

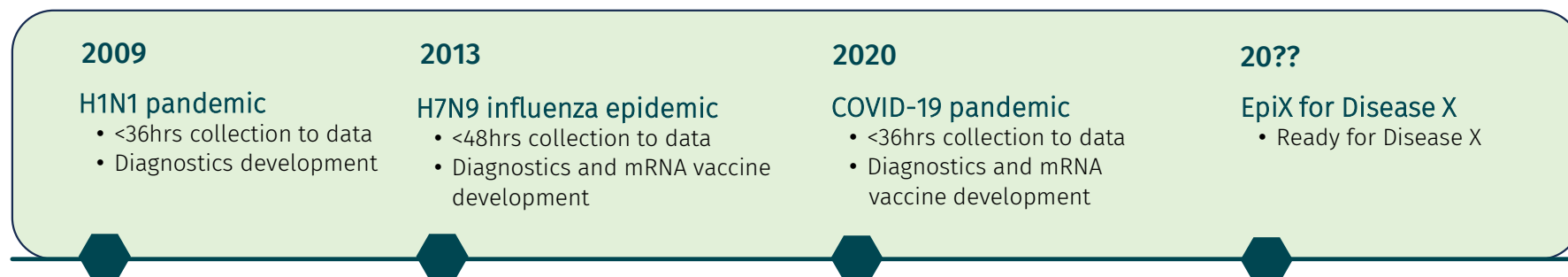
Identifying antigens from contemporary viral isolates
that are well characterized: scientific challenges

Dr. Sebastian Maurer-Stroh

GISAID Data Science Centre

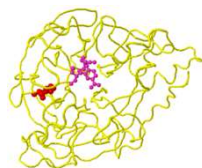


GISAID – Empowering Rapid Responses to Disease X

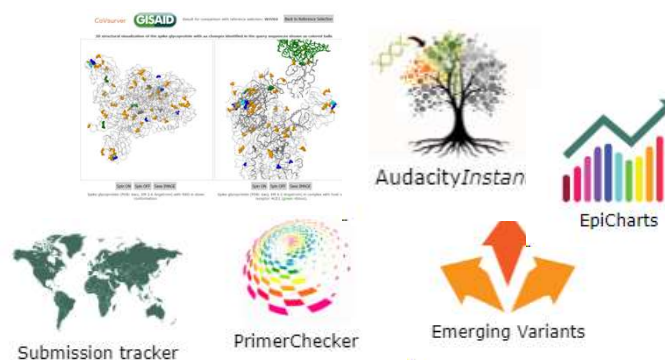


2008
Launch of GISAID and EpiFlu™

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

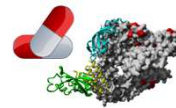
Genome Use for First Response – Same for Any **Disease X**

- How can you detect it?



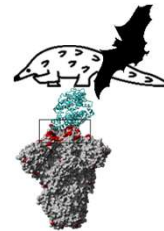
Enabling first PCR
and antigen-based
diagnostic kits

- How can you treat it?



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

- Where did it come from?

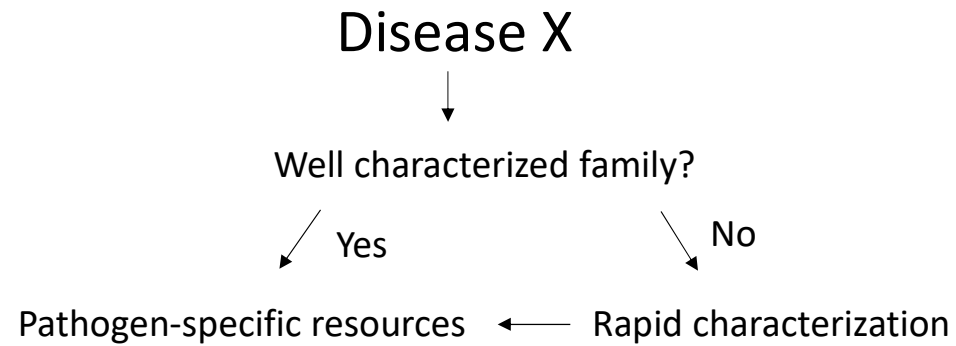


Point to likely source,
understanding animal
to human jump

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



[illegible]

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

GISAID © 2008 - 2022 | Terms of Use | Privacy Notice | Contact

Registered Users EpiFlu™ EpiCoV™ EpiRSV™ EpiPox™ EpiArbo™ EpiX™

Search Back to

Released files

EpiCoV™ Search Downloads

Search Accession ID Location Collection Substitutions

Virus name

hCoV-19/USA/AZ-ASU75332/2021
hCoV-19/USA/AZ-ASU75300/2021
hCoV-19/USA/AZ-ASU75352/2021
hCoV-19/USA/AZ-ASU75338/2021
hCoV-19/USA/AZ-ASU75322/2021
hCoV-19/USA/AZ-ASU75346/2021
hCoV-19/USA/AZ-ASU75326/2021
hCoV-19/USA/AZ-ASU75372/2021
hCoV-19/USA/AZ-ASU75336/2021
hCoV-19/USA/AZ-ASU75306/2021
hCoV-19/USA/AZ-ASU75310/2021
hCoV-19/USA/AZ-ASU75366/2021
hCoV-19/USA/AZ-ASU75292/2021
hCoV-19/USA/AZ-ASU75290/2021
hCoV-19/USA/AZ-ASU75355/2021
hCoV-19/USA/AZ-ASU75367/2021
hCoV-19/USA/AZ-ASU75335/2021
hCoV-19/USA/AZ-ASU75319/2021
hCoV-19/USA/AZ-ASU75296/2021

