Influenza Vaccines with Broader Strain Protection

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Influenza Vaccine Challenges

- Antigenic changes (drift and shift) represent a major challenge for current licensed vaccines
  - Annual immunization is required
  - Vaccine effectiveness is moderate in adults and less so in the elderly
- Current production processes are predominantly egg-based
  - Growth properties of human isolates in eggs (H3 isolation, yield)
  - Pandemic surge demands
- Pandemic-like candidate vaccines (H5 and H7) are poorly immunogenic in humans
  - 2 x 90 µg dose for H5N1
  - Concerns about adjuvant safety and public perceptions
- Next generation influenza vaccines are needed

National Pandemic Influenza Vaccine Development Strategy: Multi-Step & Integrated Approach

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Antigen-Sparing Vaccine Technology

Universal Vaccines

Recombinant-based Vaccines

FluBlOk licensed 01/16/13

Cell-based Vaccines

Flucelvax Licensed 11/20/12

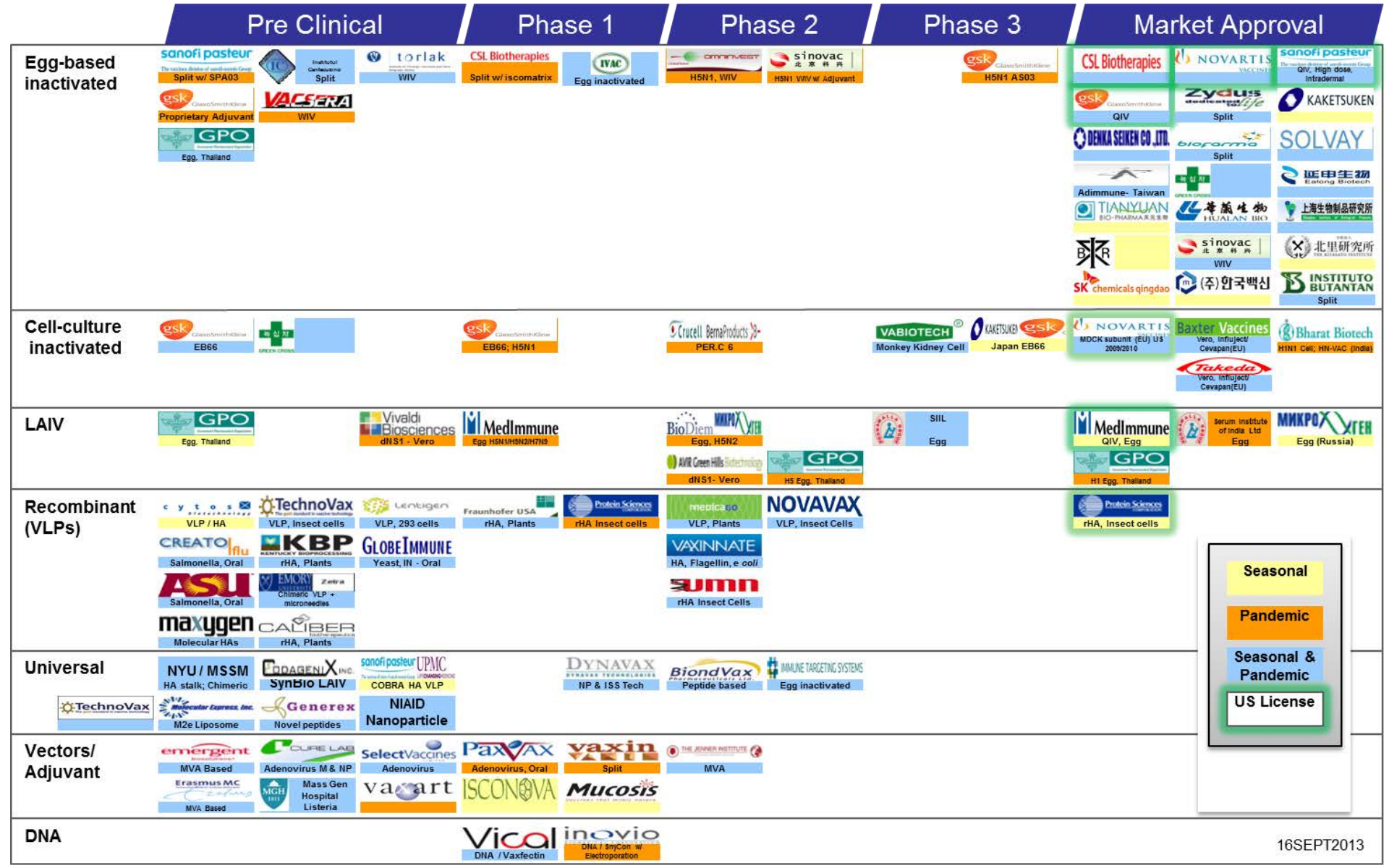
Egg-based Vaccines

