

NIAID's Priorities to Support Broadly Protective Influenza Vaccines

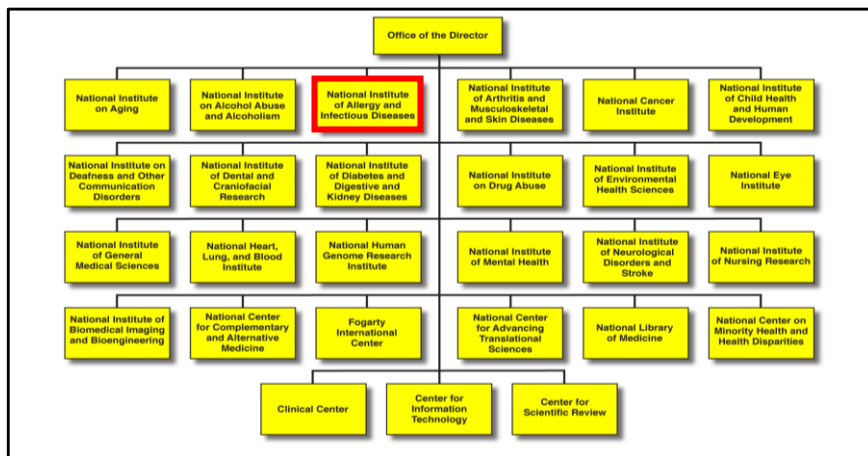
Jennifer Gordon, PhD
 Respiratory Diseases Branch
 Division of Microbiology & Infectious Diseases
 NIAID, NIH, DHHS

09 September 2018

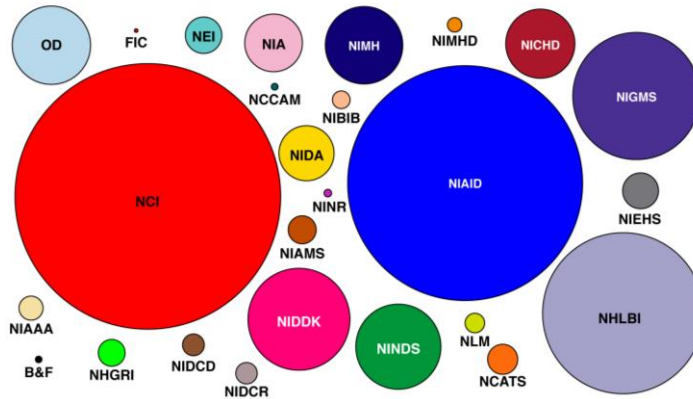


National Institutes of Health

NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.

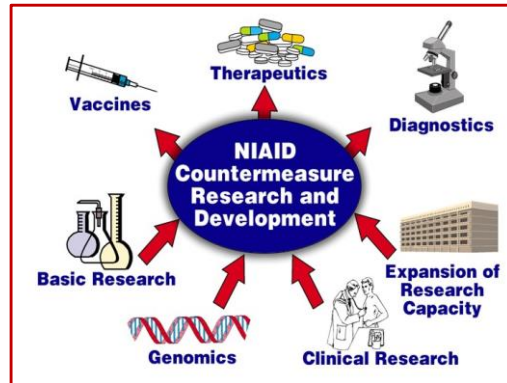


National Institutes of Health



NIAID Mission

Conduct and support basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic and allergic diseases.



NIH - A Two-Component System

Supporting the training of research investigators
Fostering communication of medical
and health sciences information

INTRAMURAL

Conducting research in NIH laboratories
(Division of Intramural Research, Vaccine Research Center, Division of Clinical
Research)

EXTRAMURAL

Supporting the research of non-Federal scientists in universities,
medical schools, hospitals, and research institutions throughout
the United States and around the world

(Division of Allergy, Immunology, and Transplantation, Division of Microbiology
and Infectious Diseases, Division of Extramural Research)

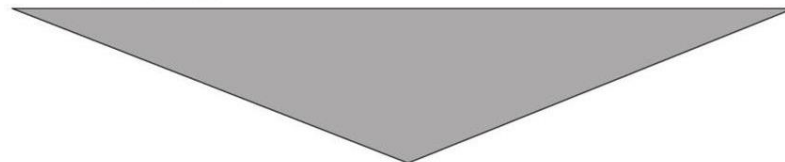


NIAID Research: A Dual Mandate

Maintain and “grow” a
robust basic and applied
research portfolio in
microbiology, infectious
diseases, immunology
and immune-mediated
diseases