Total: 368,082 isolates

Go back Help

Important note: In the GISAID EpiFlu™ Database, the Database contains data relating to non-influenza viruses, the view is bound by the terms of the GISAID EpiFlu™ Database Access Agreement.

Total: 24,401 viruses

Important note: In the GISAID EpiFlu™ Database, the Database contains data relating to non-influenza viruses, the view is bound by the terms of the GISAID EpiFlu™ Database Access Agreement.

Total: 205 viruses

GISAID © 2008 - 2022 | Terms of Use | Privacy Notice | Contact

You are logged in as Sebastian Maurer-Stroh - logout

Registered Users EpiFlu™ EpiCoV™ EpiRSV™ EpiPox™ EpiArbo™ EpiX™ My profile Administration

EpiX™ Search Upload

Single Upload

Enter and upload genetic sequence and metadata, available clinical and epidemiological data, geographical as well as species-specific data. Data will be reviewed by a curator prior to release. An email confirmation will be issued upon release.

Pathogen detail

Submission name*
X/Country/Identifier/2022

Accession ID

Pathogen Kingdom*
Pathogen Family*

Passage details/history
Example: Original, Vero

Sample information

Collection date*
Example: 2022-03-27, 2022-03 (collection in March, specific day unknown), 2022 (collection in 2022, month and day unknown)

Location*
Continent / Country or Territory / Region

Additional location information
Example: Travel history; Residence; Cruise ship; ...

Host*
Example: Human, Environment, Canine, Manis javanica, Rhinolophus affinis, unknown

Additional host information
Example: Underlying health conditions; other host relevant characteristics

Sampling strategy

Gender
Male, Female, or unknown

Patient age
Example: 65, 7 months, or unknown

Patient status
Hospitalized, Released, Live, Dec

Additional clinical information
Example: Fatal

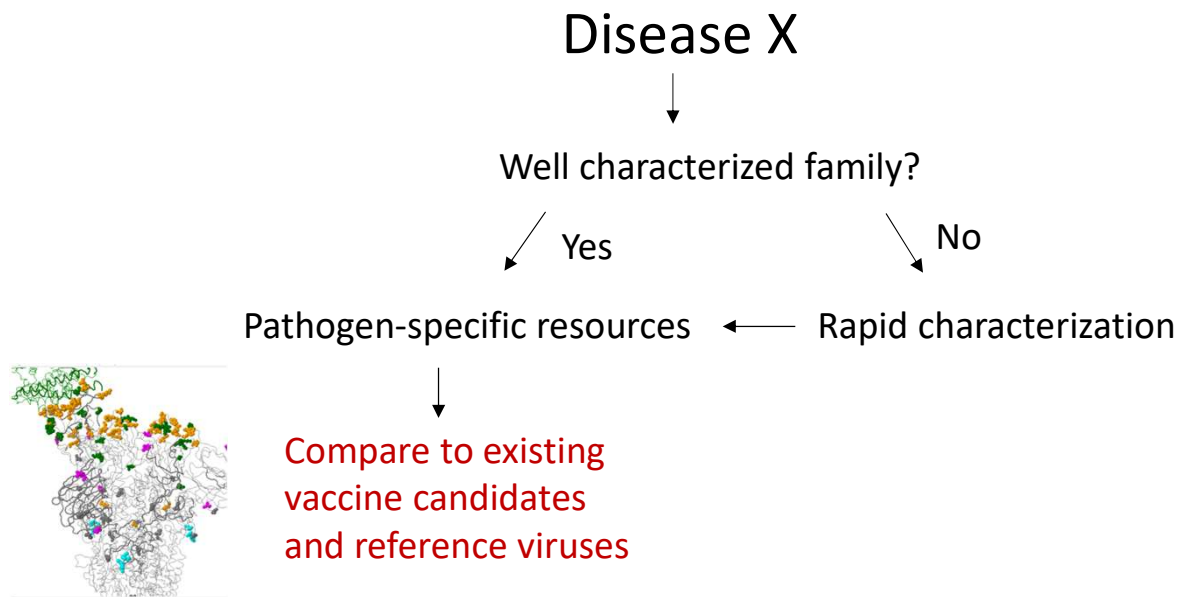
Specimen source
Example: Sputum, Alveolar lavage fluid, Oropharyngeal swab, Nasopharyngeal swab, Blood, Tracheal swab, Urine, Stool, Cloacal swab, Organ, Feces, Other

