NIAID Universal Influenza Vaccine Portfolio

Teresa Hauguel, PhD

Program Officer, Respiratory Diseases Branch

Division of Microbiology & Infectious Diseases

NIAID, NIH, DHHS

February 7, 2018

Need for a Universal Influenza Vaccine

- **Current seasonal influenza vaccines are not consistently effective**
- **Pandemics do occur and response after the fact is not effective**
- **“Chasing after” potential pandemic outbreaks (pre-pandemic viruses) is costly and ineffective**

Slide Credit: Dr. Anthony Fauci, NIAID

NIH National Institute of Allergy and Infectious Diseases

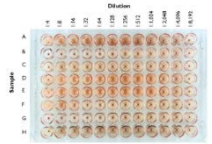
DMID Strategy For Advancing Universal Influenza Vaccines

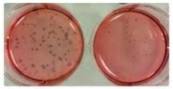
DMID Strategic Plan

- Advance Pipeline Towards Clinical Evaluation

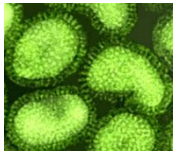
- Improve Vaccine Efficacy & Production

- Support Assay Development to Measure Efficacy & Safety





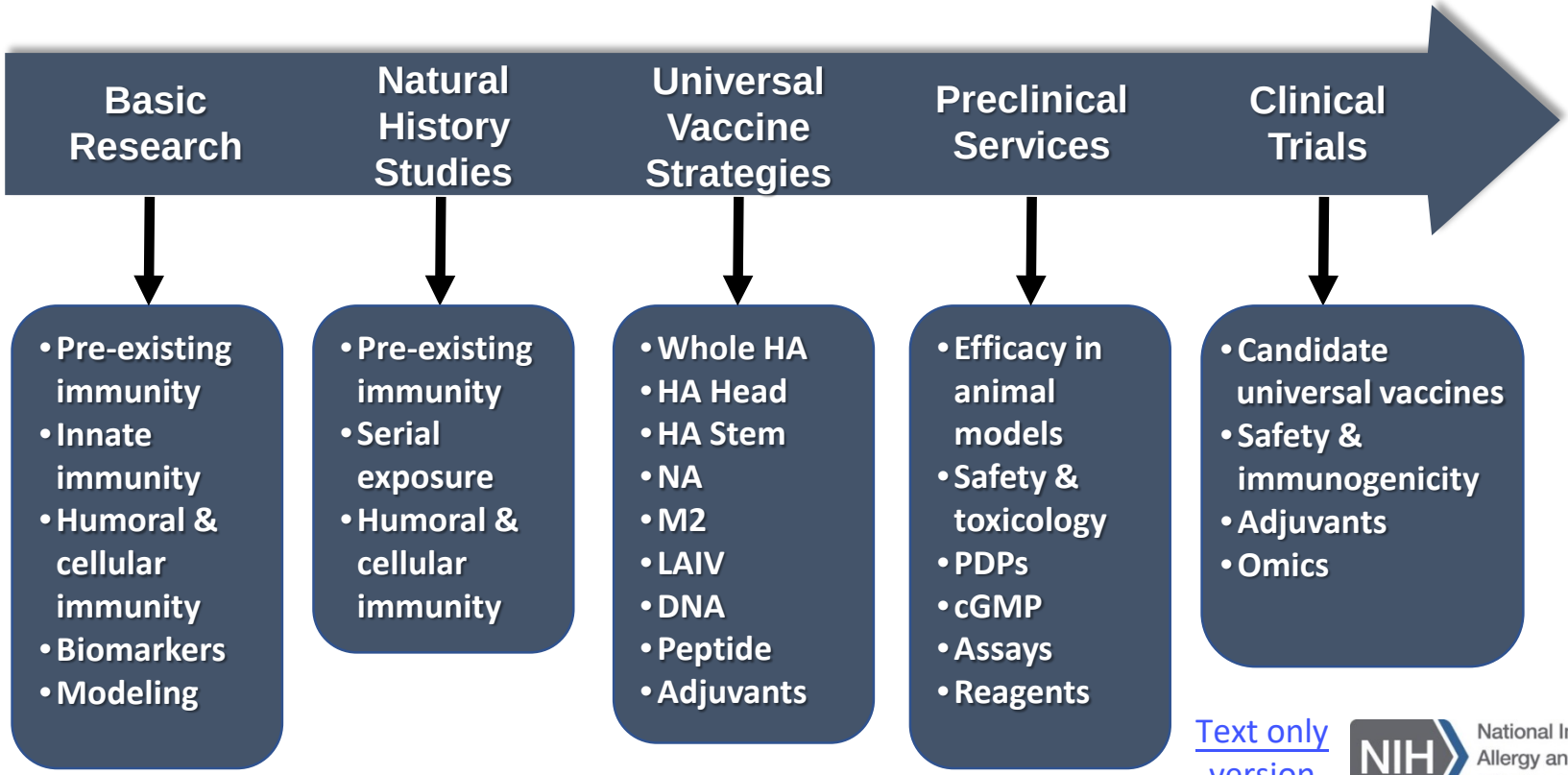
- Provide Reagents to Community for Development



