Prototype Pathogen approach for monoclonal antibody development - why do we need it?

Cristina Cassetti, PhD

DMID Deputy Director,

NIAID, NIH

Global research & innovation forum

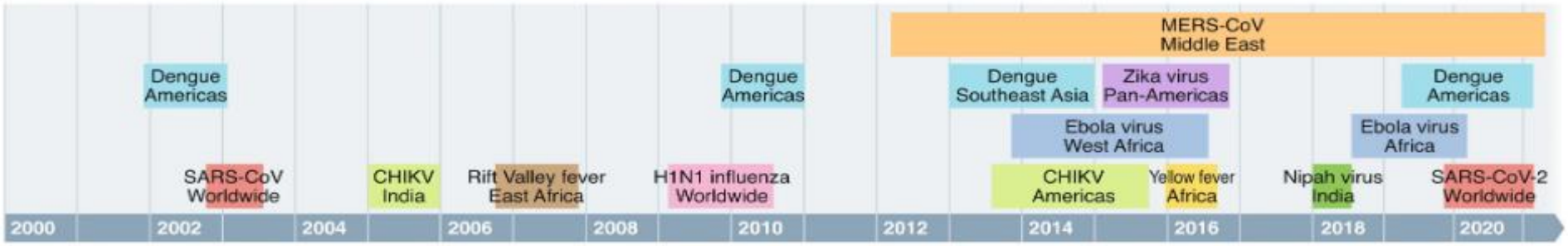
RESILIENCE AGAINST OUTBREAKS & PANDEMICS

WHO, 23-24 October 2023

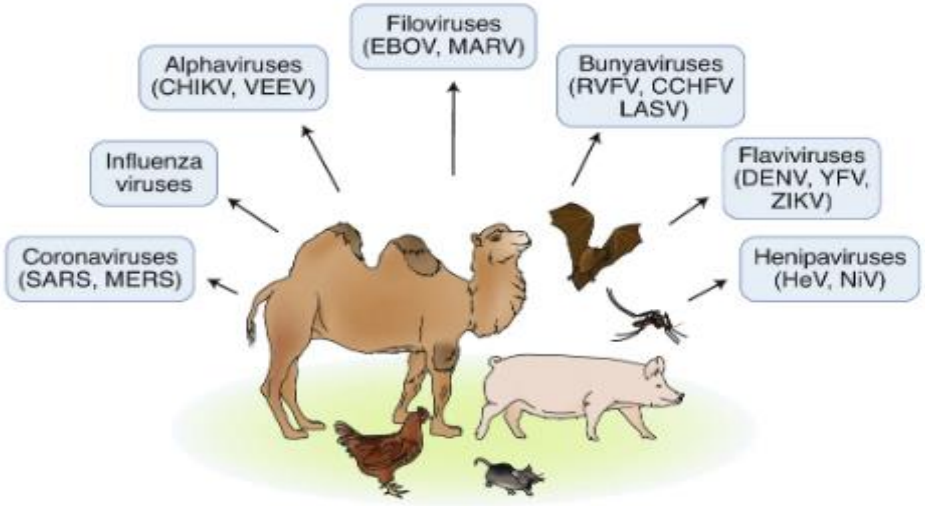
National Institute of Allergy and Infectious Diseases

Major Viral Diseases outbreaks in the last 20 years

a 21st century viral disease outbreaks



b Zoonotic reservoirs and vectors



Meganck, R.M., Baric, R.S. Developing therapeutic approaches for twenty-first-century emerging infectious viral diseases. *Nat Med* **27**, 401–410 (2021).

a, Timeline of twenty-first-century viral outbreaks, from 2000 to the present day. Viral strains and the area of outbreak are indicated along with the timeline. **b**, Animals such as the ones shown are zoonotic reservoirs or vectors for a number of virus families with pandemic potential.

