Identifying antigens from contemporary viral isolates that are well characterized: scientific challenges

Dr. Sebastian Maurer-Stroh

GISAID Data Science Centre

GISAID – Empowering Rapid Responses to Disease X

2009

H1N1 pandemic
- <36hrs collection to data
- Diagnostics development

2013

H7N9 influenza epidemic
- <48hrs collection to data
- Diagnostics and mRNA vaccine development

2020

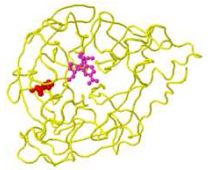
COVID-19 pandemic
- <36hrs collection to data
- Diagnostics and mRNA vaccine development

20??

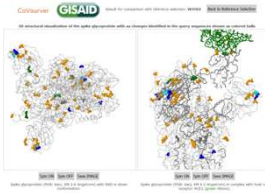
EpiX for Disease X
- Ready for Disease X

2008
Launch of GISAID and EpiFlu™

2013-2019
Integration of tools for Influenza



2020-2021
Launch of EpiCoV™ and EpiRSV™
Expansion of tools
Creation of live dashboards



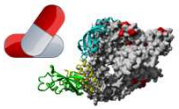
2022-2023
Launch of EpiPox™ and EpiArbo™ (Dengue, Zika, Chikungunya) and tools

Genome Use for First Response – Same for Any Disease X

- How can you detect it?

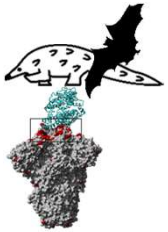
Enabling first PCR and antigen-based diagnostic kits

- How can you treat it?



Repurposed and new drugs, e.g. small molecule, mAbs, **Vaccine candidates**

- Where did it come from?

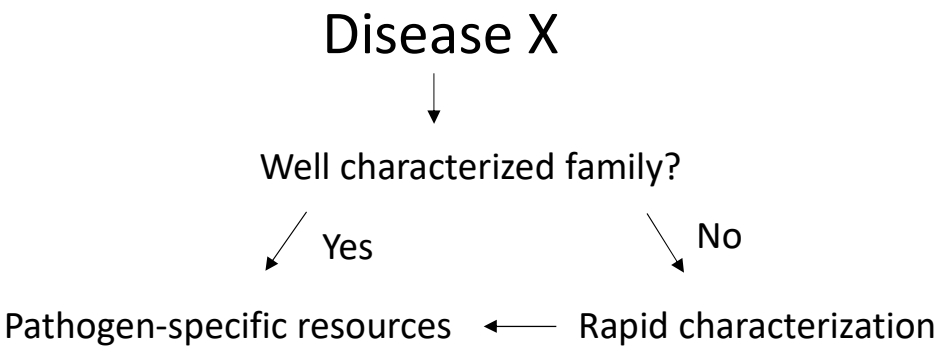


Point to likely source, understanding animal to human jump

Who needs this info?

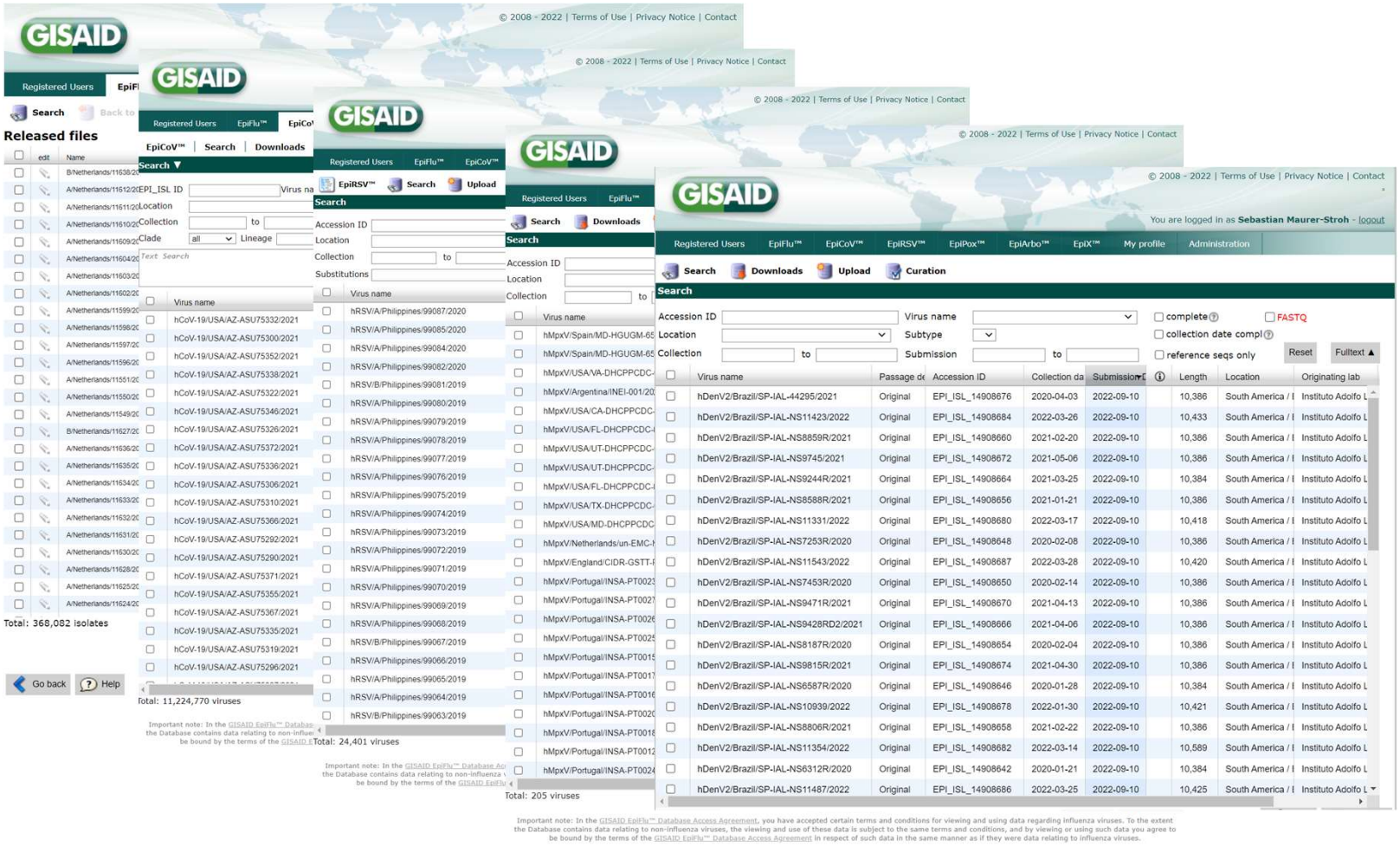
- State and national public health authorities and
- International health agencies e.g., WHO, FAO, WOAH
- Vaccine, Diagnostics, Treatment Manufacturers