Respond rapidly to
new and emerging
disease threats



New/Improved Interventions



NIAID Centers of Excellence for Influenza Research and Surveillance (CEIRS)

St. Jude Children's Research Hospital
Memphis, TN



PI
Richard Webby



Co-PI
Stacey Schultz-Cherry

University of Rochester
Rochester, NY



PI
John Treanor



Co-PI
David Tophman

Icahn School of Medicine
at Mt. Sinai
New York, NY



PI
Adolfo Garcia-Sastre

Emory University
Atlanta, GA



PI
Walter Orenstein



Co-PI
Dick Compans



Johns Hopkins University
Baltimore, MD



PI
Richard Rothman



Co-PI
Andrew Pekosz

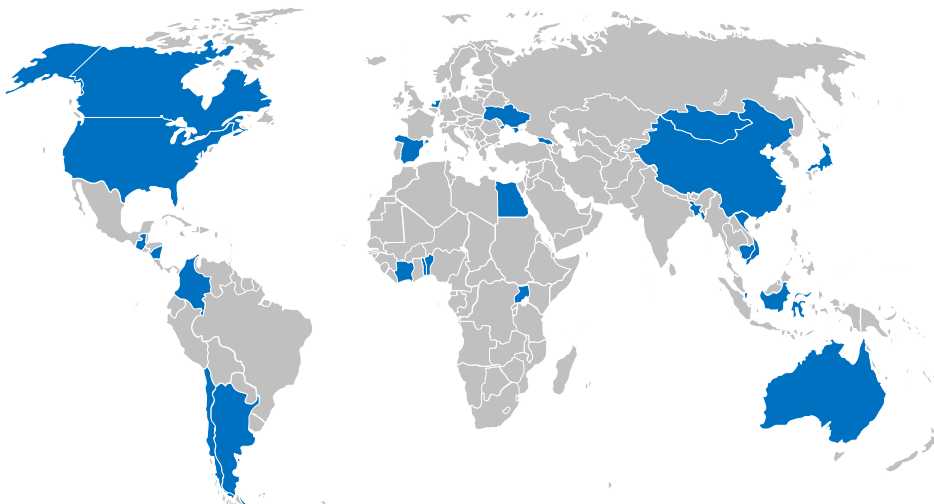
Updated 5/2014

- Established to support the research agenda of the HHS Pandemic Influenza Plan
 - 2009 H1N1 pandemic, CEIRS conducted early virus characterization studies and pre-clinical evaluation of vaccine material
 - During 2014, provided viral isolates in response to H5N8 outbreaks in birds in US and Europe
 - During 2015 H7N8 outbreak in U.S. poultry, provided >50 viral isolates
- 5 sites + 1 Core center + multiple sub-contracts