- Outreach & Partnerships

National Institute of Allergy and Infectious Diseases

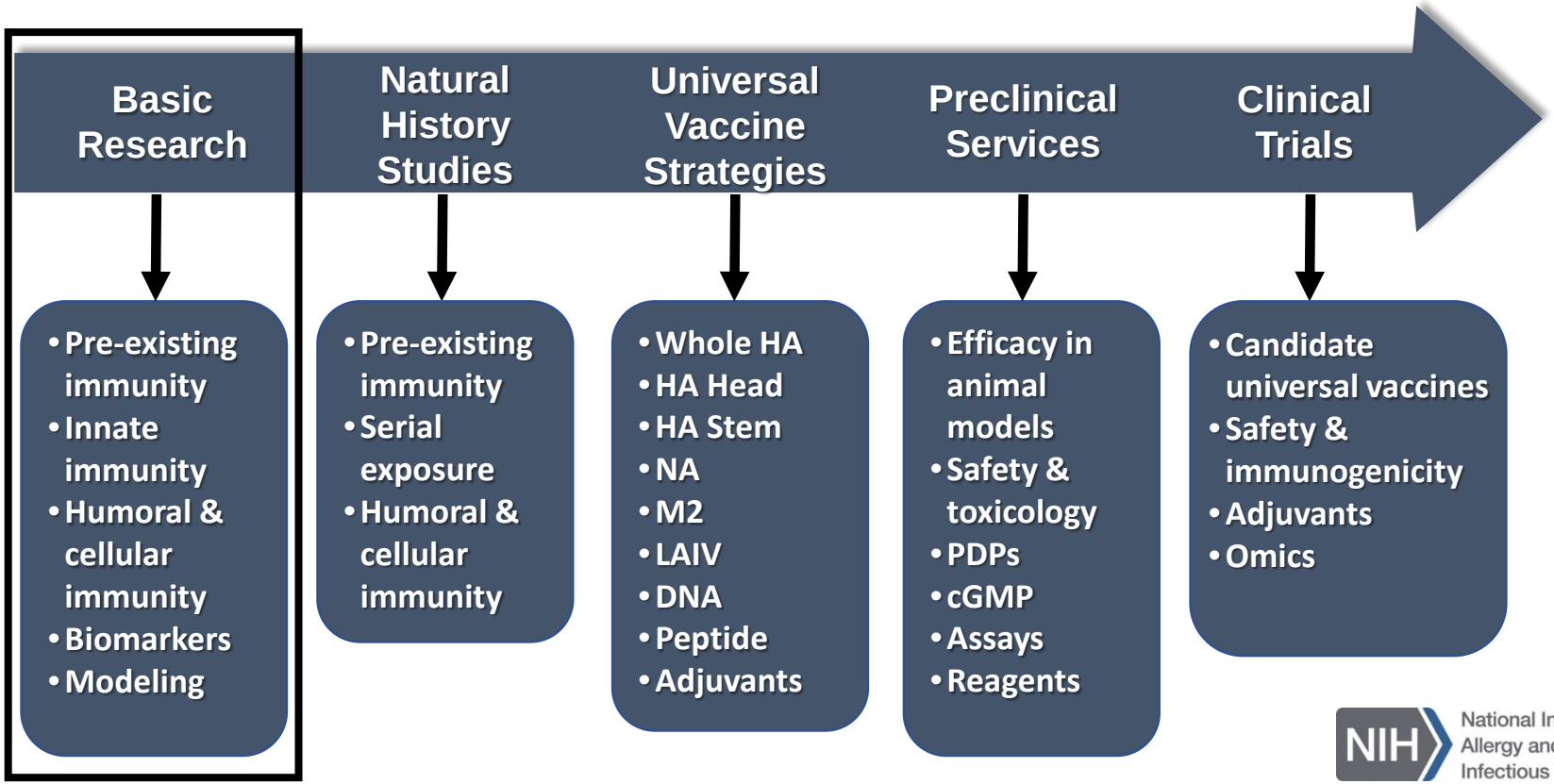
DMID Universal Influenza Vaccine Research Portfolio



Text only version

NIH National Institute of Allergy and Infectious Diseases

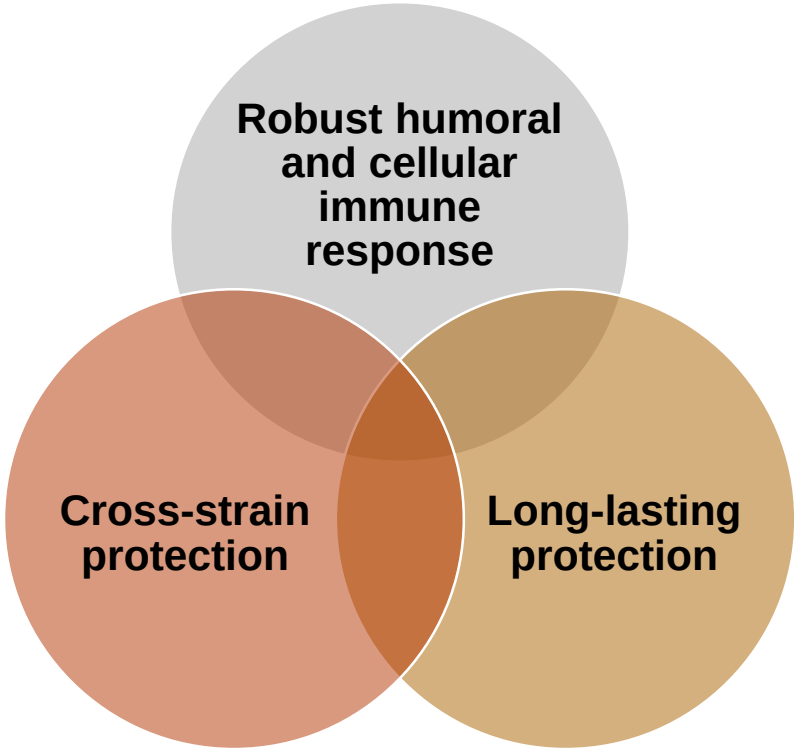
DMID Universal Influenza Vaccine Research Portfolio