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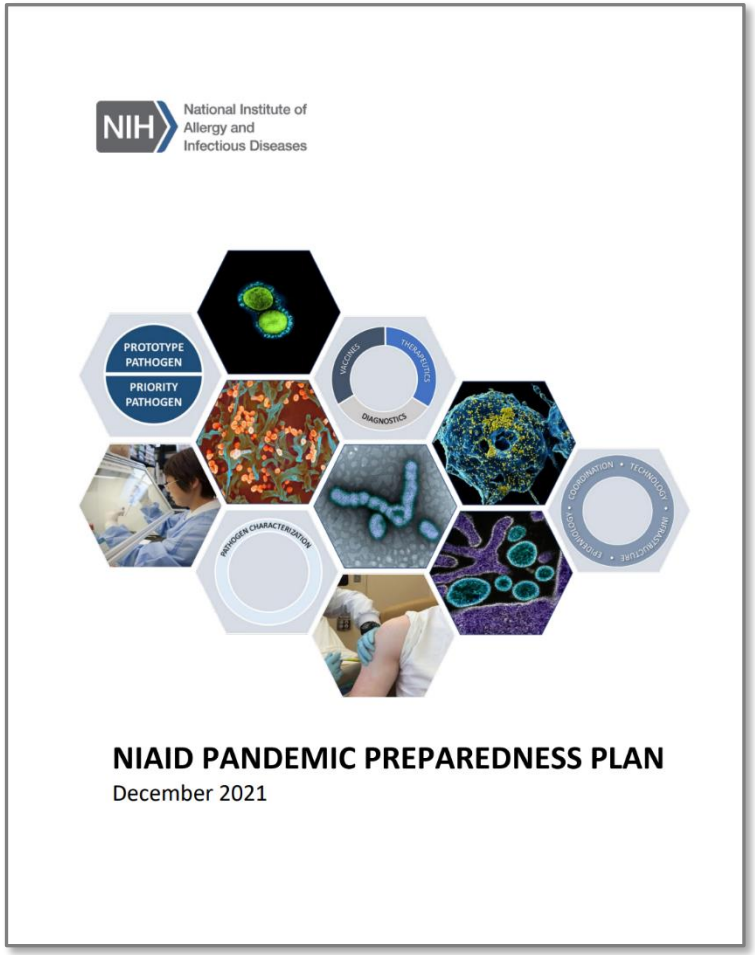
Three major goals of the NIAID Pandemic Preparedness Plan

- Systematically characterize known pathogens of pandemic concern and increase research and surveillance on novel threats before they emerge
- Shorten timelines between outbreak onset and authorization/approval of diagnostics, therapeutics and vaccines
- Fill existing gaps in research, infrastructure, technology and expand non-clinical, pre-clinical, and clinical testing capacity