Facilitating surveillance from the onset of an outbreak



GISAID EpiFlu™ | EpiCoV™ | EpiRSV™ | EpiPox™ | EpiArbo™ | **EpiX™**

Supporting other priority pathogens



EpiArbo™

Dengue
Zika
Chikungunya

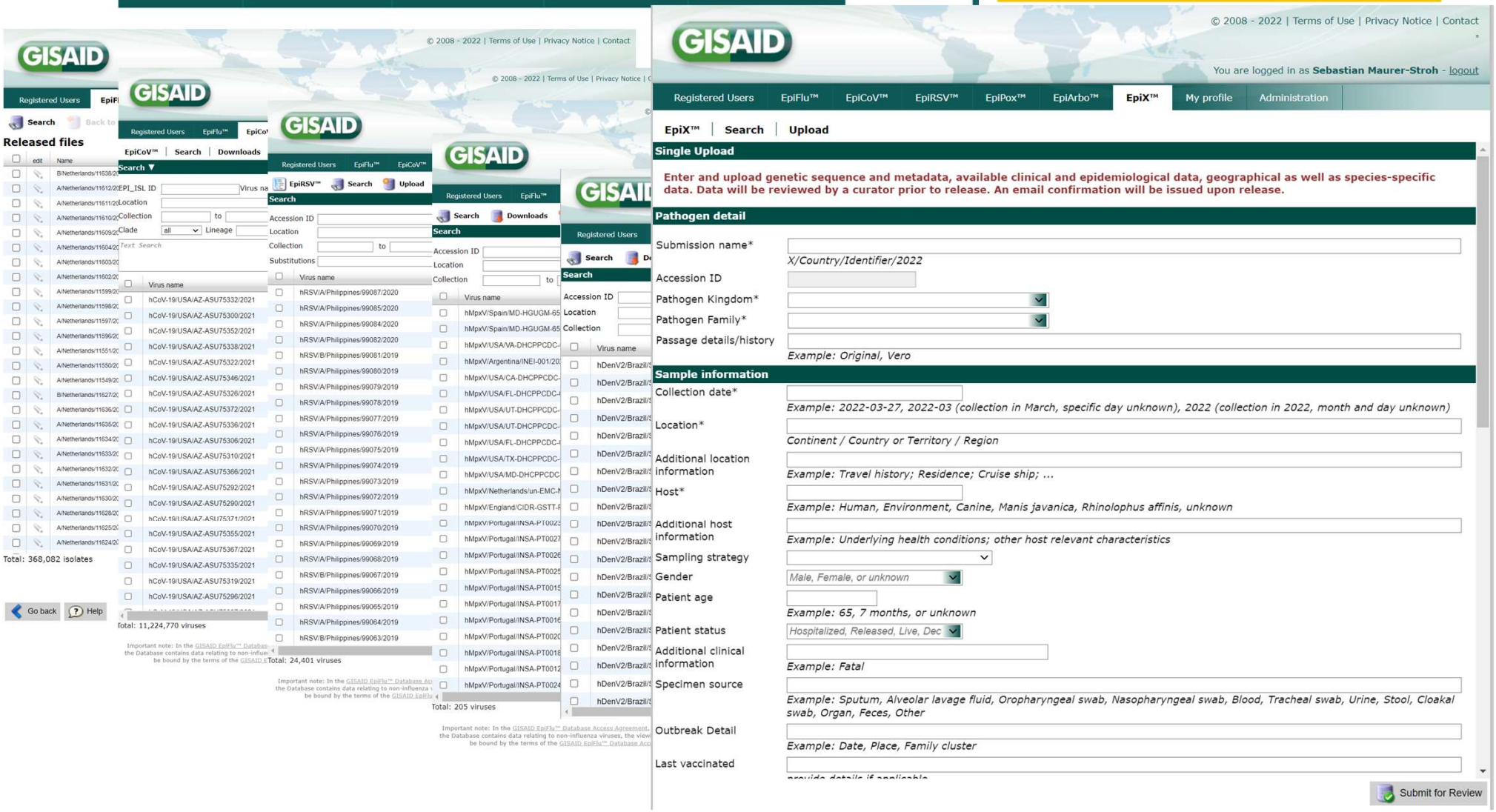
>86 new countries contributing (since August 2023)

