Viral sub-Species classification: the antigenic phenotype

Derek Smith

University of Cambridge

Summary

The importance of the antigenic phenotype for vaccine strain selection

(Richard “Aggregation of phenotypic data”, here antigenic cartography)

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(Influenza and SARS-CoV-2)

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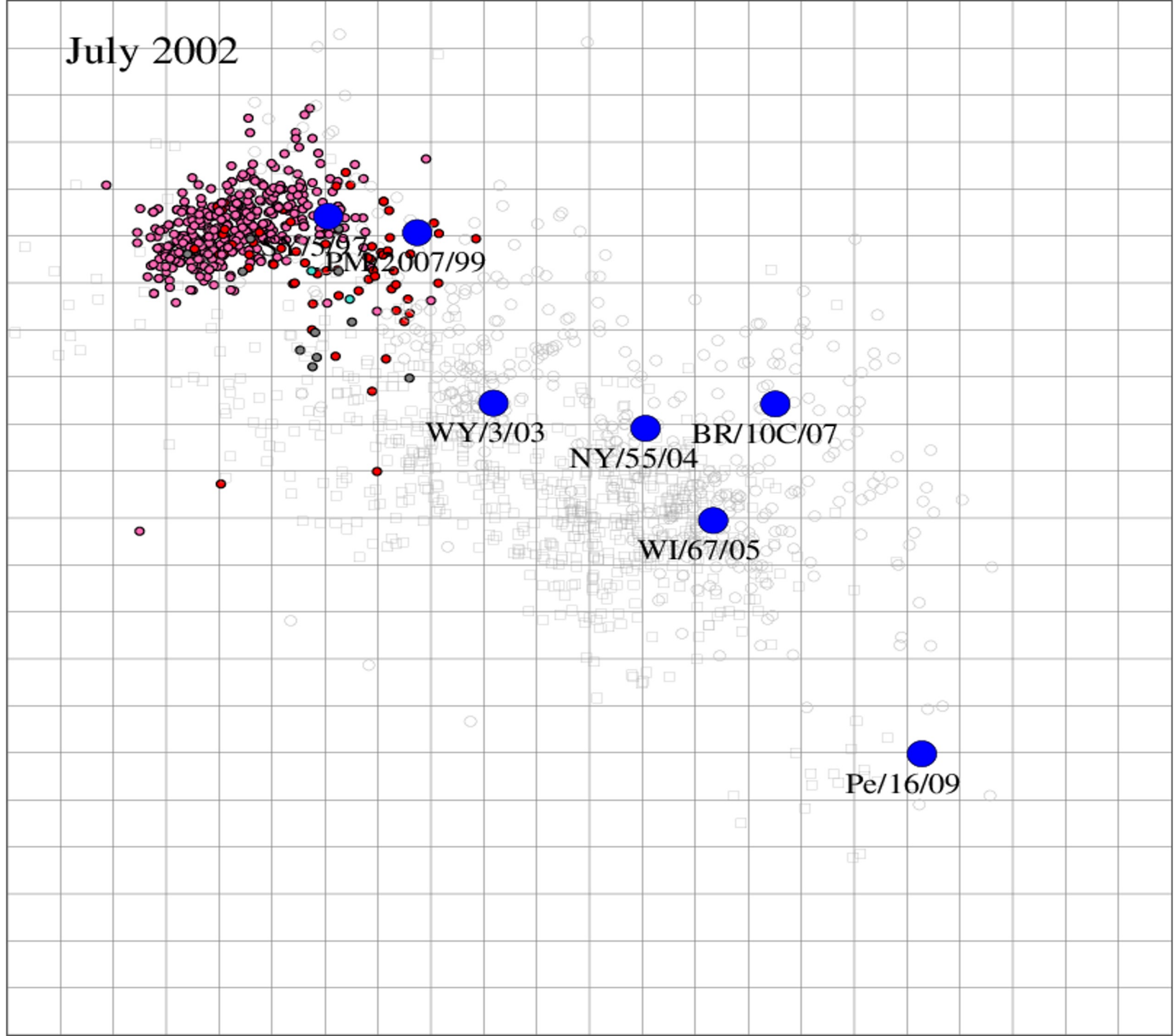
(Dengue virus, H5 influenza virus, and sometimes swine influenza viruses)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