https://www.niaid.nih.gov/sites/default/files/pandemic-preparedness-plan.pdf

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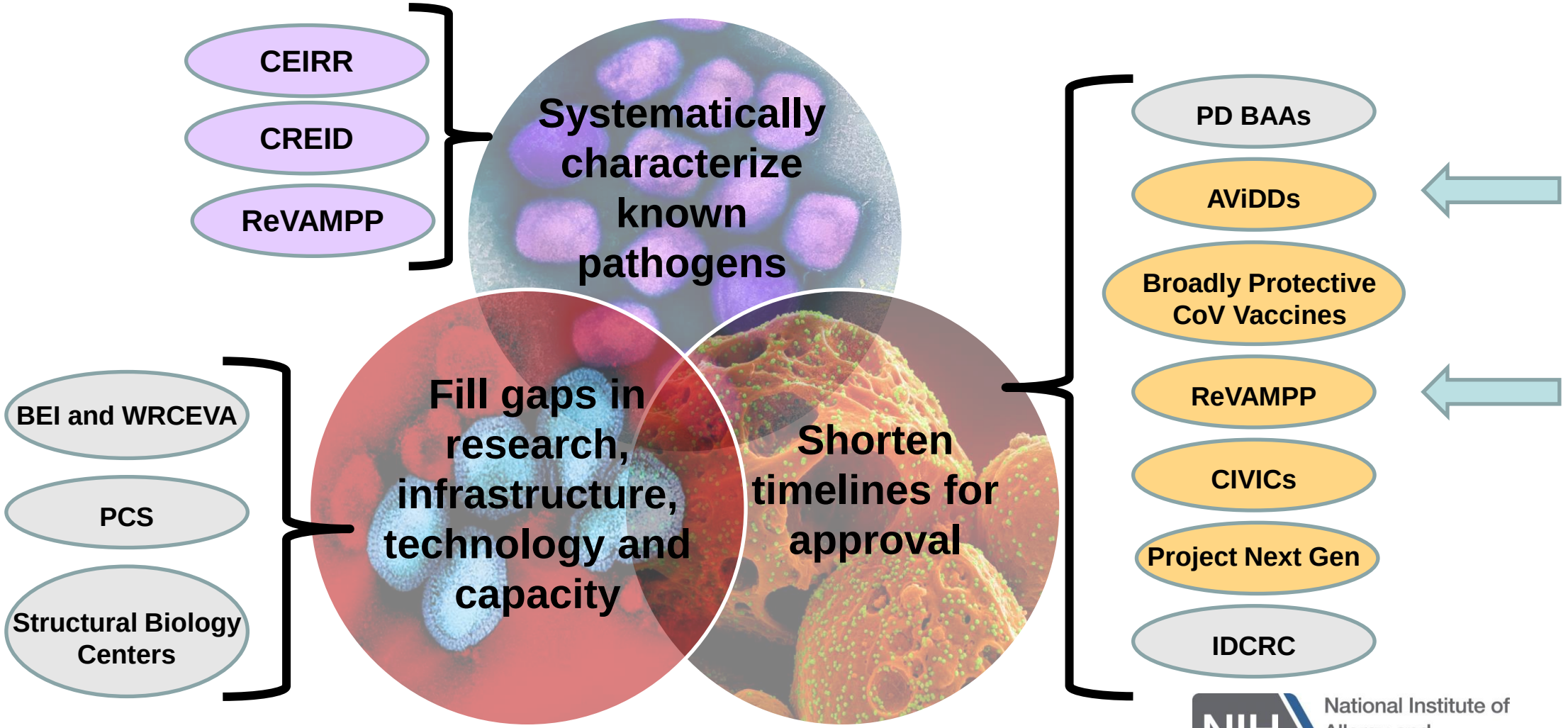
AS Fauci/NIAID