Wallau GL; Global Arbovirus Researchers United. Lancet Glob Health. 2023 Oct;11(10):e1501-e1502.

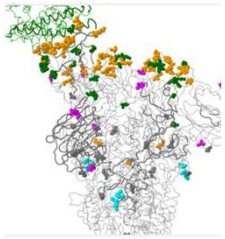
GISAID

EpiFlu™ | EpiCoV™ | EpiRSV™ | EpiPox™ | EpiArbo™ | **EpiX™**

Rapid Actionable Data of Disease X



Identifying antigens from prototype references



Disease X

↓

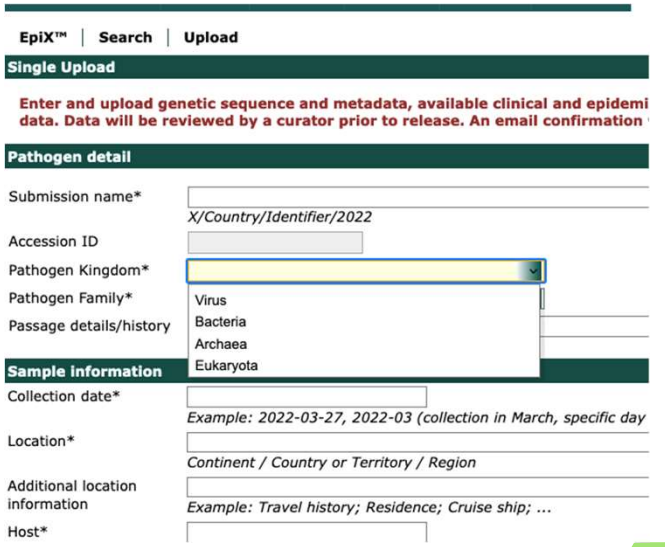
Well characterized family?