Outbreak Detail

Last vaccinated
provide details if applicable

Submit for Review

Identifying antigens from prototype references



EpiX™ Search Upload	
Single Upload	
Enter and upload genetic sequence and metadata, available clinical and epidemiological data. Data will be reviewed by a curator prior to release. An email confirmation will be sent to the user.	
Pathogen detail	
Submission name*	<input type="text" value="X/Country/Identifier/2022"/>
Accession ID	<input type="text"/>
Pathogen Kingdom*	<input type="text" value="Virus"/>
Pathogen Family*	<input type="text" value="Bacteria"/>
Passage details/history	<input type="text" value="Archaea"/>
Sample information	
Collection date*	<input type="text" value="Example: 2022-03-27, 2022-03 (collection in March, specific day)"/>
Location*	<input type="text" value="Continent / Country or Territory / Region"/>
Additional location information	<input type="text" value="Example: Travel history; Residence; Cruise ship; ..."/>
Host*	<input type="text"/>

GISAID Login

About us Database Features Events Collaborations Resources Registration Help

CoVsurver: Mutation Analysis of hCoV-19

Paste your protein or nucleotide FASTA sequence(s) into the text area below.
(Sample FASTA sequence: Example hCoV-19 genome)

```
>hCoV-19_example_genome
ATTAAAGGTTTATACCTTCCAGGTAACAAACCAACCACTTTCGATCTCTGTAGATCTGTTCTCTAAACG
GTGTGGCTGTCACCTCGGCTGCATGCTTAGTGCACTCACGCAGTATAATTAATACTACTGTCGTTGA
ACTCGTCTATCTTCTGCAGGCTGCTTACGGTTTTCGTCCTGTTGCAGCCGATCATCAGCACATCTAGGTT
ACCGAAGGTAAGTGGAGAGCCTTGTCCCTGGTTTCAACGAGAAACACACGTCACACTCAGTTTGCCI
GCGACGTGCTCGTACGTGGCTTTGGAGACTCCGTGGAGGAGGCTTATCAGAGGCACGTCAACATCTTA
TGGCTTAGTAGAAGTTGAAAAAGGCGTTTGCCTCAACTGAACAGCCCTATGTGTTTCATCAACGTTTCG
CACCTCATGGTCATGTTATGTTGAGCTGTGAGCAGAACTCGAAGGCATTAGTACGGTCGTAGTGGTGA
CTTGTCTCTCATGTGGGGCAATACCACTGGCTTACCGCAAGGTTCTCTTCGTAAGAACGGTAATAAA
```

OR upload your protein or nucleotide sequences in a FASTA file
Choose file No file chosen

The server can **automatically** determine the type of input (either protein or nucleotide) sequence among current strains to compare.

To compare with more remotely related sequences/strains, it is possible to select a specific reference strain below.

GISAID reference strain:

- hCoV-19/Wuhan/WIV04/2019
- hCoV-19/Wuhan/WIV04/2019
- Automatic detection of closest reference
- hCoV-19-like/bat/Yunnan/RaTG13/2013**
- hCoV-19-like/pangolin/Guangdong/1/2019
- SARS-like/Bat/Nanjing/SL-CoVZXC21/2015
- SARS-like/Bat/Nanjing/SL-CoVZC45/2017
- SARS/Toronto/Tor2/2004
- MERS/Netherlands/HCoV-EMC/2014
- OC43/USA/VR759/2019
- HKU1/Hong_Kong/HKU1/2005
- 229E/Wuerzburg/229E/2000
- NL63/Amsterdam/NL63/2004

Estimated time needed: <1 seconds per sequence
Estimated time needed: ~10 seconds per sequence

Questions if you are new to CoVsurver.

STAR Bioinformatics Institute (BII), Singapore

© 2008 - 2022 Freunde von GISAID e.V. | Imprint / Privacy | Terms of Use | Contact

CoVsurver: Mutation Analysis of hCoV-19

The main application scenario for CoVsurver is to highlight phenotypically or epidemiologically interesting candidate amino acid (aa) changes for further research and should ideally be combined with experimental testing and verification of any predicted phenotypes.

Result for comparison with reference selection: **hCoV-19-like/bat/Yunnan/RaTG13/2013**

3D structural visualization of the spike glycoprotein with aa changes identified in the query sequences shown as colored balls