NIH National Institute of Allergy and Infectious Diseases

DMID Immunology Research To Advance Universal Influenza Vaccines

Universal Vaccine Properties

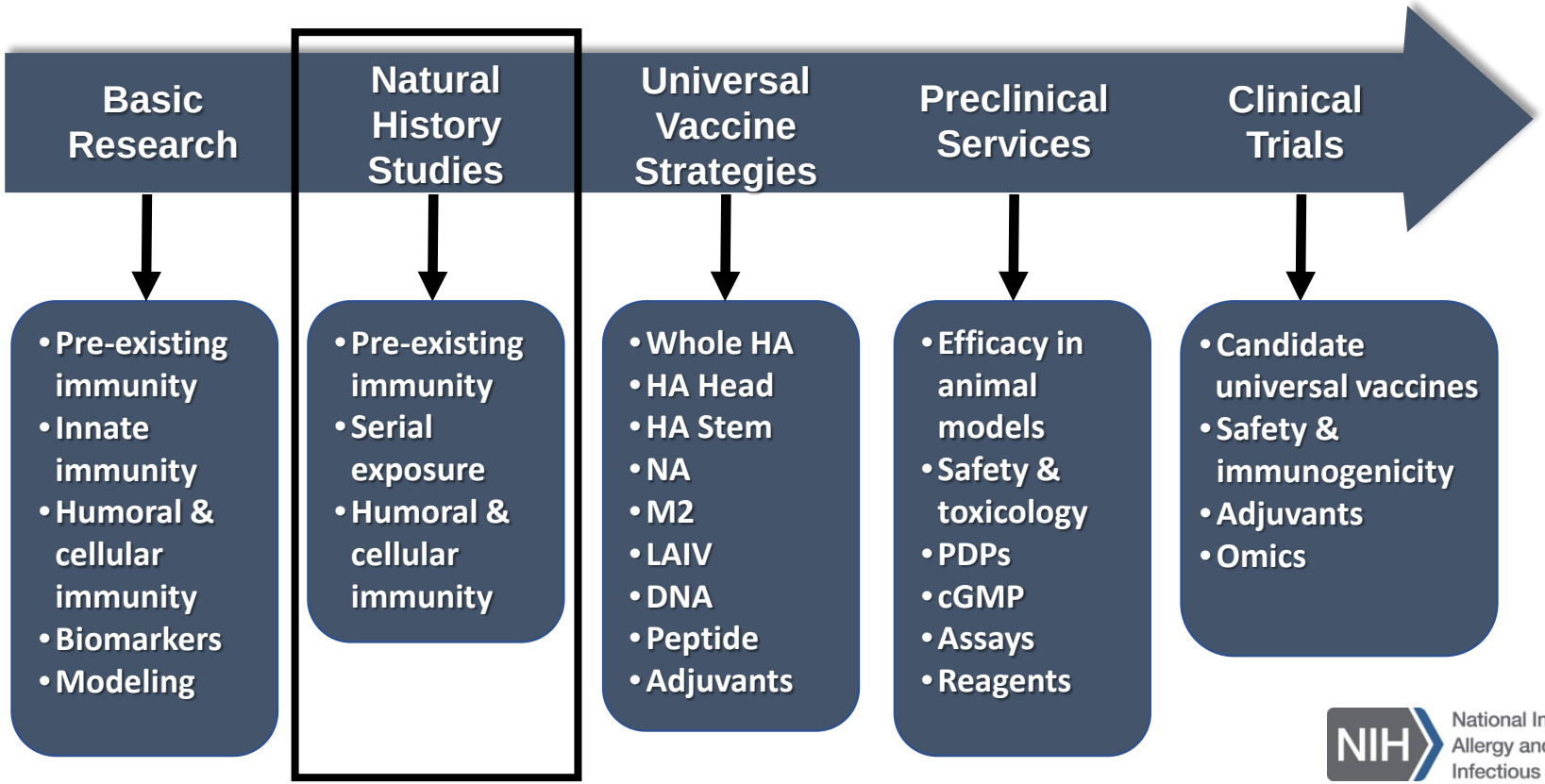


>50 active projects

- **Innate immunity**
- **B cell immunity**
- **T cell immunity**
- **Pre-existing immunity**
- **Impact of sex and age**
- **Biomarkers**
- **Modeling**
- **Systems biology**

NIH National Institute of Allergy and Infectious Diseases

DMID Universal Influenza Vaccine Research Portfolio



NIH National Institute of Allergy and Infectious Diseases

Request for Information (RFI): Prospective Longitudinal Cohort Studies of Influenza Infection and Vaccine Effectiveness

Notice Number: NOT-AI-17-043

Key Dates

Release Date: September 21, 2017
Response Date: December 5, 2017

Related Announcements

None

Issued by

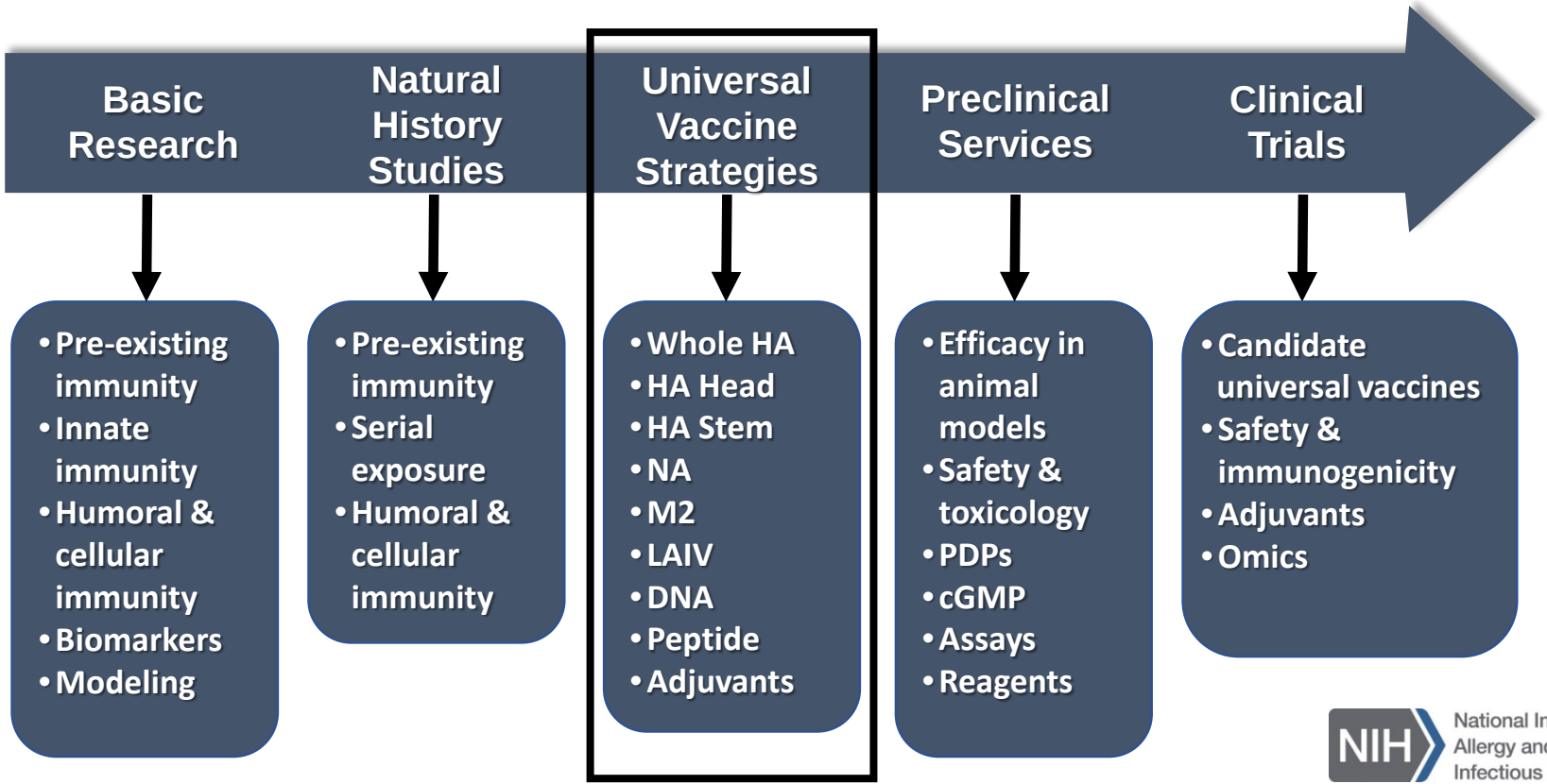
National Institute of Allergy and Infectious Diseases (NIAID)

