2013

Report from the field - Overview of the Sixth Annual Vaccine Renaissance Conference

Denice Spero

Lauren Levitz

See next page for additional authors

Citation/Publisher Attribution
Spero, D., Levitz, L., & De Groot, A. S. (2013). Report from the field - Overview of the Sixth Annual Vaccine Renaissance Conference. *Human Vaccines & Immunotherapeutics*, 9(7), 1555-1557.
Available at: http://www.tandfonline.com/doi/abs/10.4161/hv.24833

Human Vaccines & Immunotherapeutics 9:7, 1555–1557; July 2013; © 2013 Landes Bioscience

Report from the field
Overview of the Sixth Annual Vaccine Renaissance Conference

Denice Spero,[1] Lauren Levitz[2] and Anne S. De Groot[1,2,*]

[1]Institute for Immunology and Informatics; University of Rhode Island; Providence, RI USA; [2]EpiVax, Inc.; Providence, RI USA

Keywords: vaccines, immunoinformatics, biodefense, emerging infectious diseases, neglected tropical diseases, animal vaccines, vaccine design, T cell epitope, immunomodulation

The Sixth Annual Vaccine Renaissance Conference, hosted by the Institute for Immunology and Informatics (iCubed) at the University of Rhode Island (URI), took place on October 15–17, 2012. This conference provides a forum for the review of current progress in the discovery and development of vaccines, and creates an environment for the exchange of ideas. Dr Joel McCleary opened the conference with a warning about the importance of preparing for well-defined biowarfare threats, including tularemia and *Staphylococcal enterotoxin B*. Following the keynote address, sessions explored biodefense and preparation for pandemic and biowarfare threats; vaccines for emerging and re-emerging neglected tropical diseases; animal vaccines and human health; and vaccine vectors and the human microbiome. In this issue of *Human Vaccines and Immunotherapeutics*, seven Vaccine Renaissance Conference speakers will showcase their work; here, we describe a few of the conference highlights.

The sixth annual Vaccine Renaissance Conference, hosted by the Institute for Immunology and Informatics (iCubed) at the University of Rhode Island, was held in Providence, RI on October 15–17, 2012. This conference provides a forum for the review of current progress in vaccine discovery and development, and creates an environment for the exchange of ideas. In this issue of *Human Vaccines & Immunotherapeutics* (*HV&I*), seven Vaccine Renaissance Conference speakers will showcase their work; below, we describe a few of the conference highlights. The first session, "Developments in Homeland Security: From Microbe Hunters to Vaccines on Demand," started the conference with a warning from an expert in the field about the importance of preparing for well-defined biowarfare threats. Joel McCleary, the chairman and co-founder of Q Global, founder of PharmAthene, Inc., and former aide to President Jimmy Carter, presented a historical overview of the US bioweapons program and summarized his take on current bio-threats,[1] which include tularemia and *Staphylococcal enterotoxin B*.[2] McCleary stated that the US should plan to have enough of these vaccines stockpiled for the entire country and reminded the audience that there is no tularemia vaccine at present. He also emphasized that a bioterror attack would overwhelm victims' immune systems due to the high dose of pathogen, and consequently, traditional small molecule drugs like antibiotics would be ineffective for those near the epicenter of an attack.

Following on the topic of biodefense, Dr Daniel Wolfe and colleagues from the Joint Science and Technology Office of the Defense Threat Reduction Agency (DTRA) addressed the need for a tularemia vaccine highlighted by McCleary. In the current issue of *HV&I*, Wolfe et al. identified a lead candidate (Lm-IgIC) that protects F344 rats against an aerosol challenge of *F. tularensis* and established a non-human primate model for aerosolized *F. tularensis* Type A.[3] DTRA has also submitted an Investigational New Drug (IND) application for a Phase I clinical trial to test a Venezuelan Equine Encephalitis Virus (VEEV) DNA vaccine. A ricin vaccine, RVEc, is under development as well; acceptable safety and immunogenicity have been demonstrated in non-human primates, and Phase I clinical trials for RVEc began in May 2011.

