse events [AEs]) and immunogenicity. While current study designs are effective at describing the rates of AEs and immune correlates, most current studies are not able to define the molecular events underlying AEs or optimal immunogenicity. New approaches using data intensive surveys of genetic and proteomic data, coupled with novel computational designs, are being used to define the principal pathways governing the clinical and laboratory endpoints that we observe in clinical trials. This presentation will review the emergence of powerful new technologies for such investigations and illustrate their use with examples from recent experimental vaccine trials.

Reference:
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16 Vaccination of Immunocompromised Patients
Alan S. Cross, MD
Center for Vaccine Development
Baltimore, MD

Objectives: Describe the impact of various immunocompromised states on the response to various vaccines and the strategies used to improve these responses; with the advent of new vaccines for the prevention of nosocomial infections, analyze innovative approaches to their optimal use.

The advances in modern medicine have led to an enlarging population of immunocompromised patients subject to both community-acquired and nosocomial infections. Immunization provides the most cost-effective strategy for preventing these life-threatening complications, yet perceived and real impediments to optimal immune responses have resulted in the inadequate deployment of vaccines. While a considerable early literature describes relatively poor responses to influenza and pneumococcal polysaccharide vaccines, new vaccine formulations, adjuvants, and immunization strategies have led to improved immunization responses that will be reviewed. With increasing concern about nosocomial infections with organisms such as *C. difficile* and MRSA that inordinately impact the immunocompromised patient, immunization strategies for targeting these patients must be devised.

References:

17 Vaccination of Neonates
Trudy V. Murphy, MD
Centers for Disease Control and Prevention
Atlanta, GA

Objective: Discuss the circumstances that would improve outcomes for vaccination in the neonatal period and understand when immunization can be achieved.

Respiratory, diarrheal, and parasitic pathogens are major causes of severe disease among neonates and young children worldwide, accounting for more than a million deaths each year. An increasing number of vaccines provide opportunities for preventing the morbidity and mortality from these diseases. Aside from cost and regulatory issues, the epidemiology of the disease and immunologic considerations determine the age when vaccination is likely to achieve substantial reductions in the disease burden. For infections that result in morbidity starting at an early age, strategies for prevention consider ensuring immunity in pregnant women so that their infants have transient protection though passive maternal antibody, and vaccination starting in the neonatal period (≤ 28 days of life). Three vaccines have wide application in the neonatal period, hepatitis B, Bacillus Calmette-Guérin (BCG), and oral polio vaccine. The potential for inducing immunity starting in the neonatal period is being examined with other vaccines including oral rotavirus and acellular pertussis.

Although much is still to be learned, great advances have been made in understanding the immunology of neonatal responses to vaccination, broadening the potential early vaccination. Initial protection against infection often relies largely on passive maternal antibody. However, infants respond to environmental challenge from exposure to multiple foreign antigens through activation of the innate immune system, and these responses mature with repeated exposure. In this presentation, we will explore examples of successful neonatal immunization and strategies to improve immune responses to vaccination starting in the newborn period.

Reference:
18 Vaccination of Seniors
Birgit Weinberger, PhD
Institute for Biomedical Aging Research of the Austrian Academy of Sciences
Innsbruck, Austria

Objectives: Review age-related changes of the immune system, which contribute to reduced efficacy of vaccination in the elderly; explain official recommendations for vaccination of the elderly and recent improvements/novel strategies to optimize vaccination for seniors.

With increasing age, the immune system undergoes characteristic changes termed "immunosenescence." Cell types of both the innate and the adaptive immune system undergo functional and compositional alterations contributing to increased incidence and severity of infections and reduced efficacy of most vaccines in the elderly. Antibody titers induced by vaccination are generally lower in the elderly and are declining fast, leading to reduced antibody titers at any given time after vaccination. For inactivated vaccines antibody titers before and after booster vaccination are highly correlated, which means that the success of booster vaccination depends on the residual antibody titers. Numbers of vaccine-specific IFN producing T cells are also reduced in the elderly. Many countries have implemented specific details for seniors in their official vaccination recommendations. Still, specific strategies to increase the efficacy of existing vaccines need to be employed; and novel vaccines, adjuvants, and delivery systems should address the special properties and requirements of the aging immune system in order to ensure optimal protection of the elderly.

References:

19 Cattle as a Model to Evaluate New Vaccine Strategies for Tuberculosis
W. Ray Waters, DVM, PhD
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Agricultural Research Service
Ames, IA

Objectives: Discuss the current status of veterinary tuberculosis (TB) vaccine research, opportunities afforded by use of cattle for TB research, and limitations of experimental approaches for TB vaccine discovery.

Vaccines are lacking for many chronic intracellular pathogens requiring cell-mediated immunity for protection. A serious impediment to vaccine discovery is a lack of animal models predictive of efficacy in humans. For TB, vaccine efficacy studies using Mycobacterium tuberculosis in non-human primates (NHPs) offer a logical model for prediction of efficacy in humans. Availability (especially of neonates) and costs associated with BL-3 care, however, hinder widespread use of NHPs for vaccine testing. Thus, many candidate TB vaccines are tested using mice and guinea pigs; yet, only a few of the vaccines deemed effective with rodent models have emerged for evaluation in Phase 1 human trials.

Mycobacterium bovis infection of cattle results in disease that is very similar to M. tb infection in humans. Prior to pasteurization, ~25% of TB cases in humans were attributable to M. bovis. Infection with M. bovis in humans is clinically indistinguishable from infection M. tb infection and these two organisms have ~99.95% sequence identity. The neonatal calf/TB challenge model is a well-established method for evaluation of TB vaccines, including early efficacy studies by Calmette/Guerin in 1911. While the mainstay of bovine TB control has been abattoir inspection and targeted testing, vaccines are being considered as an additional tool, both in cattle and wildlife reservoirs. Vaccine efficacy parameters include: gross and histologic lesion scoring, qualitative assessment of lesion distribution (and colonization), quantitative
assessment of colonization, and morphometric analysis of lung radiographs for granulomas.

Currently, *M. bovis* BCG is the only bovine TB vaccine available. As with humans, BCG efficacy in cattle is variable and responses to BCG may interfere with standard ante-mortem tests. Other bovine TB vaccine platforms have been evaluated including DNA, subunit, live-vectored, attenuated *M. bovis* strains, auxotrophic mutants, and killed mycobacterial preparations. Of these, BCG prime and subunit boost strategies have shown improved efficacy over BCG alone. With calves, effective vaccination is associated with a reduced immune stimulation profile after virulent *M. bovis* challenge. Positive prognostic indicators include: reduced antigen-specific IFN-γ, iNOS, IL-4, and MIP1-α responses; reduced expansion of CD4+ cells in culture; and a diminished T cell activation profile. Also, vaccine-elicited TcM responses prior to challenge correlate with vaccine efficacy. In contrast, infection-elicited antibody and effector recall IFN-γ responses positively correlate with pathology. These findings demonstrate advances in experimental approaches for development of bovine TB vaccines and opportunities for use of calves for TB vaccine research.

Reference:

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Bovine Paramyxoviruses, BRSV and BPIV-3, as Models for HRSV and HPIV-3
John A. Ellis, DVM, PhD
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University of Saskatchewan
Saskatoon, Canada

Objective: Review current information on cognate respiratory virus infections as related to vaccine-development humans to broaden perspectives on available models.

The bovine paramyxoviruses, bovine respiratory syncytial virus (bRSV) and bovine parainfluenza virus-3 (bPIV3), are very closely related, genetically and antigenically, to their cognate infections in humans, hRSV and hPIV3, respectively. The epidemiology, clinical course and lesions are very similar in the respective host species. Notwithstanding some important species differences in lung anatomy and physiology, the ruminant infections are, arguably, the best non-primate models in which to test the efficacy of vaccine candidates for the human pathogens.

In contrast to the situation for the cognate infections in humans, a variety of modified-live and inactivated parenteral and intranasal (IN) vaccines are available for bRSV and bPIV3; more are in development. These are most frequently formulated as combination vaccines. Their safety and efficacy has been tested in experimental challenge models that closely mimic the disease caused by the naturally-occurring infections in cattle. The availability of a variety of immunological reagents and knowledge of the ruminant immune system has allowed the examination of a wide spectrum of vaccine-induced antibody and cell-mediated immune responses that have been correlated with protection. In addition, issues related to the neonatal immune response, passive immunization, and prime-boosting have also been examined.

References:
Swine Model for Torque Teno Virus
Steven Krakowka, DVM, PhD
Department of Veterinary Biosciences, College of Veterinary Medicine
The Ohio State University
Columbus, OH

Objectives: Describe the salient features of our piglet-pTTV-infection model; outline some of the intellectual challenges that the TTVs present to the research community.

The Torque Teno Viruses (TTVs) are subtle agents (family Circoviridae, genus Anellovirus) that encode genomic information for only two viral proteins, a nucleocapsid and a viral DNA polymerase. It is a single stranded circular DNA virus that so far has resisted all attempts at in vitro tissue culture propagation. The virology community is divided into two camps regarding the importance of TTVs in human health and disease: Some view the TTVs as orphan commensal agents without disease potential; others believe that TTVs are pathogenic, but only under unusual or ill-defined circumstances such as immune deficiency disease. The TTVs do not behave as classic “one-agent-one-identifiable-disease” viruses. Yet, suggestions of pathogenicity are accumulating in the human literature, particularly if the TTVs are considered as viruses with disease promotion and co-factor potential. This synergistic relationship is most evident for human viral respiratory diseases caused by “ordinary” pathogens in which increased severity of disease is positively correlated not to the presence/absence of TTV but rather to the amount of TTV in patients. TTV DNAs are elevated in autoimmune disease. One of the more perplexing aspects of autoimmunity is its apparent behavior as an “infectious” disease in individuals according to age (young & middle-aged), gender (female) and HLA-restrictions. The TTVs could well be the “missing infectious agent link” in autoimmunity-prone patients.

Over the last 4 years, we (OSU) have developed the only experimental model of TTV infection in the cognate species, pigs (p) and have established the natural pathogenicity of the pTTVs in swine, the first demonstration of disease-causing capabilities (interstitial pneumonia and renal membranous glomerulonephro-pathy) of any human or animal TTV. As well, we have documented the promotional/synergistic effects that pTTV infection has upon the two most economically significant and economically important viral diseases of swine, porcine respiratory and reproductive syndrome virus (PRRSV) and porcine circovirus disease (PCVD) manifest as post-weaning multisystemic wasting syndrome (PMWS).

References:
ABSTRACTS OF SUBMITTED ORAL PRESENTATIONS
Impact of Cross-Protective Vaccines on Epidemiological and Evolutionary Dynamics of Seasonal and Pandemic Influenza

N. Arinaminpathy, O. Ratmann, K. Koelle, S. Epstein, G. Price, C. Viboud, M. Miller, B. Grenfell

Objective: Discuss key epidemiological and evolutionary implications of broad-spectrum vaccines for influenza, and for antigenically variable viruses in general.

Background: A major goal of influenza vaccinology is to develop vaccines which protect against multiple strains and subtypes of the virus. The main focus of such studies has been on clinical protection, often against highly pathogenic pandemic candidates such as H5N1 viruses. Here, we build on recent experimental work illustrating how cross-protective vaccines could significantly limit viral shedding from infection with seasonal or pandemic strains. We ask how widespread use of such vaccines may impact influenza epidemiology and evolution in the human population.

Methods: We compare two ‘phylodynamic’ approaches, mathematical models integrating influenza epidemiology and evolution. The first of these offers a transparent framework for conceptually studying the population-level effects of vaccination. The second, the ‘epochal evolution’ model, is a well-established, sophisticated framework capturing key features of influenza A evolution, which enables us to test the robustness of our evolutionary findings.

Results: Our models show that sustained immunization with such vaccines could - through lowering transmission - significantly moderate pandemics and seasonal epidemics. More subtly, widespread cross protective immunization could substantively slow the antigenic evolution of seasonal influenza.

Conclusion: Through sustained suppression of transmission, cross-protective vaccines could open important new strategic options for control of influenza. Our findings have profound consequences for the persistence of the virus in the human population, and for the management of antigenically variable viruses in general.

References:

Evidence from H1N1 Supporting Development of Broad-Spectrum Vaccines Against Influenza


Objective: To discuss the role conserved T-cell epitopes may play in a universal influenza vaccine.

Background: The pattern of morbidity associated with swine-origin influenza A (H1N1) virus (S-OIV) observed in the 2009-2010 pandemic suggests that protection from severe disease might have been due to existing cross-reactive T cells specific for highly immunogenic T-cell epitopes conserved between novel H1N1 and strains in the conventional influenza vaccine (CIV).

Methods: Using EpiMatrix, a T-cell epitope prediction and comparison tool, we compared the sequences of the three hemagglutinin (HA) and neuraminidase (NA) proteins contained in 2008-2009 CIV to their counterparts in A/California/04/2009 (H1N1) looking for cross-conserved T-cell epitopes. We also validated candidate epitopes for their ability to bind HLA molecules by examining published records in IEDB and by performing HLA competition binding assays.

Results: We found >50% conservation of T helper and CTL epitopes between novel S-OIV and CIV HA for selected HLA. Conservation was lower among NA epitopes. Sixteen promiscuous helper T-cell epitopes are contained in the S-OIV H1N1 HA sequence, of which nine (56%) were 100% conserved in 2008-2009 CIV; 81% were either identical or had one conservative substitution. >60% of the predicted HA and NA T helper/CTL epitopes were tested and validated, according
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to IEDB. HLA binding assays of T helper epitopes performed in our laboratory confirm informatics predictions and demonstrate that these sequences bind multiple HLA alleles.

**Conclusion:** The results of these studies suggest that conserved influenza sequences, important to viral fitness, may also be immunologically significant as contributors to protection against newly emerging strains of influenza. The conserved epitope approach promises to answer the need for prompt preparedness and delivery of a safe and efficacious vaccine without requiring a new vaccine for every emergent influenza strain.

**References:**

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**S3**

**Antigenic Stability of H1N1 Pandemic Vaccines Correlates with Vaccine Strain**

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**Objective:** The specific influenza vaccine strain used for vaccine production can serve as a predictor of the physical and biological properties of the final vaccine.

**Background:** In 2009, a novel H1N1 influenza virus emerged and spread rapidly around the world. Initially, production of suitable vaccine strains was slow, which hampered the rapid production of initial vaccine lots. Soon after many vaccine lots were released, however, their shelf life was shortened due to an unexpected decrease in HA potency over time.

**Methods:** To investigate the reason for this loss, we used hemagglutination, protease degradation, and deglycosylation analysis as well as tandem mass spectrometry on split influenza monovalent vaccines and the vaccine strains from which they were derived.

**Results:** We found differences in both antigenic content and stability between two different vaccine preparations, which correlated with differences in the specific A/California/7/2009-like influenza strain used in their preparation.

**Conclusion:** This work suggests that more complete analysis of the specific vaccine strains under consideration will lead to an improved predictability of the antigenic content and stability of the resulting vaccine.

**References:**

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**S4**

**Aerosol Live-Attenuated Influenza Vaccine Protects Ferrets at a Reduced Dose**

J. L. Humberd Smith1, M. J. Papania2, D. Knaus1, P. Brooks1, D. Haas1, R. Mair3, J. J. Barry3, S. M. Tompkins1, R. A. Tripp1

1College of Veterinary Medicine, University of Georgia, Athens, GA, 2National Center for Immunization and Respiratory Diseases, Centers for Disease Control, Atlanta, GA, 3Creare, Inc., Hanover, NH

**Objective:** Review the potential role of aerosol delivery live attenuated influenza vaccine as a dose reduction strategy to expand influenza vaccine supply.

**Background:** The 2009-2010 influenza pandemic highlighted the limited influenza vaccine supply in the face of increasing worldwide demand. New vaccine delivery methods that allow for significant dose reduction could mitigate the vaccine supply crisis. Live attenuated influenza vaccine (LAIV) is effectively delivered by nasal spray syringe. However, improved
nasal delivery efficiency using aerosol LAIV might enable a significant vaccine dose reduction. We evaluated the efficacy of aerosol LAIV in ferrets for immunogenicity and protection against homologous influenza virus challenge.

**Methods:** Seronegative ferrets were vaccinated with 0.2 ml LAIV by aerosol (median particle size 15 microns) or by intranasal instillation (i.n.). For each vaccination route, LAIV was delivered at a conventional dose (10^7 TCID₅₀) or a reduced dose (10^3 TCID₅₀). Ferrets administered an aerosol of sterile PBS served as naïve controls. Hemagglutination inhibition assays (HAI) were performed on serum samples collected 14 days post-vaccination. Viral titers were assessed in nasal washes collected 3 and 5 days post-challenge with homologous virus.

**Results:** Mean serum HAI titers were ≥ 320 at 14 days post-vaccination for all conventional dose groups and ≥ 160 for reduced dose groups. Virus was not detected in nasal washes collected at any time point from ferrets vaccinated with the conventional dose by aerosol or i.n., or with the reduced dose by aerosol. One of three ferrets vaccinated i.n. with the reduced dose had a detectable nasal wash virus titer (10^1.6 TCID₅₀) on day 3 post-challenge. All three naive ferrets had nasal viral reproduction, with mean titers ≥ 10^4.2 on days 3 and 5 post-challenge.

**Conclusion:** Aerosol LAIV induced a robust antibody response and protected ferrets from homologous challenge, even at a significantly reduced dose.

**References:**

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**Comparison of Live-Attenuated and Inactivated Influenza Vaccines: Domain-Specific Variation in T-Cell Immunity to Viral Hemagglutinin**

**S. Basha, S. Hazanfeld, R. Brady, R. Subbramanian**  
*Division of Infectious Diseases, Cincinnati Children’s Hospital Medical Center, University of Cincinnati, Cincinnati, OH*

**Objective:** Comparison of domain-specific variation in T-cell immunity to viral hemagglutinin elicited by trivalent inactivated influenza vaccine (TIV) and a live-attenuated influenza vaccine (LAIV) in a cohort of healthy adults (18-49 years old) against H3N2 HA antigen.