CoVsurver: Mutation Analysis of hCoV-19

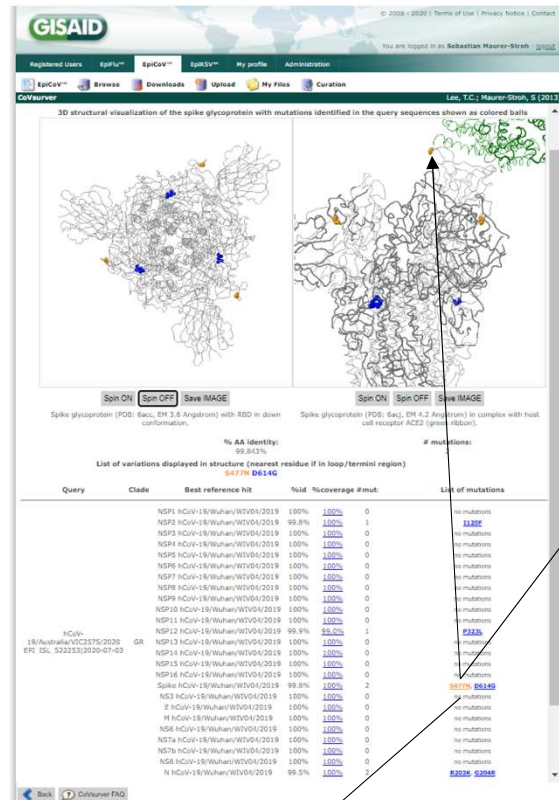
The main application scenario for CoVsurver is to highlight phenotypically or epidemiologically interesting candidate amino acid (aa) changes for further research and should ideally be combined with experimental testing and verification of any predicted phenotypes.

Result for comparison with reference selection: **SARS/Toronto/Tor2/2004**

3D structural visualization of the spike glycoprotein with aa changes identified in the query sequences shown as colored balls

Compare to existing vaccine candidates and reference viruses

Real-time surveillance for mutations that can affect antigenic changes

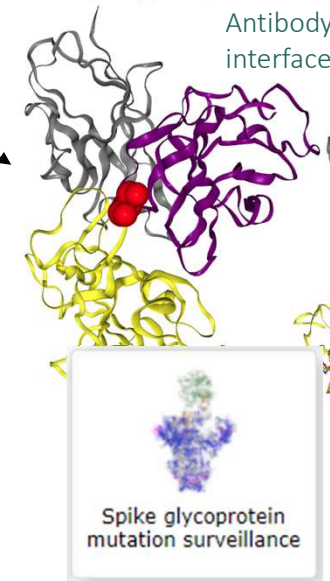


Protein: Spike
Coronavirus type: Yeast SARS-CoV-2 (2019)
Mutation (as in paper): S477N
neutral AA: S
neg. eff. AA: N
Effect: Host Change

Receptor binding

Comment:
In a deep mutational scanning experiment that expresses Spike RBD in a yeast-display platform, S477N mildly increases the binding to ACE2 (apparent dissociation constant delta-log10 value: 0.06)
[Literature reference](#)
(Mutation S477N in the paper is at an equivalent position of the mutation in your query)

Antibody interaction: The mutation position (red atoms) corresponds to position 477 on viral chain E (yellow backbone) of protein entry 6xcs, originating from Severe acute respiratory syndrome coronavirus 2 and with a label of Spike glycoprotein. The mutation is within 6 Å from antibody chain F (purple backbone).

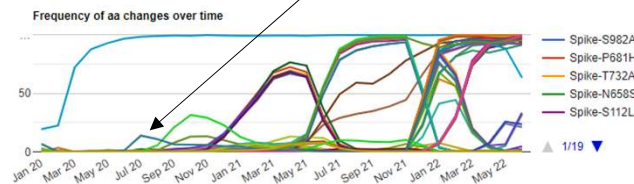


Literature-curated mutation effect database
>2,230 entries

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

FluSurfer

Result for comparison with reference selection: H7N7_Human_2003_Netherlands219

Query	Best reference hit	% AA identity	% length coverage	# mutations	List of mutations
HA_A/Anhui/1/2013_138739	HA_Netherlands/219/2003(H7N7)	96.071	98.41%	22	V18I S20I V58I T327S T156S Q198S I180V S262L S258L S286S K214D K238R R343G R454D I515M A550V
HA_A/Shanghai/1/2013_138737	HA_Netherlands/219/2003(H7N7)	96.071	98.41%	22	V18I S20I V58I T327S T156S Q198S I180V S262L S258L S286S K214D K238R R343G R454D I515M A550V
HA_A/Shanghai/2/2013_138738	HA_Netherlands/219/2003(H7N7)	96.071	98.41%	22	V18I S20I V58I T327S T156S Q198S I180V S262L S258L S286S K214D K238R R343G R454D I515M A550V

Key to alternative position numbering:

- 240 FluSurfer numbering (absolute as in 2009 H1N1 pdm)
- HA1 226 Classical H3N2 strain num
- HA1 223 Classical H1N1 strain num

Chosen reference: HA_H7N7_Human_2003_Netherlands219

Position in reference: 242

AA in reference: Q

AA in query: L

A mutation at the position equivalent to HA 242 has been reported to be related to [antigenic drift](#), [escape mutant](#) and [host specificity shift](#).

A combination of mutations including the position equivalent to HA 242 reported in the literature to be related to [host specificity shift](#).

As seen in resolved structures of proteins from related strains, the HA position equivalent to your mutation is related to [host cell receptor binding](#) and [antibody recognition sites](#).