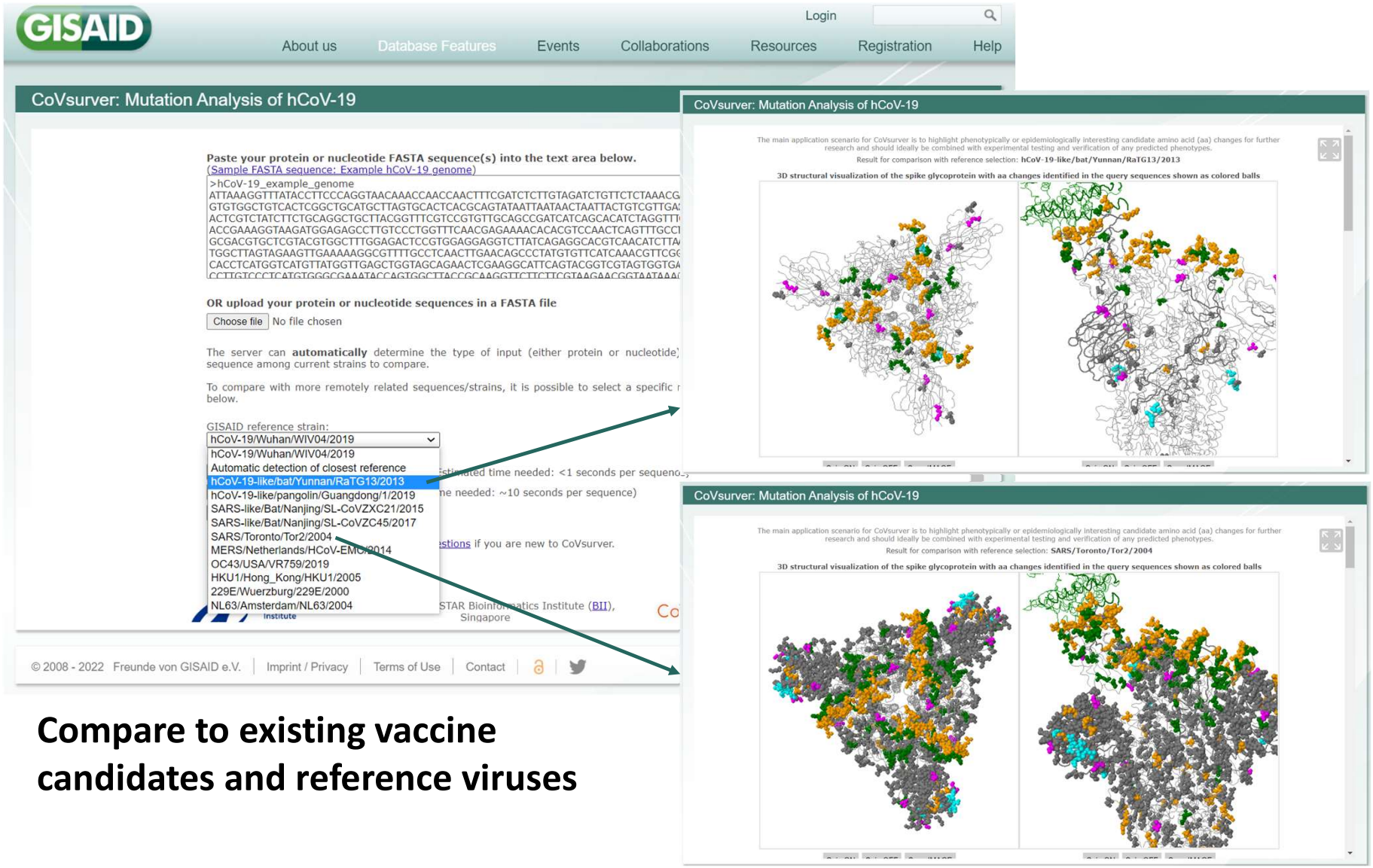
↙ Yes　　No ↘

Pathogen-specific resources ← Rapid characterization

↓

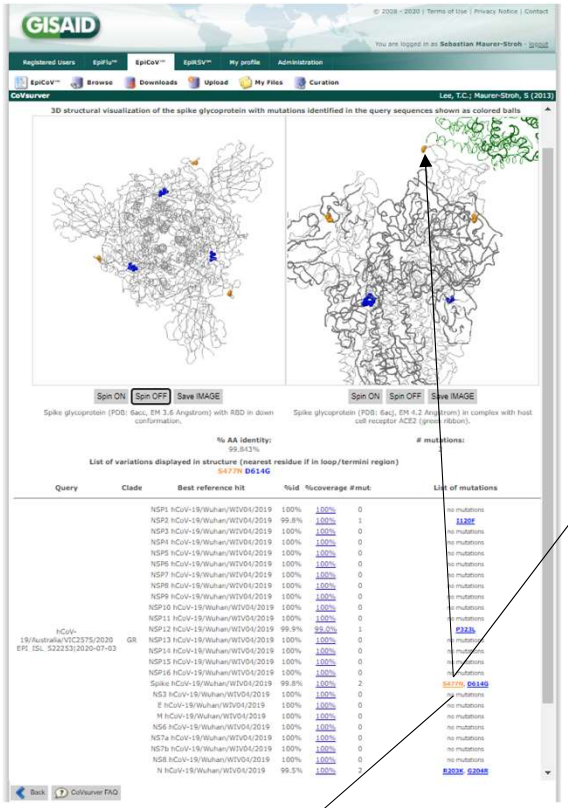
Compare to existing vaccine candidates and reference viruses

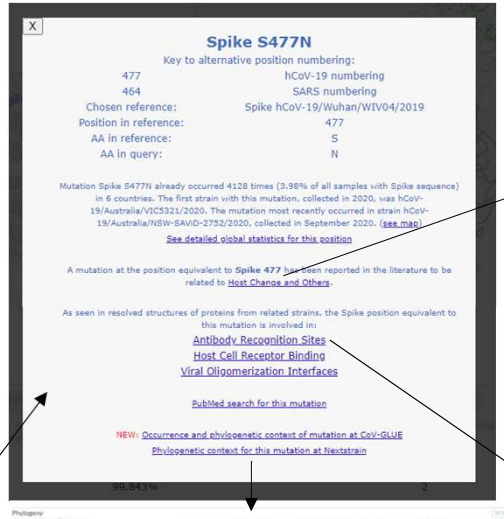


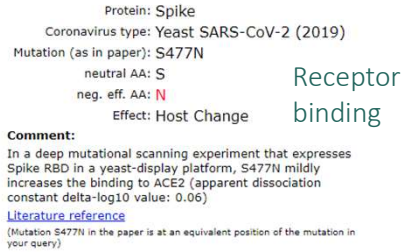


Compare to existing vaccine candidates and reference viruses

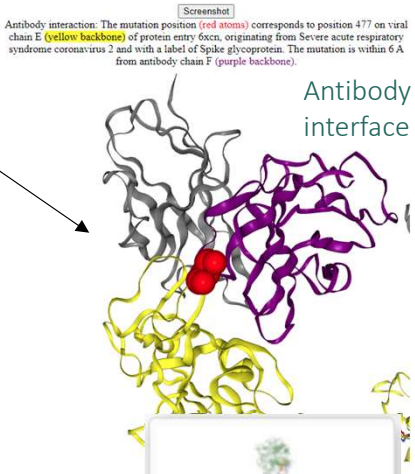
Real-time surveillance for mutations that can affect antigenic changes