**Background:** Influenza HA-specific T-cell responses are being increasingly recognized as a significant component of influenza immunity among humans. However, it is unclear if the two licensed influenza vaccines, TIV and LAIV, vary in their ability to elicit T cell responses to the conserved and the antigenically drifting variant regions of the HA antigen. Elucidating such region-specific T cell responses could shed light on the ability of T cells to provide protection against variant viruses that may escape antibody mediated neutralization.

**Methods:** To measure the T-cell responses elicited by the variant or the conserved regions of H3N2 HA protein, we performed IFN-γ ELISPOT with two peptide pools that spanned these regions individually. Influenza antibody titers were quantified using the standard serum hemagglutination inhibition (HAI) assay.

**Results:** The two licensed influenza vaccines varied significantly in their ability to elicit HA-specific antibody and T cell responses: TIV elicited higher geometric mean HAI titers than LAIV; whereas, LAIV elicited superior T cell responses. Importantly, LAIV elicited higher magnitude T cell responses toward the rapidly drifting variant region of HA that is prone to escape from antibody responses.

**Conclusion:** Ability to elicit robust T cell responses toward mutable regions of the HA antigen could render drift-variants of influenza viruses susceptible to immune control. These results have important implications for the deployment of influenza vaccines in years of antigenic mismatch and shift.

**References:**
**S6**  
**Safety, Immunogenicity, and Productivity of a Recombinant Influenza A Vaccine Constructs for HA1 California/07, Novel H1N1 in Healthy Adults 18-49 and ≥ 65 Years of Age**  
D. N. Taylor¹, L. Tussey¹, J. Treanor², T. Fitzgerald², U. Kavita¹, L. Song¹, K. Ozer³, A. Shaw¹, T. Hofstaetter¹  
¹VaxInnate Corporation, Cranbury, NJ, ²Infectious Diseases, University of Rochester, Rochester, NY, ³Cytel, Cambridge, MA  

**Objective:** Understand a new approach to influenza vaccines.  

**Background:** We evaluated 3 novel influenza vaccine constructs consisting of the globular head of the HA1 domain of the A/California/07, Novel H1N1 (VAX128) genetically fused to the TLR5 ligand, flagellin, and produced in E. coli. HA1 was fused to the C-terminus of flagellin in VAX128A, replaced the D3 domain of flagellin in VAX128B or was fused in both positions in VAX128C.  

**Methods:** 112 healthy subjects 18-49 and 100 adults ≥ 65 years old were enrolled in a double blind, placebo controlled clinical trial conducted at two centers. Vaccines were administered IM at doses ranging from 0.5-20μg. A phase 2 study was performed in 100 subjects 18-64 years old comparing 1.25 and 2.5μg doses. All subjects were followed for safety and sera were tested by hemagglutination-inhibition (HAI) pre- and post-vaccination. Serum C-reactive protein, cytokine levels and anti-flagellin antibody were also measured.  

**Results:** Serum antibody responses were seen by HAI after doses as low as 0.5 μg. Doses of 1.25 to 2.5 induced a GMT of 1:250 with over 90% seroconversion and seroprotection. In young adults, the maximum tolerated dose for VAX128A was 8 μg and VAX128B 16μg. VAX128C was safe at 20μg, the highest dose tested. In adults ≥ 65 years, all three vaccines were safe at the highest doses tested of 8, 12, and 20μg for VAX128A, B, and C, respectively.  

**Conclusion:** Altering the configuration of the HA1 and flagellin produced influenza vaccines with a large safety window. VAX128C was well tolerated at the highest dose and was highly immunogenic. The globular head of the influenza HA expressed in a prokaryotic system was able to induce a functional antibody response at low doses.  

**Reference:**  

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**S7**  
**Phase 1, Randomized, Open-Label, Study to Assess the Safety and Immunogenicity of Serogroup B Neisseria Meningitidis (Mnb) Rlp2086 Vaccine in Healthy Adults**  
E. Sheldon¹, Q. Jiang², H. Schwartz², P. Giardina³, J. Perez¹  
¹Miami Research Associates, Miami, FL, ²Pfizer Vaccine Research Statistics, Collegeville, PA, ³Pfizer Vaccine Research, Pearl River, NY  

**Objective:** Discuss the potential of a novel outer-membrane-lipoprotein Mnb candidate vaccine to elicit a strong immune response and evaluate the vaccine's safety profile in healthy adult subjects.  

**Background:** Mnb causes significant invasive meningococcal disease, but no broadly-protective vaccine is yet licensed. We assessed the safety and immunogenicity of a bivalent, recombinant, investigational Mnb vaccine composed of lipidated subfamilies A and B variants of meningococcal factor-H binding protein (rLP2086).  

**Methods:** Forty-eight 18-40 year-old adults were enrolled in a 1:1:1:1 ratio to 60, 120, or 200 μg of rLP2086 vaccine or the control group and vaccinated at 0, 2, and 6 months. rLP2086-specific binding IgG geometric mean titers (GMT) for subfamily A and B proteins were measured immediately before doses 1 and 3, and 1 month postdoses 2 and 3. Blood and urine were collected at screening and 2-3 days post-vaccination for laboratory assessments. Subjects recorded local and systemic reactions for 7 days post-vaccinations. Unsolicited adverse events (AEs) were reported throughout the study.  

**Results:** The investigational bivalent lipidated rLP2086 vaccine elicited high IgG titers postdoses 2 and 3 at all dose levels. Eleven subjects reported ≥ 1 AE(s) in each vaccine and the control groups. No serious AEs were reported. Local and systemic reactions were mainly mild to moderate. Mean laboratory data were within the normal range after each vaccination and at each dose level. No laboratory changes were associated with clinical events.  

**Conclusion:** Vaccinations were well tolerated. Strong immune responses and absence of clinically significant laboratory abnormalities support further development of rLP2086 vaccine.
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References:

S8

Live, Attenuated, Tetravalent, CYD Dengue Vaccine in Healthy Adults and Children: Randomized Controlled Phase II Trial in Viet Nam
H. Tran Ngoc, T. Nguyen, A. Wartel, R. Forrat, A. Bouckenoooghe, M. Saville
1Pasteur Institute, Ho Chi Minh City, Vietnam, 2sanofi pasteur, Singapore, 3sanofi pasteur, Marcy l’Etoile, France

Objective: To learn about the latest phase II clinical trial results and status of sanofi pasteur’s tetravalent dengue vaccine program.

Background: Dengue viruses (DENV1-4) infect >100 million individuals per year; 2 million develop severe hemorrhagic symptoms. The live, attenuated, tetravalent CYD dengue vaccine, containing four recombinant dengue viruses (CYD1-4), is in clinical phase III.1

Methods: In a partially-blinded, phase II trial in Long Xuyen, Vietnam, 180 children and adults (range: 2-45 years) were randomized 2:1 to receive 3 CYD vaccinations at months M0-M6-M12 or meningococcal polysaccharide A+C at M0, placebo at M6, and typhoid Vi polysaccharide at M12. Antibody responses against the CYD1-4 parental wild-type dengue viruses were assessed using PRNT50. Safety and reactogenicity were assessed using conventional methods. Febrile episodes lasting >/=48h with suspicion of dengue (passive surveillance) were assessed for laboratory confirmation. (ClinicalTrials.gov: NCT00875524)

Results: At baseline, 139 (77%) were seropositive against dengue or Japanese encephalitis; 36% were seropositive (PRNT50 titer >/=10 dil-1) to all four dengue serotypes. After the first CYD vaccination, 53% were seropositive to all four serotypes, increasing to 72% and 92% after the second and third vaccinations. After the third CYD vaccination, 96% were seropositive to at least 3 serotypes, and geometric mean titers against DENV1-4 were respectively 129, 216, 169, and 146. Six SAEs, unrelated to vaccination, were reported including 2 virologically-confirmed dengue cases after the second vaccination in the control group. Reactogenicity of CYD decreased after each vaccination, was slightly higher than placebo, but no higher than either active control.

Conclusion: Safety and reactogenicity of CYD were satisfactory and consistent with results from phase I.2 Three doses of CYD induced a balanced neutralizing antibody response against the four dengue serotypes in children and adults living in a dengue endemic country.

References:

S9

A Chimeric Vaccine Prevents Primary and Recurrent Clostridium difficile Infection
H. Wang, X. Sun, Y. Zhang, L. Shi, W. Nie, S. Li, R. Kumar, T. Savidge, S. Tzipori, J. Wang, H. Feng
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Objective: This study represents an important advance in the management of CDI and is the first example of a functional chimeric toxin that has been developed for vaccine purposes.

The global emergence of hypervirulent drug-resistant Clostridium difficile infection (CDI) has contributed to the recent surge in antibiotic-associated colonic disease which now represents a major public health concern. C. difficile secretes two homologous glucosylating exotoxins, TcdA and TcdB, both of which are pathogenic and require neutralization to
prevent disease occurrence. However, because of their complex multifunctional domain structure and large size, it has been a challenge to produce full-length recombinant toxins for vaccines and immunization has thus far been limited to poorly immunogenic toxoids. Here we describe a novel chimeric toxin vaccine that confers complete protection against primary and recurrent CDI in mice. Using a non-pathogenic Bacillus megaterium expression system, we generated glucosyltransferase (GT)-deficient holotoxins and demonstrated their loss of toxicity. The atoxic holotoxins induced potent anti-toxin neutralizing antibodies showing little cross-immunogenicity or protection between TcdA and TcdB. To facilitate simultaneous protection against both toxins, we generated an active clostridial toxin chimera by switching the receptor binding domain of TcdB with TcdA. Parenteral immunization with the GT-deficient chimeric toxin cTxAB induced rapid and complete disease protection against laboratory and hypervirulent C. difficile vegetative cells and spores. Further, prophylactic cTxAB vaccination prevented spore-induced disease relapse, which constitutes the most significant clinical issue in CDI. Thus, the rational design of chimeric toxins provides a novel approach for prophylactic protection of individuals at high risk of developing infectious diseases such as CDI.

References:

S10 Treatment of Human Obesity by a Therapeutic Vaccination Approach
K. N. Haffer
Braasch Biotech LLC, Garretson, SD

Objective: Initiate new thinking for therapeutic vaccines for human metabolic disease conditions.

Therapeutic effects of novel vaccines for reducing weight gain and increasing weight loss in diet induced obesity (DIO) model were studied. Male C57BL/6J mice fed a 60% kcal fat diet were vaccinated via the intraperitoneal route with two formulations (JH17 & JH18) of chimeric-somatostatin vaccines at 1 and 22 days of the study. Control mice were injected with PBS. All mice continued to be fed the 60% kcal fat diet for the 6 week study. Body weights were measured two times a week and food intake was measured weekly. At week 6, mice were euthanized and a terminal bleed was made and antibody levels to somatostatin and levels of Insulin-like Growth Factor 1 (IGF-1) were determined. Vaccination with both vaccine formulations induced a statistically significant body weight change over the study period, as compared with PBS controls. Percentage of baseline body weight was also significantly affected by vaccination during the study period. Food intake per mouse was similar in all mouse groups during the entire study. Control mice did not demonstrate any antibody titers to somatostatin, while all vaccinated mice had measurable antibody responses (&gt; 1:500,000 titer). IGF-1 levels were not statistically significant among the groups, but were elevated in the JH18 vaccinates (mean 440.4 ng/ml) when compared with PBS controls (mean 365.6 ng/ml). Vaccination with either JH17 or JH18 chimeric -somatostatin vaccines produced a statistically significant weight loss as compared with PBS controls, even though the DIO mice with continually fed a 60% kcal fat diet. The weight loss/lower weight gain observations were even more significant, as all mice consumed similar amounts of food for the entire study.

References:
S11  Alternative Delivery Protocols of an Adenovirus Vector-Based Vaccine Against Foot-and-Mouth Disease Virus Enhances Protection of Swine
M. J. Grubman¹, C. C. A. Dias², F. San Segundo², M. P. Morales²
¹Foreign Animal Disease Research Unit, Plum Island Animal Disease Center, USDA, ARS, Greenport, NY; ²Plum Island Animal Disease Center, USDA, ARS, Greenport, NY

Objective: Adenovirus vectored FMD vaccines are a practical alternative to the current inactivated FMD vaccines.

Background: Foot-and-mouth disease (FMD) is a highly contagious disease of cloven-hoofed animals. A human replication-defective adenovirus-based FMD virus (FMDV) subunit vaccine (Ad5-A24) is an effective alternative to the current inactivated whole virus vaccine and has a number of advantages including no requirement for infectious FMDV and DIVA status (differentiation of infected from vaccinated animals).¹ Recently, we demonstrated that inclusion of the complete coding region of FMDV nonstructural protein 2B in the Ad5-A24 vector resulted in a more rapid immune response and improved protection in pigs.² Nevertheless, the continuous development of this novel vaccine to overcome high dose requirements, 5x10⁹ pfu, is ongoing.

Methods: To address this limitation, we compared delivery protocols for the vaccine, specifically route and number of sites of vaccination. We vaccinated 18 swine, divided in 6 groups of 3 pigs per group; 3 groups were vaccinated with 1x10⁹ pfu, one inoculated at two sites intramuscularly (IM), one inoculated at two sites subcutaneously (SC) and one inoculated at one site IM. Another 2 groups were vaccinated with 2x10⁸ pfu, delivered IM or SC at two sites, and one group was inoculated SC at two sites with 1x10⁹ pfu of control Ad5 vector. Animals were challenged with FMDV at 21 days post-vaccination.

Results: All vaccinated animals had reduced clinical signs of FMD compared with the control group. In addition, both groups vaccinated SC and the group receiving 1x10⁹ pfu IM at two sites was completely protected, showing no lesions, viremia, or virus in nasal swabs.

Conclusion: The results demonstrate that we could reduce the protective dose at least 25-fold when the animals were vaccinated SC at two sites.

References:

S12  Inoculation of Swine with Foot-And-Mouth Disease Virus SAP-Mutant Induces Early Protection Against Disease
T. de los Santos, F. Diaz-San Segundo, M. Weiss, E. Perez-Martin, C. C. Dias, M. J. Grubman
Plum Island Animal Disease Center, NAA, ARS, USDA, Greenport, NY

Objective: Use of a live attenuated vaccine deserves consideration as a viable strategy to control foot and mouth disease (FMDV).

Background: FMDV is one of the most contagious agents of cloven-hoofed species. Current vaccines require 7 days to protect against disease.¹ We have previously reported that mutation of FMDV Lpro [SAP-mutant] results in attenuation in vitro. Here we study the virulence of SAP-mutant FMDV in vivo and explore the use of this strain as a live attenuated vaccine candidate.

Method: Two animal experiments were performed in swine. 1. In vivo virulence: groups of 3 swine each were inoculated with 105, 106 and 107 pfu of SAP-mutant or 105, 106 of wild type (WT) virus. 2. Evaluation of protection against WT FMDV challenge: groups of 3 swine each were vaccinated with 106 pfu of SAP-mutant virus and challenged either at 2, 4, 7, 14, and 21 days with WT FMDV. Clinical signs, viremia, shedding, cytokine profile, antibody titers and cellular mediated immunity were evaluated throughout the experiments.

Results: Animals inoculated with different doses of SAP-mutant did not develop clinical signs, viremia, or shedding...
even when the inoculation dose was 100-fold higher than the WT-virus dose sufficient to cause disease. Interestingly, the induction of neutralizing antibodies was equivalent for both viruses but a differential profile of some cytokines was detected in sera. Remarkably, animals inoculated with SAP-mutant are protected against challenge with WT-FMDV as early as 2 days post-vaccination even in the absence of detectable neutralizing antibodies. In addition, animals inoculated with SAP-mutant developed a memory T cell response resembling infection with WT-FMDV.

**Conclusion:** Although design improvement is still required, these results suggest that use of a live attenuated FMD vaccine candidate deserves further consideration as a viable strategy to control FMD.

**References:**

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**S13 MF59 Adjuvant Enhances Antibody Specificity, Affinity Maturation, and Virus Neutralization Titers to Swine-Origin and Avian Influenza A Virus Vaccines**

S. Khurana1, N. Verma1, J. Yewdell2, G. D. Giudice3, R. Rappuoli3, H. Golding1

1.CBER, FDA, Bethesda, MD, 2.NIH, Bethesda, MD, 3.Novartis Vaccines, Siemens, Italy

**Objective:** Role of adjuvants in development of antibody repertoires and affinity maturation following influenza vaccination.

**Background:** Rapid response against pandemic influenza viruses requires development of effective vaccines. Oil-in-water adjuvants were found to significantly increase virus neutralizing titers, heterosubtypic immunity, and afforded dose sparing. However, the complete impact of these adjuvants on antibody repertoire and affinity maturation was not investigated before.

**Methods:** We employ Whole Genome Fragment Phage Display Libraries (GFPDL) and surface plasmon resonance (SPR) to elucidate the effects of MF59 adjuvant on the diversity, specificity, and affinity of human antibody responses to avian influenza H5N1 and swine origin-H1N1 vaccine vaccines in toddlers, young children and adults.

**Results:** Using GFPDL and SPR, we found that the oil-in-water adjuvant (MF59) induced epitope spreading from HA2 to HA1 in the hemagglutinin (HA) and to neuraminidase, when compared with unadjuvanted or aluminum-adjuvanted inactivated H5N1 vaccines. Furthermore, a 2-3 fold increase in the binding avidity of antibodies to properly folded HA1 was measured in SPR, which correlated with broadening of cross clade neutralization. A similar expansion of HA1 epitopes recognition and increased binding avidity was observed in sera from pandemic H1N1 immunized individuals receiving the MF59 adjuvanted vaccine compared with unadjuvanted vaccine. Importantly in the most naïve population (12-35 month) MF59 enhanced serum antibody affinity as measured by increased 7M urea resistance and 10-fold drop in binding off-rate constants using SPR. A close correlation between inferred serum antibody affinity and virus-neutralizing titers was demonstrated (r > -0.8).