Despite important advances in the strategic preparedness of the US agencies for biowarfare preparedness, delays in vaccine design, development, and manufacture remain significant obstacles to effective national biodefense. This is particularly true for the very real threat of novel pathogens and emerging influenza pandemic strains. Conventional approaches to vaccine development and production are incompatible with the prompt deployment needed for an effective public health response. One potential solution to the problem is developing vaccines on demand, as elucidated by Dr Mark Poznansky, Director of the Vaccine and Immunotherapy Center at the Massachusetts General Hospital. Poznansky provided an overview of the DARPA-funded program for rapid vaccine production that was established in 2011 and executed in 2012; the VaxCelerate Consortium features local biotech company EpiVax, Inc. as one of its members.

*Correspondence to: Anne S. De Groot; Email: AnnieD@EpiVax.com
Submitted: 04/16/13; Accepted: 04/25/13
http://dx.doi.org/10.4161/hv.24833

Dr Anne De Groot continued this discussion by detailing progress on "FastVax," a program to produce vaccines on demand for biodefense. De Groot outlined the feasibility of producing a vaccine for a novel biowarfare agent within 60 days, which would be 2-fold faster than the rate at which the most recent pandemic influenza vaccine was produced. The rapid, nimble vaccine design tools and production technologies currently in use at iCubed and EpiVax can significantly accelerate vaccine development while enhancing national security against emerging pathogens and biowarfare agents. In her article in an upcoming issue of *HV&I*, De Groot will report on an innovative and distributed solution to the need for rapid vaccine production capability, and suggests this approach might be highly relevant to the development of a vaccine for emerging H7N9 influenza.[4]

The focus of the conference then shifted from vaccines for bioterror applications to vaccines for emerging and re-emerging tropical diseases in the session entitled, "Neglected Tropical Diseases." Dr Stephen Thomas, director of the Viral Diseases Branch at the Walter Reed Army Institute of Research, described the high social, financial, and healthcare resource costs caused by the millions of dengue virus infections each year. He stressed that a safe, efficacious, and widely used dengue vaccine in conjunction with strategic vector control is necessary to reduce the global dengue burden. As no correlates of protection or validated animal model of dengue disease have yet been defined, Thomas advocated for continued exploration of the dengue human infection model with partially attenuated dengue viruses to advance dengue vaccine development. In the current issue of *HV&I*,[5] Thomas describes the potential application of this human infection model to the development of new vaccines and therapeutics.

Also in the neglected tropical diseases session, Dr Jonathan Kurtis (Warren Alpert Medical School of Brown University) detailed his exciting progress toward a vaccine candidate for pediatric *Plasmodium falciparum* malaria. Kurtis et al. demonstrated the protein PfSEP-1, which is involved in schizont egress, protected from lethal parasite challenge in a mouse model.[6] On a related note, Dr Steven Williams, Gates Professor of Biology and Biochemistry at Smith College, gave an overview of neglected tropical diseases and advocated for breaking the cycle of disease and poverty to improve the economies of developing world countries. Williams, who has long worked in the areas of elephantiasis and African river blindness, noted that despite 40 years of research, there are still no parasite vaccines available.

While not a neglected tropical disease, hepatitis C virus (HCV) is a considerable contributor to the global burden of disease, affecting an estimated 180 million people worldwide and causing a large proportion of chronic liver disease. Dr Phyllis Losikoff (Department of Medicine, Rhode Island Hospital and the Warren Alpert Medical School of Brown University) presented the problem of chronically HCV-infected individuals who are unable to maintain the broad $CD4^+$ and $CD8^+$ T cell responses required to resolve primary HCV infection. Losikoff et al. provide evidence in the current issue of *HV&I*[7] demonstrating the role of T regulatory (Treg) cells in the pathogenesis of chronic hepatitis C, as increased Treg populations in the tissues of HCV-infected patients correlated with persistent viral infection. These findings have important implications for future development of vaccines and therapeutics. Correlates of protection were also explored by Dr Sharone Green (University of Massachusetts Medical School), who described how the mechanisms behind heterologous secondary infections could be exploited for rational vaccine design.[8] Green et al. demonstrated protection against secondary heterologous Japanese encephalitis virus infection in a murine model following primary infection with West Nile virus. These results have broad implications for neglected tropical disease vaccine development, as cross-conserved epitopes could be selected to create broadly protective flavivirus vaccines.