NIAID CEIRS Surveillance Sites

Currently collaborates with 27 international and ~20 domestic surveillance sites

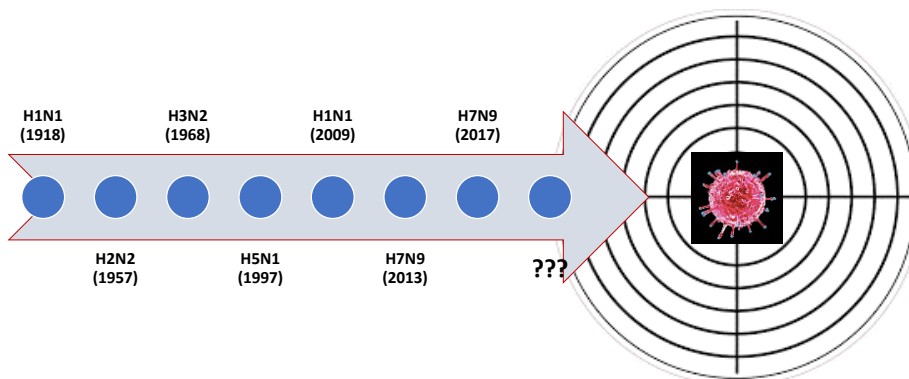


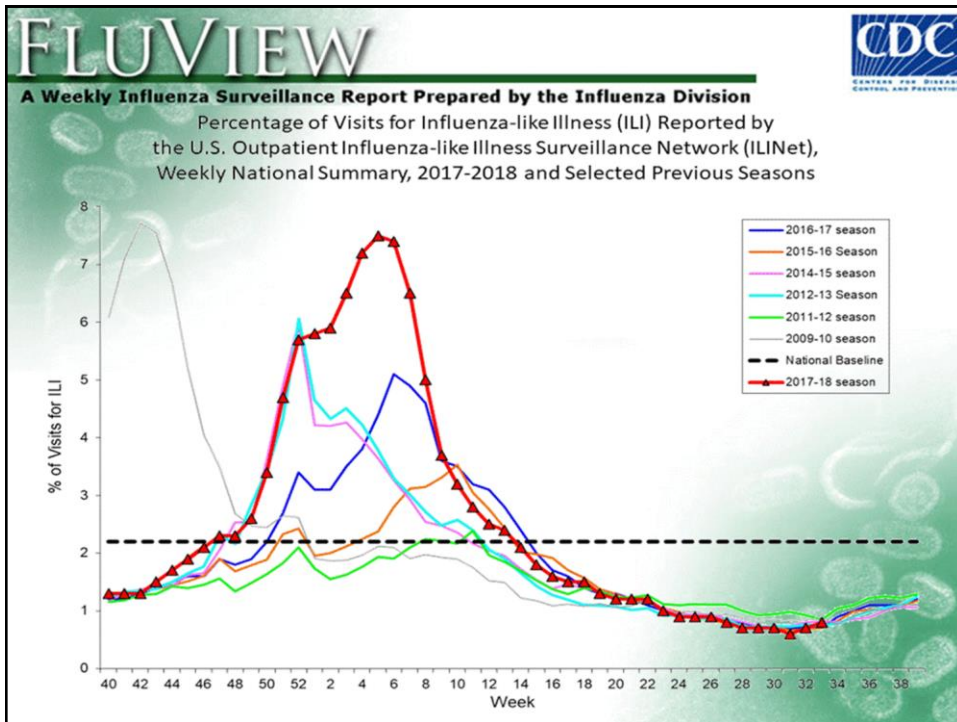
NIAID Support of H5 and H7 Pandemic Preparedness Clinical Trials

- Mix and Match Studies +/- adjuvant
 - Dose ranging using stockpiled monovalent split IIVs with and without adjuvant (AS03 and MF59) (e.g., H5N1, H5N8, 2013 H7N9 and 2017 H7N9)
- Heterologous Prime/Boost Studies to broaden cross-clade response
 - H5N1: A/Vietnam and A/Indonesia
 - H7: H7N7 and H7N9
 - LAIV prime followed by IIV boost; IIV prime followed by LAIV boost
- System biology and comprehensive assessment of T, B and Innate Immune Responses



Influenza is Difficult to Predict and Remains a Moving Target for Pandemic Preparedness