H5N1 Vaccine Licensed 04/17/07

Manufacturing Improvements

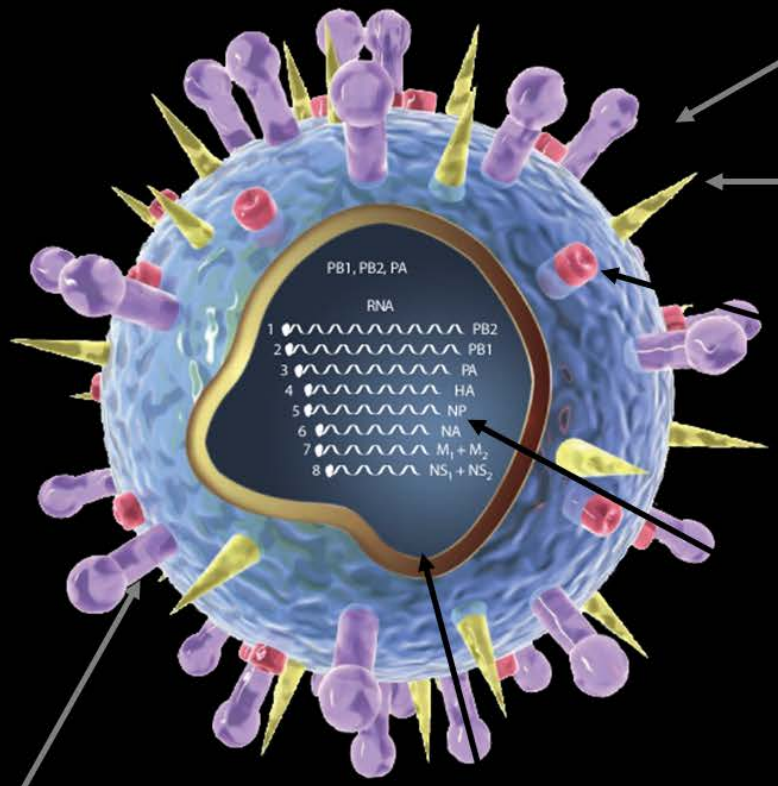
ASPR: Resilient People. Healthy Communities. A Nation Prepared.

Influenza Vaccine Landscape



Universal Influenza Vaccine

- Many definitions for a universal influenza vaccine
  - A single influenza vaccine that would provide “protection” against any given subtype of influenza A
  - Could be used for several influenza seasons before reformulation
    - Reduce annual “guesswork” for strain selection
    - Reduce production costs (thus vaccine costs/year round production)
    - Reduce vaccine “mismatches”
    - Reduce the potential for vaccine shortages
    - Increase the global supply of vaccine
- Could be stockpiled for epidemics/pandemics
- Surge capacity
  - Rapid scale-up, reduce production bottlenecks



HA: surface, immunogenic
Highly variable. Drift. Shift.

NA: surface, immunogenic
Variable. Drift. Shift.

M2e: surface, immunogenic??
Fairly conserved. Ab-mediated.
Protective? Reduce severity.

NP (nucleoprotein): internal
Highly conserved.
Induces CMI. Reduce severity?

