GVIRF 2014: Workshop 1: Towards the Development of a Universal Influenza Vaccine	
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Session Outline	**Chair:** David Spiro (NIAID) **Opening remarks:** David Spiro introduced the limitations of current influenza vaccine strategies and the potential for universal influenza vaccines to overcome these issues. **Presentations:** Each of the discussants addressed the opportunities and challenges in the development of universal influenza vaccines based on their scientific expertise in virology, vaccinology, and regulatory issues. **Discussants:** 1. Norman Baylor (Biologicals Consulting Group) 2. Ruben Donis (CDC) 3. Hana Golding (FDA) 4. Gary Nabel (Sanofi Pasteur) 5. Peter Palese (Mount Sinai) 6. Rino Rappuoli (Novartis) **Closing Remarks**: Progress towards universal influenza vaccines may be achieved now by increasing the pipeline of these vaccines and implementing efforts to improve influenza vaccines now such as movement to cell-based vaccines and adjuvants.
Objectives of the session	Discuss the opportunities and challenges in the development of universal influenza vaccines.
Main outcome	Critical opportunities and challenges in the development of universal influenza vaccines were identified. Discussants concurred that within the next decade significant advances towards vaccines with increased breadth and duration of protection against influenza are feasible.
Summary	Universal influenza vaccines have the potential to shift paradigms for seasonal and pandemic influenza preparedness by providing increased breadth and duration of protection against influenza. Development of universal influenza vaccines may occur as a step-wise process in the direction of a true universal vaccine that provides long term immunity against all influenza viruses. Multiple strategies are currently being taken to develop these novel vaccines and each will present different hurdles in efficacy assay development, preclinical and clinical evaluation, licensure indications, and post licensure marketing. The discussion addressed the question of how to make a universal influenza vaccine and focused on the following questions: 1) <u>What are the outstanding questions in the basic biology of the immune response to influenza antigens that elicit broadly cross-reactive antibodies?</u> To achieve increased breadth of protection, one strategy will be to design vaccines that direct the human immune response to conserved epitopes of influenza viruses. It is important to note that these epitopes will need to generate high avidity immune responses that are sufficient to protect against infection and disease. Studies need to be conducted that go beyond simple binding and rather focus on neutralization and protection. The ability to generate vaccines with increased duration of protection was also discussed. Discussants noted that long term immunity to influenza in humans has been observed in nature. Thus there are prospects that some universal vaccine strategies may extend protection beyond one season of influenza. 2) <u>What gaps need to be filled to facilitate the development of universal influenza vaccines?</u> One of the key challenges to the development of universal influenza vaccines is the need for novel assays that predict immunogenicity, protection, and safety. Currently, influenza vaccine efficacy is correlated with hemagglutination titers. Not only are there limitations with the use of this assay for current licensed influenza vaccines, but it may not be applicable for universal influenza vaccines which do not induce hemagglutination. The importance of also developing assays to assess the safety of these novel vaccines was also discussed. Certainly novel assay development is one area of research where further efforts will be need. 3) <u>What are the efficacy endpoints for a universal vaccine and how do we design pivotal clinical trials?</u> The discussants addressed how designing appropriate clinical trials will be central to advancing universal influenza vaccines. They noted a clear need for human data to assess the potential of these novel vaccines to increase breadth and duration of protection. The issues of vaccination schedule and clinical endpoints will vary based on the universal influenza vaccine strategy being tested in humans. Support for clinical trials is viewed as key to de-risking the process of developing universal influenza vaccines. The discussants also noted that there are differences in issues related to licensure versus utilization of universal influenza vaccines. Licensure will primarily require evidence of non –inferiority to current standard of care, seasonal influenza vaccines. In contrast, utilization of these vaccines will need clear health and economic benefits to ensure recommendation of use by healthcare advisory committees. The session concluded with discussants predicting what efforts may be accomplished in the next decade towards the development of universal influenza vaccines. There was consensus that clinical trials of some universal influenza vaccine candidate would be possible to achieve. The experts also emphasized that all short term goals toward improving current influenza vaccines , such as generation of cell-based vaccines and the use of adjuvants, will help advance the field toward the discovery of truly universal vaccines.
Key references or quotes	