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

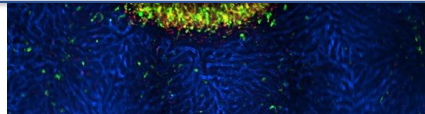
Workshop Meeting Report



The Pathway to a Universal Influenza Vaccine

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

October 2017

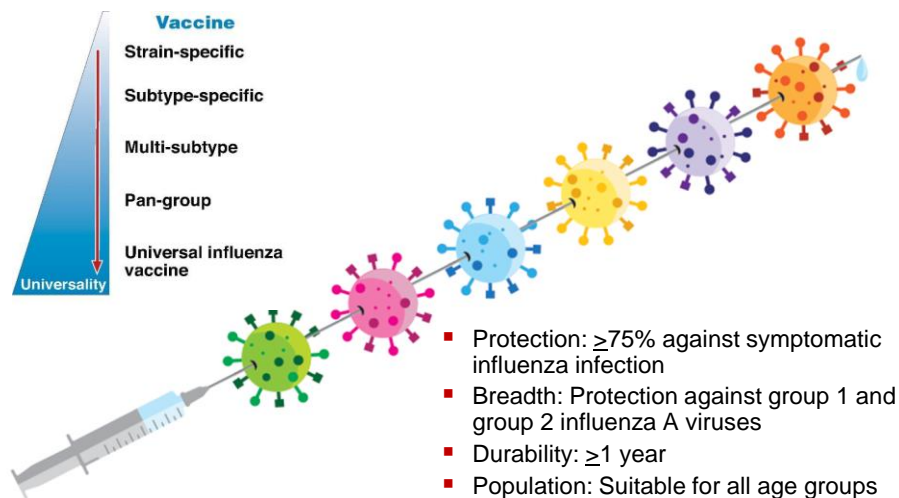


- Established definition for a **universal influenza vaccine to serve as a goal** for future research efforts
- Identified current **research tools** and discussed advantages/disadvantages
- **Coordination** of the influenza research field is critical for success
- Identified **key gaps in knowledge**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

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



Universal Influenza Vaccine Strategy



NIAID Universal Influenza Vaccine Strategic Plan

The Journal of Infectious Diseases

MAJOR ARTICLE

IDSIA
Infectious Diseases Society of America

hivma
HIV medicine association

OXFORD

A Universal Influenza Vaccine: The Strategic Plan for the National Institute of Allergy and Infectious Diseases

Emily J. Erbeling,^{1,2} Diane J. Post,^{1,2} Erik J. Stemmy,^{1,2} Paul C. Roberts,^{1,2} Alison Deckhut Augustine,^{1,2} Stacy Ferguson,^{1,3} Catharine I. Paules,¹ Barney S. Graham,^{1,4} and Anthony S. Fauci¹

¹National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, ²Division of Microbiology and Infectious Diseases, ³Division of Allergy, Immunology, and Transplantation, and ⁴Vaccine Research Center.

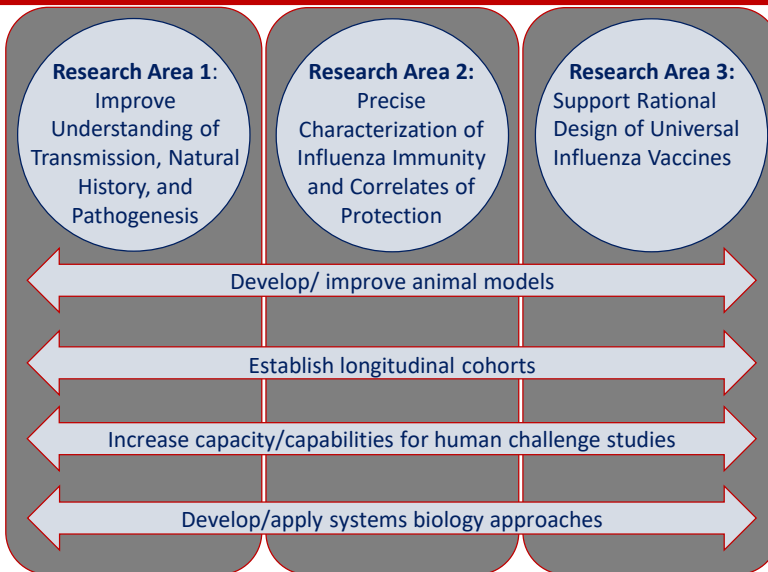
A priority for the National Institute of Allergy and Infectious Diseases is development of a universal influenza vaccine providing durable protection against multiple influenza strains. NIAID will use this strategic plan as a foundation for future investments in influenza research.

Keywords. Strategic plan; influenza; universal vaccine.

- NIAID priority to develop a universal influenza vaccine that provides durable protection against multiple influenza strains
- Foundation for future investments in influenza research

NIH National Institute of Allergy and Infectious Diseases

NIAID Strategic Plan for a Universal Influenza Vaccine



Implementation of NIAID's Universal Influenza Vaccine Strategic Plan

Alison Augustine, PhD
Basic Immunology Branch
Division of Allergy, Immunology & Transplantation
NIAID, NIH, DHHS

