Can we identify pathogens with future pandemic potential?

Scientific Strategies from Recent Outbreaks to Help Us Prepare for Pathogen X
WHO R&D Blueprint Consultation
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Zoonotic and Vector-borne Viral Threats

- Hanta virus
- Nipah/Hendra
- West Nile virus
- SARS
- Influenza
- Chikungunya
- Ebola
- MERS
- Zika
- EV-D68
- SARS-CoV-2
New Human Viral Pathogens in the 20th Century

EIDs are recognized primarily in HICs

Jone KE et al Nature 2008; 451:990
• ~75% of emerging viral diseases are zoonotic
• EIDs more frequently discovered in HICs, but EID event risk is higher in LMICs
Technology Advances Provide New Options for Pandemic Preparedness

Graham and Sullivan. Nature Immunology 2018
Prototype Pathogen Approach for Pandemic Preparedness

- ~120 viruses from 27 families known to infect humans with potential for increased human-to-human transmission and virulence
- Develop vaccines for ~30 prototype viruses through phase 1
- Develop vaccine candidates (& reagents) for other ~90 through animal testing

Graham & Sullivan.
Nature Immunology 2018
Prototype Pathogen Approach to Pandemic Preparedness

* A Large but Tractable Endeavor

For each viral family:

- **Detailed Knowledge of viral characteristics**
  - Natural immunity, correlates of protection, vaccine targets, atomic-level structures

- **Preclinical & clinical development of prototype vaccines**
  - Vaccine modalities; phase 1, 2 immunogenicity, dose, schedule

- **Manufacturing and Storage**
  - Platform engineering, formulation, scale, cold chain requirements
# Viral Families that Infect Humans (licensed vaccine exist)

<table>
<thead>
<tr>
<th>Family</th>
<th>Prototype(s)</th>
<th>Other Viruses of Concern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paramyxo</td>
<td>Nipah</td>
<td>Measles, Mumps, Hendra, Langya, Cedar, PIV1–PIV3</td>
</tr>
<tr>
<td>Matona</td>
<td>Rubella</td>
<td></td>
</tr>
<tr>
<td>Reo</td>
<td>Rotavirus</td>
<td>New rotaviruses, Banna virus, Nelson Bay orthoreoviruses</td>
</tr>
<tr>
<td>Orthomyxo</td>
<td>Influenza A</td>
<td>Multiple subtypes of influenza A, Dhori, Thogoto, Bourbon, Influenza B</td>
</tr>
<tr>
<td>Adeno</td>
<td>Adenovirus 4, 7</td>
<td>Adenovirus 14, 41, 81 or other serotypes</td>
</tr>
<tr>
<td>Corona</td>
<td>SARS-CoV-2</td>
<td>MERS, other SARS-like bat-derived viruses</td>
</tr>
<tr>
<td>Rhabdo</td>
<td>Rabies</td>
<td>VSV</td>
</tr>
<tr>
<td>Picorna</td>
<td>EV-D68</td>
<td>EV71, poliovirus serotype 1 &amp; 3, rhinoviruses, Ljungan</td>
</tr>
<tr>
<td>Papilloma</td>
<td>HPV 6, 11, 16, 18</td>
<td>Other HPV serotypes</td>
</tr>
<tr>
<td>Pox</td>
<td>Variola</td>
<td>Monkeypox</td>
</tr>
<tr>
<td>Pox</td>
<td>Variola</td>
<td></td>
</tr>
<tr>
<td>Hepadna</td>
<td>Hepatitis B</td>
<td></td>
</tr>
<tr>
<td>Herpes</td>
<td>Varicella</td>
<td>CMV, EBV, HSV-1, HSV-2, HHV-6, HHV-7, HHV-8</td>
</tr>
<tr>
<td>Flavi</td>
<td>Zika, HCV</td>
<td>Dengue, West Nile, St. Louis encephalitis, Powassan, Omsk hemorrhagic fever, Murray Valley encephalitis, Rocio encephalitis, Kyasanur forest, Alkhurma, Russian spring and summer encephalitis, Central European tick-borne encephalitis, Wesselsbron, Bussuquara, Cacipacore, Ilheus, Iguape, Usutu</td>
</tr>
<tr>
<td>Hepe</td>
<td>Hepatitis E</td>
<td></td>
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## Viral Families that Infect Humans (no licensed vaccine)

