Collaborative basic research to study viral structures for vaccines development

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01/19/2024
Improved pandemic preparedness could be achieved by proactively managing emerging virus threats focused on four discreet activities using currently available tools:

- Discovery and Surveillance
- Targeted Basic Research
- Translational Research and Product Development
- Clinical Trial Infrastructure and Deployment Capacity

Adapted from the World Health Organization Website
Integrated pipeline for Response to Pathogen X

- Discovery and Surveillance
- Targeted Basic Research
- Translational Research and Product Development
- Clinical Trial Infrastructure and Deployment Capacity
Structural biology in understanding a virus and in vaccine development

Antibody epitope visualization

Complete Structural Characterization of the HIV-1 glycan-V3 targeting DH270 broadly neutralizing antibody lineage

Details of protein structure and dynamics

Vaccine immunogen design
The power of structural surveillance: SARS-CoV-2 as a case study

Structural Biology provides unique information on viral antigen conformation

Phylogenetic tree generated from GISAID.
All pre-Omicron variants preferred spike conformation that maximized receptor interaction and enabled transmissibility

Omicron prefers spike conformation that maximizes immune evasion

Information from structure of viral antigens can help predict the course of an epidemic while informing a response in the form of a vaccine or a therapeutic
**Structure-guided sequence surveillance predicted structures of emerging variants**

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| RBD |
|-----|-------|-----|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| D614G | D | R | L | F | P | F | T | D | R | N | K | V | S | L | F | N | K | A | F | F | S | R | Y | H |
| BA.1 | D | R | L | F | P | F | T | D | R | N | K | V | G | L | F | N | K | A | F | F | S | R | Y | H |
| BA.5 | D | R | L | F | P | F | T | D | R | N | K | V | G | L | F | N | K | A | F | F | S | R | Y | H |
| XBB.1.5 | H | T | I | F | P | F | A | N | S | N | K | P | S | L | F | K | N | R | A | P | S | Q | G | R | Y | H |
| XBB.1.6 | H | T | I | F | P | F | A | N | S | N | K | P | S | L | F | K | N | R | A | P | S | Q | G | R | Y | H |
| EG.5 | H | T | I | F | P | F | A | N | S | N | K | P | S | L | F | K | N | R | A | P | S | Q | G | R | Y | H |

- Ubiquitous mutation
- Shared mutation
- Unique BA mutation
- Unique XBB/EG.5 mutation
- Unique mutation
- ACE2 binding interface
- * inter-down-down RBDs
- ^ inter-down-up RBDs

**AI-enabled structural analysis to further bridge between structure and sequence**
What priority research should be triggered immediately after the declaration of a pandemic?

- Sequence surveillance
- Population level sequence surveillance (for example, wastewater)
- Immune surveillance
- Structural surveillance
  - Expedite structural research.
  - Leverage existing knowledge on related viruses: we may know more than we think we do.
  - AI-enabled structural biology.
  - Facilitate cross-talk between different arms of a required response.