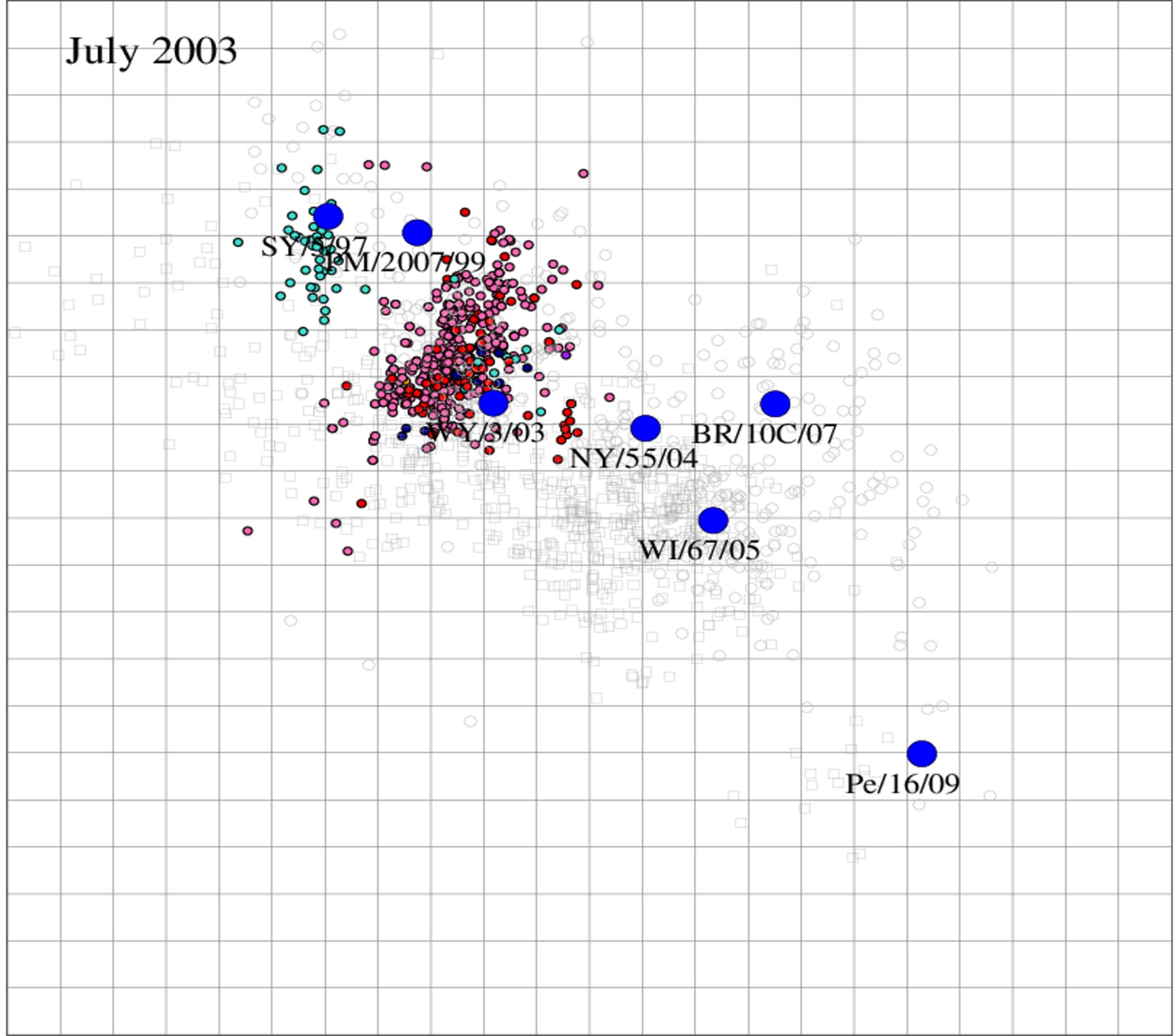
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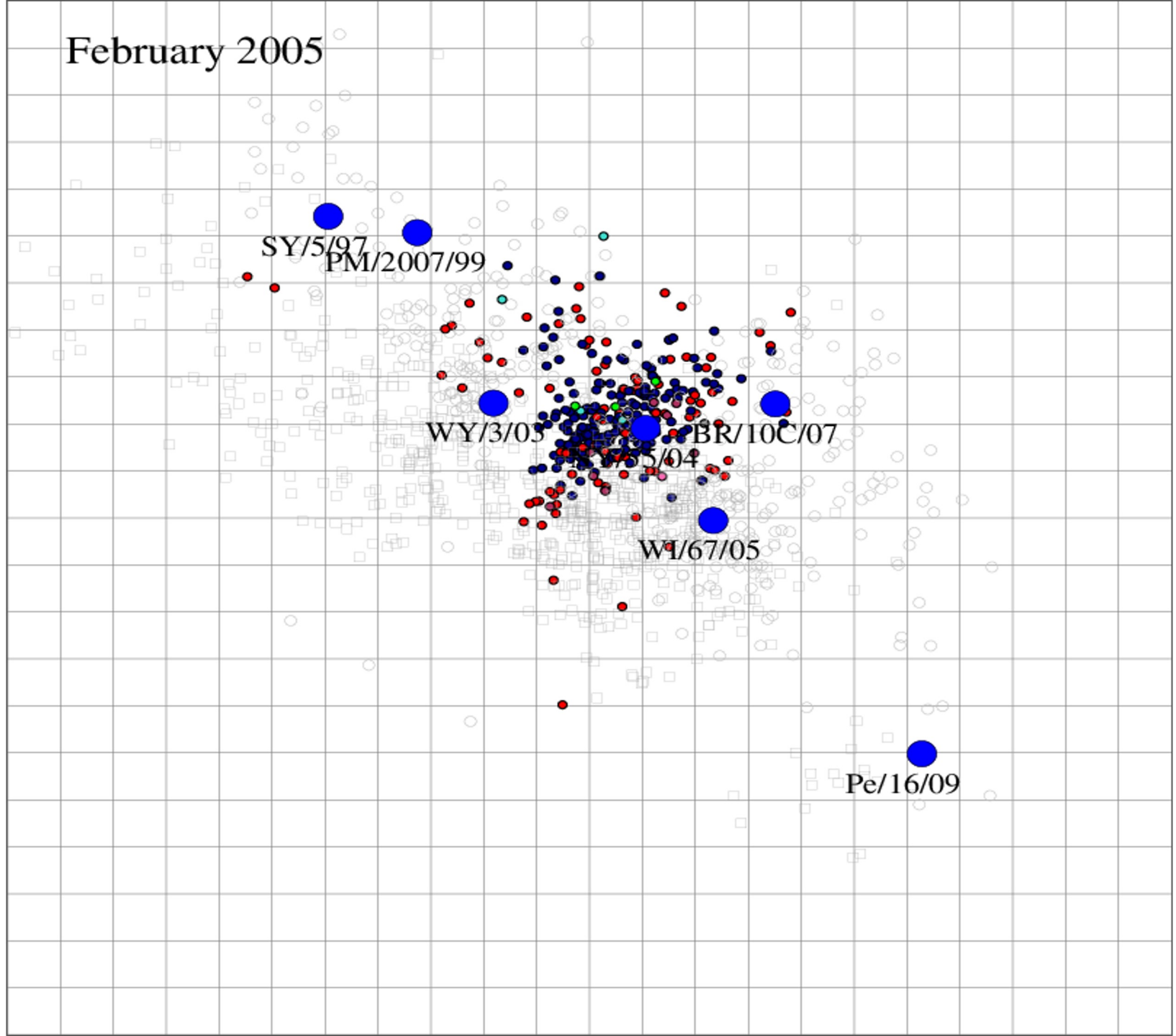
Pe/16/09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