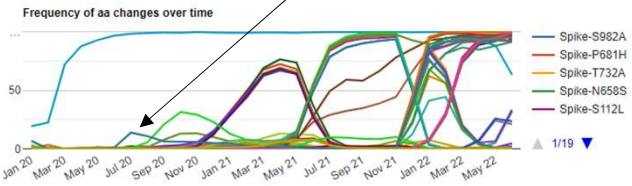


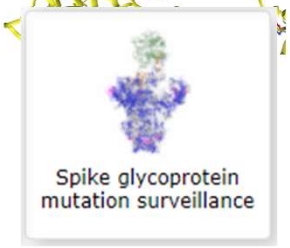


Receptor binding



Antibody interface





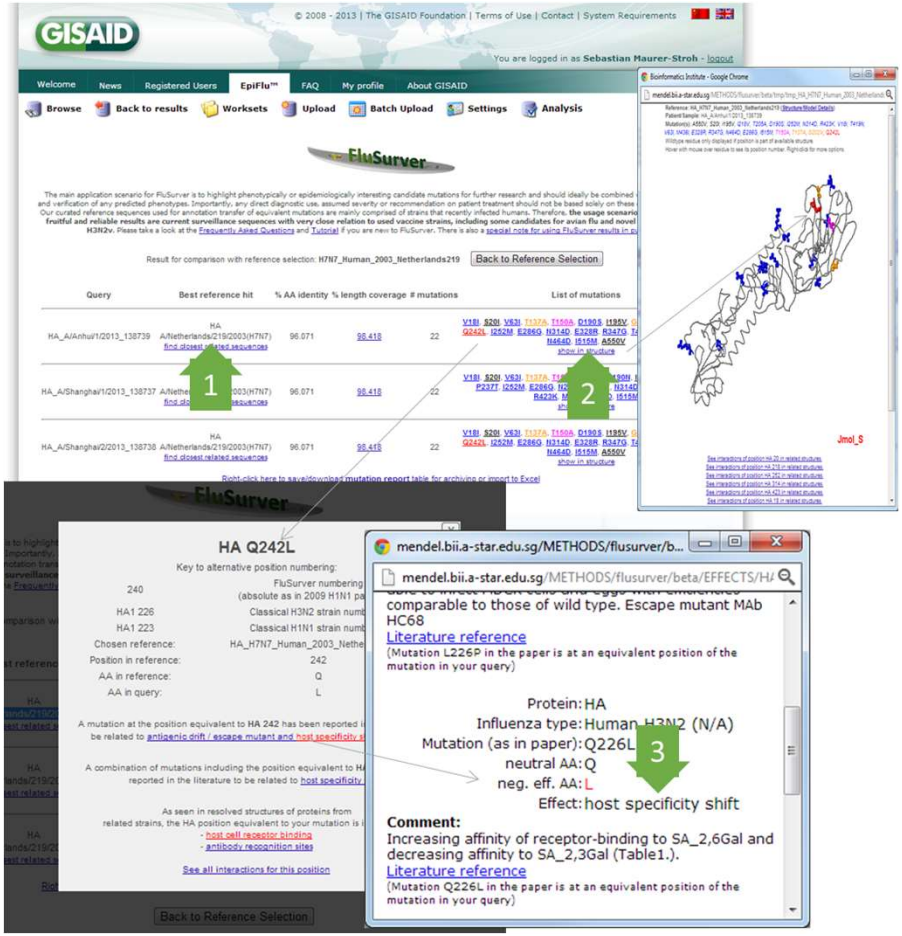
Literature-curated mutation effect database
>2,230 entries

drug resistance	7
virulence	23
antigenic drift / escape mutant	1,336
host specificity change/shift	369
Other (enzyme activity, affects protein accumulation/ stability/function)	496

3D structure interaction mutation position database
>3,800 entries

self/oligomerization	2,686
small ligand	497
antibody	356
host protein	241
host cell receptor	46