Purpose

NIAID is seeking information related to prospective, longitudinal cohort studies on influenza infections. The primary goal of this request is to gather information about existing community-based, prospective, longitudinal cohort studies of influenza, or other acute respiratory infections that may allow assessment of influenza immunity from banked samples. Also of interest are longitudinal cohort studies examining the effectiveness of influenza vaccination.

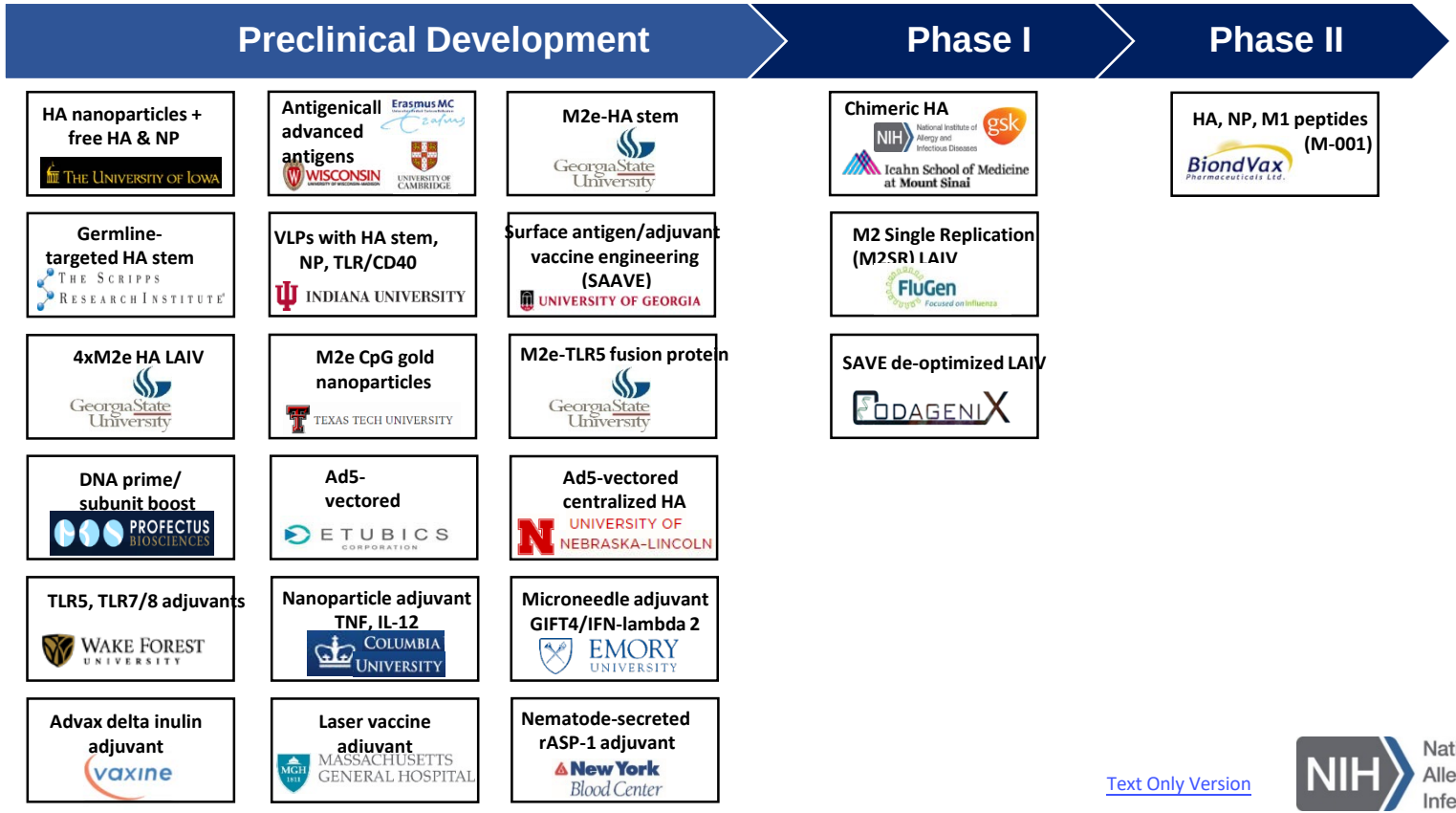
NIAID seeks to understand the breadth of existing cohort studies including cohort characteristics (e.g., the size, participant population, ages, location, and period of time the cohort has been studied); the types of samples that have been collected; and the quantity of samples banked for future use. Of particular interest are cohorts (including international cohorts) that might be leveraged to examine gaps in understanding how immunity develops to influenza, especially in the context of vaccination vs natural infection. Information from this RFI will be used in developing a research agenda.