**Conclusion:** MF59 enhances functional antibody responses to pandemic influenza vaccines by improving antibody affinity, expanding repertoires, and focusing on protective epitopes. These effects were most prominent in the naïve populations.

**References:**
**S14** Nanoemulsion (NE) Intranasal Adjuvant Facilitates Uptake of Antigen Loaded Epithelial Cells (EC) by Dendritic Cells (DC)


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**Objective:** Describe mechanism of action of intranasal adjuvant.

**Background:** NEs are emulsions (~400 nm droplet size) composed of innocuous surfactants, solvent, soybean oil, and water. NEs are effective mucosal adjuvants when mixed with whole microbes or protein antigens. NEs enhance antigen penetration of nasal mucous and increase intracellular uptake of antigens by ECs. Subsequently, antigen-loaded DCs are observed in regional lymph nodes within 24 hours after NE nasal administration. The present studies address the hypothesis that NEs enhance both “direct” uptake of antigen and “indirect” phagocytosis of NE-antigen-loaded ECs by DCs as a central mechanism for adjuvant activity.

**Methods:** Fluorochrome-labeled ovalbumin (DQ-Ova) mixed with NE was used to evaluate uptake into cell lines including epithelial TC-1, Jaws II, and primary BMDCs. The cells were labeled with CFSE or PKH-26 dyes. The impact of NE on cell cycle was determined by DNA content analysis and RT-PCR.

**Results:** NE-DQ-Ova addition to TC-1 epithelial cells yields a NE-dose-dependent increase in fluorescence (>2-30 fold) as compared to DQ-Ova alone after 2-4 hours exposure at 37°C. Cell cycle analysis and RT-PCR revealed that NE uptake also caused a dose-dependent cell cycle arrest in the G2M compartment followed by apoptosis and necrosis of exposed cells. Interestingly, unlike staurosporine treated apoptotic TC-1 cells NE-antigen pre-treatment induced rapid phagocytosis of epithelial TC-1 cells by Jaws II or BMDCs.

**Conclusion:** NE augments direct uptake of antigen into EC and facilitates rapid phagocytosis of antigen-loaded EC by DC. NE facilitated uptake of antigen-loaded ECs by DCs at mucosal surfaces may enable an efficient priming of the cellular immune response without induction of inflammation.

**References:**

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**S15** The Effects of Novel Adjuvant Complex on Host Immune Response to Recombinant Eimeria Profilin Vaccine

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**Objective:** Discuss the modulation of chicken protective immunity and transcriptional profiles during coccidiosis by novel adjuvant formulations.

**Background:** This study investigated the ability of two novel adjuvant formulations, QCDC (Quil A/cholesterol/DDA/Carbopol) and QCDCR (QCDC/Bay R1005), in combination with a recombinant profilin vaccine, to modulate host protective immunity and to alter new gene expression during experimental avian coccidiosis.

**Methods:** Chickens were immunized with PBS, profilin alone, profilin with QCDC, or profilin with QCDCR and orally infected with E. acervulina. Body weights, oocyst shedding, and lesion score were measured and total mRNA was prepared from spleen lymphocytes. The proliferation of blood lymphocytes by profilin was measured using Cell-Counting Kit-8. Chicken 44K Agilent microarray was used to compare global transcriptional changes between the following groups: (a) profilin alone vs. PBS, (b) profilin plus QCDC vs. profilin alone, and (c) profilin plus QCDCR vs. profilin alone. Microarray data were analyzed using GeneSpring GX10 and Ingenuity Pathway Analysis software.

**Results:** Immunization with profilin plus QCDC or profilin plus QCDCR had no effect on body weight gain or fecal oocyst shedding of chickens infected with Eimeria acervulina compared with animals vaccinated with profilin alone. By contrast, vaccination with profilin plus QCDCR significantly reduced the severity of intestinal lesions and increased mitogen-induced lymphocyte proliferation in infected chickens. The results of global gene expression analysis revealed that compared with
animals vaccinated with profilin alone, (a) chickens given profilin plus QCDC had 60 up- and 104 down-regulated transcripts and (b) chickens immunized with profilin plus QCDCR had 103 up- and 130 down-regulated mRNAs.

**Conclusion:** Biological function and network analyses revealed that the majority of altered transcripts in response to the profilin vaccine administered with the QCDC or QCDCR adjuvants were encoded by immune-related genes and pathways.

**References:**

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**S16 Development of New Adjuvants - A Role for the National Institute of Allergy and Infectious Diseases**

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**Objective:** Raise awareness of NIH funding support for adjuvant development.

The development of adjuvants by commercial entities is complicated by the need to protect proprietary and intellectual property (IP) rights as the regulatory requirements in the US currently only permit the licensing of vaccine/adjuvant combinations. Some of the IP complications could be addressed through public funding of adjuvant development studies. Recent discoveries in adjuvant research indicate that understanding the mechanism of adjuvant action is critical in correctly matching an adjuvant with an antigen and attaining the correct formulation required to achieve maximum vaccine efficacy.

**Method:** The NIH grants database was accessed through the Query View Report (QVR) system to retrieve award information on all DMID grants for the 2009 and 2010 grant years in which an adjuvant was involved. Both the database and the QVR are secured systems designed to protect sensitive information. The adjuvant in each study was identified and this information was summarized into adjuvant types, and further identified as Basic research, Research and Development, or Clinical research.

**Results:** Most of the adjuvant research projects involved cytokines, followed by oligonucleotides, toll-like receptors, lipids and emulsions, recombinant proteins, T cell activators, and alum, in that order. Furthermore, although most of the projects were at the level of Basic or Research and Development stages, up to 10% were clinical studies. Details of these studies will be provided.

**Conclusion:** These preliminary results confirm that DMID grant support activity for adjuvant development is broad based and extends through the critical product development phases. Future efforts to extend this analysis are warranted and are in progress.

**References:**

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**S17 Rapid Pre-Season Trial of the Safety of 2010-2011 H1N1 Pandemic Vaccine; A PHAC/CIHR (PCIRN) Influenza Research Network Study**


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Objective: To be aware of TIV vaccine safety issues in young children and the need for enhanced preseason vaccine safety surveillance.

Background: During the AH1N1 pandemic, a universal immunization program with monovalent oil-in-water (AS03) adjuvanted vaccine Arepanrix™ (GSK Biologicals) (AV) was offered to Canadians. Given high vaccine immunogenicity and attack rates of infection in YC, high levels of immunity were expected.

Methods: YC immunized with 1 or 2 doses of AV, with or without 2009-10 TIV, received 1 or 2 doses of 2010-11 TIV in an open study in 5 Canadian centers. Safety monitoring day (D) 0-6 and D21 was enhanced by phone follow-up on severe adverse events (AE) by phone in the 24 hours post-TIV, when AE were expected to be at peak intensity. Blood was collected for serology on D0 and D21-post TIV.

Results: Enrollment of 207 YC began 7Sep10; D2 safety data was provided to public health on 30Sep10 prior to public TIV programs. Any local AE was reported by 53.6% (95% CI, 46.4, 60.6) post-dose (PD)1 and by 62.5% (40.6, 81.2) PD2; one severe (S) local AE occurred. Any general AE was reported in 60.9% PD1, and in 58.3% PD2. Fever ≥ 38.5 ºC occurred PD1 in 2 (1.0%, 95% CI 0.1, 3.5) and PD2 in 4 YC (16.7%, 95% CI 4.7, 37.4). No unsolicited SAE considered related to immunization occurred. Of 21 PR unsolicited AE, severity was moderate in 3 (2 vomiting, 1 eczema) and mild in 18 (10 gastrointestinal, 2 rash, 2 headache, 4 other). No seizures were observed day 0-6.

Conclusion: YC who received AS03-adjuvanted influenza AH1N12009 vaccine in 2009-10, subsequently immunized with 2010-11 TIV had acceptable rates of local and general reactogenicity. Fever episodes were increased with the second TIV dose.

References:

S18 Safety and Immunogenicity of Re-vaccination with H1N1-Containing 2010-11 Seasonal Influenza Vaccine After Priming with 2009 Adjuvanted Pandemic Vaccine

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Objective: Discuss the safety of ongoing use of the H1N1 vaccine antigen in the first post-pandemic year.

Background: Many Canadians in 2009 had adjuvanted H1N1 vaccine or H1N1 infection, both of which elicited robust immune responses. We wondered if high anti-H1N1 titers would persist to next season and, if so, could result in increased or unusual reactions to H1N1-containing seasonal vaccine.

Methods: Adults (20-59 yoa) who had AS03-adjuvanted H1N1 vaccine (Arepanrix™, GSK Canada) about 9 months earlier were enrolled in a randomized, blinded, cross-over trial to receive 2010-11 trivalent, inactivated vaccine (Fluviral™, GSK Canada) and saline placebo 10 days apart. Daily safety monitoring followed each injection, with interviews 1 and 7 days afterward. Blood was obtained at baseline and 21-28 days post-vaccination. Paired sera were tested for HAI antibodies. Adverse event rates were calculated. HAI titers were analyzed using standard CHMP criteria.

Results: Among 5 centers, 326 subjects were enrolled, 323 had both injections, 318 supplied all safety data, and 321 provided both blood samples per protocol. At baseline, H1N1 antibodies were detectable (titer ≥10) in 303/324 subjects (94%) but only 176 (54%) had protective titers (≥40), with an overall geometric mean (GMT) of 37.6. Adverse event rates were as expected after seasonal vaccine except for myalgia (25%) and generalized itchiness (3 instances). Myalgia was more
frequent with baseline titers ≥80 (31/106, 29%) than ≤20 (25/136, 18%, p<0.05); all 3 pruritus cases had baseline titers ≥40. Post-immunization, 96% of subjects had H1N1 titers ≥40, with GMT 167.4 (4.4X increase).

Conclusion: H1N1 seroprotection persisted 9 months after pandemic vaccine in half the subjects and boosted readily with seasonal vaccine. Adverse effects were typical of seasonal vaccines except for myalgia and pruritus, reported more often by subjects with higher baseline titers.

References:

S19 Randomized Controlled Trial of Dose-Response to Influenza Vaccine in Children 6-23 Months of Age
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Objective: Understand the influence of dose on antibody response to influenza vaccine in infants and toddlers.

Background: We assessed whether two full-doses of trivalent inactivated influenza vaccine (TIV) in previously unimmunized infants and toddlers could improve immunogenicity without increasing reactogenicity compared to the recommended North American practice of administering two half-doses in this age group.

Methods: Previously unimmunized children 6-11moa and 12-23moa were separately randomized to receive two spaced injections of either 0.25mL (“half-dose”) or 0.5mL (“full-dose”) 2008-09 TIV. Sera were collected at enrolment and 27-45days after the second dose. Parents recorded adverse events for 7days after each injection. Antibody responses were evaluated by hemagglutination-inhibition (HI) and microneutralization (MN) assays. Primary immunogenicity outcome was superiority (one-sided;α=0.025) of the full- vs. half-dose based on >10% increase in sero-protection rates (SPR;% with HI≥40). Primary reactogenicity outcome (one-sided;α=0.025) for full- vs. half-dose was based on <10% increase in the rate of axillary temperature ≥38ºC within 3days of either injection.

Results: 252 participants (6-11moa:126; 12-23moa:126; full-dose:124; half-dose:128) were included in per-protocol analyses. Post-immunization SPRs exceeded 85% for all three vaccine components in the 12-23moa group without significant difference based on dose received. Conversely, the full-dose induced significantly higher HI responses for all three vaccine components in infants 6-11moa, meeting the >10% test of superiority for the H3N2 (75.4% vs.47.6%;Δ=27.8%(95%CI 11.2%, 44.5%);p=0.02) and B/Yamagata (70.2% vs.41.3%;Δ=28.9%(95%CI 11.9%,45.9%);p=0.02) components but not the H1N1 component (71.9% vs.54.0%;Δ=18.0%(95%CI 1.0%,34.9%);p=0.2). Compared to the half-dose, full-dose recipients in both age groups experienced lower rates of fever in the 3days following either injection (5.6% vs.12.7% combined).

Conclusion: Compared to the currently recommended two half-dose TIV schedule, administration of two full TIV doses improved immunogenicity in infants 6-11moa (but not toddlers 12-23moa) without increasing reactogenicity. Current TIV dosing recommendations for young children warrant further evaluation.

References:
Case Definition, Data Collection Guidelines, and Yellow Fever Vaccine Causality Assessment for Viscerotropic Disease as an Adverse Event Following Immunization


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Objective: Describe the structure of the Brighton Collaboration case definition and causality assessment for viscerotropic disease (VTD) and their importance to the standardized evaluation and reporting of VTD as an adverse event following immunization.

Background: The international Brighton Collaboration strives to enhance our understanding of adverse events following immunization by improving the comparability of vaccine safety data through development of globally accepted, standardized case definitions, and associated guidelines. A Brighton Collaboration working group was formed to develop a case definition and guidelines for viscerotropic disease (VTD) applicable for surveillance, health care, and research in diverse geographic regions. VTD is rare, frequently fatal, acute multiple organ dysfunction/failure that has been reported following administration of live-attenuated yellow fever (YF) vaccine.

Methods: We performed a systematic literature review for VTD/multiple organ failure following immunization. Sources included MEDLINE, EMBASE and the Cochrane Library. Thirty-six published and unpublished case reports from surveillance systems were identified and reviewed for clinical details. The definition, guidelines, and causality algorithm were then developed using case report data and through expert consensus.

Results: We developed the VTD case definition and a YF vaccine causality algorithm, each with three hierarchical levels of diagnostic certainty. The case definition utilizes major and minor criteria representing the following clinicopathologic categories: hepatic, renal, musculoskeletal, respiratory, hematologic, blood pressure, and coagulation. More diagnostic certainty is conferred by major criteria than minor criteria (e.g., serum bilirubin > 1.5 times normal versus clinical jaundice). YF vaccine causality is assessed by isolation or amplification of YF vaccine virus/viral RNA, detection of YF viral antigen by immunohistochemistry, or demonstration of histopathologic changes consistent with YF virus in clinical specimens.

Conclusion: The Brighton VTD case definition and YF vaccine causality algorithm provide immunization safety research standards for VTD. Studies to test their usefulness and applicability in surveillance systems and clinical trials are encouraged.

References:
**Objective:** Discuss the rationale for, and safety of, maternal pertussis immunization.

**Background:** Due to shifting epidemiology, pertussis incidence continues to increase in infants <6 months of age who are too young to be fully vaccinated. Maternal vaccination offers the possibility to protect infants from birth until immunity is induced by active vaccination. We sought to determine if immunization against pertussis in the late third trimester of pregnancy is safe, and provides passive protection to the infant sufficient to protect the infant in the critical neonatal period without suppressing the infant’s immune response to active immunization.

**Methods:** 50 healthy pregnant women were recruited for stage 1 of the study. At 34-35 weeks gestation women deemed eligible based on obstetrical algorithm were randomized in a 1:1 ratio to receive either Tdap or Td. Solicited adverse events were collected for 7 days post immunization; all medically significant and serious adverse events in mothers/babies were recorded for the duration of the study. Prior to enrolling the remaining 390 women (stage 2), all data from stage 1 is undergoing an interim blinded combined safety analysis of women who received Tdap or Td.

**Results:** In the first 7 days post-vaccination, 39/50 (78%) mothers reported having any local reactions (injection site redness, swelling, pain): 25/50 (50%) were mild; 15/50 (30%) were moderate; 2/50 (4%) were severe. 19/50 (38%) reported having any general reactions (headache, fever, muscle aches, fatigue): 12/50 (24%) were mild, 8/50 (16%) were moderate, 5/50 (10%) were severe. 50 adverse events were reported in 25/50 (50%) of babies: 13 were serious; none were deemed related to vaccine.

**Conclusion:** Interim analysis indicates that vaccination of women with Tdap or Td during pregnancy is not associated with significant adverse maternal or fetal outcomes.

**References:**

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**Objective:** Assess the long term effectiveness of pertussis vaccines.

**Background:** During the widespread 2010 California pertussis outbreak, we evaluated the risk of laboratory-confirmed pertussis among vaccinated members of Northern California Kaiser Permanente (NCKP).

**Methods:** From December 2005 through 2010, we compared the vaccination history of NCKP members who tested polymerase chain reaction (PCR) positive for pertussis with two different control populations: 1) persons testing PCR negative for pertussis and 2) persons matched 5:1 from the general NCKP population. Pertussis risk was assessed in relation to both time since date of last vaccination (4th or 5th dose of DTaP) and whether they had ever received a Tdap vaccine, using logistic regression, adjusted for age, sex, and medical facility.

**Results:** PCR testing was performed on 22,470 members during the study period. 1,287 tests (5.73%) were positive for B. pertussis. Rates of pertussis were highest in infants and in children ages 8 to 14 years old. Decreasing rates of pertussis from ages 10 to 14 coincided both with the use of the adolescent formulation of Tdap and with the change from whole cell to acellular vaccines in infancy. Analyzing time since last dose of DTaP showed that each year since vaccination was associated
with a 20% increased risk of acquiring pertussis (OR 1.20, p<0.0001). Odds of pertussis decreased following receipt of Tdap (OR 0.62, p<0.0001).

**Conclusion:** Tdap appeared to be moderately effective without evidence for waning in the 5 years since licensure. DTaP showed signs of waning effectiveness with each year after vaccination. Ecologic data suggests that pertussis immunity following acellular pertussis is shorter lived than after whole cell pertussis vaccine.