09 September 2018

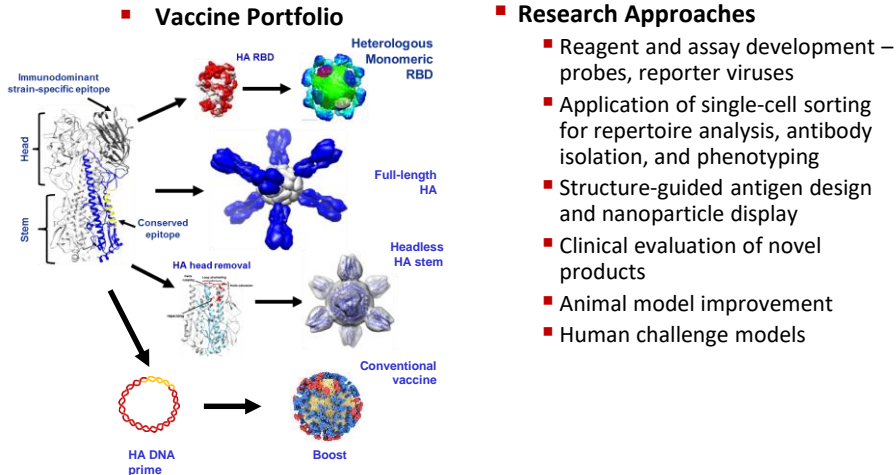


Filling Research Gaps Leading to a Universal Influenza Vaccine

- Expand existing programs
- Use NIAID clinical trial sites
- Expand human challenge studies
- Increase support for investigator-initiated applications
- Develop targeted funding opportunities
- Launch a multidisciplinary consortium for development of universal influenza vaccines
- Coordinate activities to advance all research areas



NIAID Intramural Universal Influenza Vaccine Program

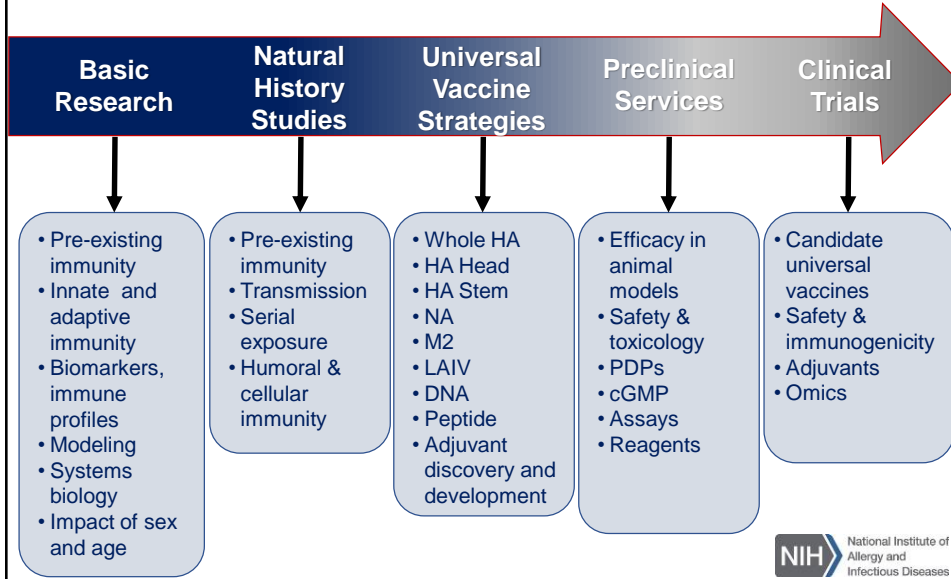


<https://www.niaid.nih.gov/research/vaccine-research-center-labs>

Confidential to NIAID VRC



Extramural Universal Influenza Vaccine Research Portfolio



Impact of Initial Influenza Exposure on Immunity in Infants

- New Program to establish longitudinal cohorts of infants to determine how initial and repeated infections and/or vaccinations shape infant and childhood immunity to future influenza exposures (RFA-AI-18-01)
- Applications received and will undergo peer review soon
- Awards expected in Spring or Summer 2019



Advancing Research Needed to Develop a Universal Influenza Vaccine

- Funding opportunities for investigator-initiated research, US domestic and international applicants welcome
- Supports areas of interest outlined in NIAID's Universal Influenza Vaccine Strategic Plan
 - viral transmission, natural history and pathogenesis
 - immunity and correlates of immune protection
 - rational design of universal influenza vaccines
- Funding mechanisms:
 - PA-18-858: R21, innovative research, 2 year award, \$275,000 direct costs over 2 years
 - PA-18-859: R01, up to 5 year award, average of \$250,000 direct costs/year