The health of animals has a significant bearing on the health of humans (infectious diseases in particular), and this served as the impetus behind the "Animal Vaccines and Human Health" session. Dr Jennifer Steele and her colleagues at Tufts University Cummings School of Veterinary Medicine reported how hyperimmune bovine colostrum (HBC) harvested from cows vaccinated during gestation can be used to treat gastrointestinal infections in humans. HBC, which is rich in targeted immunoglobulins, has demonstrated efficacy in treating or preventing numerous diseases, including *Clostridium difficile* infection (CDI). Steele et al. inoculated cows with a novel recombinant vaccine containing the two most important virulence factors of *C. difficile*, TcdA and TcdB, and demonstrated in preliminary results that this HBC product successfully treated CDI in the gnotobiotic piglet model. Steele notes in the current issue of *HV&I* that HBC could be utilized as a valuable alternative to traditional antibiotic treatment, which would have the added benefit of lowering the risks of damage to the gut microflora, disease recurrence, and antibiotic resistance.[9]

Animal vaccination can additionally be applied to the problem of Lyme disease, as demonstrated by Dr Samuel Telford (Tufts University Cummings School of Veterinary Medicine). Telford argued that "vector control" such as mass vaccination of local mouse populations could be implemented concurrently with a revival of the Lymerix vaccine to halt the spread of Lyme disease.[10] Although the Lymerix vaccine demonstrated 50–70% efficacy in a Phase II clinical trial, Smith Kline Beecham withdrew the product due to pressure from advocacy groups and poor sales. In a review of Lyme disease pathology and the history of Lymerix, Telford found no peer-reviewed evidence of arthritis as a side effect, even 10 years post vaccination. Telford believes that Lymerix is both safe and effective in preventing Lyme disease, which would be of great interest to those who reside in, or visit, rural areas.

Dr Peter Burkhard, Associate Professor at the University of Connecticut and CEO of Alpha-O Peptides AG, rounded out this session with a presentation of his work to develop a protein nanoparticle vaccine against rodent malaria. The P4c-Mal vaccine tested by Burkhard et al. conferred long-lasting immunity against *Plasmodium berghei* sporozoite challenge in BALB/c and C57Bl/6 mice,[12] while a prototype *P. falciparum* human-indicated vaccine demonstrated protection against lethal challenge in Wild Type and MHC I knockout C57Bl/6 mice.[13] As Burkhard noted, this vaccine platform has a wide range of applications

that could be expanded through the inclusion of small molecule attachments (e.g., nicotine vaccine) or full-length protein attachments (e.g., norovirus vaccine).

Vaccine platform design was further explored in the last session, "Vaccine Vectors and Human Microbiome." In his presentation, Dr James Galen (Center for Vaccine Development at the University of Maryland School of Medicine) laid out a new strategy for the development of bacterial live vector vaccines. By integrating antigen-encoding gene cassettes into multiple chromosomal sites within an attenuated *Salmonella enteric* serovar Typhi vaccine candidate, immunogenic chromosomally encoded antigens can be delivered without sacrificing loss of gene dosage or further attenuating the vaccine strain. Galen et al. demonstrated the effect of integration site on expression levels of the green fluorescent protein (GFPuv), and notably observed that GFPuv expression increased in a growth phase-dependent manner. As Galen points out in the current issue of *HV&I*,[14] this novel platform expression technology holds high potential for facilitating development of multivalent live vector vaccines.

The final day of the conference was devoted to hands-on immunoinformatics and immunology training. This yearly event trains researchers to use the suite of immunoinformatics tools developed at EpiVax, Inc. and iCubed. Computational and lab-based training provides opportunities for researchers to learn directly from the informatics and immunology experts in order to enhance their own research programs. This training session also provides an opportunity for researchers to network and establish collaborations.

A valuable role of the Vaccine Renaissance Conference is to support women and students from diverse and underrepresented backgrounds who are embarking on scientific careers. Each year, the organizers award a conference scholarship to a student studying immunology or bioinformatics. This year's recipient was Alicia Francis, a student of Jamaican heritage studying bioinformatics at Washington Adventist University in Maryland. Francis aspires to become a pediatrician and plans to apply her bioinformatics training to the improvement of women's and children's health. Furthermore, the annual "Polly Matzinger Fearless Scientist Award" recognizes women who entered scientific careers later in life or who returned to scientific careers after taking time off. This award, named for NIH scientist and thought leader in the field of immunology Dr Polly Matzinger, was presented to Dr Carey Medin, Assistant Research Professor at iCubed. Medin took time off from her research pursuits to raise her young family but has since returned to academia; in her current position at iCubed in the laboratory of Dr Alan Rothman, she is analyzing the pathogenesis of dengue virus.