Compare to existing vaccine candidates and reference viruses



H7N9 (2013) first analysis highlighted Q226L host specificity role automatically

A/Indiana/10/2011(H3N2v) - swine-origin H3N2 with M segment from human H1N1pdm - vaccine candidate
A/Equine/Miami/1/1963(H3N8)
A/Equine/Sussex/1/1989(H3N8)
A/Equine/Kentucky/1/1992(H3N8)
A/Duck/HongKong/24/1976(H4N2)
A/Duck/EasternChina/108/2008(H5N1)
A/Goose/Guangdong/1/1996(H5N1)
A/VietNam/1203/2004(H5N1) - clade 1 avian-origin H5N1 - vaccine candidate
A/Anhui/1/2005(H5N1)
A/Indonesia/5/2005(H5N1) - clade 2.1.3.2 avian-origin H5N1 - vaccine candidate
A/Egypt/1394-NAMRU3/2007(H5N1) - clade 2.2.1v - vaccine candidate
A/Egypt/2321-NAMRU3/2007(H5N1) - clade 2.2.1p - old poultry vaccine strain
A/Hubei/1/2010(H5N1) - clade 2.3.2.1 avian-origin H5N1 - vaccine candidate
A/Chicken/BCFAV8//2014(H5N2)
A/Sichuan/26221/2014(H5N6) - novel avian flu with rare zoonosis
A/Baikalteal/Korea/Donglim3/2014(H5N8) - novel avian flu 2014
A/Duck/Taiwan/0526/1972(H6N1)
A/Taiwan/2/2013(H6N1)
A/Canada/RV504/2004(H7N3) - avian flu with rare zoonosis - North American lineage
A/Netherlands/219/2003(H7N7) - avian flu with rare zoonosis - Eurasian lineage

H7N9 in 2013 was another “test” for a Disease X and enabling to quickly connect and check against reference viruses allows to identify related vaccine antigens

Facilitating antigenic surveillance from genomic data

Disease X

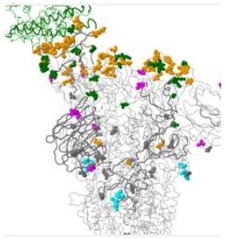
↓

Well characterized family?

↙ Yes No ↘

Pathogen-specific resources ← Rapid characterization

↓



Compare to existing vaccine candidates and reference viruses

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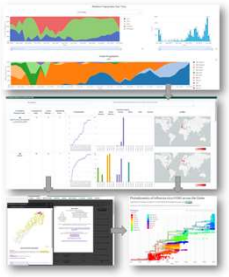
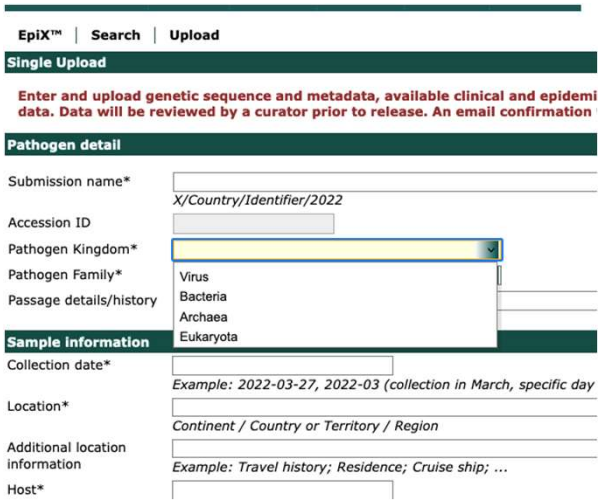


Monitor diversity and evolution of the virus



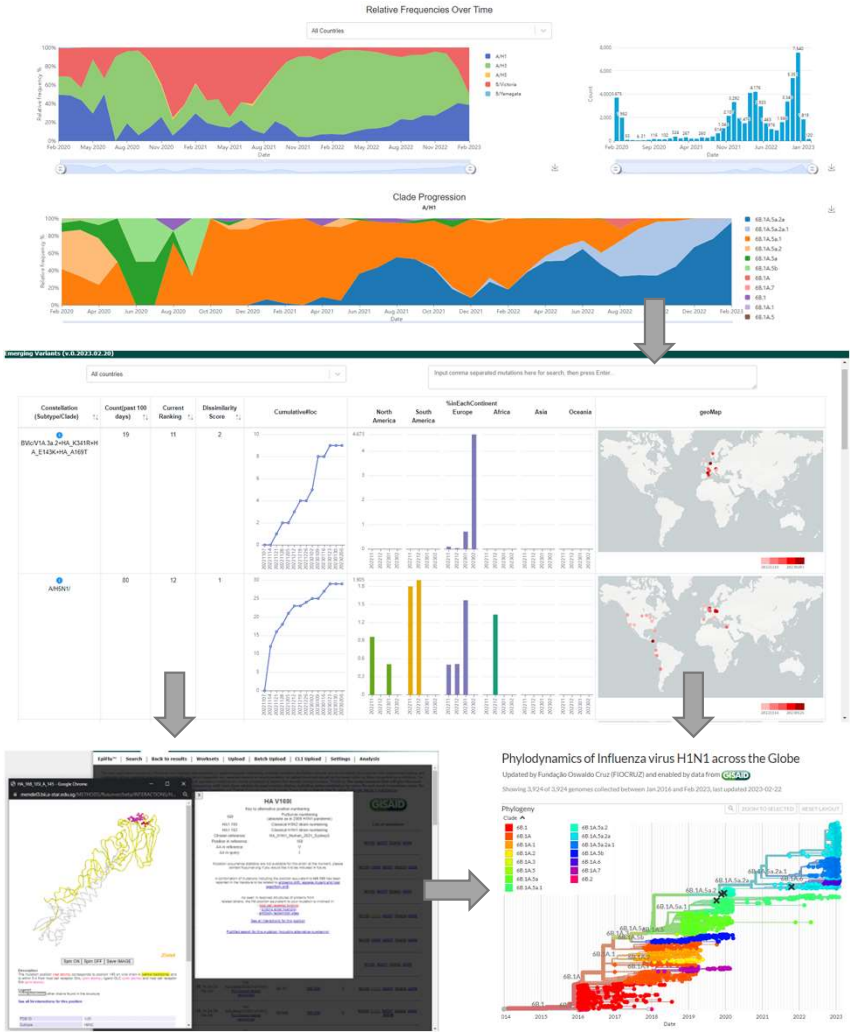
An ecosystem of integrated tools supporting scale-free view of virus evolution