**References:**

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**S23** Changes in the Epidemiology of Varicella in the Post-Vaccine Era (1995-2009)

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**Objective:** Interpret the changing epidemiology of varicella since introduction of the vaccine.

**Background:** When varicella vaccine was licensed in the US in 1995, there were concerns that it might shift varicella incidence towards older age groups where the disease is more severe. This 15-year study was conducted to assess changes in varicella epidemiology in 5-19 year old children and adolescents as well as changes in varicella and herpes zoster (HZ) hospitalization rates in people of all ages.

**Methods:** Five cross-sectional telephone surveys, each sampling approximately 10,000 members 5-19 year olds from Kaiser Permanente Health Plan in Northern California, were conducted in 1995 (pre-licensure), 2000, 2003, 2006, and 2009. The surveys collected information on varicella history, vaccination, and occurrence during the past year. Incidence rates and proportion of susceptible subjects were calculated by age groups across survey years. Varicella and HZ hospitalization rates were calculated for the entire Kaiser population of all ages.

**Results:** Between 1995 and 2009, the overall varicella incidence in 5-19 year olds decreased from 25.8 to 1.3 per 1,000 person-years (PY) (~10 to 20 fold in the various age groups) while the proportion of susceptible decreased in all age groups. Meanwhile, age-adjusted varicella-associated hospitalization rates in the general Kaiser population decreased from 2.13 to 0.25 per 100,000 PY while HZ-associated hospitalization rates increased from 2.26 to 4.14.

**Conclusion:** Overall, in the 15 years following varicella vaccine implementation, there was a dramatic decrease in varicella incidence and hospitalization with no evidence of a shift in the epidemiology of varicella toward older age groups. The observed increase in HZ hospitalization deserves further evaluation but may in part be due to coding practice changes and a major increase in the very old population at Kaiser.

**Reference:**

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**S24** Trends in U.S. Pediatric Influenza Vaccination from 2006 to 2011 Among Privately Insured Children

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**Objective:** Discuss recent trends in the use of influenza vaccine among US children.

**Background:** US recommendations for pediatric influenza vaccination have expanded significantly in recent years. However, limited data are available on influenza vaccine utilization by US pediatric providers.

**Methods:** Electronic healthcare reimbursement claims data representing more than 60% of all medical claims from the US outpatient setting were analyzed. Weekly counts of influenza vaccinations given to children and adolescents 6 months through 18 years of age between August 1 and March 31 for the 2006-2007 through 2009-2010 seasons and between

Conclusion: Consistent with national recommendations, pediatric influenza vaccination has increased significantly in recent years. From 2006-2007 to 2010-2011, pediatric influenza vaccination began and peaked 1 week earlier each season. Despite efforts to extend vaccination into later months, there was no evidence of increased late-season vaccination. Additional research is needed to identify barriers to late-season vaccination.

References:


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Objective: Understand that non-specific effects of vaccines are important for the overall assessment of vaccinations.

Background: Measles vaccination (MV) is more effective against measles infection when administered after maternal antibodies have waned. Surprisingly, epidemiological studies from low-income countries have suggested that general survival is greater when MV is given before the recommended age of vaccination of 9 months of age, when many still have maternal antibodies. In a recent randomized trial, an additional MV at 4.5 months was associated with a marked non-specific benefit for general child survival.

Methods: We explored the hypothesis that vaccination in presence of maternal antibodies may confer non-specific beneficial effects. In the trial of early MV, a subgroup of 450 children had pre-vaccination measles antibodies measured as well as antibodies from their mothers; 948 controls were included in the same period. The children were followed for survival to 5 years of age.

Results: Among the 450 trial participants, 249 had measurable measles antibodies. The children with maternal measles antibodies at vaccination had 4-fold lower mortality between 4.5 months and 5 years of age than those with undetectable measles antibody levels, the mortality rate ratio (MRR) being 0.23(0.06-0.82). None of the potential confounding factors, including HIV-status of mother, explained this pattern. The children with maternal antibodies had 4-fold lower mortality than controls receiving the usual MV at 9 months of age (MRR=0.23(0.07-0.75)). Children vaccinated at 4.5 month but with no measurable maternal antibodies had the same mortality as controls receiving MV at 9 months.

Conclusion: MV in presence of maternal antibody may enhance general child survival and be the explanation of the non-specific beneficial effects of MV noted in many studies. It may reduce child mortality to lower the age of MV.

References:
S26 Early Impact of PCV13 on Nasopharyngeal Colonization among American Indian Children and Household Members of the Navajo and White Mountain Apache Communities

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Objective: Describe the early epidemiology of NP colonization among Navajo and White Mountain Apache households following PCV13 introduction.

Background: 7-valent pneumococcal conjugate vaccine protects against nasopharyngeal (NP) colonization with vaccine serotypes. The 13-valent pneumococcal conjugate vaccine (PCV13) was licensed on February 24, 2010 and introduced in March among Navajo and White Mountain Apache (N/WMA) communities. This study evaluates the impact of PCV13 against serotype-specific NP colonization in the 2 years following vaccine introduction.

Methods: N/WMA children (7-<24m) and their family members enrolled into this prospective, community-based, cross-sectional NP study. Using continuous enrollment before and throughout PCV13 introduction, an NP swab was collected from each study participant. Pneumococci are isolated by culture following broth enrichment and serotyped by Quellung reaction. Statistical analyses compare the prevalence of overall, vaccine-type and non-vaccine-type NP colonization before and after PCV13 introduction.

Results: Enrollment began in January 2010 and will continue through March 2012 when an estimated 4500 participants will have been recruited. As of January 24, 2011, approximately 2900 participants have been enrolled (N=855,<2y; N=579,2-<8y; N=252,8-<18y; N=1132,18<49y; N=67,>=50y). Preliminary analyses of specimens from January 2010 through July 2010, demonstrate that 35% (332/963) of study participants are colonized with pneumococcus (52%,<2y; 54%, 2-<8y; 23%,8-<18y; 13%,18<49y; 7%,>=50y). Of the pneumococci isolated (N=336), 19% (N=65) are PCV13 vaccine-type; among those <5 years, 10% (N=44) are vaccine-type. The most common serotype isolated is 19A (N=40), which is most frequently isolated from children 12-<24m (9.8%, 20/205).

Conclusion: NP colonization remains very common among N/WMA children through 8 years of age. Serotype 19A is the most frequent colonizing serotype among N/WMA of all ages, but particularly among young children. Serotype-specific NP colonization data from the first 12 months of PCV13 use will be presented to establish if an early impact is observed.

References:

S27 Projected Public Health Impact and Cost-Effectiveness of Adult Pneumococcal Conjugate Vaccination in 50-Year-Olds

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Objective: Examine the use of decision analysis techniques in the evaluation the effectiveness and cost-effectiveness of adult pneumococcal vaccination strategies.

The effectiveness and cost-effectiveness of 13-valent pneumococcal conjugate vaccine (PCV13) compared to 23-valent pneumococcal polysaccharide vaccine (PPV) in adults are unclear. In a Markov state-transition model, we used available data and projections of herd immunity effects based on pre- and post-PCV7 licensure data to estimate the cost-effectiveness of PCV13 strategies in 50-year-old adult cohorts. The 6 strategies were no vaccination, present US adult vaccination recommendations, present recommendations with PCV13 substituted for PPV, PCV13 (age 50) then PPV (age 65), PCV13 (50/65), and PCV13 (50/65) then PPV (75). Costs were 2006 US$, discounting costs and effectiveness 3%/yr. An expert panel estimated PPV and PCV13 effectiveness; other probabilities and utilities were estimated from published
We found that, in most scenarios, PCV13 given at ages 50 and 65 was the preferred strategy, costing $14,202 per quality adjusted life year gained while preventing more pneumococcal disease cases and deaths than all but one competing strategy. The most effective strategy, PCV13 at ages 50 & 65 then PPV at age 75, was very expensive, costing more than $500,000/QALY gained. Results were robust in sensitivity analyses and in a variety of alternative scenarios, except that PCV13 given as a substitute for PPV in the present adult pneumococcal vaccination recommendations (i.e., vaccination at age 65 and vaccination at younger ages if comorbidities are present) became more favored if both low vaccine efficacy and observed age- and comorbidity-based vaccination uptake are modeled. We conclude that these data support a two-dose strategy for vaccinating adults with PCV13 at ages 50 and 65 to prevent pneumococcal disease.

References:

Replication Study of Measles Vaccine-Specific Immune Responses and CD46, SLAM and CD209 Genes
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Objective: Discuss the effect of cellular receptor gene (CD46, SLAM and CD209) polymorphisms on the variation of measles vaccine immune responses observed in healthy subjects who received two doses of measles-containing vaccine.

Background: In our previous population-based study of 346 subjects, we found several specific polymorphisms in the CD46 and SLAM measles virus (MV) receptor genes that demonstrated an allele-dose response-related decrease in MV antibody level.

Methods: We genotyped a new cohort of 745 subjects (ages 11-22 years; 56% males; 598 Caucasians, 89 African-Americans) after measles vaccine for 55 SNPs in CD46, SLAM and CD209 genes using the Illumina genotyping platform. Humoral responses were determined by MV-PRMN assay. Cellular responses were assessed by MV-specific IFNγ-Elispot. MV-specific secreted cytokines (IL-2, IL-6, IL-10, IFNa, IFNγ, IFNα, and TNFα) were measured by EIA. Associations between SNP genotypes/haplotypes and immune response measures were determined using ANCOVA.

Results: A previously found association of the CD46 SNP rs2724384 with measles-specific antibodies was replicated in this study. Specifically, increased representation of the minor allele G for an intronic CD46 SNP was associated with an allele-dose-related decrease in antibodies (median value [mIU/ml]=978 for genotype AA vs. 522 for GG, p=0.0007). A coding polymorphism (rs164288) in the SLAM gene which was associated with measles antibody and IFNγ-Elispot responses in our previous study was also replicated. A minor allele G for this synonymous SNP in exon 3 (rs164288, Thr210Thr) of the SLAM gene was associated with variations in IFNγ-Elispot responses (p=0.04) in African-Americans. Another SLAM polymorphism (rs11265452) previously associated with measles antibodies (p=0.04), demonstrated a significant association with MV-specific IL-10 secretion (p=0.0008) in African-Americans. We also found associations between haplotypes, AACCGAATGGAAAG (p=0.009) and GGCCGAGGGAGAG (p<0.001), in the CD46 gene and MV-specific TNFα secretion in Caucasians.

Conclusion: Replication of several associations provides confidence that these specific SNPs can be considered as candidates for identification of causative genetic variants.

References:
Monitoring the Breadth of Coverage of Meningococcal Vaccines: An Overview and Progress Update on the Pfizer Bivalent LP2086 Vaccine Program
K. Jansen, A. Anderson, T. Jones, S. Harris, L. McNeil, J. Perez, E. Murphy, S. Hoiseth, E. Emini, J. Eiden
Pfizer, Pearl River, NY

Objective: Evaluate protein vaccines using a surrogate.

Background: Pfizer is developing a bivalent factor H binding protein (fHBP, also known as LP2086) vaccine for the prevention of Neisseria meningitidis serogroup B (MnB) disease. fHBP is an outer membrane lipoprotein with a key role in protecting the organism from the host alternative complement pathway. The fHbp gene is found in all MnB strains evaluated to date (>2500), and sequence analysis demonstrates that the protein exists in two genetically and immunologically distinct subfamilies. Preclinical studies have identified the importance of including one protein from each subfamily in a vaccine to generate broad SBA reactivity against heterologous strains. Since vaccines for MnB will be evaluated and licensed based on serum bactericidal antibody responses using human complement (hSBA), the evaluation of vaccine performance in the context of circulating strain epidemiology is an important component for vaccine licensure.

Methodology: The epidemiology of fHBP was monitored from N. meningitidis clinical isolates in the context of sequence, expression, and age of subject with disease. Breadth of vaccine coverage was then evaluated by hSBA using serum from human clinical trials where the bivalent vaccine was given to healthy subjects on either a 0-1-6 month or a 0-,2-6 month schedule.

Results: Studies in humans with the bivalent, lipidated rLP2086 vaccine have demonstrated significant hSBA cross-reactivity against heterologous MnB strains. Compiled data from phase I/II studies in adults, adolescents, and toddlers will be reviewed in the context of ongoing epidemiological studies to assess potential breadth of strain coverage.

Conclusion: The bivalent rLP2086 investigational vaccine confers broad protection against MnB clinical isolates. Efficacy will be determined using the hSBA surrogate and clinical isolates with heterologous fHBP sequences to the vaccine variants.

References:

Improved Antibody and CTL Immunogenicity of HIV-1 Envelope Antigen by consensus DNA Prime/Protein Boosting
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Objective: Vaccines (DNA prime and Protein boost) that can stimulate both cellular and humoral responses to HIV may be able to control the virus early in infection before it causes major immune damage.

It is agreed that the induction of strong T cell responses and cross neutralizing antibodies as well as antibodies that drive ADCC could play a role in HIV vaccine-induced protection. DNA vaccines in the past have been poor inducers of seroconversion. However, recent enhancements in construct design and through delivery and formulation appear to be improving the immune potency of this approach. We have previously demonstrated the induction of strong HIV/SIV antigen specific cellular immune responses in mice and macaques using consensus DNA immunogens delivered via electroporation. While these studies have demonstrated the increased magnitude and breadth of cellular immune responses induced by DNA immunogens via electroporation, the ability of the DNA-EP platform to induce neutralizing antibody responses has not been previously explored.

Here we tested the immunogenicity of a consensus DNA encoding gp140 constructs from individual HIV-1 subtypes A, B, C and D in DNA prime/protein boost vaccine regimen in Guinea pigs. Immunization with env alone induced low-titer
antibodies; in contrast, high-titer antibodies were seen after rgp120 boost in DNA-primed animals. Furthermore, sera from DNA prime/protein boost regimen groups were able to neutralize not only a significantly higher percentage of viruses than the sera immunized with DNA alone, but also elicited antibodies that neutralized tier 1 clade B viruses with some neutralizing multiple clade A and C viruses. The EP prime substantially improved the resulting antibody responses induced by the protein boost. This study suggests that such improved DNA constructs and delivery may provide additional benefit in protein prime boost strategies. Understanding the impact on immune breadth of this approach is under further investigation.

Reference:

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**S31 DNA Prime-Protein Boost Approach Was Effective in Eliciting Neutralizing Antibody Responses Against a High Percentage of Subtype BC HIV-1 Viruses Circulating in China**

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**Objective:** Discuss DNA prime-protein boost HIV-1 vaccine.

**Background:** Our previous data showed that DNA prime-protein boost is effective in eliciting neutralizing antibodies (NAb) against randomly selected HIV-1 isolates. Given the genetic diversity of HIV-1 viruses and that different geographic regions have unique predominant subtypes, it is critical to test the DNA prime-protein boost approach against circulating viral isolates in key HIV endemic areas. In the current study, an experimental DNA prime-protein boost vaccine was tested based on envelope glycoprotein (Env) of HIV-1 clade BC, a major subtype circulating in China.

**Method:** A codon optimized gene coding for BC clade consensus Env antigen sequence was produced according to bioinformatics analysis. A BC Env DNA vaccine was constructed and a stable CHO cell line expressing the same consensus BC Env protein was produced. The immunogenicity of the consensus BC Env was examined in New Zealand White rabbits by DNA prime-protein boost or protein alone approaches. Solid phase Env-specific IgG (via ELISA) and functional NAb responses against pseudotyped viruses were measured.

**Results:** High levels of Env-specific antibody responses were elicited by both protein alone and DNA prime-protein boost approaches. However, only DNA prime-protein boost but not the protein alone sera contained significant levels of NAb against HIV-1 BC Env pseudotyped viruses. In addition, high frequency of CD4 binding site-targeted antibodies were found in the DNA prime-protein boost rabbit sera indicating that the positive NAb may be the result of antibodies against conformation sensitive epitopes on HIV-1 Env.

**Conclusion:** The DNA prime-protein boost approach was effective in eliciting NAb against a key HIV-1 virus subtype in China, suggesting that it is feasible to develop regional HIV vaccines by using this approach.

**References:**

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**S32 Circulating Cytokine Levels and Responses to Influenza Vaccine**

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**Objective:** Discuss the immune response to influenza vaccination in regards to serum cytokine levels.
Background: Currently it is difficult to assess if an older individual will have a robust immune response to influenza vaccination. Age, alone, is not a reliable predictor of immune function. We hypothesized that elevated levels of Th2 cytokines would predict poor responses to influenza vaccination.

Methods: Adults aged ≥ 50 years were enrolled in the fall of 2008 to study immune response to influenza vaccination. Hemagglutinin inhibition assays (HAIs) were performed on the day of vaccination and 21 days later. Serum Th2 cytokines, IL-4, IL-5, IL-6, and IL-10, were measured using cytokine bead assays on frozen serum specimens obtained on day 0. We identified subjects with detectable levels of at least 3 cytokines associated with Th2 responses and compared them to those without detectable Th2 cytokines.

Results: 385 of 386 total enrolled subjects had remaining S1 serum samples for cytokine testing. Of these 385 subjects, 34 (8.8%) had at least 3 detectable Th2 cytokines in the serum specimen and 62 (16.1%) subjects had none detected. Subjects with detectable Th2 cytokines were older, had lower HAI antibody levels on days 0 and 21 associated with H3N2 and B vaccine strains but higher H1N1 antibodies on days 0 and 21.

Conclusion: Subjects with detectable Th2 cytokines had lower HAI titers postvaccination for H3N2 and B influenza strains.

Reference:

S33 Trivalent Inactivated Vaccine Containing Influenza B/Victoria Induces Strong Recall of B/Yamagata but Inadequate B/Victoria Antibody Responses in Children Primed With Two Doses of B/Yamagata

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Objective: Review the pediatric prime-boost antibody response to trivalent inactivated influenza vaccine when there has been a major change in the influenza B/lineage in sequential years.