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<th>Prototype(s)</th>
<th>Other Viruses of Concern</th>
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</thead>
<tbody>
<tr>
<td>Pneumo</td>
<td>RSV, hMPV</td>
<td></td>
</tr>
<tr>
<td>Filo</td>
<td>Ebola, Marburg</td>
<td></td>
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<tr>
<td>Retro</td>
<td>HIV-1, HTLV-1</td>
<td></td>
</tr>
<tr>
<td>Parvo</td>
<td>B19, Bocavirus</td>
<td></td>
</tr>
<tr>
<td>Calici</td>
<td>Norovirus</td>
<td></td>
</tr>
<tr>
<td>Polyoma</td>
<td>JC, BK, SV40, Merkel cell</td>
<td></td>
</tr>
<tr>
<td>Toga (alpha)</td>
<td>Chikungunya</td>
<td>Western equine encephalitis, Eastern equine encephalitis, Venezuelan equine encephalitis, Mayaro, Ross River, Barmah Forest, O'nyong'nyong, Semiliki Forest, Getah, Sindbis</td>
</tr>
<tr>
<td>Arena</td>
<td>Lassa, Machupo, Junin, Guanarito, Chapare, Sabia, Flexal, lymphocytic choriomeningitis, Lujo</td>
<td></td>
</tr>
<tr>
<td>Hanta</td>
<td>Sin Nombre, Hantaan, Andes, Seoul, Dobrava-Belgrade, Puumala,</td>
<td></td>
</tr>
<tr>
<td>Nairo</td>
<td>Sin Nombre, Hantaan, Andes, Seoul, Dobrava-Belgrade, Puumala,</td>
<td></td>
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<tr>
<td>Peribunya</td>
<td>Bunyavera</td>
<td>La Crosse, Oropouche, California encephalitis, Batai, Tahyna, Cache Valley, Jamestown Canyon, Snowshoe hare</td>
</tr>
<tr>
<td>Phenui</td>
<td>RVF, SFTS, Phlebovirus Toscana, Heartland, Bhanja Bandaviruses</td>
<td></td>
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<tr>
<td>Astro</td>
<td>Astrovirus</td>
<td></td>
</tr>
<tr>
<td>Arteri</td>
<td>Simian hemorrhagic fever (Not yet reported to infect humans)</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Graham & Sullivan. Nature Immunology 2018
What I Worry About the Most

• Pandemic Influenza
• Paramyxoviruses
  • Morbillavirus (Rhinderpest-like)
  • Henipavirus (Nipah-like)
• Bunyavirus converted from vector-borne to respiratory spread (Plague-like)
• Virus with delayed symptom onset (Retroviruses, Polyomaviruses, Herpesviruses)
• New virus family with zoonotic then human-to-human spread (Arteriviruses)
• Expansion of vector geographic range (Flaviviruses and Alphaviruses)
• Not being ready for things that have effective approved medical countermeasures on the shelf (e.g. Monkeypox)
Mosaic multiple full-length HA subtypes on custom designed icosahedral nanoparticles

mRNA delivery of full-length HA or HA ectodomain on ferritin

Group 1/2 headless HA stem trimer on ferritin

Pandemic response

Pandemic preparedness

Supraseasonal
Readiness for COVID-19 and its Consequences

- HIV-1 vaccine development
- Precision vaccinology including structure-based vaccine design and protein engineering for RSV and CoV
- Human monoclonal antibody discovery
- Pre-existing public-private and academic partnerships
- RSV vaccine-enhanced disease pathogenesis
- Prior responses to PHEIC and interagency coordination
- Platform manufacturing technologies – DNA, vectors
- Prototype Pathogen Approach for Pandemic Preparedness and Response
- Novel Vaccine Technologies Essential Components of an Adequate Response to Emerging Viral Diseases
- Human monoclonal antibody discovery
- Emerging viral diseases from a vaccinology perspective: preparing for the next pandemic

Be Part of the Solution