Subtype

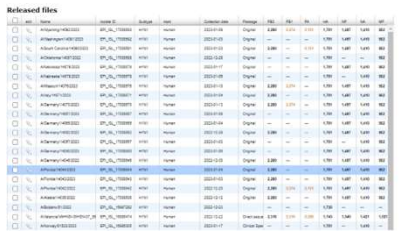
Clade

Emerging Variant
(unique set of mutations)

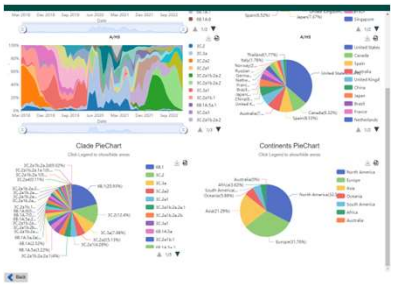
Individual
mutation



Single
entry
detail



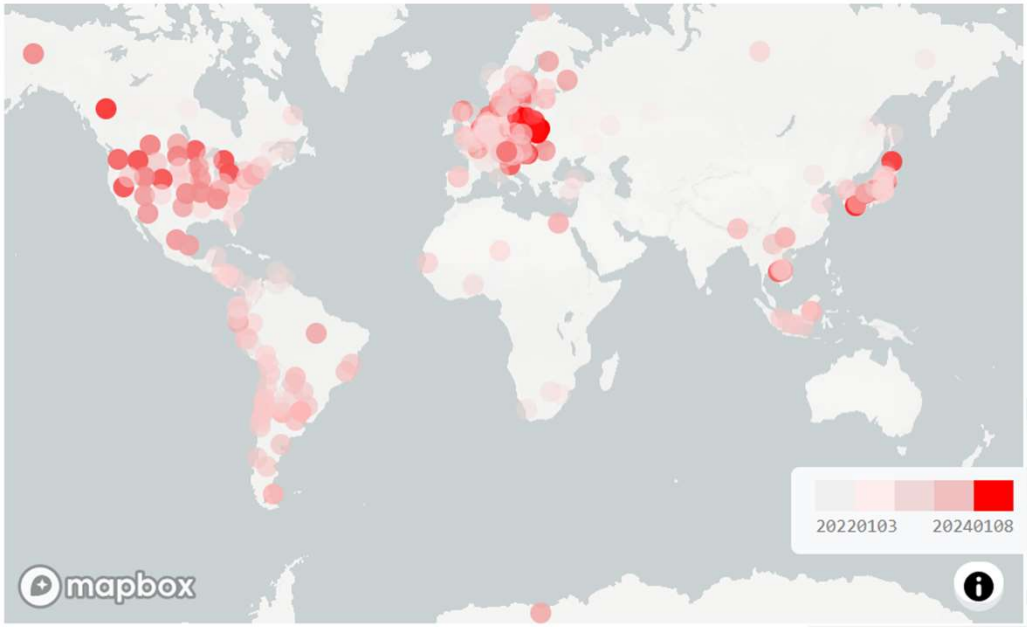
Set of
entries in
the database



Set of
entries
graphical
summary

Oversight of lineage distribution enables decisions making

H5N1 major lineage distribution 2022-2024



2.3.4.4b

2.3.2.1c

Facilitating antigen identification through genomic surveillance

Disease X

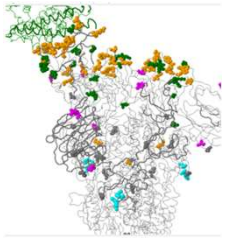
Well characterized family?