Key DMID Pandemic Preparedness Programs



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July 25, 2022

The Journal of Infectious Diseases

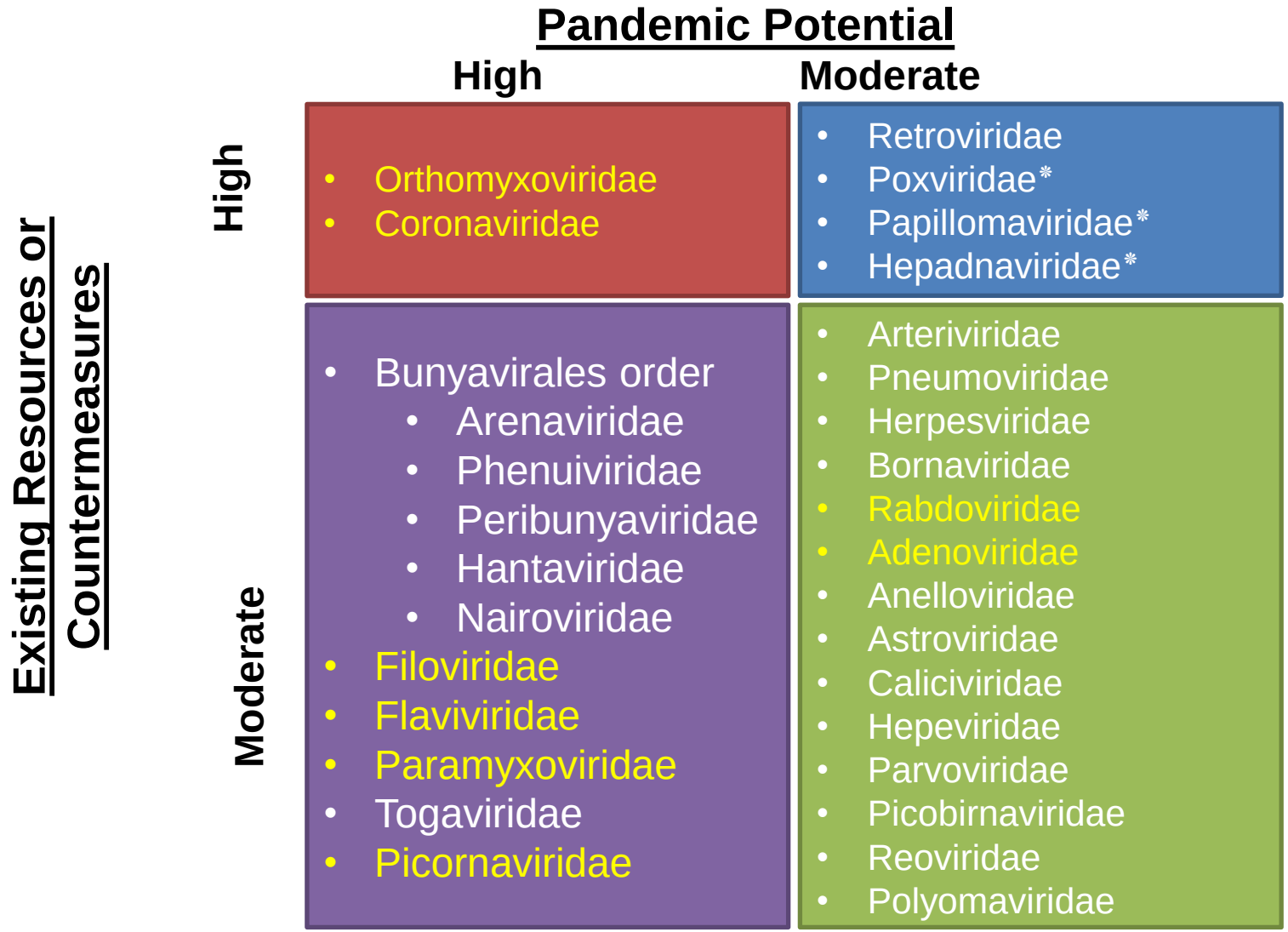
IDSA Infectious Diseases Society of America

hivma hiv medicine association

Prototype Pathogen Approach for Vaccine and Monoclonal Antibody Development: A Critical Component of the NIAID Plan for Pandemic Preparedness

MC Cassetti, TC Pierson, LJ Patterson, K Bok, AJ DeRocco, AM Deschamps, BS Graham, EJ Erbelding, AS Fauci

Virus families were prioritized based on pandemic potential and existing resources and countermeasures



*Existing vax solutions for entire family
Yellow text-Existing vax solutions for some viruses in that family