Background: Trivalent inactivated influenza vaccine (TIV) contains one of two influenza B/lineages annually (B/Yamagata or B/Victoria). Children who have received two prior TIV doses are recommended to receive a single dose annually thereafter. We assessed vaccine prime-boost responses in young children following major influenza B/lineage change in sequential years.

Methods: Participants had well-defined influenza B priming during an earlier randomized-controlled-trial as infants (6-11moa) or toddlers (12-23moa) with two full-(0.5mL) or half-(0.25mL) doses of 2008-09TIV containing A/Brisbane/10/07(H3N2); A/Brisbane/59/07(H1N1); and B/Florida/4/06(Yamagata-lineage) antigens. In this follow-up study, participants received a single recommended dose of 2009-10TIV containing the same influenza A antigens but a changed influenza B antigen (B/Brisbane/60/08(Victoria-lineage)). Sera were collected at baseline and 28-42days post-immunization. Serologic response was assessed by hemagglutination-inhibition (HI), summarized as geometric-mean-titres (GMTs) and sero-protection rates (SPR: titres ≥40), and also by microneutralization (MN).

Results: Fifty-six children 20-39moa were included. Before their 2009-10 TIV dose, HI antibody to all 2008-09TIV components had fallen to low levels with B/Florida/4/06(Yamagata-lineage) and B/Brisbane/60/08(Victoria-lineage) SPRs<10% and GMTs<10. A single 2009-10TIV dose boosted HI antibody to the influenza A antigens present in both 2008-09 and 2009-10 TIVs with SPRs ≥90%. The SPR for the 2008-09 B/Florida/4/06(Yamagata-lineage) antigen was ≥80%. However, antibody to the influenza B/Brisbane/60/08(Victoria-lineage) antigen contained in the 2009-10TIV remained low with SPR ≤25%. In follow-up among a subset of 36 children administered a further B/Brisbane/60/08(Victoria-lineage) dose in the subsequent year's 2010-11TIV, antibody response to the B/Victoria lineage was not improved.

Conclusion: A single TIV dose containing a changed influenza B/lineage strongly boosted antibodies to the influenza B/lineage antigen of first vaccine priming. Conversely, not even two full 0.5mL TIV doses primed children for response to a single dose of the alternate B/lineage.

References:
ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS
P1 Characterization of the Mechanism of Protection Mediated by CS-D7, a Monoclonal Antibody to Staphylococcus Aureus Iron Regulated Surface Determinant B (IsdB), with Functional Activity In Vitro and In Vivo

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Objective: Describe the characteristics of an efficacious monoclonal antibody to S. aureus

A fully human monoclonal antibody (CS-D7, IgG1) specific for the iron regulated surface determinant B (IsdB) of Staphylococcus aureus, with high specificity and affinity was isolated from the Cambridge Antibody Technology (CAT) scFv antibody library. The antibody recognized a conformational epitope spanning amino acids 50 to 285 of IsdB. The antibody mediated opsonophagocytic (OP) killing in vitro and mediated significant protection in a murine lethal sepsis model. In an effort to understand the mechanism of protection mediated by CS-D7 in vivo, the mAb was engineered to introduce a point mutation, at aa 297 (CS-D7•N297A). This point mutation prevents glycosylation of the IgG Fc, and thereby reduces Fc effector functions. In vitro analysis of the mutein confirmed that it had essentially no in vitro OP activity when compared to CS-D7. The mutein surprisingly conferred equivalent protection to CS-D7 in the murine lethal challenge model in Balb/c mice. Additionally, both mAbs were efficacious in Fcy KO mice (both FcγRII KO mice and FcγRI, III, IV KO mice), indicating that these receptors were unnecessary for mAb mediated protection in vivo. Depletion of C′ using cobra venom factor in Balb/c mice, or lymphocytes using SCID mice, or SOD using p47phox deletion mice, lead to loss of protection mediated by CS-D7. Lastly, CS-D7 was examined to determine if it could block heme binding to IsdB in vitro, and the mAb was not found to have heme blocking activity under those conditions. Nor did the mAb prevent bacterial growth under in vivo conditions. CS-D7 apparently mediated survival in challenged mice through a mechanism involving C′, neutrophils, and lymphocytes, but which did not depend on Fcγ receptors, nor on blocking iron uptake.

References:

P2 Genomic Sequence of Live, Attenuated Salmonella Typhi Vaccine Strain Ty21 -- Towards an Understanding of Attenuation

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Objective: Review genomic sequence findings to help delineate the mutations responsible for Ty21a attenuation.

Background: The licensed live, attenuated Salmonella typhi Ty21a oral typhoid vaccine has been administered safely to > 200 million recipients worldwide. This vaccine has stimulated efficacies ranging from 67-96% in several large field trials. Ty21a was originally derived from the virulent parent strain Ty2 by successive rounds of random chemical mutagenesis, followed by screening for stable mutations in the galE gene and in Vi capsule expression. These genomic studies were aimed at obtaining a better understanding of how this strain is attenuated.

Methods: The Ty21a genomic sequence was determined from a chip-based resequence analysis compared to the Ty2 genome and from a 4X random 454-based genomic sequence of Ty21a, and was completed by double-strand sequence analysis of contested regions. Preliminary gene microarray analysis was conducted by comparing the gene responses of Ty21a to Ty2 under stress conditions.

Results and Conclusion: Ty21a was determined to be 4,791,958 bp containing 4,339 coding regions. Comparison to
the published Ty2 genomic sequence revealed >600 SNPs and 3 nucleotide deletions in Ty21a relative to the parent. Approximately half of these SNPs were silent mutations. Analysis of the Vi capsule biosynthetic operon revealed 7 mutations in 4 essential genes, but complementation studies showed that only one mutation (i.e. in \textit{tviE}) was functional. Other potentially attenuating metabolic and virulence mutations have been defined. Microarray studies showed that Ty21a downregulates approx. 30 genes relative to Ty2 during stress conditions. Recent reports show that \textit{galE} is a global regulator of cell function and that the Vi capsule normally downregulates the immune response in the gut—but other factors also likely play a role in overall attenuation.

References:

**P3**

**Safety and Immunogenicity of a DNA Vaccine Expressing H5 Hemagglutinin Delivered by Intramuscular or Intradermal Route in Healthy Adults**


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**Objective:** Provide an update on development of the DNA vaccine targeted against avian influenza and report the results of two phase I studies evaluating safety and immunogenicity of this vaccine.

**Background:** Avian influenza causes outbreaks in domestic and wild birds around the world; sporadic human infections have been reported. The DNA vaccine, VRC-AVIDNA036-00-VP, encoding hemagglutinin (HA) protein from the A/Indonesia/5/05 (H5N1) strain was tested in two randomized Phase I clinical studies.

**Methods:** VRC 304 was a placebo-controlled, double-blinded study with 45 subjects randomized to placebo, 1 mg, or 4 mg vaccine (n=15/group) by intramuscular (IM) Biojector® injection. VRC 305 was an open-label study with 44 subjects randomized to intradermal (ID) injections of 0.5 mg by needle/syringe or by Biojector®, or 1 mg delivered by two 0.5 mg Biojector® injections in the same arm or by 0.5 mg in each arm (n=11/group). Three injections at weeks 0, 4, 8 were administered in both studies. Antibody responses were assessed by ELISA, HAI, and neutralization assays and compared between groups by Fisher’s exact test for response rate and Wilcoxon test for response magnitude.

**Results:** There were no vaccine-related serious adverse events; reactogenicity was no more than moderate. At 1 mg, ID compared to IM vaccination induced greater frequency and magnitude of response by ELISA (p<0.05), but there were no significant differences in frequency or magnitude of response between ID and IM routes in the HAI or neutralization assays.

**Conclusion:** The H5 DNA vaccine was well-tolerated and induced antigen-specific immune responses. The ID injection route did not offer an advantage over the IM route, and no difference was detected in one arm versus two arms for ID vaccine administration. Therefore, the 4 mg dose (IM) will be used in future prime-boost regimens.

**References:**
Lack of Protective Efficacy of an Adenovirus-vectored *P. falciparum* Malaria Vaccine in the Absence of DNA Priming


1US Military Malaria Vaccine Program, Naval Medical Research Center/Walter Reed Army Institute of Research, Silver Spring, MD, 2GenVec Inc., Gaithersburg, MD, 3USAID, Washington, DC

**Objective:** Describe the clinical outcome of a Phase 1/2a malaria vaccine trial testing the protective efficacy of an Adenovirus-vectored malaria vaccine and compare this to results when the same vaccine is given after DNA priming.

**Background:** Pre-clinical models of immunity to malaria indicate that cell mediated responses targeting the intrahepatic development of the parasite can provide sterile protection. The U.S. Military Malaria Vaccine Program recently demonstrated that priming with a DNA vaccine encoding the malaria antigens circumsporozoite protein (CSP) and apical membrane antigen 1 (AMA1) followed by boosting with an Adenovirus 5-vectored vaccine incorporating the same antigens (the AdCA Vaccine) steriley protected 4 of 15 (26.7%) human volunteers against sporozoite challenge in association with strong CD8+ T cell-dependent interferon-gamma ELISpot responses. The current trial evaluated the protective efficacy of the AdCA vaccine given without DNA priming.

**Methods:** A single dose of AdCA (1 x 10^10 pu/antigen) was administered to 20 healthy, malaria naïve, Ad5 seronegative volunteers. Four weeks later, 18 immunized and 6 unimmunized infectivity controls underwent homologous *P. falciparum* sporozoite challenge.

**Results:** The AdCA vaccine was safe and well-tolerated. IFN-gamma ELISpot responses were higher following Ad CA in the absence of a DNA prime (CSP range 34-2508 sfc/10^6 PBMCs, geometric mean 236; AMA1 range 399-4456 sfc/10^6 PBMCs, geometric mean 1102) than when the prime had been given in the previous trial (CSP range 5-375 sfc/10^6 PBMCs, geometric mean 43; AMA1 range 14-1165 sfc/10^6 PBMCs, geometric mean 177). However, all challenged volunteers become parasitemic with no significant delay to patency in the immunized compared with the control group (Log Rank test: p=0.489).

**Conclusion:** The AdCA vaccine administered alone stimulates quantitatively superior ELISpot responses against whole proteins than when following DNA priming, but does not confer sterile protection, indicating that DNA priming is required. The nature of the protective T cell response requires further investigation.

**References:**

**Efficacy of Pentavalent Human-Bovine Reassortant Rotavirus Vaccine Among American Indian Children**


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**Objective:** Describe the efficacy of the pentavalent human-bovine reassortant rotavirus vaccine among Navajo and White Mountain Apache American Indian children.

**Background:** Acute gastroenteritis (AGE) is a significant global health problem among children with rotavirus contributing to a majority of the AGE burden. Historically, Native American infants have had higher rates of rotavirus AGE compared to general United States population.

**Methods:** From 2002-2004, Navajo and White Mountain Apache (N/WMA) American Indian infants 6-<12 weeks of age were enrolled into the phase-III, double-blind, placebo-controlled efficacy trial of pentavalent human-bovine reassortant rotavirus vaccine (PRV). Participants received three doses of vaccine or placebo with 28-70 days separating each dose. Active surveillance identified AGE episodes after enrollment and serious adverse events (SAEs) within 42 days after each
dose. AGE was defined as 3 or more watery or looser-than-normal stools within a 24-hour period and/or forceful vomiting. Stool specimens from AGE episodes were tested for rotavirus by an enzyme immunoassay and serotyped. AGE severity was determined by a 24-point clinical scoring system.

Results: We enrolled 1,008 N/WMA infants; 509 received PRV, 494 placebo and 5 were not dosed. Among placebo recipients, the rotavirus AGE incidence was 118.3/100,000 child-years; the percent of AGE caused by serotypes G1, G2 and G3 was 76%, 22% and 2%, respectively. The efficacy of PRV against rotavirus AGE caused by serotypes G1-G4 was 77.1% (95% confidence interval [CI]: 59.8-87.6). PRV prevented 89% (95% CI: 65.9-97.9) of moderate and severe rotavirus AGE (severity score >11). There were no cases of intussusception or death within the 42 day safety reporting period.

Conclusion: PRV is highly efficacious against rotavirus AGE caused by vaccine serotypes and moderate and severe AGE among N/WMA children, a group at high risk of rotavirus AGE. PRV demonstrated an excellent safety profile.

References:

P6 Barriers and Drivers to Introduction of New TB Vaccines in High Burden Countries: A Market Research Study
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Objective: Describe how valuable early input from decision makers in target countries regarding introduction of new vaccines can help guide product development and introduction planning.

Background: There are policy and implementation choices for countries considering introduction of new vaccines, e.g., how they fit into healthcare budgets, immunization systems, and priorities. To understand barriers and drivers to introduction of new TB vaccines, Aeras commissioned a 2010 market research study of the perspectives of decision makers and stakeholders in high burden countries.

Methods: Interviews were performed in the following countries: China, India, South Africa, Brazil, Russia, Mozambique, Cambodia, and Romania. Respondents included Ministry of Health (MoH) civil servants, Finance Ministry civil servants; public health clinicians; NGOs interested in public/children’s health; parliamentarians; and journalists. Scenarios presented included (1) a BCG replacement that was as effective but safer than current BCGs and that would prime well for a second booster vaccine; (2) a prime boost regimen starting with current BCG or a BCG replacement followed by infant and later boosts with a different vaccine that would reduce TB disease by 60%; and (3) the regimen with the booster delivered by aerosol rather than needle injection.

Results: Analysis of interview data indicate that TB is considered a major public health issue but often does not get the importance it needs as a health care priority. There was a mixture of interest in the three scenarios and also in likelihood of rapid adoption of new TB vaccines. Overall there was enthusiasm for new, partially effective TB vaccines and willingness to pay assuming low cost.

Conclusion: Most interviewees favored use of new TB vaccines in one or more of the scenarios, often subject to clinical data bearing out safety and efficacy. The spectrum of stakeholder perspectives can help inform strategies for development and introduction of new TB vaccines.

References:


**P7**

**Pediatric Compliance to Iraqi’s Immunization Guideline**

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**Objective:** Discuss the evaluation of immunization compliance with Iraqi immunization guideline in pediatric younger than two years and to explore the possible errors associated with the immunization practice.

Immunizations have reduced dramatically the incidence rates of infection. The pediatric immunization schedule is increasingly complex to develop and achieve a well-immunization system. In Iraq, children younger than two years of age require 7 combination doses or 15 individual doses of vaccines to be protected against 9 infectious diseases.¹ A cohort study of 528 Iraqi children born between 1 January 2003 and 31 Jun 2008 was selected to ensure completeness of 2 years immunization histories. Immunization history of each individual child was collected retrospectively from pediatric immunization card. This study was restricted the analyses to types of vaccines administered before age 2 years. Immunization doses were classified as one of five types:² A normal dose was administered at the recommended age; an early dose was administered before the recommended age; a missed dose was an indicated dose that the child did not receive; a late dose was one given later than the recommended age; and an extra dose meant that the child received more than the recommended number of doses. When the child received all the vaccine doses without any missed immunizations, it was considered complete immunization compliance, while if the child missed at least one immunization dose, it was considered partial immunization compliance. Only 286 children were found to be in complete compliance with recommended immunization practices. Less than half of the population was considered to be in partial compliance. Among 3,696 scheduled immunization doses received by 528 children, 25.3% of doses were normal doses, 8.3% early doses, 13.6% were missed doses, 47.5% of doses were late doses, and 5.3% were categorized as extra doses. Immunization errors occur frequently, leading to improper immunization. This study supports the need to decrease immunization errors and optimize childhood infectious disease prevention.

**References:**


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**P8**

**Research Roadblocks: Attempts to Measure the Influence of Adverse Events Following Immunization on Parental Immunization Behaviors**

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**Objective:** Understand the recruitment challenges faced by immunization program researchers conducting behavioral research. While we support the need to protect the public’s privacy, this can lead to unforeseen complications with data collection.

**Background:** In British Columbia, vaccination is not mandatory and coverage hovers around 64% for 2 year old children.¹ We hypothesized health system response to adverse events following immunization (AEFI) may affect future parental immunization behavior and sought to evaluate parental and health system response to AEFI.

**Methods:** A baseline and 9 month follow up questionnaire were administered to parents of immunized children < 2 years old. The intended sampling frame for the study was a random sample of parents, with (cases) and without (controls) reported AEFI, extracted from public health immunization registries. An opt-out recruitment strategy was selected to minimize volunteer bias.²
Results: Although ethics approval was obtained from local research ethics boards, public health lawyers were concerned about the use of immunization registries for a sampling frame and opt-out recruitment. Negotiations occurred over a 12 month period leading to a delayed study start and necessitated a change in recruitment strategy. Cases were recruited from public health AEFI records. One district allowed only passive recruitment. Potential participants were sent an invitation letter with a phone number to call to participate. Zero participants were recruited using this method. Other districts permitted active recruitment. Invitation letters were followed with a phone call from public health. The contact information for interested parents was forwarded onto the researchers. This resulted in 52 participants. 48 controls were recruited actively from the children's hospital where the researchers work and have access to patients.

Conclusion: Recruitment constraints increased study costs and delayed data collection. Our study highlights the importance of strong collaborations with public health. Because of privacy concerns, recruitment would not have been possible without public health's active participation.

References:

P9 Parents’ Decision-Making for Seasonal Influenza Vaccination for Children Ages 2 to 12

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¹Oxford Outcomes, Bethesda, MD, ²MedImmune, LLC, Gaithersburg, MD, ³Kentucky Pediatric Research, Bardstown, KY, ⁴Marshfield Clinic, Marshfield, WI

Objective: Discuss the rationale for parental decision-making regarding influenza vaccination for their children.