See all interactions for this position

Protein: HA

Influenza type: Human H3N2 (N/A)

Mutation (as in paper): Q226L

neutral AA: Q

neg. eff. AA: L

Effect: host specificity shift

Comment: Increasing affinity of receptor-binding to SA₂6Gal and decreasing affinity to SA₂3Gal (Table1.).

Literature reference

(Mutation Q226L in the paper is at an equivalent position of the mutation in your query)

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)

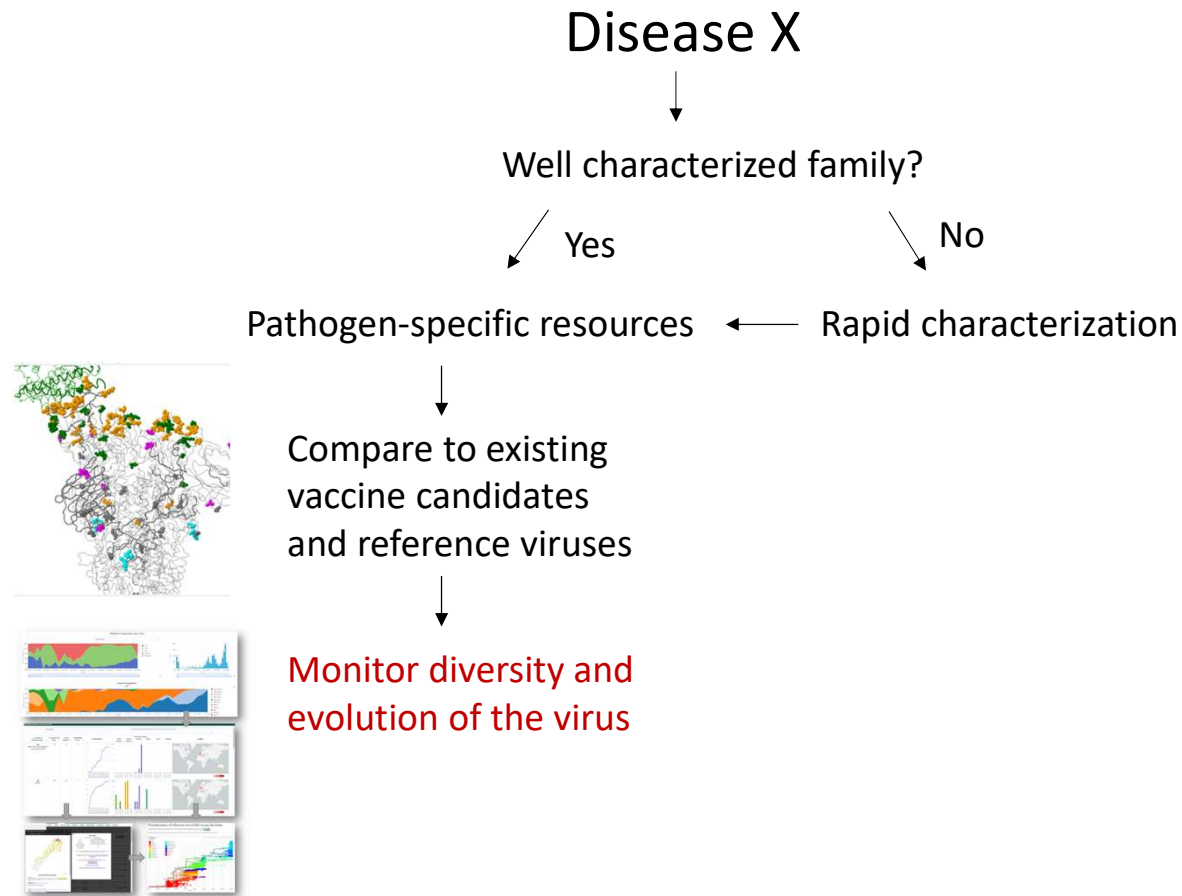
A/Canada/RV504/2004(H7N3) - avian flu with rare zoonosis - North American lineage

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

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

Facilitating antigenic surveillance from genomic data



EpiX™ | Search | Upload

Single Upload

Enter and upload genetic sequence and metadata, available clinical and epidemi data. Data will be reviewed by a curator prior to release. An email confirmation