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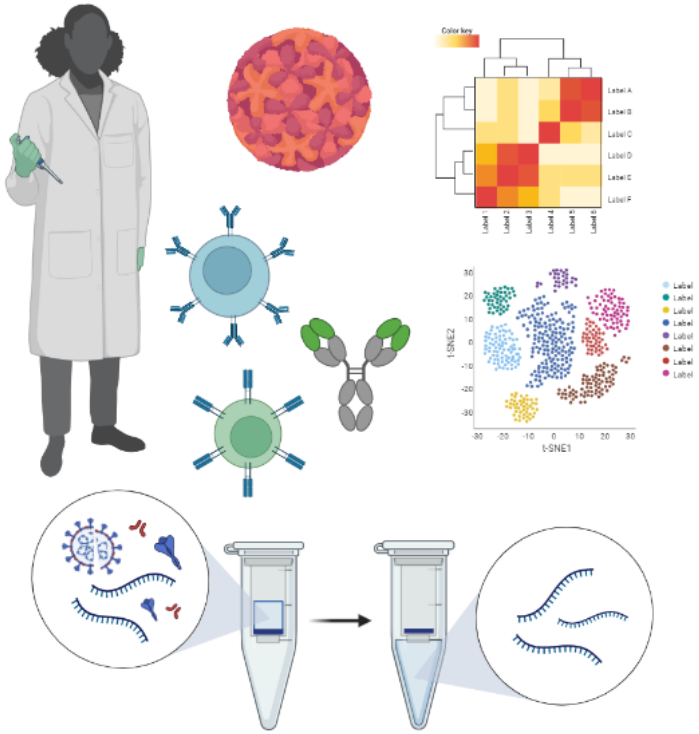
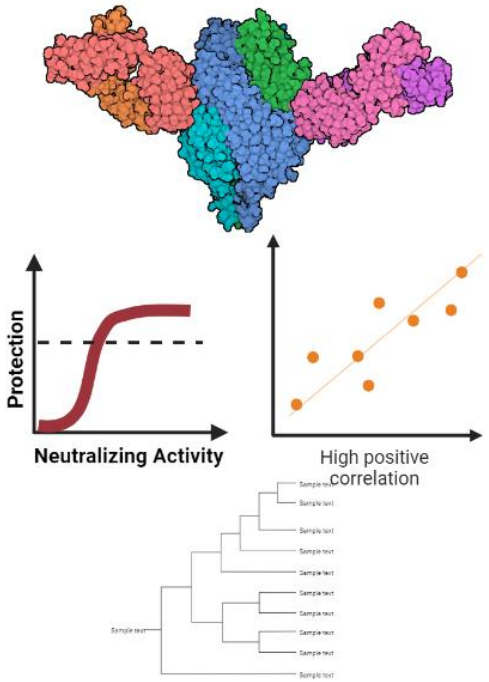
Prototype Pathogens: A Large But Finite Effort

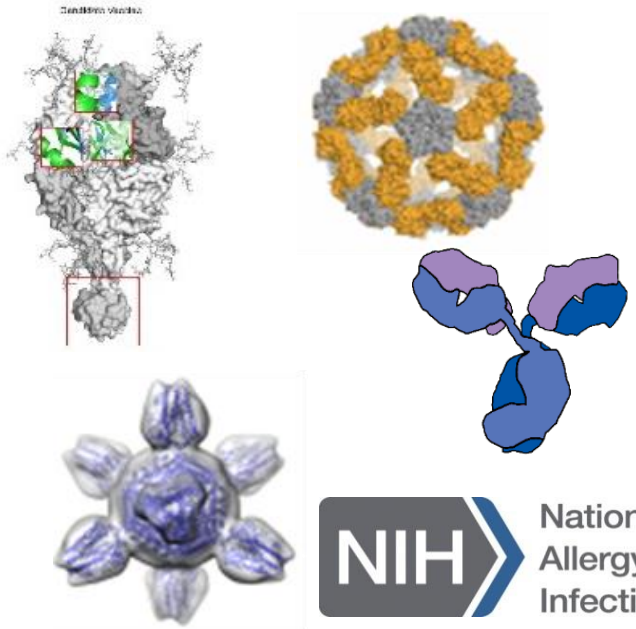
Research on Known Prototype

Foundational Knowledge

Generalizable Vaccine/mAb Strategies







Images created using Biorender

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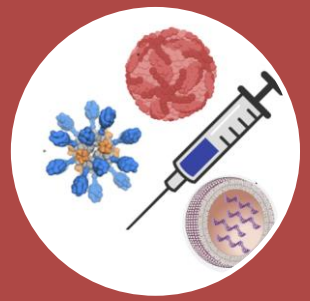
Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness (ReVAMPP) Network

