Workshop 1.
Towards the Development of a Universal Influenza Vaccine

Global Vaccine and Immunization Research Forum (GVIRF)

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Panelists

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Ruben Donis
- Associate Director for Policy, Evaluation and Preparedness, CDC Influenza Division

Hana Golding
- Chief, Laboratory of Retroviruses, Office of Vaccine Research and Review, FDA/Center for Biologics Evaluation and Research

Gary Nabel
- Chief Scientific Officer and Senior Vice President at Sanofi

Peter Palese
- Horace W. Goldsmith Professor and Chair, Department of Microbiology, Professor, Department of Medicine, Icahn School of Medicine at Mount Sinai

Rino Rappuoli
- Global Head of Vaccines Research, Novartis Vaccines & Diagnostics

Workshop Overview

- Summary of Key Findings of Narrative Report
- Panelist Introductory Statements
  - Main Promises and Main Challenges
- Panel Discussion
- Questions from the floor
- Wrap up by Panel
  - What is achievable by 2020?

The Burden of Seasonal Influenza

- 250,000 to 500,000 deaths globally/yr; 3-5 million cases of severe illness
- ~3,300 to ~49,000 deaths/yr in the U.S. plus substantial medical costs, hospitalizations, and lost productivity
- $40.2 billion in economic costs/yr in U.S. related to influenza and pneumonia

Sources: CDC, WHO, Am. Lung. Assoc.

Pandemics of the Past Century

Year	Subtype	Deaths
1918	H1N1	>40 million
1957	H2N2	>2 million
1968	H3N2	~1 million
2009	H1N1	~12,000

Source: WHO

Vaccines Currently Available

Inactivated Trivalent or Quadrivalent Vaccine

- Intramuscular injection
- Split virus, whole virion (EU) virosome (EU)
- Indicated for 6 months and older
- Standard Dose or High Dose
- Egg based or Cell based
- Adjuvanted (EU)

Live attenuated vaccine (LAIV)

- Intranasal spray
- Live attenuated virus
- Indicated for 5 to 49 years of age.

Recombinant trivalent influenza vaccine

- Intramuscular injection (TIV)
- Indicated for persons age 6 months and older

Current Vaccines: Benefits

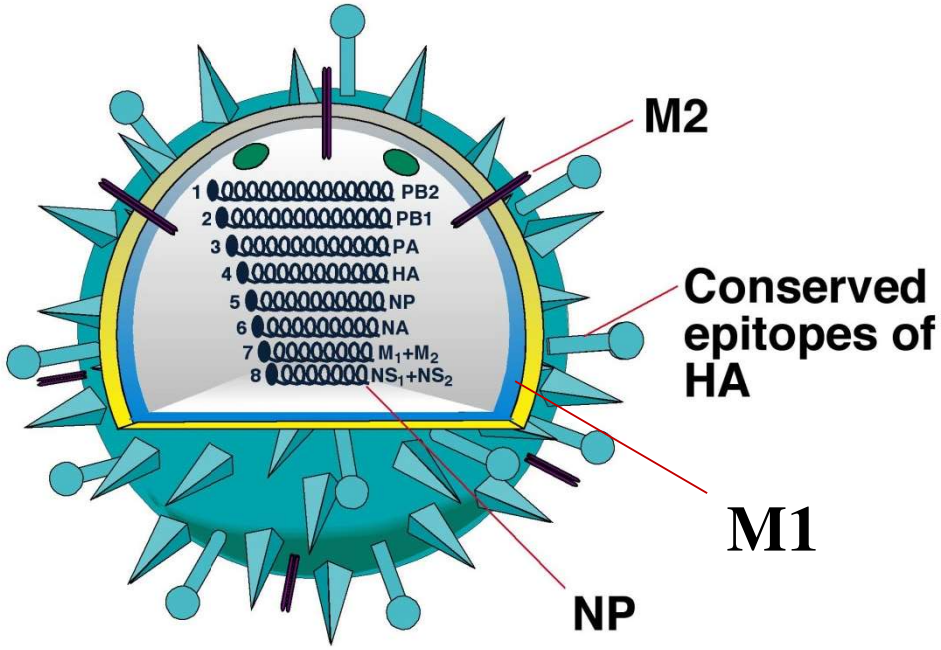
- Manufacturing process is well tested
- Strain change is well accepted
- Dramatically reduce complications from influenza, including hospitalization and death.
- Can reduce the risk for outbreaks by inducing herd immunity

Current Vaccines: Limitations

- HA protein evolves rapidly so that circulating viruses may escape the protective effect of a vaccine.
- Mismatch between vaccine and virus greatly decreases vaccine efficacy.
- Requires global surveillance and a new vaccine has to be generated every year.
- Emergence of pandemic strain requires months of preparation to mount a response
- Inactivated vaccine has limited efficacy in the elderly

Universal Influenza-Vaccine

- Universal influenza vaccine needs to:
  - elicit humoral and cellular responses like natural infection
  - provide long-lasting and cross-strain protection



Targets for Universal Influenza Vaccine

Approaches to the Development of Universal Influenza Vaccines

- HA stem region based vaccines
- Vaccines based on common determinants of the HA head.
- DNA based vaccines (e.g. nucleic acid coding for HA followed by HA protein boost).
- Vaccines comprised of conserved internal proteins (NP, M2e)
- Multimeric universal vaccines (conserved regions from HA and internal proteins)
- Live attenuated influenza vaccines

Opportunities

- Recent scientific findings demonstrate the potential efficacy of a universal influenza vaccine in vivo; provide support for a universal vaccine strategy inducing antibodies to common proteins and in particular the HA stem.
- Promising results have stimulated significant interest from pharmaceutical companies.
- Increased interest and support from government to improve seasonal vaccine efficacy and address potential pandemics.

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Discussion Topic

- What are the outstanding questions in the basic biology of the immune response to influenza antigens that elicit broadly cross-reactive antibodies?

Discussion Topic

- What gaps need to be filled to facilitate the development of universal influenza vaccines?

Discussion Topic

- What are the efficacy endpoints for a universal vaccine?
- How do we design pivotal clinical trials?

Discussion Topic

- What are the regulatory hurdles and what role can governmental and multi-governmental bodies play?

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Conclusions

- What is achievable by 2020?