Pathogen detail

Submission name*

Accession ID

Pathogen Kingdom*

Pathogen Family*

Passage details/history

Sample information

Collection date*

Location*

Additional location information

Host*

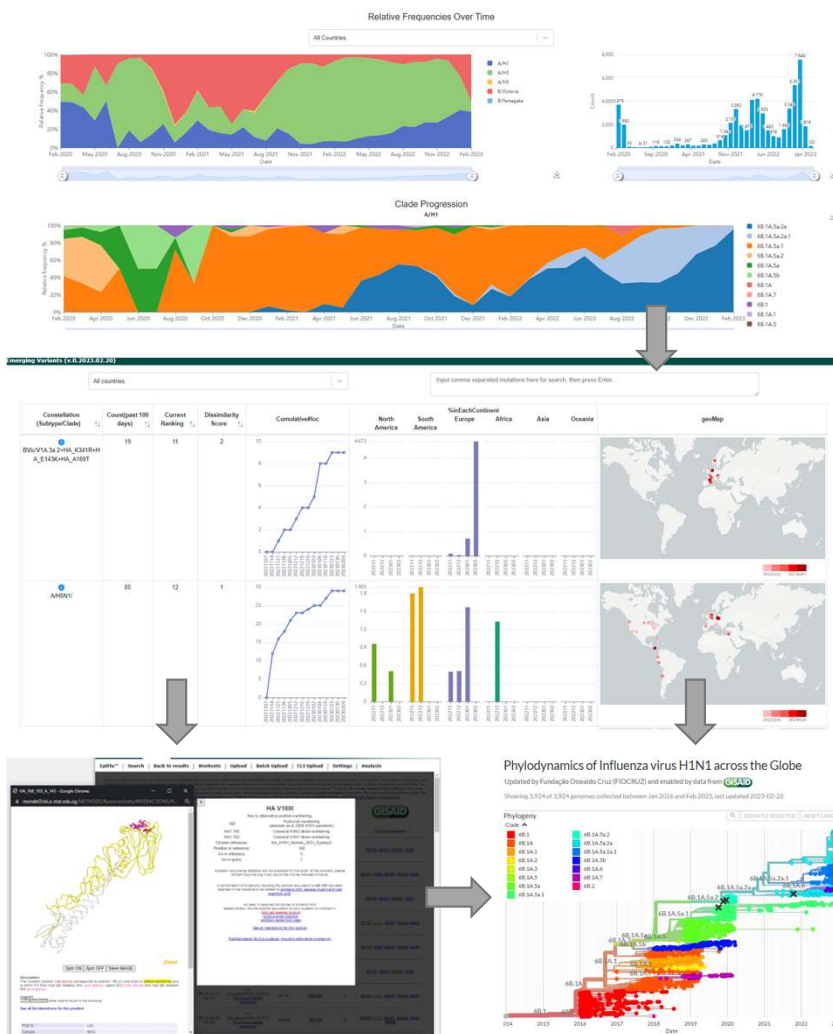
An ecosystem of integrated tools supporting scale-free view of virus evolution

Subtype

Clade

Emerging Variant
(unique set of mutations)