Collaborative Influenza Vaccine Innovation Consortium (CIVICs)

- **Objective:** Develop innovative influenza vaccine approaches that provide robust, durable, broadly protective mucosal and systemic immunity
- Broad Agency Announcement (BAA): [HHS-NIH-NIAID-BAA2018 Amendment 1](#)
- Program Structure:
 - Component A: Vaccine Center (at least 2)
 - Component B: Vaccine Manufacturing and Toxicology Core (1)
 - Component C: Clinical Core (1)
- Applications due November 29, 2018 5pm Eastern Time; separate applications for each component
- Separate initiative (RFP) for Statistical and Data Management Coordination Center (SDMCC): RFP-NIAID-DAIT-NIHAI201800018
- 7 year program; first year Total Cost for entire CIVICs = \$30M



Collaborative Influenza Vaccine Innovation Consortium (CIVICs)

External Advisory Board and NIAID
Extramural Staff

Vaccine Center

- Iterative Immunology-based Vaccine Design and Testing
- Assays & Reagents
- Project Management

Vaccine Center

- Iterative Immunology-based Vaccine Design and Testing
- Assays & Reagents
- Project Management

Cross-cutting Cores

Statistical, Data
Management &
Coordination
Center

Vaccine
Manufacturing,
Formulation,
Delivery, and GLP
Toxicology Core

Clinical Trials and
Human Challenge
Core

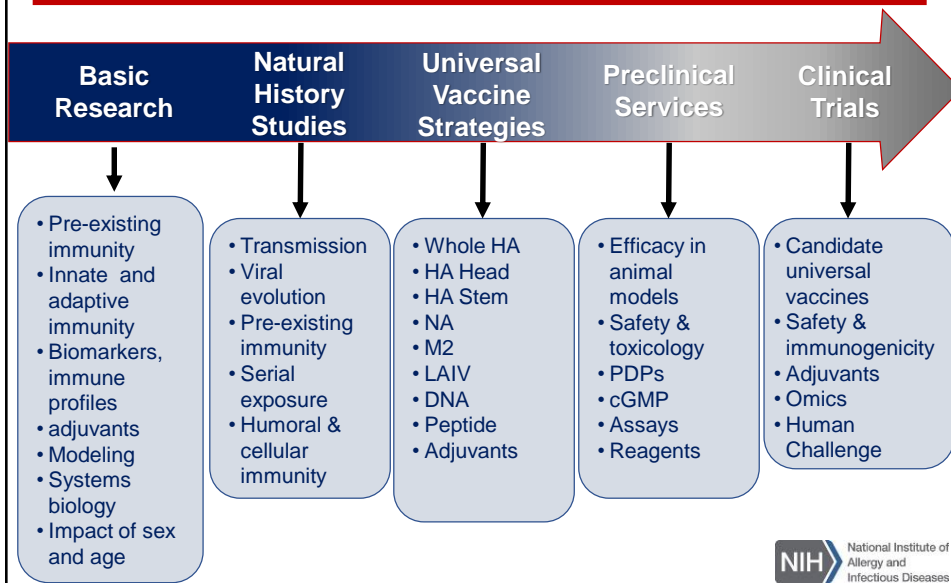


CIVICs Scope and Activities

- Rational, iterative design and development of universal influenza vaccines and improved seasonal influenza vaccines
 - Vaccine optimization, formulation and manufacturing
 - Safety and toxicity testing
- Pre-clinical evaluation of innovative influenza vaccine immunogens, antigen/adjuvant combinations and delivery platforms
- Phase I/II clinical trials of promising vaccine candidates
- Human challenge studies
- Detailed immunological studies to support the design and testing of vaccine candidates
 - Comprehensive analyses of systemic and mucosal immunity
 - Identification of correlates of protection



NIAID's Comprehensive Universal Influenza Vaccine Research Portfolio



谢谢

Jennifer Gordon
Jennifer.gordon2@nih.gov

Alison Augustine
augustine@niaid.nih.gov