Yes

No

Pathogen-specific resources

Rapid characterization



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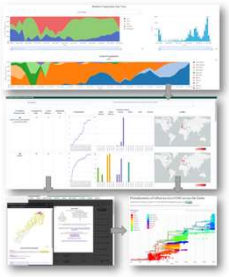
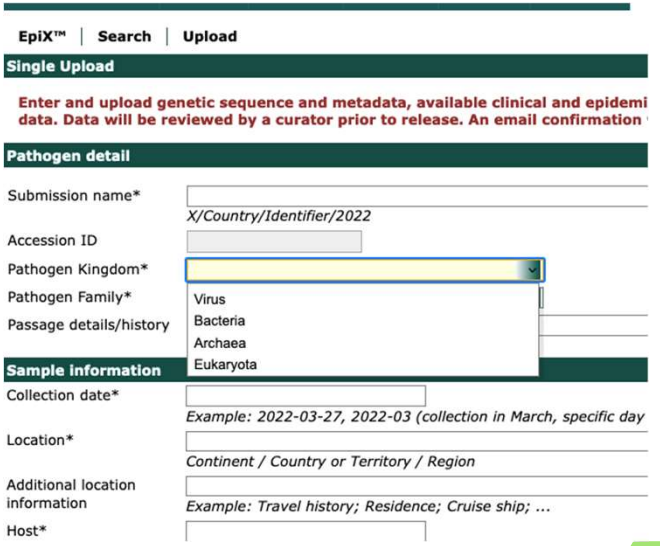
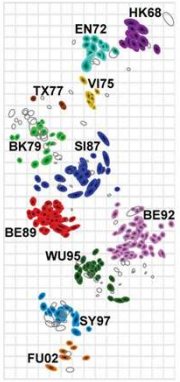


Monitor diversity and evolution of the virus

Iteration between computational prediction and experimental verification

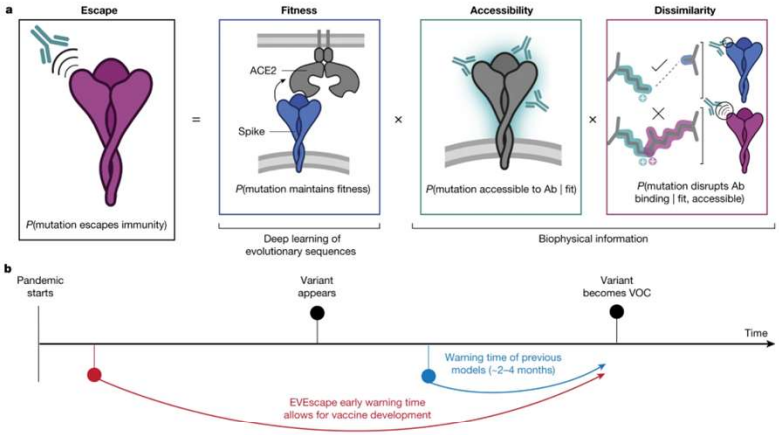




Learning from prepandemic data to forecast viral escape

Nicole N. Thadani, Sarah Gurev, Pascal Notin, Noor Youssef, Nathan J. Rollins, Daniel Ritter, Chris Sander, Yarin Gal & Debora S. Marks

Nature **622**, 818–825 (2023) | Cite this article

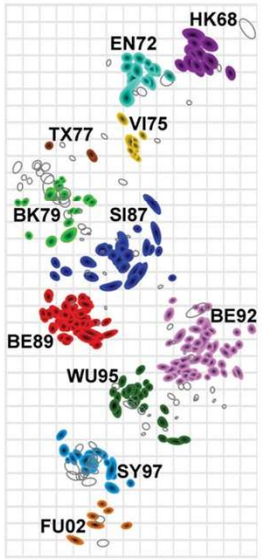


a, EVEscape assesses the likelihood of a mutation escaping the immune response on the basis of the probabilities of a given mutation maintaining viral fitness, occurring in an antibody epitope and disrupting antibody binding. **b**, EVEscape requires only information available early in a pandemic, before surveillance sequencing, antibody–antigen structures or experimental mutational scans are broadly available. This provides further early warning time critical for vaccine development. Ab, antibody. Panel **a** created with BioRender.com.

Mapping the Antigenic and Genetic Evolution of Influenza Virus

DEREK J. SMITH , ALAN S. LAPEDES, JAN C. DE JONG, THEO M. BESTEBROER, GUUS F. RIMMELZWAAN, ALBERT D. M. E. OSTERHAUS, AND RON A. M. FOUCHIER Authors Info & Affiliations

SCIENCE • 16 Jul 2004 • Vol 305, Issue 5682 • pp. 371-376 • DOI: 10.1126/science.1097211



GISAID - Facilitating step-wise approach in antigen identification

Disease X

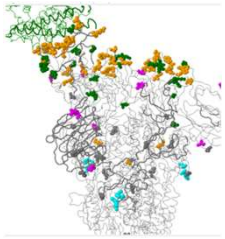
Well characterized family?

Yes

No

Pathogen-specific resources

Rapid characterization



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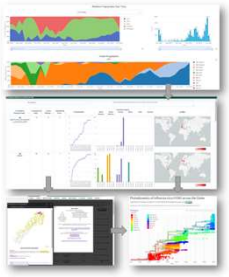

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