DMID Universal Influenza Vaccine Research Portfolio



NIH National Institute of Allergy and Infectious Diseases

DMID Universal Influenza Vaccine Strategies



Text Only Version

NIH National Institute of Allergy and Infectious Diseases

DMID Universal Influenza Vaccine Development: Assays & Reagents

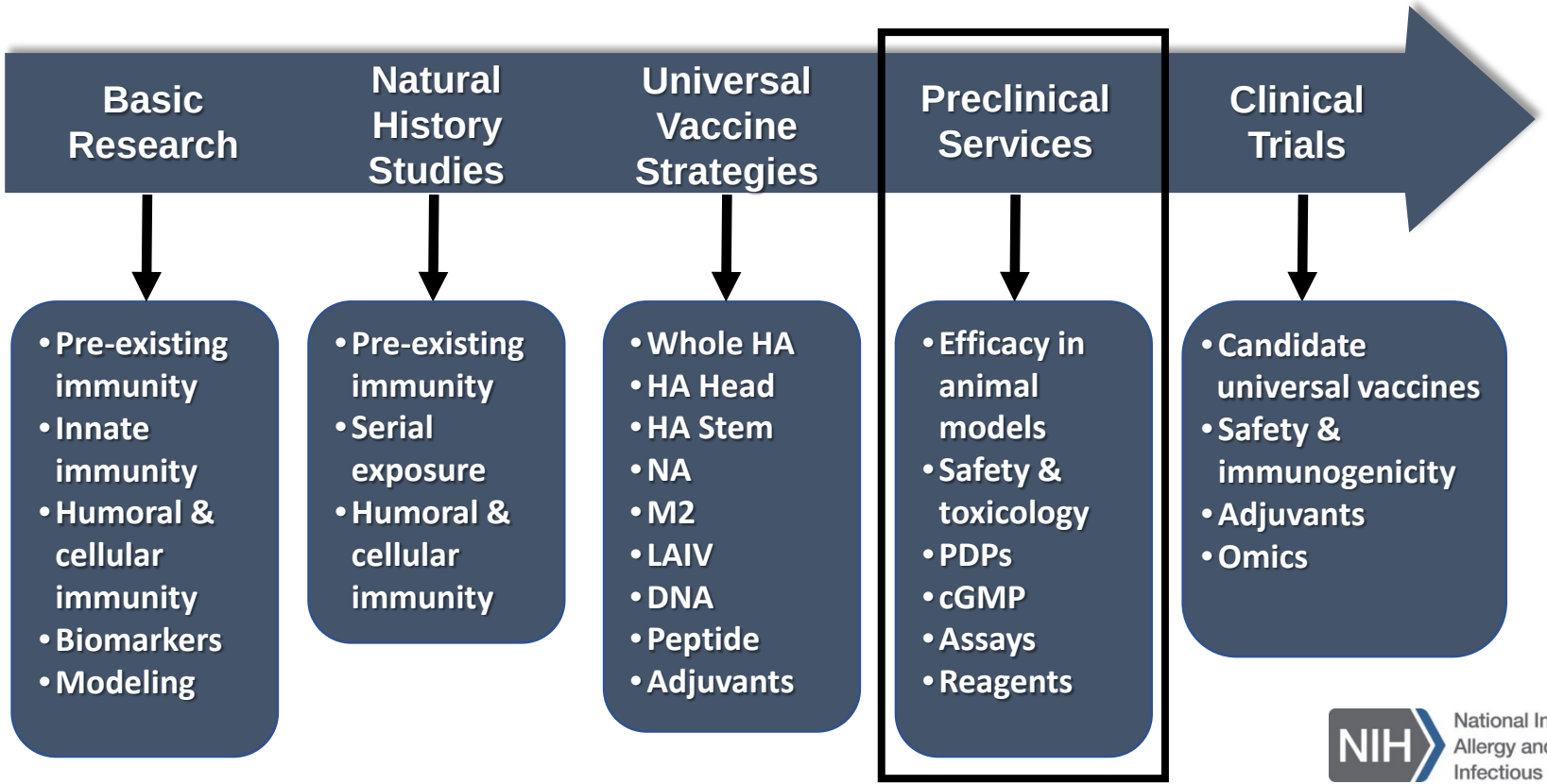
Assays

Assay	Institution
VaxArray® influenza potency assay	InDeVr, Inc.
Cypher One optical analysis of HA & HI assays	InDeVr, Inc.
Improved ADCC assay	St. Jude Children's Research Hospital
Binding of antibody to an array of expressed HAs	University of Rochester
Quantification of antigenic drift & neutralizing antibody breadth	Mt. Sinai School of Medicine

Reagents

Reagent	Institution
General influenza reagents & ferret immunological reagents	St. Jude Children's Research Hospital
Reagents for analysis of stalk-specific immunity & generation of stable chimeric HA expressing viruses	Mt. Sinai School of Medicine
Cell lines for highly efficient replication of vaccine viruses	University of Wisconsin