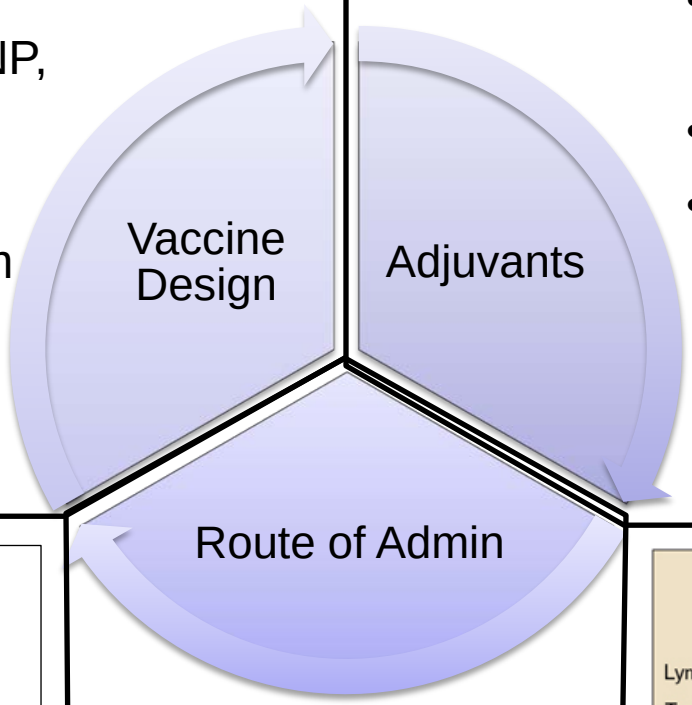
HA Stalk
Highly conserved
Transiently accessible on infected cell surface
Need to engineer a vaccine to target

Matrix: internal
Highly conserved.
Induces CMI.

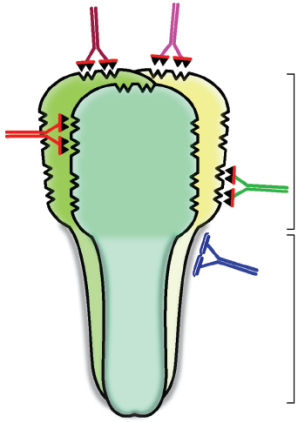
Adapted from: Paul Lewis, MD
Oregon State Public Health

Universal Vaccine Strategies

- Identify broadly reactive targets (HA Stalk, M2e, NP, M)
- Combination vaccines
- Vector expression system

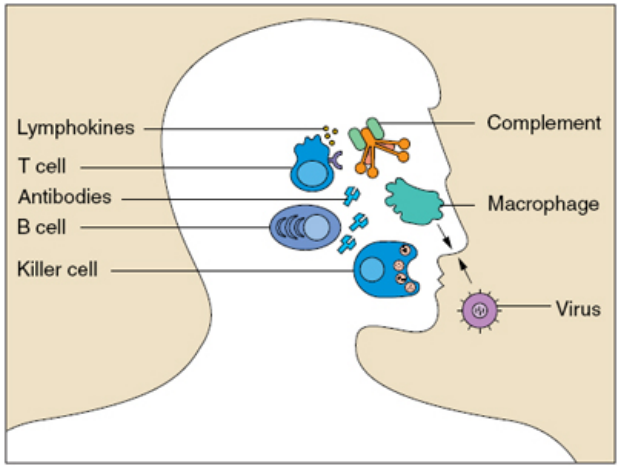


- Broaden immune recognition
- Th1 vs Th2 responses
- Humoral and Cell-mediated



R. Rappuoli, *F1000 Medicine Reports* 3 (2011): 16.

- Intranasal stimulation of mucosal immunity
- Intradermal delivery to target dendritic cells



Source: NIAID http://tinyurl.com/69n9lap

Advanced Development of Universal Influenza Vaccine - Points to Consider

- Manufacturability and scalability
- Novel potency release assay
  - Most regulators are accustomed to SRID or SRH
- Clinical development
  - Non HI immune response
    - Current regulatory guidelines are based on HI
  - Potential safety concern/disease enhancement
  - Mono-specific immune response/drift potential
    - Will a single amino acid change render vaccine ineffective?
  - May require large scale efficacy trials over multiple seasons or other non-traditional clinical development plans
    - Challenge studies for cross protection

Universal Flu Vaccine Program at BARDA

- Collaborating within HHS to develop projects
- Current activities
  - Developing a Request for Information and/or sponsoring international symposium on universal influenza vaccine
  - Planning for an Acquisition Plan to support advanced development of promising programs demonstrating improved cross-reactivity and/or duration of effectiveness.
  - Foster public-private partnerships
    - BARDA Industry Day!

Pandemic Influenza
BAA-13-100-SOL-00019

- Novel influenza vaccine candidates that improve key vaccine attributes
  - dose schedule
  - time to onset of protection
  - induction of improved immunogenicity
  - broader cross-protection across influenza A virus subtypes,
  - duration of protection
- Use of approved or novel adjuvants may be a component of the advanced development program.
- Technology readiness level 6
  - Data demonstrating statistically relevant improvements in immunogenicity/efficacy as compared to existing vaccines.