Individual mutation



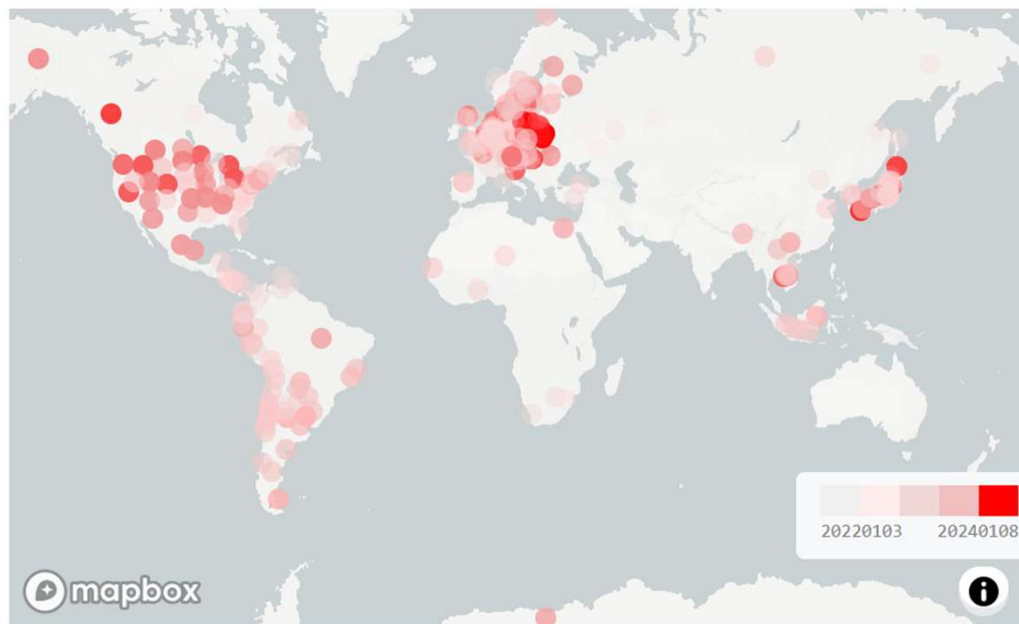
Single entry detail

Set of
entries in
the database

Set of
entries
graphical
summary

Oversight of lineage distribution enables decisions making

H5N1 major lineage distribution 2022-2024

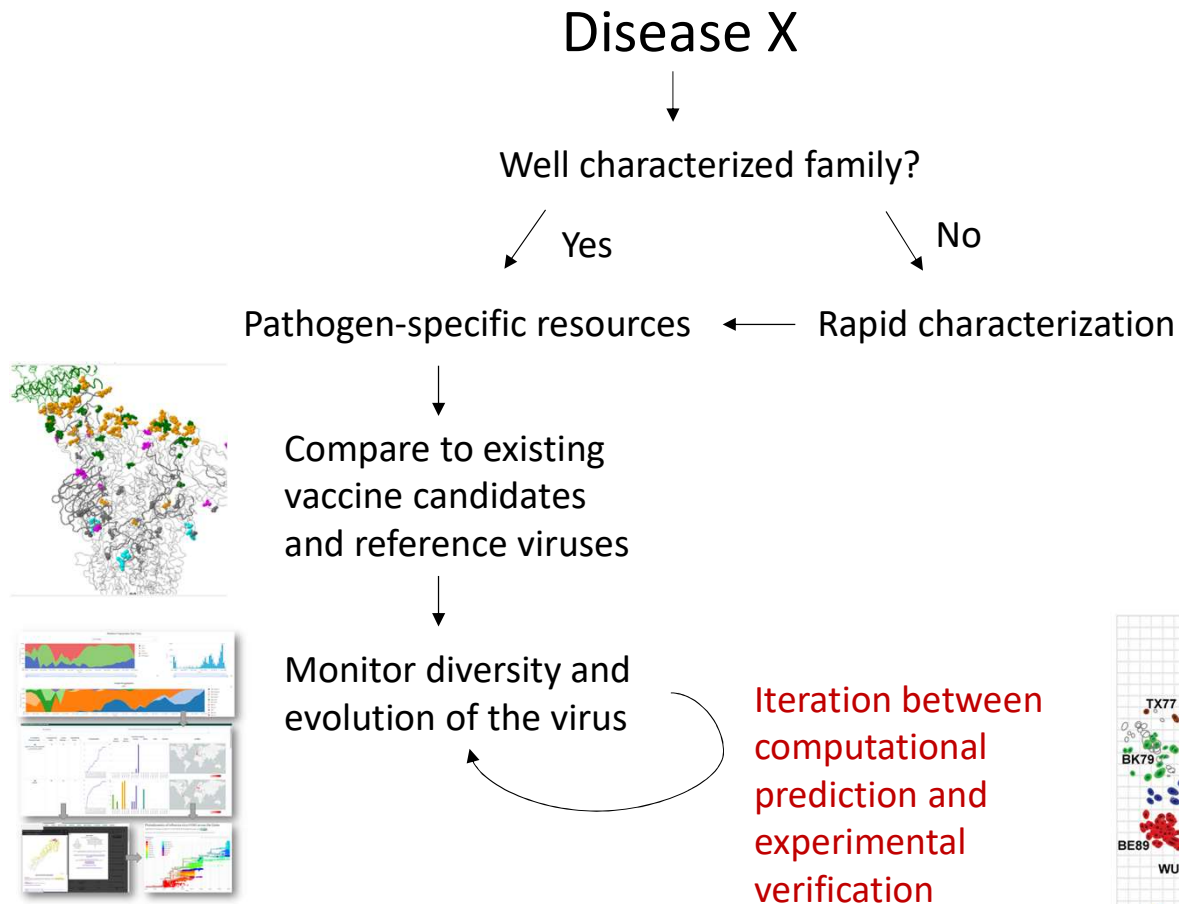


2.3.4.4b

2.3.2.1c



Facilitating antigen identification through genomic surveillance



EpiX™ | Search | Upload

Single Upload

Enter and upload genetic sequence and metadata, available clinical and epidemiological data. Data will be reviewed by a curator prior to release. An email confirmation will be sent.

Pathogen detail

Submission name*

Accession ID

Pathogen Kingdom*

Pathogen Family*

Passage details/history

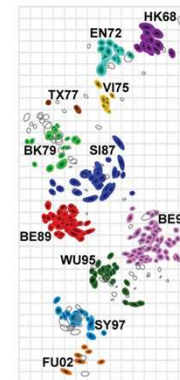
Sample information

Collection date*

Location*

Additional location information

Host*

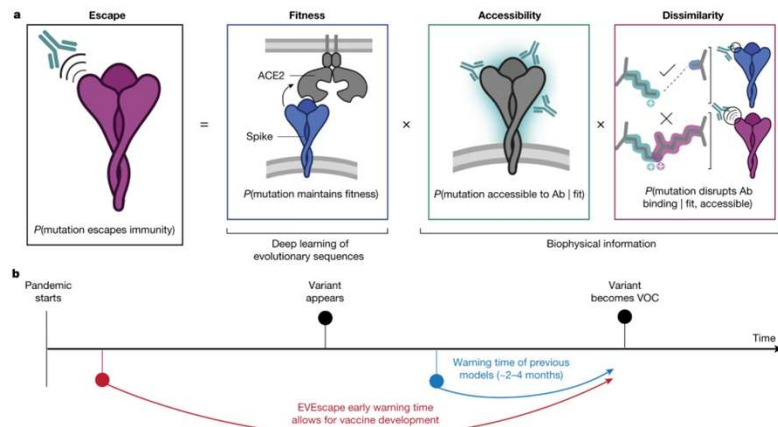


Learning from pre-pandemic data to forecast viral escape

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](#)

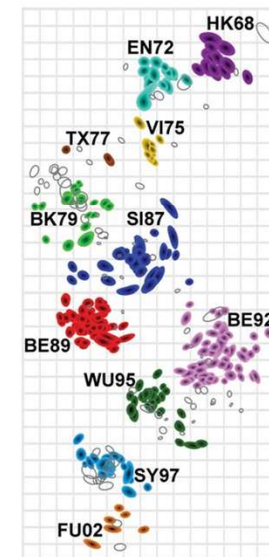


a, EVEScape assesses the likelihood of a mutation escaping the immune response on the basis of the probabilities of a given mutation maintaining viral fitness, occurring in an antibody epitope and disrupting antibody binding. **b**, EVEScape requires only information available early in a pandemic, before 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](#).