DMID Universal Influenza Vaccine Research Portfolio



NIH National Institute of Allergy and Infectious Diseases

DMID Vaccine Development Services

Supports vaccines, adjuvants, devices and challenge materials

Vaccine Manufacturing

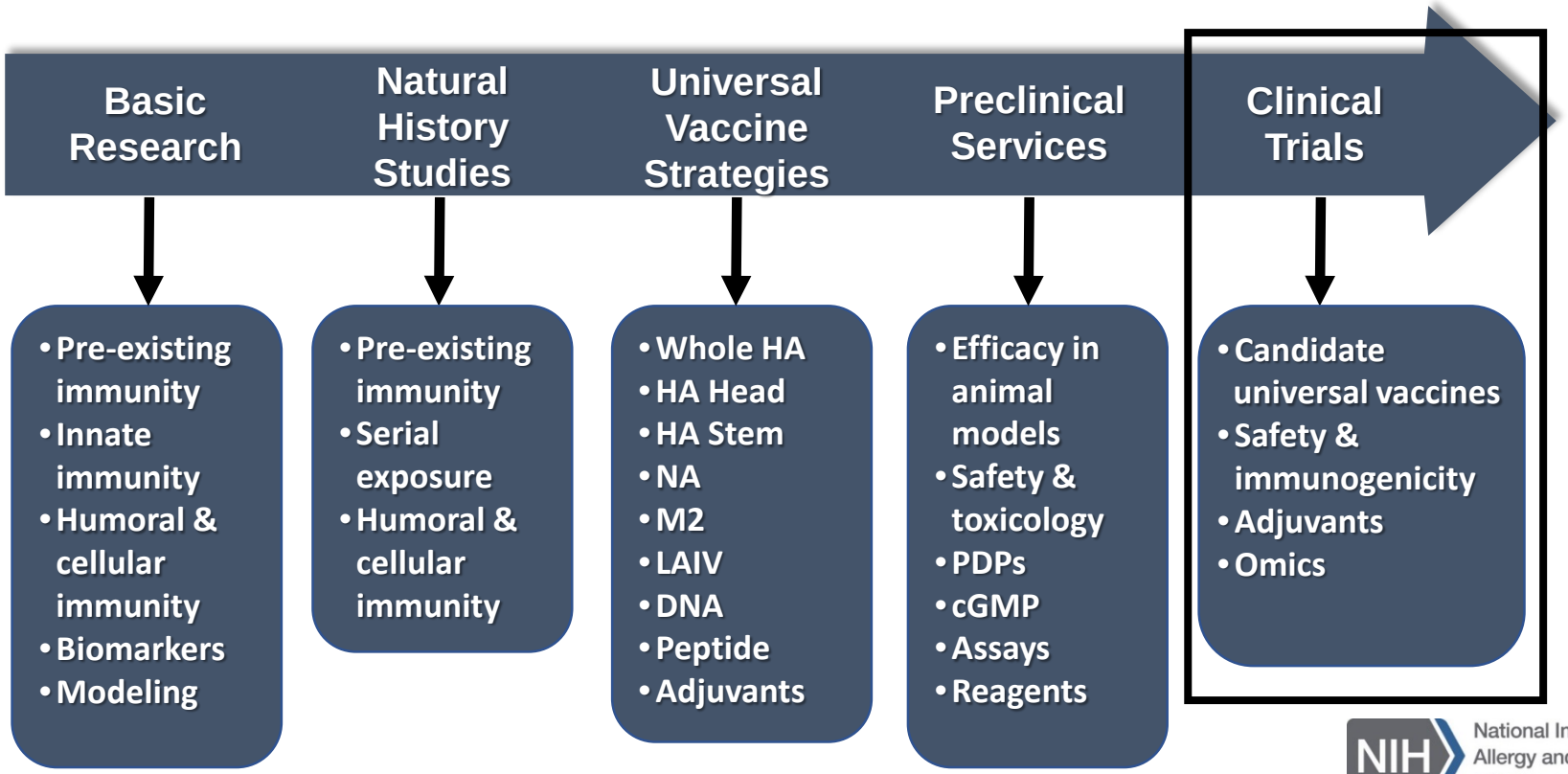
- Feasibility, Gap Analysis, & Product Development Plan (PDP) Support
- Process Development
- Product Release Assay Development
- Potency Assays
- Pilot & cGMP Manufacturing
- Audits
- Regulatory Activities

Vaccine Testing

- Assay Development for Non-Clinical & Clinical Samples
- Non-Clinical & Clinical Sample Testing
- Non-Clinical Immunogenicity & Efficacy Studies (including non-GLP & GLP)
- Safety & Toxicity Testing

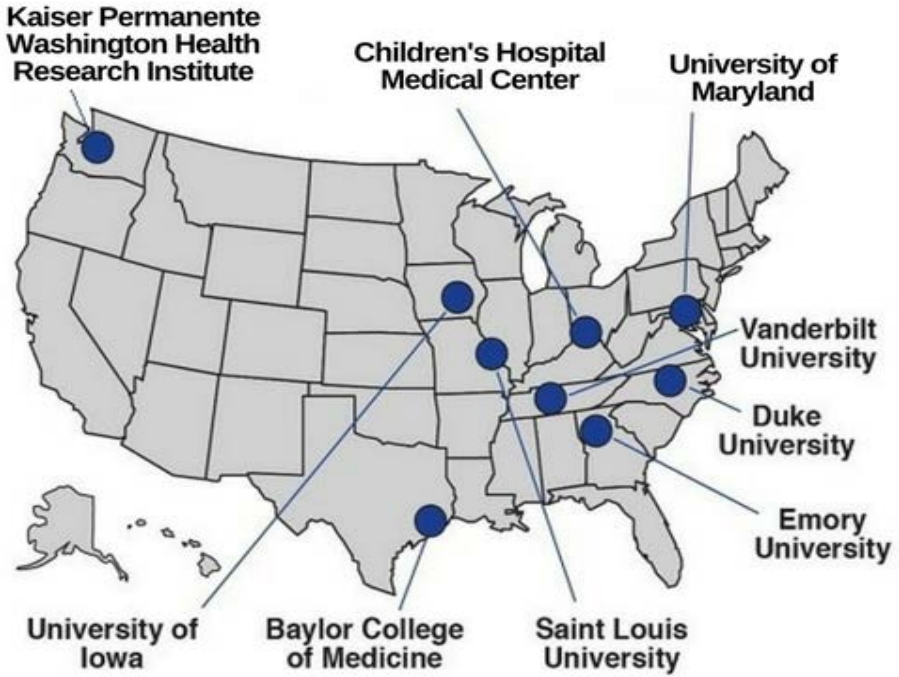
NIH National Institute of Allergy and Infectious Diseases

DMID Universal Influenza Vaccine Research Portfolio



NIH National Institute of Allergy and Infectious Diseases

DMID Vaccine and Treatment Evaluation Units (VTEUs)



- **Rapid-response capabilities**
- **Testing novel vaccines**
- **Developing combination vaccines**
- **Testing novel delivery systems**

NIH National Institute of Allergy and Infectious Diseases

DMID Supported Clinical Trials For Universal Influenza Vaccine Strategies

Icahn School of Medicine at Mount Sinai

NIH National Institute of Allergy and Infectious Diseases

gsk

MSSM/GSK/NIAID VRC Chimeric HA

- DMID 17-0086, Phase I DNA prime (chimeric H8/1, N1 NA) & IIV boost (chimeric H5/1, N1 NA) in healthy adults
- Analysis of humoral NA and HA stalk-specific responses

FluGen

RedeeFlu (M2SR LAIV)

- DMID 17-0112, Phase I H3N2 M2SR prime & IIV4 boost in pediatric subjects
- Analysis of humoral & CMI responses including NA immune responses & HA stalk-specific responses

BiondVax Pharmaceuticals Ltd.