- Highly collaborative network focused on prototype pathogen approach to identify and validate generalizable vaccine and optionally mAb solutions for virus families with high pandemic potential
- Applications due June 8, 2023; awards anticipated in March 2024

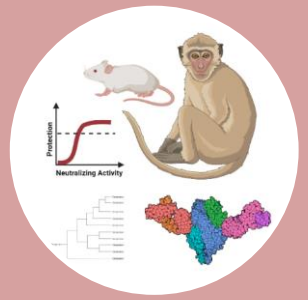


Vaccine Development

- Validation of same approach for other family members
- "Plug and Play" technologies

Early mAb Development

- Validation that antibodies with similar properties/functions are protective against other family members



Foundational Research

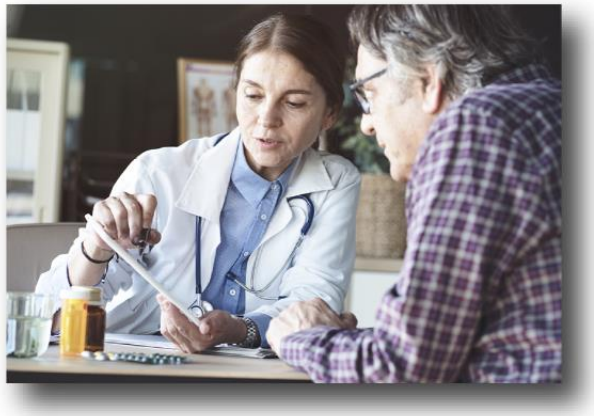
- Knowledge, reagents, models, and assays needed to enable vaccine development

Basic through IND-enabling translational research

Why mAbs?

- mAbs libraries are normally generated during vaccine development to identify the epitopes that induce strongly neutralizing antibodies.
- mAbs have been successfully used as prophylactics and therapeutics against a variety of IDs
  - RSV in high risk infants
  - Antrax
  - C.Difficile
  - HIV
  - Ebola
  - COVID-19
- Advantages
  - Rapid development (approval during COVID was obtained in only 9– 10 months from the initial discovery of mAbs)
  - Prophylactics mAbs provide immediate protection during an outbreak (e.g. nursing homes) and protect individuals that don't respond well to vaccines
- Limitations
  - development of viral escape mutants
  - the need to large scale manufacturing
  - Development of administration modalities outside of hospital settings.

Antiviral Drug Discovery (AViDD) Centers



Objective: To establish multidisciplinary Centers focused on discovery and development of antivirals against coronaviruses (CoVs) and other viruses of pandemic potential

Awards: 9 U19 Cooperative Agreement grants, each with 5-7 Research Projects and supporting Scientific Cores

Industry: Centers include industry participation for expertise with optimization of novel antiviral lead series

Scope: Aligned with APP - small molecules and non-antibody biotherapeutics that directly block viral targets

Program budget: $1B over 5 years planned (3 years secured)

