HOW COULD VACCINE RESEARCH FOR A PROTOTYPE PATHOGEN INFORM VACCINE DEVELOPMENT FOR RELATED PATHOGENS?

WHO CONSULTATION: CRITICAL RESEARCH FOR PRIORITY PATHOGENS WITH EPIDEMIC POTENTIAL

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Director of Pandemic Preparedness and Emergency Response
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To prepare for Emergencies and Pathogen X:

- Characterize known pathogens
- Bridge or eliminate existing gaps
- Shorten timelines
PROTOTYPE PATHOGEN APPROACH

120 viruses that infect humans

For each of 26 viral families:

- Understand viral characteristics
- Design vaccine and treatment candidates using structure-based design
- Manufacture vaccine
- Conduct clinical studies through Phase 1 (and 2)
- Transition to Pandemic Response with large-scale manufacturing and distribution
PROOF OF CONCEPT FOR INVESTMENT IN PROTOTYPE APPROACH: INVESTMENT IN BASIC RESEARCH WAS KEY TO DEVELOPING COVID-19 VACCINES

- **Early 2000s**
  - Optimal Structure of HIV-Env Determined

- **2013**
  - Structure of RSV Stabilized Pre-Fusion F Determined

- **2017**
  - Structure of Stabilized MERS-CoV Spike Protein Determined

- **2020**
  - Structure of Stabilized SARS-CoV-2 Spike (S2P) Protein Determined
### VIRAL FAMILIES — ARE WE PREPARED?

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<tr>
<th>PREPAREDNESS LEVEL</th>
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<td>Lacking at least one prototype with a candidate vaccine</td>
<td>1</td>
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### AVAILABILITY OF VACCINE

Karin Bok, Alan Embry, Cristina Cassetti, Barney Graham et al, NIAID/NIH
VACCINE DEVELOPMENT DECISION MAKING ROADMAP

- Antigenic Design
- Vaccine Platform
- Safety and Efficacy Considerations
- Development Pathway/Logistics
ANTIGENIC DESIGN

Proof of Concept (preclinical or clinical)
Feasibility of protection with selected target protein

Epitope Mapping
Key neutralizing epitopes
Antigenic Evolution considerations
Breadth and Durability of response
VACCINE PLATFORM

- **Extracellular or Intracellular Antigen delivery**
  - Antibody and/or cellular mediated protection

- **Humoral vs Mucosal Immunity**
  - Prevention of Severe Disease vs Infection/Spread

- **Prototype experience with a particular platform**
  - A vaccine is already approved/licensed for a prototype pathogen

- **Availability/Timeline for large scale manufacturing**
  - Facilities, Reagents, Consumables
SAFETY AND EFFICACY CONSIDERATIONS

Possibility of Enhanced Disease
Antigenic designs or adjuvants that objectively direct the immune response

Safety of delivery platform and adjuvant
Vaccine needs to target special populations (pregnancy or pediatrics)
Known risk of adverse events
Risk/benefit ratio

Epitopes with superior immunogenicity
Engineered epitopes
Delivery of epitopes
Innate immunity and T-Cell targeting
DEVELOPMENT PATHWAY/LOGISTICS

Regulatory considerations
- Viable and efficient licensure pathway
- CMC
- Biomarkers and Correlates of Protection research

Availability of delivery devices

Acceptance of vaccine
ADDITIONAL CONSIDERATIONS FOR PROTOTYPE RESEARCH BASED VACCINE DEVELOPMENT

- Animal Models
- Clinical Testing; endpoints definitions and solicited adverse events
- Assay Development; Diagnostics and Immunogenicity
- Process development might vary with change of antigen