Background: The CDC recommends annual influenza vaccination for all children older than 6 months; however, vaccination rates for children remain low. This study investigated the factors that influence parental decision-making regarding influenza vaccination for their children.

Methods: In August and September 2009, an internet-based survey was administered to a nationally representative US sample of 500 parents of children aged 2-12 years. The survey was based on conceptual models and included a list of reasons for and against (i.e., drivers and barriers) vaccinating children against influenza. The importance of each driver or barrier was assessed on a 5-point scale (1= a little important, 5=extremely important). Mean importance ratings were derived for all drivers and barriers.

Results: The most commonly selected drivers for children’s influenza vaccination were prevention of flu (95%), doctor recommendation (90%), and reduction of flu symptoms (83%). Highest mean [SD] importance ratings were: prevention of flu (4.37 [0.83]), other health issues (4.25 [0.98]), and reduction of flu symptoms (4.20 [0.92]). Barriers for vaccination were more variable; however, the top 3 barriers were: low risk for flu (46%), vaccine can cause the flu (44%), and vaccine-related side effects (sore arm, runny nose) (37%). Highest mean importance ratings were: vaccine contains thimerosal (4.21 [0.99]), vaccine weakens the immune system (3.89 [0.90]), and vaccine is not safe (3.83 [1.15]).

Conclusion: Prevention of influenza, reduction of influenza-related symptoms, and doctor recommendation were overwhelmingly endorsed as drivers for vaccination. Barriers to vaccination were more variable but primarily included risk of adverse events and perceived low risk for influenza. Health care providers should consider these drivers and barriers when addressing low influenza vaccination rates for children.

References:
**P10  Rotavirus and Bacterial Pathogens in Diarrheal Stools of Children Under 3 Years in Lagos, Nigeria**

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**Objective:** Identify challenges to diarrhea vaccine coverage in children under 3 years in Nigeria for better management of diarrhea.

**Background:** Rotavirus causes severe diarrhea among infants and young children¹ and is the single important cause of infectious severe dehydrating diarrhea and death globally in children under 5 years². The virus is transmitted by fecal-oral route. More than 85% of the 600,000 deaths in children under five due to rotavirus infection occur in Africa and Asia³. In 2004 six countries including Nigeria accounted for more than 50% of all rotavirus diarrhea in under 5. Rotarix vaccine came into Nigerian market in 2006. In view of the seriousness of this disease burden worldwide, WHO recommends the use of rotavirus vaccines in countries with under five mortality of more than 10%. This study was therefore designed to determine the prevalence of rotavirus diarrhea in under 3, the rotavirus vaccine coverage, and possible challenges to the vaccine coverage. A preliminary report is presented.

**Methods:** With informed consent, biodata of caregivers and rotavirus vaccination status of children presenting with diarrhea in 3 hospitals in Lagos Mainland were obtained. Stool samples collected were processed using standard microbiological methods to identify rotaviruses and bacteria.

**Results:** Results obtained so far showed that the rotavirus isolates were much lower than the bacterial isolates and that 13.6% of the children had received the Rotarix vaccine. Occupation of the caregivers did not influence the vaccination status of the children whereas education was a factor as 9.1% of caregivers with primary education vaccinated their children while 36.4% and 45.5% of those with secondary and tertiary education respectively, vaccinated their children. Also 60.7% claimed to purify their drinking water by boiling and addition of water guard.

**Conclusion:** Enlightenment programmes will be required to improve the vaccine coverage.

**References:**


**P11  Preclinical Development of ACAM529, a Replication-Defective Vaccine Against Herpes Simplex Virus Type 2**


_Biotherapeutics Discovery US, sanofi pasteur, Cambridge, MA_

**Objective:** Become acquainted with ongoing efforts to develop a genital herpes vaccine.

Herpes simplex virus type 2 (HSV-2), and the closely related herpes simplex virus type 1 (HSV-1) both cause genital herpes, the most prevalent sexually transmitted infection. HSV-2 is found throughout the world, including in the United States where, in the year 2000, infections were estimated to cost over $1.8 billion annually. Antivirals available commercially are effective at controlling genital herpes and reducing transmission, however they cannot cure HSV infections, do not prevent acquisition of infection, and are not 100% effective. As a result, significant efforts have been expended over the last six decades to develop a vaccine against this virus. ACAM529 is a replication-defective HSV-2 vaccine better known in the scientific literature as dl5-29, which is currently being prepared for clinical trials. The vaccine has been cloned, grown in a complementing cell line, purified, and administered to mice via various routes to assess immunogenicity as well as protective efficacy in a vaginal challenge model. ELISA and neutralization titers, as well as measurements of morbidity, mortality, and vaginal shedding of the challenge virus indicate that two doses of ACAM529 delivered intramuscularly are optimal to protect animals against a lethal challenge.
**P12** Determination of Cellular Immune Responses Induced by Consensus or Mosaic HIV-1 Env Vaccines in HLA-B7 Transgenic Mice

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**Objective:** Discuss the study of cellular immune responses induced by mosaic or consensus HIV-1 envelope antigens.

**Background:** The genomic variability of HIV viruses circulating in different countries of the world has impeded the development of globally relevant HIV vaccines. DNA vaccines require significant engineering in order to produce strong immune responses in non-human primates and humans. Recently we have reported that our optimized HIV-1 DNA consensus vaccines drive strong and broad T cell responses in humans that for the first time surpass most viral vector systems. We have now further focused on improving this technology.

**Methods:** We developed a novel optimized clade B consensus envelope vaccine (pEY2E1-B) with the goal of increasing vaccine antigen immune potency. An optimized mosaic gp160 envelope vaccine was also constructed (pMosEnv). Cellular immune responses were assayed by IFN-γ ELISPOT in human HLA-B7 (mouse MHC KO) transgenic mice.

**Results:** We observed that pEY2E1-B induced stronger cross-reactive immune responses against consensus peptides from individual subtypes than pMosEnv. The average additive number of SFU/10⁶ splenocytes induced by pEY2E1-B against four pools of consensus subtype A, B and C peptides were 238, 1150 and 372, respectively. While the additive immune responses induced by pMosEnv were 54, 415 and 168, respectively. Therefore, the consensus immunogen was up to three times more potent at driving subtype-specific responses that cross-recognized the different clade immunogens. When the PTE peptide set was used, pMosEnv was more immune potent than pEY2E1-B.

**Conclusion:** It is clear that these different strategies have unique strengths and specific differences in their immune targeting abilities. The consensus immunogen has improved ability to focus on conserved regions while it appears the mosaic immunogen targets more variable epitopes. Further exploration of these types of immunogens are valuable and in progress.

**References:**


**P13** An Integrated Genomic and Immunoinformatic Approach to *H. pylori* Vaccine Design

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**Objective:** Illustrate how to harness genomics and immunoinformatics to produce vaccines.
Background: Ineffective host immune response to H. pylori results in persistent infection and chronic gastric inflammation. Current eradication strategies are limited by emerging antibiotic resistance. Because immunity to H. pylori is T-cell dependent, development of a T cell-directed vaccine would be valuable in preventing H. pylori-associated diseases. We describe a genomes-to-vaccine approach to H. pylori vaccine design that takes advantage of bioinformatics methods to rapidly identify T-cell epitope sequences from large genomic datasets.

Methods and Results: We set out to identify vaccine immunogens common to seven H. pylori genomes, associated with geographically diverse populations and a range of different clinical sequelae. A core genome comprised of 676 open reading frames was identified in amino acid relatedness and sequence identity searches across genomes. Of 1,241,153 9-mer sequences encoded by these genes, 106,791 were identical across all seven genomes and 23,654 scored in the top 5% of predicted HLA ligands for at least one of eight archetypal Class II HLA alleles when evaluated by the EpiMatrix algorithm. 1,805 immunogenic consensus sequences (ICS) were assembled to computationally construct vaccine immunogens with maximal epitope density over 20-25 amino acid stretches. 76% of select ICS peptides bound strongly to a panel of 6 HLA Class II haplotypes, representing >90% of the global human population. Pools of ICS peptides stimulated human gastric and peripheral blood CD4 and CD8 T cells to secrete IFN-gamma, IL-2 and TNF-alpha in vitro.

Conclusion: The breadth of H. pylori genome datasets was computationally tamed to rapidly and carefully select a core set of genes. Application of immunoinformatics tools to this gene set accurately predicted epitopes with promising properties for T cell-based vaccine development.

References:

P14 Rapid, Non-Invasive Imaging of Encephalitic Viruses: Reducing Animal Numbers and Morbidity to Identify Efficacy of Potential Vaccines and Anti-Virals

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Objective: Discuss utilization of in vivo imaging systems technology in neuro-invasive infections to study the efficacy of vaccines and therapeutics while reducing animal numbers and morbidity.

Quick and accurate identification of disease progression are key factors in testing novel vaccines and anti-virals. Old-fashioned efficacy studies usually utilize a large number of animals and a severe morbidity or mortality as an endpoint. New technologies provide a means to reduce and refine the animal use as proposed in Hume's 3Rs. In vivo imaging systems (IVIS) and bioluminescent enzymes are a few technologies which we propose to utilize to accomplish the reduction of animal requirements while increasing scientific accuracy. Utilizing a murine model of Venezuelan equine encephalitis virus (VEEV) in which CNS invasion is a key endpoint for disease development, we infected imprinting control region (ICR) mice intra-nasally with the vaccine strain of VEEV, TC83, expressing a luciferase gene. Daily imaging of the mice was completed to track viral progression and tissue invasion. Using the same infectious model we also confirmed the protective capability of Ampligen®, a TLR-3 agonist, in preventing CNS invasion. The IVIS system enabled us to create multiple images throughout the study from an individual animal. We are able to accurately track and identify both CNS invasion and nasal virus clearance in real time without the need to sacrifice the animal. Furthermore, we were able to identify the invasion of the CNS days before any clinical development of disease. An analysis of Ampligen® as a prophylactic and therapeutic IFN agonist also showed inhibition of CNS invasion. The IVIS system can greatly reduce the requirement for animals through multiple data point collections without requiring animal sacrifice. The speed of the system also allows for reduction of animal morbidity providing a humane means of disease and vaccine research while obtaining scientific data accurately and rapidly.

References:
Objective: Understand and discuss new methods for assessing potency and relative potency of NTD vaccines.

Over the next decade, a new generation of vaccines will target the neglected tropical diseases (NTDs). The goal of most NTD vaccines will be to reduce the morbidity and decrease the chronic debilitating nature of these often-forgotten infections - outcomes that are hard to measure in the traditional potency-testing paradigm. The absence of measurable correlates of protection, a lack of permissive animal models for lethal infection, and a lack of clinical indications that do not include the induction of sterilizing immunity required us to reconsider the traditional bioassay methods for determining vaccine potency. Owing to these limitations, potency assay design for NTD vaccines will increasingly rely on a paradigm where potency testing is one among many tools to ensure that a manufacturing process yields a product of consistent quality. This potency test is a bioassay using BALB/c mice, which evaluates the immunogenicity of the vaccine at set time interval post manufacture. Herein, we discuss the results of 12 month potency testing of Necator americanus-glutathione-S-transferase-1 (Na-GST-1) vaccine. The Effective Dose 50 (ED50), with its 95% fiducial limits (FL) for each time point was determined along with the Relative Potency with its 95% FL for 3, 6, 9 and 12 months post manufacture. Potency testing has shown that storage at 4° C decreases the ED50 and increases the relative potency of Na-GST-1 vaccine. We proposed that the change in ED50 and relative potency coincide with higher affinity binding of the Na-GST-1 to the Alhydrogel® that occurred during storage at 4° C. These preclinical results lay the foundation for moving forward with Phase 1 clinical trial in Brazil.

Reference:

Objective: Discuss the strategies to overcome difficulties related to the properties of different influenza B viruses and to variation in yields.

Background: For influenza vaccine manufacture it is essential to produce seed viruses that consistently allow high yields of influenza virus antigen. Most seasonal trivalent inactivated influenza vaccines are prepared in embryonated eggs from accredited egg grown seed viruses. Yields of influenza A subtypes are enhanced by the selection of high yielding reassortants after co-infection of egg grown epidemic strains. However, the yield of influenza B viruses grown in eggs is low in comparison since a system for generating consistent B reassortants is yet to be established. Several reports have suggested the use of cold adaptation to improve the yield of B viruses (Hoffmann E. et al. 2005). We examined cold adaptation, classical reassorting and reverse genetics of circulating B viruses to determine whether the yield of B viruses can be improved.

Methods: In order to enhance influenza B virus yields, we first characterized the growth (plaque forming ability, HA levels, TCID₅₀, EID₅₀) of seasonal influenza B isolates. Three strains, B/Malaysia/2506/2004, B/Florida/4/2006, B/Brisbane/60/2008, were selected and grown at gradually lower temperatures in eggs, classical reassortment by co-infection or reverse genetics to determine the best method to improve B viral growth.

Results: Serial passage of B viruses (n=10) indicated an inconsistent growth pattern. Different cold adaptation strategies (n=7) were attempted yet improved the growth in 3/3 strains only after greater than 50 passages in eggs. Applications of reassorting and reverse genetic techniques also demonstrated an inconsistent growth pattern of the resulting B virus.
Conclusion: Our results suggest that current methods to manipulate influenza B virus do not overcome growth variability.

Reference:

P17 Improved Vaccine Delivery by Removal of Tolerogenic Signals in Dendritic Cell Targeting Antibodies

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Objective: Describe a novel dendritic cell targeted vaccine delivery platform.

Background: The highly specific capacity of antibodies for targeting dendritic cell endocytic receptors can be harnessed for efficient vaccine antigen delivery to the antigen presentation pathway. However, conserved IgG sequences that induce T cell tolerance may limit their ability to elicit protective T cell and antibody responses, without the addition of unsafe, non-specific dendritic cell maturation factors. We set out to eliminate tolerogenic sequences in the well-studied dendritic cell targeting antibody, anti-DEC-205, to produce a vaccine delivery platform that will be independent of additional non-specific immuno-stimulators. This goal is based on our recent discovery of a set of natural regulatory T-cell epitopes derived from human immunoglobulins that induce tolerance by stimulating regulatory T cells.

Methods and Results: We screened the anti-DEC-205 sequence computationally for putative HLA DR4-restricted, regulatory T-cell epitopes as targets for mutations that will reduce epitope binding affinity for HLA. Amino acid substitutions predicted to interfere with HLA binding were identified and experimentally verified in HLA DR4 binding assays. Sequence modifications that prevented binding were incorporated into an array of anti-DEC-205 antibody variants recombinantly fused to test antigens, ovalbumin and HIV gag, and produced in a mammalian expression system. Binding of the de-tolerized antibodies to dendritic cells was confirmed by flow cytometry. Variant antibodies are being evaluated for reduced tolerogenicity, as well as for enhanced ovalbumin and HIV gag immunogenicity, in terms of cellular and humoral responses.

Conclusion: We predict that the modification of regulatory T-cell epitopes will significantly diminish tolerogenicity, enabling the use of modified anti-DEC-205 as an antigen-delivery system that obviates the dangers associated with non-specific activation of the immune system.

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Reference:

P18 Immunogenic Consensus Sequence T Helper Epitopes for a Pan-Burkholderia Biodefense Vaccine

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Objective: Discuss an immunome-derived vaccine development approach applied to burkholderia.

Background: Biodefense vaccines against Category B bioterror agents Burkholderia pseudomallei (BPM) and Burkholderia mallei (BM) are needed, as they are both easily accessible to terrorists and have strong weaponization potential. Burkholderia cepaciae (BC), a related pathogen, causes chronic lung infections in cystic fibrosis patients. Since BPM, BM, and BC are intracellular bacteria, they are excellent targets for T cell-based vaccines. However, the sheer volume of available genomic data requires the aid of immunoinformatics for vaccine design.

Methods: Using EpiMatrix™, ClustiMer, and EpiAssemblerax, a set of immunoinformatic vaccine design tools, we screened the 31 available Burkholderia genomes for cross-conserved HLA ligands and performed initial HLA binding assays of
predicted sequences for an epitope-based multi-pathogen vaccine against *Burkholderia* species.

**Results:** Immunoinformatics analysis of 31 *Burkholderia* genomes yielded 350,004 9-mer peptides of which 133,469 were completely identical across 10 BM genomes, 175,722 across the 11 BPM genomes and 40,813 across the 10 BC genomes. Further screening with EpiMatrix™ yielded 54,010 high-scoring Class II epitopes; these were assembled into 2,880 longer highly conserved ‘immunogenic consensus sequence’ T helper epitopes. 100% of the peptides bound to at least one HLA class II allele in vitro, 92.7% bound to at least two alleles, 82.9% to three, and 75.6% of the overall binding results were consistent with the immunoinformatics analysis.

**Conclusion:** Our results show it is possible to rapidly identify promiscuous T helper epitopes conserved across multiple *Burkholderia* species and test their binding to HLA in vitro. The next step in our process will be to test the epitopes *ex vivo* using peripheral leukocytes from BC, BPM infected humans and for immunogenicity in human HLA transgenic mice.

**References:**

**P19 Vaccine Potential of Nipah Virus-Like Particles**

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**Objective:** Acquire latest information on NiV vaccine development.

Nipah virus (NiV) was first recognized in 1998 as the causative agent of a highly lethal febrile encephalitis in humans and predominantly respiratory disease in pigs. Since then, the occurrence of periodic deadly outbreaks, documentation of person-to-person transmission in some cases, and its potential as an agent of agroterror reinforces the need for effective means of therapy and prevention. We are evaluating a virus-like particle (VLP)-based approach to develop NiV vaccine. We have demonstrated that under optimized conditions, co-expression of NiV G, F and M proteins resulted in quantifiable amounts of VLPs with many virus-like/vaccine desirable properties including some that have not been reported previously, namely, their ability to induce syncytia formation, induce innate immune responses, a neutralizing antibody response, and to boost IgG subclasses in Balb/c mice. Based on these findings, we believe that VLP-based vaccination approach shows promise not only for NiV, but it will serve as platform technology for developing vaccines for other important pathogens of this group that cause human disease.