M-001 Peptide Vaccine

- DMID 14-0112, Phase II M-001 prime & seasonal IIV3/IIV4 boost in healthy adults
- Analysis of CMI responses

3M

Imiquimod (Aldara) Topical Adjuvant

- DMID 16-0050, Phase II: Imiquimod with H5N1 vaccine in healthy adults
- Analysis of humoral & CMI responses

NIAID Intramural Universal Influenza Vaccine Program

Viral Pathogenesis & Evolution Section (VPES) Influenza Program

- **Universal Influenza Vaccine Platform**
  - Cocktail of inactivated avian influenza viruses expressing at least 4 different HA subtypes
  - Currently in preclinical development
  - Demonstrated near 100% protection against influenza viral challenge regardless of subtype in animals
  - Phase I safety and immunogenicity studies to be conducted within one year

- **Human Volunteer Influenza Challenge Studies**
  - Key component of efforts to develop a universal influenza vaccine
  - Studies of viral pathogenesis and immune responses
  - Efficient model for early Phase II clinical evaluation of novel vaccines

Dale and Betty Bumpers
VACCINE RESEARCH CENTER
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Department of Health and Human Services

NIH National Institute of Allergy and Infectious Diseases

NIAID Vaccine Research Center (VRC)
Influenza Vaccine Program

Confidential to NIAID VRC

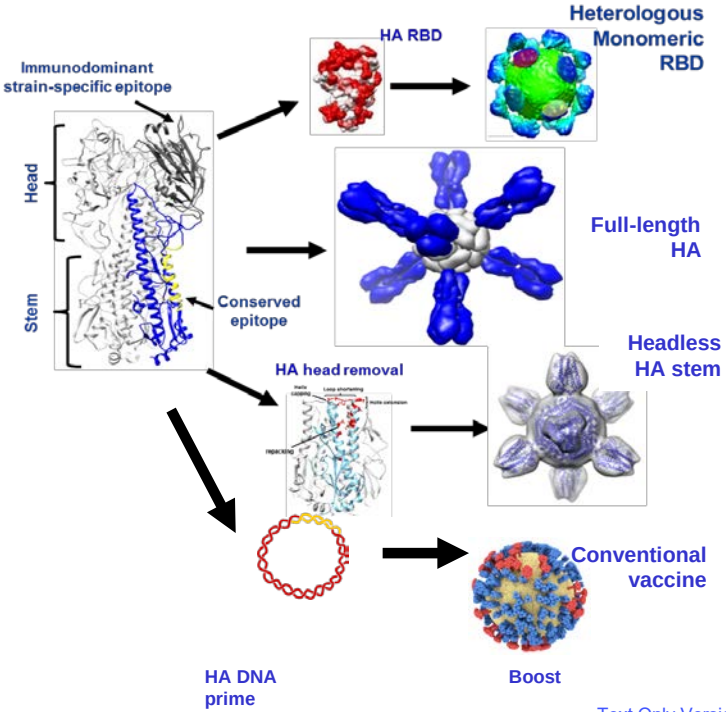
VRC Influenza Program

- **Research Approaches**
  - Reagent and assay development – probes, reporter viruses
  - Application of single-cell sorting for repertoire analysis, antibody isolation, and phenotyping
  - Structure-guided antigen design and nanoparticle display
  - Clinical evaluation of novel products
  - Animal model improvement

- **Vaccine Development Goals**
  - Improve magnitude or quality of response
  - Durability of protection extended beyond 1 year
  - Protect against future seasonal (drifted) and pandemic (shifted) strains
    - Protection within subtype
    - Protection within HA group
    - Protection against all known HAs

Confidential to NIAID VRC

VRC Influenza Vaccine Portfolio



Text Only Version

Avoiding immunodominant strain-specific antibody responses allowing cross-reactive antibodies to emerge

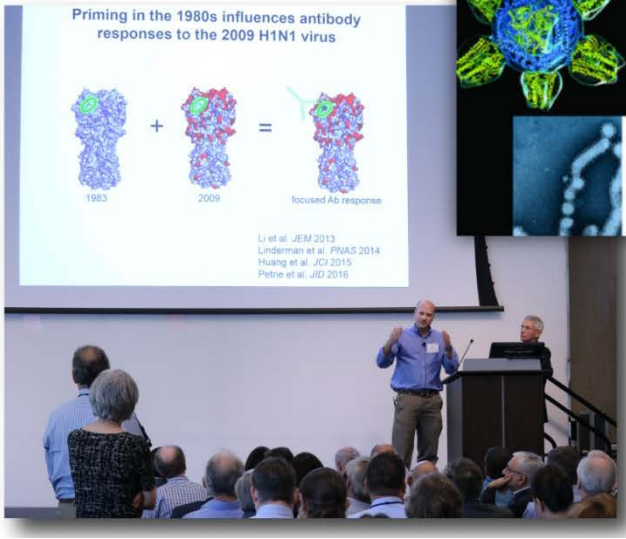
Combined or serial heterologous antigen regimens to recruit and accumulate antibodies to diverse antigen sites and strains