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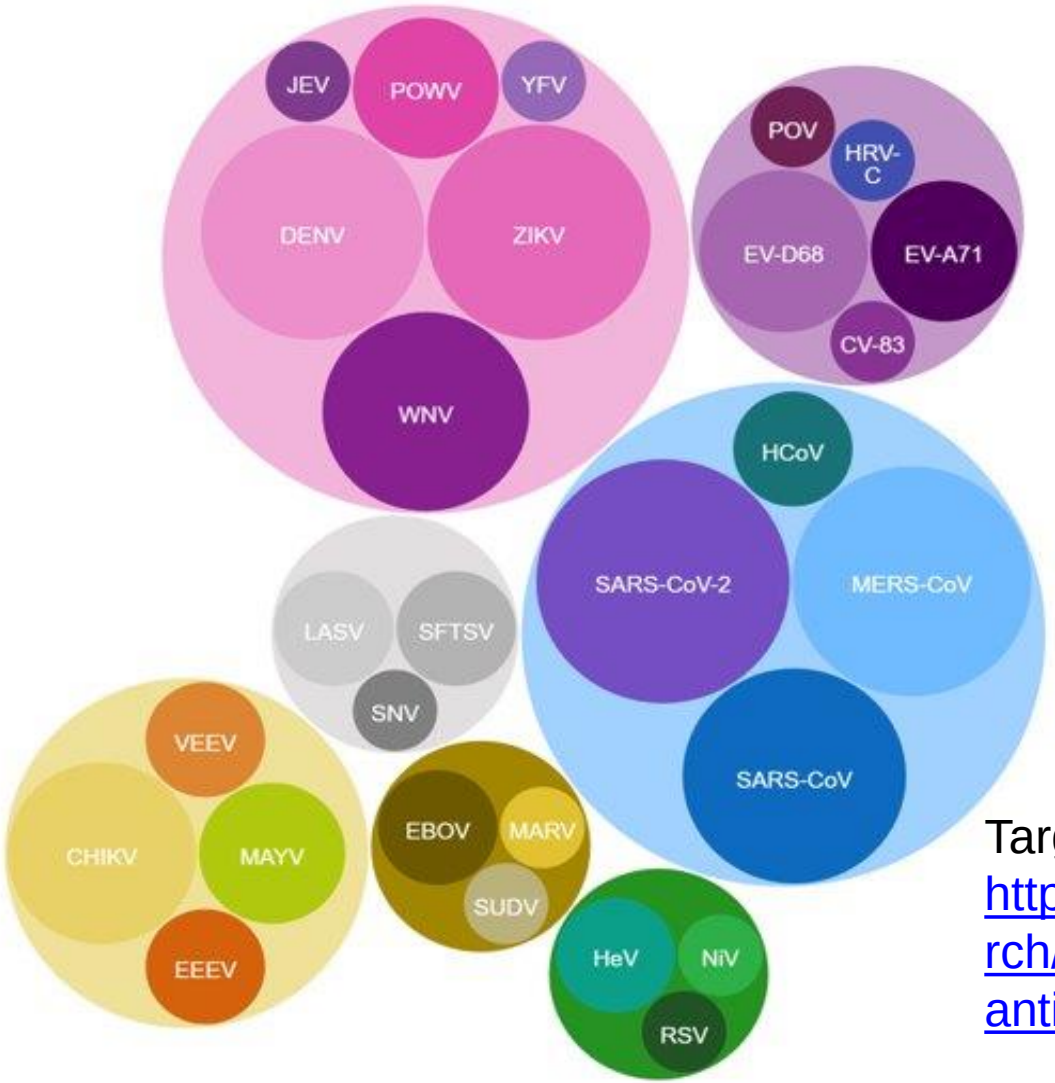
Pathogens & Targets Covered across AViDD Centers



Virus Family or Order

- Bunyavirales
- Coronaviridae
- Filoviridae
- Flaviviridae
- Paramyxoviridae
- Picornaviridae
- Togaviridae

Protease
Polymerase
Helicase
Endonuclease
Entry/Fusion
eProtein
NSP-other
Spike
NSP2
Methyltransferase
vRNA

Target Product Profiles: https://www.niaid.nih.gov/research/target-product-profiles-antivirals

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Cross-cutting DMID programs play key roles in pandemic preparedness and response

Basic research and discovery

Target ID, pathogenesis, immune response

Non-clinical development

Lead Candidate and IND-Enabling

Early clinical development

Early Clinical Evaluation (Phase 1/2a)