**References:**

**P20 Alphavirus Vaccines: A Novel Inactivation Approach Towards Better Vaccine Development**

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**Objective:** Describe a novel approach for alphavirus inactivation.

**Background:** Classically inactivated viral vaccines have been developed using formalin inactivation, gamma irradiation, UV irradiation, and heat inactivation. Such inactivated viral vaccines have been successfully used for both human and veterinary immunizations for decades. However, these vaccines have several limitations such as poor immunogenicity due to loss of epitopes and short-lived immunity. Live attenuated viral vaccines have advantage over inactivated vaccines as these are more immunogenic and usually provide long-lasting immunity. Yet residual virulence associated with the live attenuated viral strains and the possibility of reversion to a virulent phenotype are deterrents for their use as vaccine candidate for highly pathogenic alphaviruses.

**Methods:** We have used a novel approach for inactivating alphaviruses that overcome the limitations of both the classically inactivated and live attenuated virus vaccines. A photoactive aryl azide, 1,5 iodonapthyl azide (INA), was used to inactivate Venezuelan and eastern equine encephalitis viruses (VEEV and EEEV) and chikungunya virus (CHIKV). INA has been shown to partition into the hydrophobic domain of the biomembrane and upon short irradiation with UV light covalently binds to the transmembrane domain of the membrane proteins without affecting their ectodomains.

**Results:** INA-inactivated alphaviruses are completely safe with no residual virulence and protect mice from virulent virus challenge.

**Conclusion:** Alphaviruses have been identified as reemerging viruses that have been weaponised and thus could be used as bio-terror agents. Currently there are no licensed alphavirus vaccines for human immunizations presenting a great risk in the event of their use as bio-terror agent. Our findings are a first step forward in developing a highly immunogenic inactivated alphavirus vaccine. This work was supported by funding from the Defense Threat Reduction Agency.

**References:**
P22  *Salmonella Enteritidis Core-O Polysaccharide (COPS) Conjugated to Enteritidis Flagellin (H:g,m) as a Candidate Vaccine for Protection Against Salmonella Enteritidis Infection*


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**Objective:** Describe a novel polysaccharide-protein conjugate parenteral vaccine incorporating a homologous pathogen TLR ligand as the carrier protein for protection against enteric disease.

**Background:** Non-typhoidal *Salmonella* organisms are a major cause of severe gastroenteritis in the USA and worldwide, and a significant cause of systemic bacteremia in sub-Saharan Africa. *Salmonella* O polysaccharide (OPS) and flagellin protein are important virulence factors and protective antigens for *Salmonella* infection. Covalent attachment of bacterial polysaccharides to carrier proteins dramatically enhances their immunogenicity and confers immunologic memory. Conjugate vaccines comprised of *Salmonella* enteritidis flagellin and COPS were constructed to enhance the immunogenicity of COPS, supply an inherent systemic adjuvant boost through the host innate immune receptor TLR5, and provide immunity to both the carrier and hapten homologous pathogen antigens.

**Methods:** COPS and flagellin were purified from a genetically attenuated (guaBA) reagent strain of an invasive *Salmonella* enteritidis Malian clinical isolate, engineered for increased flagellin production (clpPX). COPS-flagellin conjugates were constructed by linkage either at random COPS hydroxyls with CDAP chemistry or at the Core-KDO terminus with aminooxy chemistry to solvent-exposed lysines on flagellin. Mice immunized intramuscularly three times at 28 day intervals with 2.5 µg of purified conjugate or controls, were bled at 21 days following each dose. IgG to LPS and flagellin was measured by ELISA. Serum opsonophagocytic activity was assessed with wild-type *Salmonella* enteritidis and J774 macrophages. Intraperitoneal challenge was at 28 days after the final immunization, with an LD100 dose of virulent wild-type *Salmonella* enteritidis.

**Results:** COPS-flagellin conjugates elicited high anti-LPS (as compared to unconjugated COPS) and anti-flagellin titers that were functional in vitro for opsonophagocytosis. Mice immunized with COPS-flagellin conjugate constructs were significantly protected from lethal challenge with wild-type *Salmonella* enteritidis, demonstrating 80-100% vaccine efficacy.

**Conclusion:** COPS-flagellin conjugate vaccines elicit functional immunity in mice, and mediate protection against lethal *Salmonella* infection.

**References:**


P23  *Dengue Tetravalent Consensus DNA Vaccine Induces Antibodies Against All Four Serotypes of Dengue Virus*


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**Objective:** Discuss the immunogenicity of this dengue vaccine.
Background: Co-circulation of four serotypes of dengue virus resulting in multiple infections with more than one serotype is very common in dengue epidemic areas. Increasing severity has been hypothesized to be caused by the mechanism of antibody-dependent enhancement (ADE) occurring in the secondary infection with a heterotypic infection. Therefore, an ideal dengue vaccine should induce a broad immune response against all four serotypes, thus avoiding the issues of ADE. In this regard, domain III of dengue virus envelope protein has emerged as a promising region for vaccine candidate since it has been implicated for receptor binding and target for neutralizing antibody.

Methods: We developed a synthetic human codon/RNA optimized consensus dengue envelop domain III DNA vaccine. The consensus DIII domains of dengue serotypes 1-4 envelope proteins were cloned and expressed as a single open reading frame in a mammalian expression vector (pDV-U-DIII). The DNA vaccine was delivered via electroporation (EP) using the CELLECTRA constant current device. Each mouse received 3 immunizations, 3 weeks apart. One week after last immunization, mice were sacrificed. The spleenocytes were harvested to perform B-ELISPOT and sera were used to perform the binding ELISA assay. The values were demonstrated as the mean ± standard error of the mean (SEM) calculated from triplicate samples from each experimental group.

Results: Vaccination with pDV-U-DIII DNA vaccine enhanced the production of anti-DIII specific B cells. After three immunizations, pDV-U-DIII vaccinated mice induced high level of anti-DIII specific antibodies. These antibodies were highly specific for all four serotypes of dengue virus.

Conclusion: Vaccination of mice with a synthetic consensus pDV-U-DIII vaccine delivered by CELLECTRA® EP induces tetravalent immunity against all four serotypes of dengue virus.


P24 Induction of False-Positive PTT Elevations by Investigational Adenoviral Vector Vaccines

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Objective: Apply knowledge of induction of anti-phospholipid antibody in association with adenoviral vector vaccines and recognize that this observation may be an artifact of the in vitro assay method rather than a clinically relevant finding.

Background: Prolonged partial thromboplastin time (PTT) has been observed in preclinical evaluation of adenoviral vector vaccines in rabbits and in an investigational rAd5-Ebola vaccine study; the latter was investigated and determined to be a laboratory artifact, not associated with a clinical coagulation defect. Membrane phospholipids are a limiting ingredient in the PTT assay. The presence of anti-phospholipid antibody (APA) can thereby result in a false-positive prolongation of PTT. Evaluation of PTT was included in the Phase I safety and immunogenicity study of two prototype HIV vaccines, VRC-HIVADV027-00-VP (rAd35-EnvA) and VRC-HIVADV038-00-VP (rAd5-EnvA).

Methods: In VRC 012 Part II, 20 healthy adults were randomized to 4 blinded, heterologous prime-boost schedules of rAd5-EnvA and rAd35-EnvA (12 week interval). rAd35-EnvA was given at 10^{10} or 10^{11} particle units (PU); all rAd5-EnvA injections were 10^{10} PU. PTT was evaluated through 4 weeks after each vaccination. The PTT normal range was 25.3-37.3 seconds. Additional hematologic evaluations were performed for PTT adverse events (AE); defined as 1.1 times the upper limit of normal or higher.

Results: Eighteen of 20 subjects completed both vaccinations. Four had prolonged PTT values as defined by normal range at follow-up 2 weeks after both prime and boost injections. At 3 of these timepoints, values did not attain grade 1 severity defined per protocol; 5 of these timepoints met criteria for an AE. Four PTT AEs were grade 1; one was grade 3 (maximum=57.9 sec). None were associated with clinical symptoms and all resolved without treatment.

Conclusion: The PTT prolongation observed with these adenoviral vector vaccines was not clinically significant and was consistent with an in vitro effect on the laboratory assay for PTT due to induction of APA.

References:

P25 The Unintended Consequences of Vaccine Delivery Devices Used to Eradicate Smallpox: Lessons for Evaluating Future Vaccination Methods

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Objective: Review the actual and theoretical evidence for transmission of bloodborne pathogens between consecutive vaccines by multi-use-nozzle jet injectors (MUNJIs) and bifurcated needles (BNs) without intervening sterilization.

Background: After smallpox eradication, evidence emerged that its vaccine-delivery devices could transmit bloodborne pathogens such as hepatitis B (HBV) through inherent design defect or unsafe use. Learning from past mistakes might prevent future ones with novel delivery methods.

Methods: Published literature and unpublished CDC data on high-speed, multi-use-nozzle jet injectors (MUNJIs) and bifurcated needles (BNs) were reviewed, along with standards for auto-disabling needle-syringes and related policies on vaccine safety and nosocomial disease. Smallpox eradication experience of authors and others was recalled, and novel vaccination technologies assessed.

Results: Laboratory and animal model studies, epidemiologic investigations and analyses, and human trials of the Ped-O-Jet® and similar MUNJIs once used in smallpox campaigns demonstrated these “jet guns” capable of HBV transmission, even when nozzles were alcohol-swabbed between injections per manufacturer instructions. In the 1990s, the Ped-O-Jet® was recalled, its use abandoned by the U.S. military, and contraindicated by WHO and CDC. The latest 2008 study detected HBV contamination by PCR after 8% of MUNJI injections of HBV-carrier volunteers. The BNs were sometimes re-used in eradication without sterilization by minimally-trained vaccinators in challenging field environments. Without health officer supervision to assure sterilization and lacking auto-disabling features, BNs would not satisfy current WHO and UNICEF policies for safe injection. Although HBV transmission during smallpox eradication cannot be documented retrospectively, many involved countries have moderate-to-high prevalence of chronic infection, suggesting transmission opportunities.

Conclusion: Some iatrogenic infections with HBV likely occurred in countries where unsafe MUNJIs and unsterile BNs were used. Nonetheless, the overall benefits of eradication are overwhelmingly positive and lasting. Modern emphasis on injection safety should apply to future vaccine delivery systems now in development which re-use vaccine pathways.

References:

P26 Serological Cross-Reactivity of the 2009 Pandemic H1N1 Virus with Current Swine Influenza Viruses and Implications for Protection with a Commercial Vaccine

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Objective: Determine whether swine may be protected against the pandemic H1N1 virus due to pre-existing immunity derived from current swine H1 strains or from commercial inactivated vaccines

Background: The 2009 H1N1 influenza pandemic virus (pH1N1) was a severe liability to public health worldwide. The
pH1N1 virus genome is derived from Eurasian and N. American swine influenza viruses. Therefore, the role of swine as possible reservoirs of pH1N1 could be influenced by pre-existing immunity to pH1N1 viruses either from exposure to circulating field strains or commonly used commercial vaccines. In this study, we have assessed the serological cross-reactivity of pH1N1 to current vaccine and field swine influenza strains.

**Methods:** Anti-sera against two pH1N1 strains, eight current field swine influenza virus strains including H1N1, H1N2, and H3N2 strains and strains present in a commercial vaccine were prepared by experimental inoculation of piglets with the corresponding viruses. Antibody responses were assessed by an ELISA. The presence of cross-reactive antibodies was evaluated by a partial two-way cross-hemagglutination inhibition assay.

**Results:** We found that pH1N1-specific antisera showed low levels of cross-reactivity with a reassortant H1N1 vaccine strain and no cross-reactivity with the human-like H1N1 vaccine strain. Among the field strains tested, the best cross-reactivity was noticed with the A/Swine/H1N2/WI/R33f/01 and A/Swine/H1N1/IA/40776/92 with mean reciprocal HI titers of 42.5 and 33 respectively. As expected, no serological cross reactivity was noted with the H3N2 field strains tested.

**Conclusion:** Therefore, a large percentage of the US swine population may have low levels of cross-reactive antibodies to the pH1N1 virus. However, due to the low magnitude of the cross-reactive responses it is possible that protection against pH1N1 viruses may not be complete. Considering the public health significance, in vivo studies will be important in determining whether a pH1N1 strain should be included in current swine influenza vaccines.

**Reference:**

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**P27**

**A Cytopathic Effect Reduction Assay for Measuring Anti-Foot and Mouth Disease Virus (FMDV) Activity of Bovine Interferons**

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**USDA, Agriculture Research Service, Plum Island Animal Disease Center, Orient Point, NY**

**Objective:** Understand the newer approaches currently being undertaken to develop better biotherapeutics for the prevention of Foot and Mouth Disease virus.

**Background:** Type I interferon (IFN) delivered by human replication-defective adenovirus vectors (hAd5-IFN) can completely protect pigs from foot-and-mouth disease virus (FMDV) challenge, but in cattle receiving a similar dose of Ad5-IFN only induces partial protection and delays the onset of disease (Wu et al., 2003). In order to enhance their potential use as biotherapeutics, bovine IFN (bIFN) with a higher anti-FMDV activity must be identified. Currently, there are no reported methods that directly measure anti-FMDV IFN activity in bovine cells.

**Methods:** Bovine IFNs were expressed in a human cell line. Expressed bIFNs were harvested and used in anti-viral assays, Western blotting, and ELISA. Antiviral activity of IFN was assessed by an MTT based cytopathic effect reduction (CPER) assay. Briefly, bovine cells were treated with 2-fold serial dilutions of bIFN for 24 hours before infection with FMDV. Viable cells were measured using a MTT assay kit.

**Results:** Polyclonal antibodies against bovine type I IFN peptides capable of detecting all bIFNs in Western blot and ELISA was utilized in semi-quantitative tests to determine bIFN expression. Fetal bovine serum in culture medium can significantly enhance the anti-FMDV activity in the CPER assay though it did not display antiviral activity. The differences in anti-FMDV activity of several bIFNs were determined based on a 50% reduction of cytotoxic effect with normalized IFN concentrations. More than 100 fold differences in anti-FMDV activity were measured among different bIFNs using this method.

**Conclusion:** The MTT-CPER based assay allows measuring anti-FMDV activity of bIFNs and it is sensitive and easy to perform. There are substantial differences in anti-FMDV activity among bIFNs.

**References:**
P28 Surface Display of Immunogenic Epitopes of FMDV in E. coli
S. H. Khodadad, Sr.1, M. Karbalayi Ali2, A. Mohabati Mobare2; 
1Microbiology, Tonekabon Islamic Azad University, Tehran, Iran, 2Bacteriology, Tarbiat Modares University, Tehran, Iran

Objective: Discuss designing new viral vaccine.

Background: Foot-and-mouth disease (FMD) is a highly contagious disease of livestock that causes severe economic loss in susceptible animals and it may lead to a new outbreak of FMD because of either incomplete inactivation of FMDV or the escape of live virus from vaccine production workshop. Thus, it is urgent to develop a novel FMDV vaccine that is safer, more effective, and more economical. We have designed a peptide-based vaccine for FMD effective in livestock. Display of heterologous proteins on the surface of microorganisms, enabled by means of recombinant DNA technology, has become an increasingly used strategy in various applications in microbiology, biotechnology, and vaccinology.

Methods: Several different FMDV peptides containing the immunogenic regions of vp1 were fused to the OMPA of Salmonella and transferred into E. coli. After induction, the expression was shown by SDS PAGE and to confirm the presence of this fused protein on the surface of E. coli, fractionation method performed. By ELISA method the activity of the epitopes approved and the lyophilized bacteria was inoculated to the mice feed and the immunogenicity was evaluated.

Results: The immunogenicity of these recombinant bacteria was tested by immunizing the mice. Ten days after the last inoculation, the animals were bled and the sera analyzed to evaluate the presence of antibody against FMDV by ELISA and Western blot. The results show extra stimulation in the immune system of the mice which the recombinant bacteria were inoculated in their daily feed.

Conclusion: These results suggested that designing a recombinant peptide vaccine would be a good and possible way to gain high levels of immunity in veterinary medicine but there is still a strong need for additional studies.

Reference:

TRAVEL GRANT RECIPIENTS (TG1-TG10)

TG1 Local Development of Safe and Effective Recombinant Hepatitis B Vaccine at the WHO GMP Standard Plant in Myanmar
W. Aung, Sr. 
Department of Medical Research (Lower Myanmar), Ministry of Health, Yangon City, Myanmar

Objective: Describe the successful development of the safe and effective recombinant Hepatitis B vaccine in accordance with WHO GMP requirements in one of the developing countries, Myanmar.

The hepatitis B (HB) viral infection is an important health problem worldwide and Myanmar is hyperendemic for HB viral infection with carrier rate of 10-12 % and infection rate of 35-65%. Since vaccine is the best protection against HB infection, the WHO GMP standard vaccine plant was built in Yangon in 2002 and development of Hansenula polymorpha yeast-derived recombinant HB vaccine was carried out at the Department of Medical Research (Lower Myanmar) after transfer of technology from the Republic of Korea in 2003. Vaccine production, quality control, quality assurance, and logistics in accordance with WHO GMP were applied in this plant. Test production was carried out and was successfully completed in 2004. The product passed the quality control tests recommended by WHO. In 2005, phase I clinical trial for vaccine safety was carried out on 17 healthy adult volunteers, showing no undesirable side effects. Phase III clinical trial was carried out on 123 healthy newborns in 2006. The results showed that after completion of the second and third doses of vaccination, seroconversion rates were found to be 86.57% and 100% with mean antibody titres of 129.8 mlU/ml and 610.7 mlU/ml respectively without undesirable side effects. Therefore, this vaccine is recommended to be safe, immunogenic, and capable of protecting HB viral infection. These vaccines have been distributed all over the country since May, 2008. In the near future, this vaccine will be introduced into the National Immunization Program to prevent and reduce the morbidity and mortality resulted from HB viral infection in Myanmar.
References:

TG2

**Evaluating Accessibility of Children Under Two Years to Measles Vaccination at Health Districts with Challenges of Vaccine Preservation**

A. A. Adeiga¹, J. Onyewuche¹, S. Ahmad²
¹Nigeria Institute of Medical Research, Yaba, Lagos, Nigeria, ²Sokoto State Ministry of Health, Sokoto, Nigeria

**Objective:** Describe evaluation of immunization coverage and missed opportunities in Gada Local Government Area in order to establish the cause of frequent mortality of children during measles outbreaks.