Targeting conserved antigenic sites in stem to induce cross-reactive antibodies

Priming with DNA improves magnitude and avidity of vaccine-induced antibody

Confidential to NIAID VRC

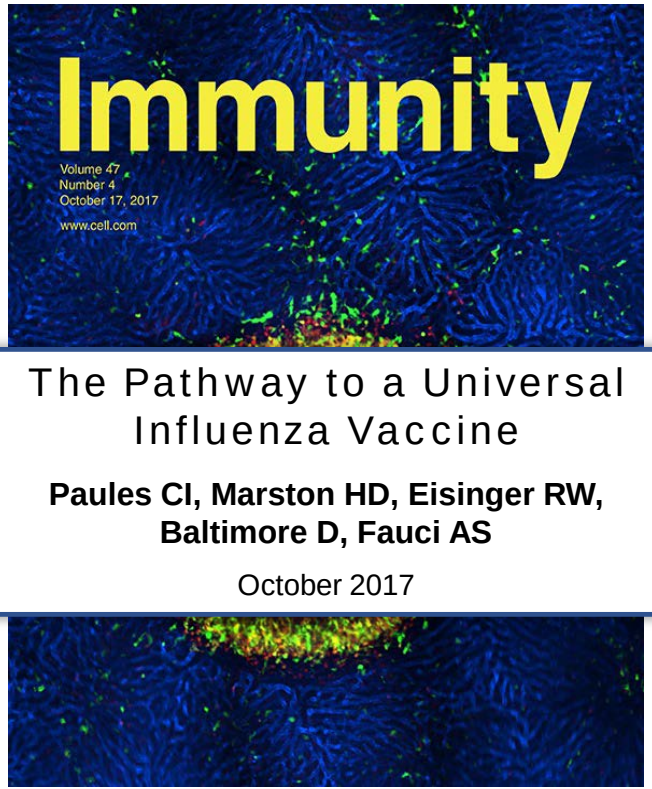
NIH National Institute of Allergy and Infectious Diseases



Slide Credit: Dr. Anthony Fauci, NIAID

NIH National Institute of Allergy and Infectious Diseases

Workshop Meeting Report



The Pathway to a Universal Influenza Vaccine

Paules CI, Marston HD, Eisinger RW, Baltimore D, Fauci AS

October 2017

- **Established definition for a universal influenza vaccine to serve as a goal for future research efforts**
- **Identified key gaps in knowledge to guide strategic planning**
- **Identified current research tools and discussed advantages/disadvantages**
- **Coordination of the influenza research field is critical for success**

Slide Credit *(adapted from)*: Dr. Anthony Fauci, NIAID

NIH National Institute of Allergy and Infectious Diseases

Definition of a Universal Influenza Vaccine

- **Protection: ≥75% against symptomatic influenza infection**
- **Breadth: Protection against group 1 and group 2 influenza A viruses**
  - **Influenza B a secondary target**
- **Durability: ≥1 year**
- **Population: Suitable for all age groups**

Slide Credit: Dr. Anthony Fauci, NIAID

NIH National Institute of Allergy and Infectious Diseases

Key Gaps & Priorities

- **Improve understanding of transmission, natural history and pathogenesis of influenza infection**
- **Precise characterization of influenza immunity and correlates of immune protection**
- **Support rational design of universal influenza vaccines**
- **Develop research resources and cross-cutting tools to improve influenza vaccines**
  - **Develop/improve animal models**
  - **Establish longitudinal cohorts**
  - **Increase capacity and capability for conducting human challenge studies**
  - **Develop/apply systems biology approaches**

DMID Universal Influenza Vaccine Research Portfolio

1. Basic Research
    - Pre-existing immunity
    - Innate immunity
    - Humoral & cellular immunity
    - Biomarkers
    - Modeling
2. Natural History Studies
    - Pre-existing immunity
    - Serial exposure
    - Humoral & cellular immunity
3. Universal Vaccine Strategies
    - Whole HA
    - HA Head
    - HA Stem
    - NA
    - M2
    - LAIV
    - DNA
    - Peptide
    - Adjuvants
4. Preclinical Services
    - Efficacy in animal models
    - Safety & toxicology
    - PDPs
    - cGMP
    - Assays
    - Reagents
5. Clinical Trials
    - Candidate
    - Universal vaccines
    - Safety & immunogenicity
    - Adjuvants
    - Omics

DMID Universal Influenza Vaccine Strategies

- Preclinical Development
    - HA nanoparticles + free HA & NP (with The University of Iowa logo)
    - Germline-targeted HA stem (with The Scripps Research Institute logo)
    - 4xM2e HA LAIV (with Georgia State University logo)
    - DNA prime / subunit boost (with Profectus Biosciences logo)
    - TLR5, TLR7/8 adjuvants (with Wake Forest University logo)
    - Advax delta inulin adjuvant (with Vaxine logo)
    - Antigenicall advanced antigens (with Erasmus MC, University of Cambridge, and University of Wisconsin-Madison logo)
    - VLPs with HA stem, NP, TLR/CD40 (with Indiana University logo)
    - M2e CpG gold nanoparticles (with Texas Tech University logo)
    - Ad5-vectored (with Etubics corporation logo)
    - Nanoparticle adjuvant TNF, IL-12 (with Columbia University logo)
    - M2e-HA stem (with Georgia State University logo)
    - Surface antigen/adjuvant vaccine engineering (SAAVE) (with University of Georgia logo)
    - M2e-TLR5 fusion protein (with Georgia State University logo)
    - Ad5-vectored centralized HA (with University of Nebraska-Lincoln logo)
    - Microneedle adjuvant GIFT4/IFN-lambda 2 (with Emory University logo)
- Phase I
    - Chimeric HA (with NIH National Institute of Allergy and Infectious Diseases, gsk, and Icahn School of Medicine at Mount Sinai logos)
    - M2 Single Replication (M2SR) LAIV (with FluGen logo)
    - SAVE de-optimized LAIV (with CodageniX logo)
- Phase II
    - HA, NP, M1 peptides (M-001) (with BiondVax Pharmaceuticals Ltd. logo)

VRC Influenza Vaccine Portfolio

Immunodominant strain-specific epitope

- HA REB
    - Heterologous Monomeric RBD
- Full-length HA
- HA head removal
    - Headless HA stem
- HA DNA Prime
    - Conventional vaccine