Preclinical Services (PCS) Contracts

Early Clinical Phase Contracts

IDCRC

Investigator-initiated grants

Product Development/Public-Private Partnership Contracts

Systems Biology, Genomics, Bioinformatics

CETRs

BEI/WRCEVA

RBL/NBLs

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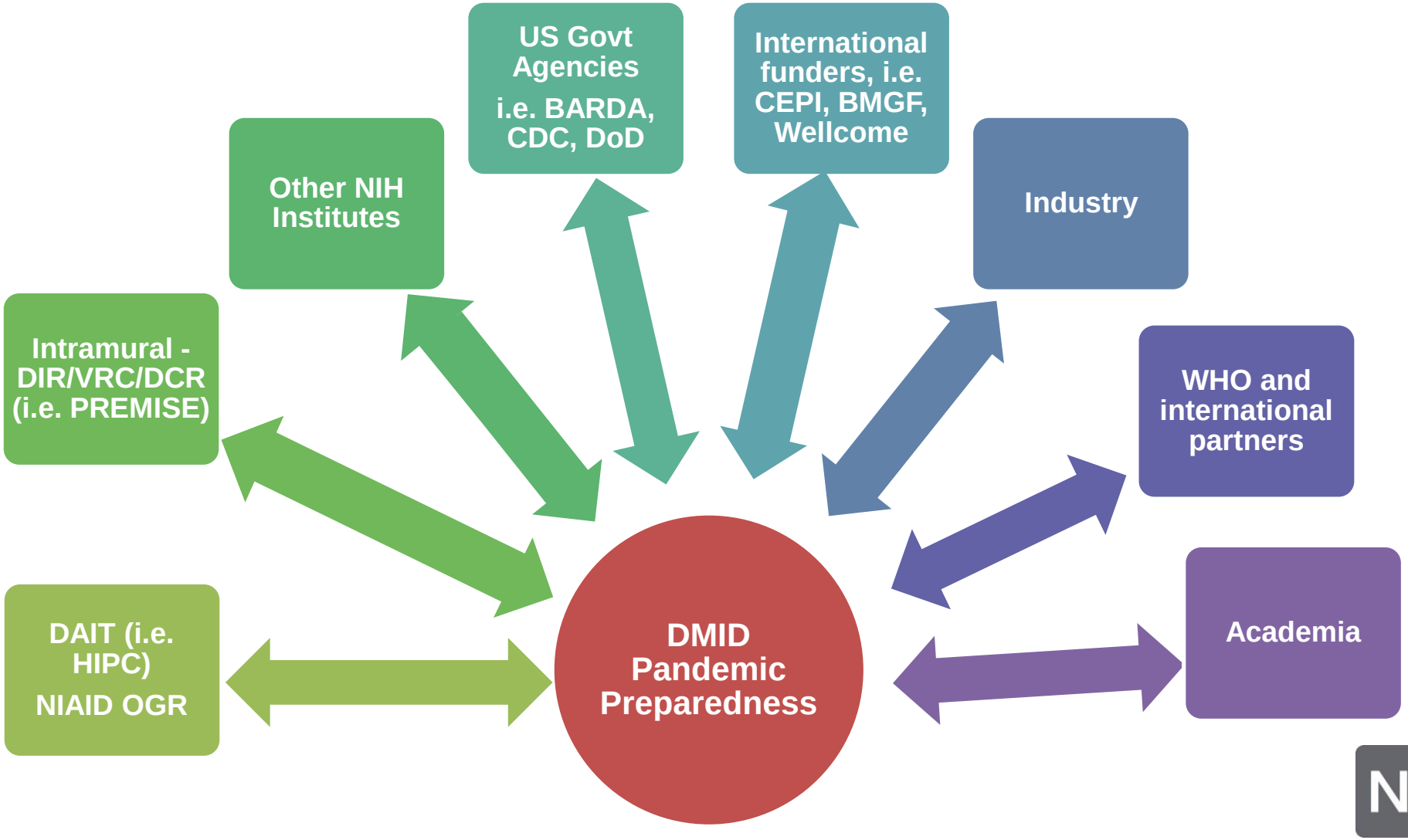
Collaborations with other Pandemic Preparedness Efforts



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Q&A

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