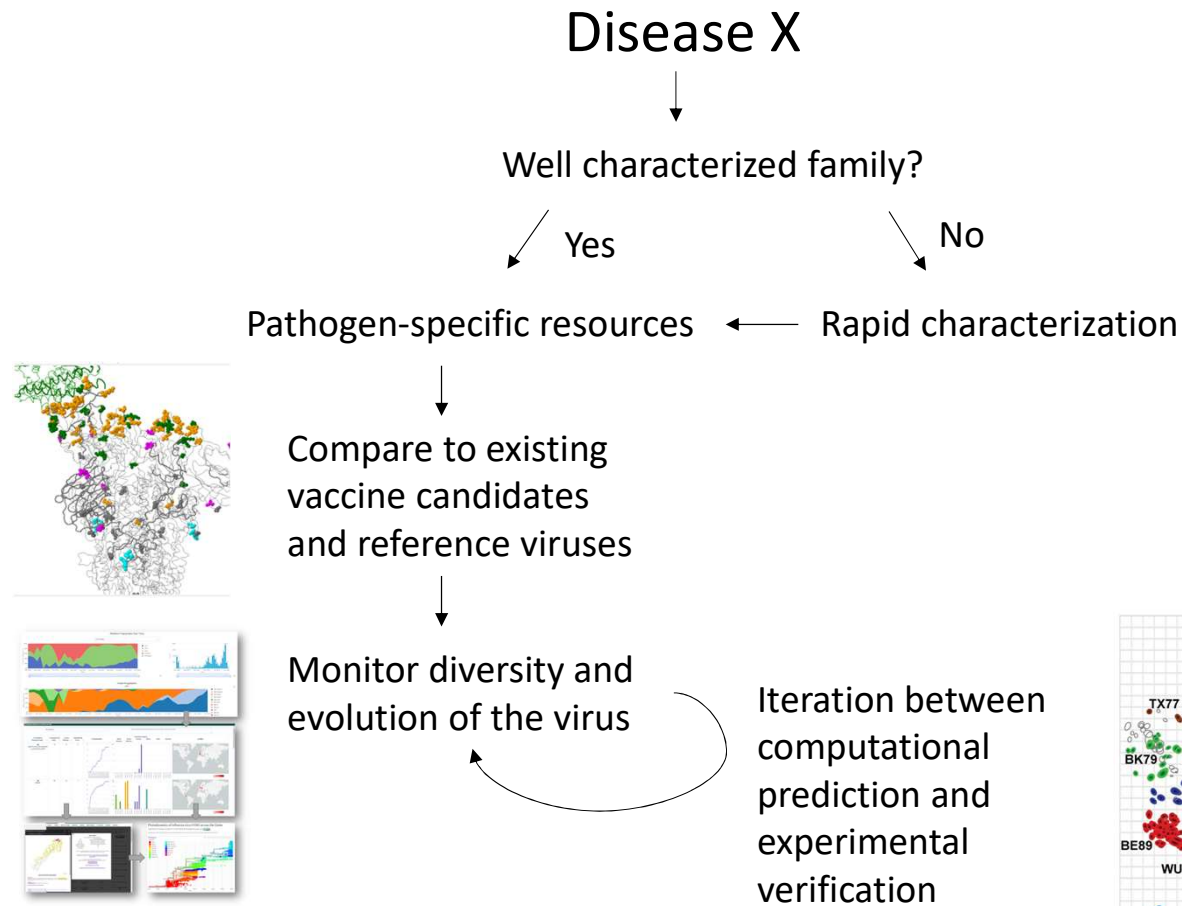
Mapping the Antigenic and Genetic Evolution of Influenza Virus

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



EpiX™ | Search | Upload

Single Upload

Enter and upload genetic sequence and metadata, available clinical and epidemiological data. Data will be reviewed by a curator prior to release. An email confirmation will be sent to the user.

Pathogen detail

Submission name*

Accession ID

Pathogen Kingdom*

Pathogen Family*

Passage details/history

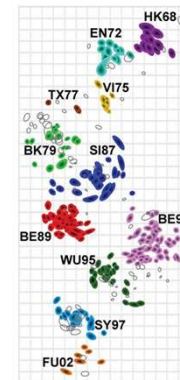
Sample information

Collection date*

Location*

Additional location information

Host*



GISAID