**Background:** Measles vaccination is routinely conducted in Nigerian children. This imparted measles prevalence in urban areas, but yet to be abated in rural areas. Frequent high mortality was reported during measles outbreaks in Gada Local Government Area (LGA) of Sokoto state in Nigeria.

**Method:** Survey of infant immunization coverage for measles and cold-chain facilities using structured questionnaire was conducted in 4 health districts at Gada LGA which are Gada A, Gada B, Waaru, and Kaffe.

**Results:** Of the four health districts, only Waaru had functional cold-chain facilities with good terrain, although cold-chain facilities were in good condition at the LGA headquarters. At the four health districts, only Waaru had 500 doses of measles vaccine. Others had none in stock. Vaccine supplies were made available only on immunization days by health officers from the LGA headquarters. Terrains of Gada B and Kaffe health districts were bad and difficult to reach. No staff was stationed at these health districts. Inadequate staffing and bad terrain were challenges to vaccine distribution that resulted in missed opportunities and low immunization coverage. Measles immunization coverage at the districts were 6.3%, 5.3%, 5.1%, and 25.8% for Gada A, Gada B, Kaffe, and Waaru health districts respectively. Missed opportunities at the districts were 35%, 52%, 47%, and 15% for Gada A, Gada B, Kaffe, and Waaru health districts respectively.

**Conclusion:** Lack of health facilities, poor cold-chain facilities, and vaccine distribution at 3 of the 4 health districts of Gada LGA caused the missed opportunities that resulted in low immunization coverage. The study showed that many children were unvaccinated and therefore explained the high mortality reported.

References:

TG3

**Cytokine Signatures of Innate and Adaptive Immunity in 17DD Yellow Fever Vaccinated Children and its Association with the Level of Neutralizing Antibody**

M. Luiza-Silva¹, A. C. Campi-Azevedo¹, M. A. Batista¹, M. A. Martins¹, R. Sathler-Avelar¹, D. Silveira-Lemos², L. A. B. Camacho³, R. M. Martins³, M. L. S. Maia³, M. S. Freire³, R. Galler³, A. Homma³, J. G. L. Ribeiro³, J. A. C. Lemos⁴, S. M. Eloisantos⁴, A. Teixeira-Carvalho², O. A. Martins-Filho¹
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**Objective:** Discuss the immunogenicity of 17D-Yellow Fever vaccine in children.
Background: The live attenuated Yellow Fever vaccines have been available for decades and are considered highly effective and one of the safest vaccines worldwide.

Methods: The impact of YF-17DD-antigens recall on the cytokine profiles of innate/adaptive immunity of YF-17DD-vaccinated children were characterized using short-term cultures of whole blood samples and single-cell flow cytometry. This study enrolled seroconverters and non-seroconverters after primo-vaccination (PV-PRNT+ and PV-PRNT-), seroconverters after revaccination (RV-PRNT+), and unvaccinated volunteers (UV-PRNT-).

Results: Our findings demonstrated that PV-PRNT+ displayed a pro-inflammatory microenvironment, mediated by IL-12+ and TNF-α+ neutrophils (NEU) and monocytes (MON) and down-regulation of IL-4+CD4+ T-cells, whereas PV-PRNT- showed a regulatory status with lower index of IL-12+ and TNF-α+ NEU and MON, along with up-regulation of IL-5+ and IL-10+CD8+ T-cells. Interestingly, RV-PRNT+ shifted the cytokine profile towards a pro-inflammatory status, mediated by TNF-α+ NEU, MON and B-cells and lower levels of IL-4+CD4+ and IL-10+CD8+ T-cells. The analysis of high cytokine producers demonstrated in PV-PRNT+ a balanced involvement of pro-inflammatory/regulatory adaptive immunity with a prominent participation of the innate immunity pro-inflammatory events (IL-12+ and TNF-α+ NEU and MON). PV-PRNT- presented a striking lack of innate immunity pro-inflammatory response along with an increased adaptive regulatory profile (IL-4+CD4+ T-cells and IL-10+ and IL-5+CD8+ T-cells). Conversely, the RV-PRNT+ shifted the overall cytokine signatures towards an innate immunity pro-inflammatory profile and restored the adaptive regulatory response. Additional analysis demonstrated that the overall cytokine signature was associated with the levels of PRNT antibodies.

Conclusion: A distinct immunological profile was observed in children that did not seroconvert as compared to those that seroconvert after 17DD primo-vaccination as well as to the unvaccinated children, with no polarization of the immune response toward a pro-inflammatory/regulatory cytokine pattern.

References:

TG4 Positive Selection on the Member of Plamodium falciparum SURFIN

M. K. M. Kombo, II
National Institute of Biomedical Research, Kinshasa, Democratic Republic of the Congo

Objective: Discuss knowledge that can be translated into recommendations to putative end-users involved in research, clinical studies, control, and surveillance on malaria.

Malaria is still the world’s most important parasitic disease and is responsible for high mortality and morbidity mainly in tropical and sub-tropical regions. Recently a new multigene family of Placiparum falciparum-infected erythrocyte surface antigens, the SURFIN, was identified. SURFIN is a polymorphic antigen expressed on P. falciparum merozoites and infected erythrocytes. The orthologus genes encoding PvSTP-1 were identified in P. vivax genome, thus this gene family is the first molecule likely expressed on the infected erythrocyte surface throughout malaria species. In the previous polymorphic analysis using 3 laboratory lines, N-terminal potential extracellular region showed high polymorphism. To elucidate the degree of diversity of the extracellular domain of SURFIN, SURFIN4.2 was selected. Nucleotide diversity and positive selection were evaluated using P. falciparum 5 field isolates obtained in Thailand. To this end, it was found that the polymorphism of P. falciparum SURFIN4.2 extracellular domain was extensively high and positive selection was detected by comparing synonymous and nonsynonymous substitutions, suggesting SURFIN4.2 was under selective pressure, presumably by host immunity. Thus SURFIN represents an attractive vaccine candidate and could induce antibodies that prevent both cytoadherence and erythrocyte invasion by the malaria parasites.
References:

TG5  *Leishmania Donovani* Vaccine Candidate Arrest in Intracellular Replication Induces Th1 Specific Immune Response Towards Lasting Protection Against Experimental Leishmaniasis

A. Selvapandiyan¹, R. Dey², S. Nylen³, R. Duncan², S. David¹, H. Nakhasi²
¹Institute of Molecular Medicine, New Delhi, India, ²Division of Emerging Transfusion and Transmitted Diseases, FDA, Bethesda, MD, ³Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, MD

Objective: Discuss live attenuated leishmania vaccine candidate to further take in to preclinical evaluation.

The fatal visceral leishmaniasis caused by protozoan parasite *Leishmania donovani* is a major public health problem in the developing world. There is no vaccine yet for this disease. This study addresses whether our centrin gene deleted *L. donovani* parasite with arrest in the replication of the intracellular stage, survives only for 5 weeks in mice, and protects the animals from virulent challenge elicits a protective immune response. The immunized mice after virulent challenge exhibited a significant increase in IFNg, IL2 and TNF producing CD4⁺ and CD8⁺ T cells (each cytokine produced either singly or in combination) and an increase in IFNg/IL10 ratio among CD4⁺ T cells, in spleen. Immunized mice also showed increased IgG2a immunoglobulins and NO production in macrophages. In addition such immunized mice displayed an increase in CD4⁺ CCR7⁺ central memory T cells all indicative of a protective Th1-type immune response in the absence of a persistent mutant parasite. The observed Th1 response correlated with a significantly reduced parasite burden in spleen and no parasites in liver compared to non-immunized mice 10 weeks post challenge. Protection was observed, when challenged even after 16 week post immunization, signifying a sustained immunity. Protection by immunization with attenuated parasites was also seen in hamsters. Further studies are underway to see the mechanistic involvement of Th1 response in protecting the animals from virulent challenge.

References:

TG6 Challenges of Retaining the Fisher Folk in an HIV Vaccine Preparatory Cohort Study

A. N. N. Nanvubya
UVRI/IAVI HIV Vaccine Program, Entebbe, Uganda

Objective: Discuss strategies of retaining mobile populations in clinical research.

The prevalence of HIV among the fisher folk is approximately two-three times more than that of the national average. HIV vaccine research is critical especially among vulnerable populations such as the fisher folk. The UVRI-IAVI HIV Vaccine program conducted an 18-month follow up study of volunteers aged 13-49 years from 5 fishing villages of Lake Victoria in Uganda as part of a larger epidemiological study determining HIV incidence and behavioral characteristics in preparation for future HIV vaccine efficacy trials. A standard questionnaire was administered to consented participants to obtain socio-demographic characteristics including mobility patterns and sexual behavior data. HIV and pregnancy were tested at a 6-monthly interval while syphilis was tested for at screening and after a year. From the 1000 participants enrolled, a retention rate of 80% was achieved. Scheduled visits were missed especially during seasons when the fish catch was low. About 50% of the study population was reportedly absent from their homes for at least two nights in a month. Twenty two
percent have so far missed scheduled visits. Only 48% of the participants returned for scheduled visits without reminders. Telephone contacts were made to remind the rest of their scheduled visits. Approximately 40% of the participants had home visits made because they couldn’t be contacted on phone. Peer and participant leaders were employed to assist in participant tracing. The fisher folk are highly mobile which makes their retention in research a challenge. Despite their mobility, a good retention rate can be achieved. Engaging the fisher folk in research calls for innovative retention strategies such as engagement of community gate keepers, use of telephones, and physical contacts.

**References:**

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**TG7**

**Survey of Human Papilloma Virus Vaccine Awareness and Vaccination History in Relation to the Presence of HPV Antibodies in Patients Attending STI Clinics in Lagos and Ibadan, Nigeria**

A. O. Faneye
Institute of Medical Research, Yaba, Lagos, Lagos, Nigeria

**Objective:** Provide information on the human papilloma virus (HPV) vaccine awareness and vaccination history in relation to the level of antibodies to HPV in the population at risk.

**Background:** HPV is one of the most common causes of sexually transmitted disease in both men and women worldwide. It is transmitted through vaginal, anal, and oral sex. HPV can spread without visible warts. In developing countries, cervical cancer is often the most common cancer in women and may constitute up to 25% of all female cancers. HPV has been found in 99.7% of cervical carcinomas worldwide with HPV 16 and 18 the predominant genotype in these carcinomas (de Sanjos, et al. 2007).

**Methods:** Target population: patients attending STI clinics at Lagos and Ibadan were accessed. Informed consent was obtained from all the patients participating in the study. Using semi structured questionnaire, vaccination history, demography, and past experiences of the patients were obtained. Whole blood samples were obtained and the sera screened for specific antibodies to HPV using ELISA test kits for determination of IgG to HPV by DIA.PRO Diagnostic Bioprobes Milano-Italy according to the manufacturer’s instructions.

**Results:** Of the one hundred and seventy samples analyzed, 50 (29.4%) samples were positive for HPV, 30 (17.6%) of which are females and 20 (11.7%) are males. Thirty five percent (35%) of the 100 women who filled out the questionnaires were aware of HPV vaccine. 15 percent (15%) of women did not take the vaccine because they did not know where to get it while twenty percent (20%) of women could not afford it.

**Conclusion:** A high prevalence of HSV and HPV antibodies was observed in the study yet none of the participants had received the HPV vaccine thus the antibodies are from infection. Implication is that the 30 women who tested positive for the HPV antibodies are at risk of cervical cancer.

**References:**
TG8  Avidity Of IgG Antibodies Against Meningococcal Serogroup A Polysaccharide and Correlation with Bactericidal Activity in Sera of Meningitis Patients and Controls from Ethiopia

M. M. Gebreselassie
AHRI, Addis Ababa, Ethiopia

Objective: Discuss the avidity of IgG antibody against serogroup A polysaccharide in Ethiopian sera and its correlation with SBA.

In order to determine the level of antibodies against meningococcal A polysaccharide (APS) which correlates with protection for the “meningitis belt” area, it may be important to consider quality of the antibodies along with quantity. Though quality of antibodies might be affected by several factors, this study has taken into account only one factor, namely avidity, which was assumed to better correlate with the serum bactericidal activity (SBA). Two ELISA methods using the chaotropic agent ammonium thiocyanate were compared, and employed to measure avidity indexes (AI) of anti-APS IgG in sera from Ethiopian controls meningococcal patients (Geometric means of test groups were calculated at 95% confidence interval and since the data obtained was non-normally distributed, the IgG concentrations and the avidity indices were compared using non-parametric tests). The antibody levels in the patients increased significantly from acute to early convalescent phase, but declined in late convalescent sera to same levels as in the controls. High correlations (r≥0.8) between avidity indexes determined by the two methods were observed. The AI of sera from controls was significantly higher than in the acute sera from meningococcal patients. A positive correlation between serum bactericidal titres and IgG levels against APS was observed by both methods; however, the correlation was moderate and there was no significant difference in the correlation coefficients determined with or without 120 mM thiocyanate. The geometric mean avidity indices increased with time indicating affinity maturation in the patient sera. However, further studies are needed to standardize avidity measurement for serogroup A N. meningitidis and other factors that might affect quality of antibody responses (eg IgG subclasses) should also be considered.

References:

TG9  Immunization Cost Among Iraqi Pediatric Practice Younger Than 2 Years

O. Q. B. Al-lela1, M. B. Bahari1, M. G. Al-abbassi2, A. Y. Bashar3
1Pharmaceutical School, Universiti Sains Malaysia (USM), Pinang, Malaysia, 2Pharmacy College, Al-Mustansaria University, Baghdad, Iraq, 3Advance Medical and Dental Institute, Universiti Sains Malaysia (USM), Pinang, Malaysia

Objective: Discuss the overall cost involved in pediatric immunization (<2 years) in Mosul, Iraq.

The cost of pediatric immunization in Iraq has increased in recent years due to problems in the supply system. The overall cost of immunization is important in the development of a national immunization system. Mixed cost study design was used which included human service cost based on activity time spent for immunization, and immunization dose error cost (extra dose and invalid dose). Five public health clinics in Mosul, Iraq participated in the study, and 50 vaccine doses were required to achieve stability of time and cost estimates. 528 pediatric immunization cards (each pediatric received seven doses) and 3696 doses were collected to evaluate immunization history and dose error. Children who received more than the recommended number of doses of any vaccine considered extra doses. Immunization doses were considered invalid doses if they were administered before the minimal interval between-doses and must be repeated1. Clinic member salaries and vaccine costs were provided by the Ministry of Health2. The mean time of child registration was 6.7 minutes per dose, while the physician spent approximately 10 minutes per dose. Nurses needed more than 5 minutes per dose. The total cost of immunization activities (excluding vaccine cost) accounted for $1.67 per each immunization dose. The cost of 288 invalid doses was $744.55 ($499.15 as an immunization service cost and $245.40 as medication cost). While the total cost
of 195 extra doses was $503.85 ($326.62 as an immunization service cost and $177.23 as medication cost). The cost of immunization dose errors may have a negative impact on immunization system. Health clinic staff knowledge regarding proper immunization timing should be conducted to reduce the administration of immunization dose errors.

References:

TG10 Qualitative and Quantitative Analysis of Rubella IgG Antibody Among Pregnant Women in Ibadan, Nigeria

O. M. Adewumi, B. R. Olusanya, A. B. Oladunjoye, A. J. Adeniji
University of Ibadan, Ibadan, Nigeria

Objective: Discuss evaluation of rubella antibodies in susceptible populations to help improve immunization programme and facilitate control/elimination of the virus in the population.

Background: Rubella is a vaccine-preventable viral infection of the skin and lymph nodes often culminating in a mild rash. The aetiologic rubella virus has been identified as a human teratogen capable of causing a spectrum of birth defects collectively referred to as congenital rubella syndrome (CRS) or fetal death. Despite the availability of a safe and effective vaccine, a significant number of adults including women of childbearing age remains susceptible to rubella infection. Consequently, this study evaluates the level of immunity against rubella virus in pregnant women with the aim of assessing the feasibility of virus elimination in the country and beyond.

Methods: A total of 273 consenting rubella vaccine naïve ante-natal clinic attendees aged 15-42 years were randomly selected and their sera analyzed for anti-rubella IgG antibody detection using DIA.PRO® Diagnostic Bioprobes Srl Enzyme Immunoassay in accordance with the manufacturer’s description.

Results: Overall, 247 (90.5%) of the pregnant women had protective level (Titre >10 IU/mL) of anti-rubella IgG (Median Titre = 165 IU/mL; Range = <10 - >250 IU/mL). Further analysis shows highest and lowest rates of seropositivity in age groups >40 and 21-29 years respectively.

Conclusion: Results of the study confirm previous reports of exposure, infection, and continuous circulation of rubella virus in Nigeria. More significantly, it is evident that Nigeria has an opportunity to eliminate the virus since the herd immunity is high and susceptible population is definite. Therefore, establishment of health policy that promotes improved and continuous surveillance network for rubella and CRS cases, vaccination of vulnerable populations, and periodic evaluation of health policies to achieve immunization will facilitate prevention and control/elimination of rubella virus in Nigeria and beyond.

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