In conclusion, the Vaccine Renaissance Conference continues to provide an important forum for discussions of cutting-edge vaccine research to address unmet public health and biodefense needs. The small size of the conference creates ample opportunity for dialog, and a number of important scientific collaborations have resulted from encounters between researchers at this annual event.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

This conference was supported by the NIH CCHI grant U19AI082642–01 and NIH Research Conference Grant R13AI094946–01.

References

1. Gilfillan L, Smith BT, Inglesby TV, Kodukula K, Schuler A, Lister M, et al. Taking the measure of countermeasures: leaders' views on the nation's capacity to develop biodefense countermeasures. Biosecur Bioterror 2004; 2:320-7; PMID:15650441; http://dx.doi.org/10.1089/bsp.2004.2.320
2. Patrick WC. Interviews with Biowarriors. Interview by Broad B, Wolfinger K. NOVA. PBS. 2001 Nov 01. Accessed at: http://www.pbs.org/wgbh/nova/bioterror/biow_patrick.html.
3. Wolfe DN, Florence W, Bryant P. Current biodefense vaccine programs and challenges. Hum Vaccin Immunother 2013; 9: In press; PMID:23428906; http://dx.doi.org/10.4161/hv.24063
4. De Groot AS, Einck L, Moise L, Chambers M, Ballantyne J, Malone RW, et al. Inc. Ardito M, Martin W. FastVax: Biodefense Vaccine Production "On Demand". Hum Vaccin Immunother 2013; 9: In press.
5. Thomas SJ. Dengue human infection model: Re-establishing a tool for understanding dengue immunology and advancing vaccine development. Hum Vaccin Immunother 2013; 9: In press; PMID:23466948; http://dx.doi.org/10.4161/hv.24188
6. Raj DK, Nixon CP, Fried M, Duffy PE, Kurtis JD. Vaccine candidate identification for pediatric falciparum malaria. Poster presentation. American Society of Tropical Medicine and Hygiene 60th Annual Meeting. Philadelphia, PA. 2011 Dec 4-8. Am J Trop Med Hyg 2011; 85(Suppl 6):222
7. Self AA, Losikoff PT, Gregory SH. Regulatory T cells promote the pathogenesis of chronic hepatitis C infection. Hum Vaccin Immunother 2013; 9: In press; PMID:23732899.
8. Trobaugh DW, Yang L, Ennis FA, Green S. Altered effector functions of virus-specific and virus cross-reactive CD8+ T cells in mice immunized with related flaviviruses. Eur J Immunol 2010; 40:1315-27; PMID:20213733; http://dx.doi.org/10.1002/eji.200839108
9. Steele J, Sponseller J, Schmidt D, Cohen O, Tzipori S. Hyperimmune bovine colostrum for treatment of GI infections: A review and update on Clostridium difficile. Hum Vaccin Immunother 2013; 9: In press; PMID:23435084; http://dx.doi.org/10.4161/hv.24078
10. Bhattacharya D, Bensaci M, Luker KE, Luker G, Wisdom S, Telford SR, et al. Development of a baited oral vaccine for use in reservoir-targeted strategies against Lyme disease. Vaccine 2011; 29:7818-25; PMID:21816190; http://dx.doi.org/10.1016/j.vaccine.2011.07.100
11. Sam TAR. Hum Vaccin Immunother 2013; 9: In press.
12. Kaba SA, Brando C, Guo Q, Mittelholzer C, Raman S, Tropel D, et al. A nonadjuvanted polypeptide nanoparticle vaccine confers long-lasting protection against rodent malaria. J Immunol 2009; 183:7268-77; PMID:19915055; http://dx.doi.org/10.4049/jimmunol.0901957
13. Kaba SA, McCoy ME, Doll TA, Brando C, Guo Q, Dasgupta D, et al. Protective antibody and CD8+ T-cell responses to the Plasmodium falciparum circumsporozoite protein induced by a nanoparticle vaccine. PLoS One 2012; 7:e48304; PMID:23144750; http://dx.doi.org/10.1371/journal.pone.0048304
14. Wang JY, Harley RH, Galen JE. Novel methods for expression of foreign antigens in live vector vaccines. Hum Vaccin Immunother 2013; 9: In press; PMID:23406777; http://dx.doi.org/10.4161/hv.23248.