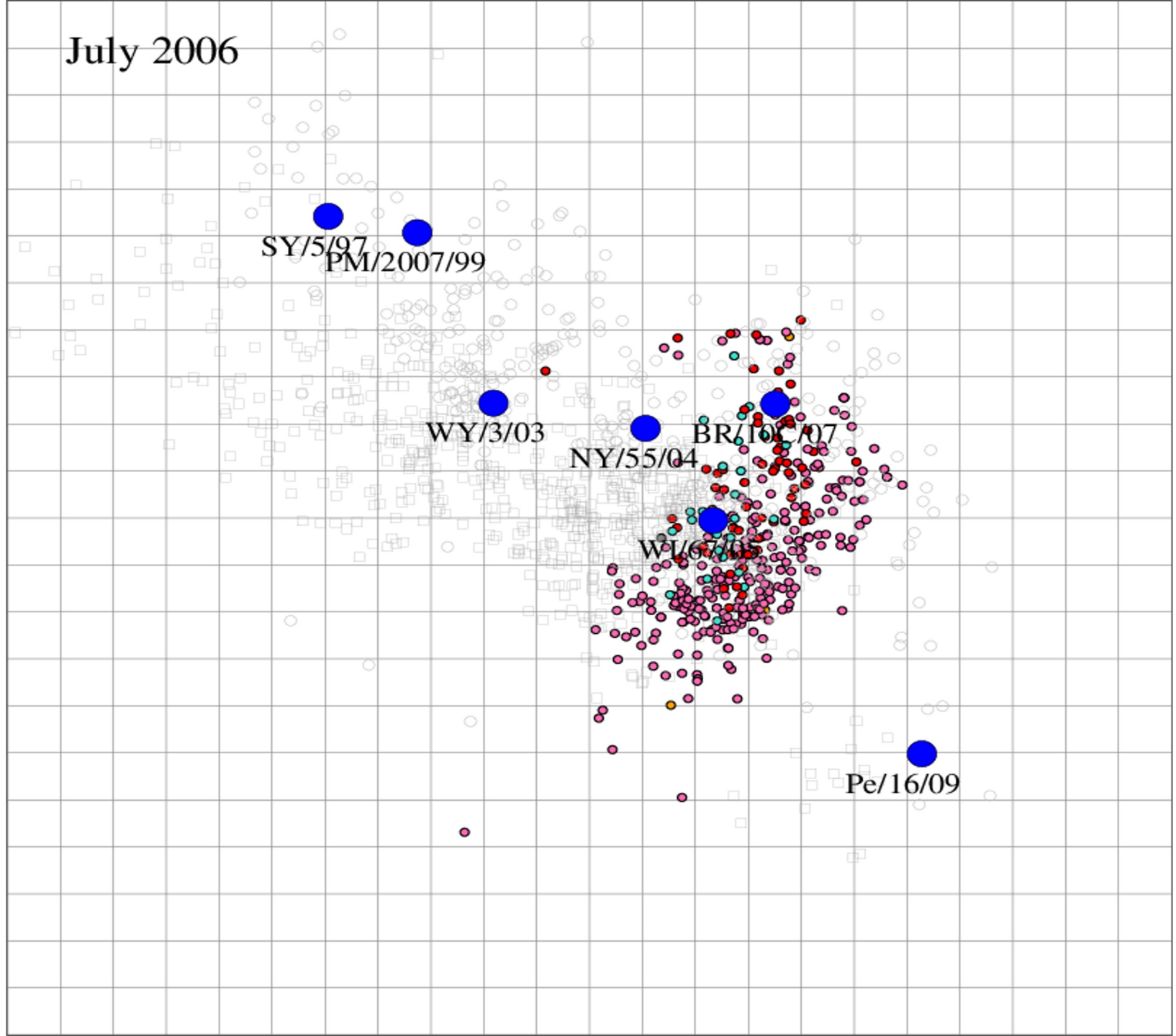
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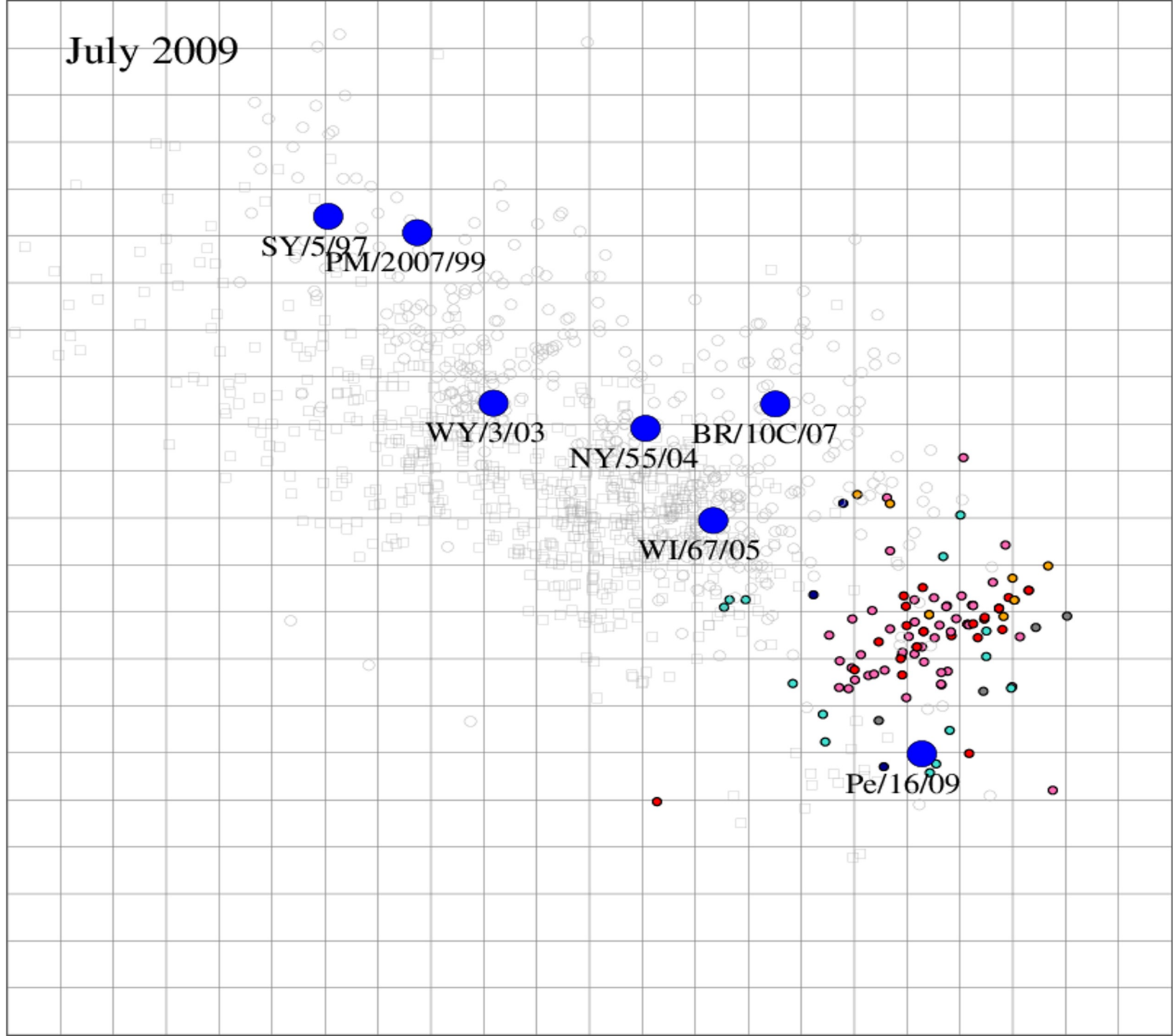
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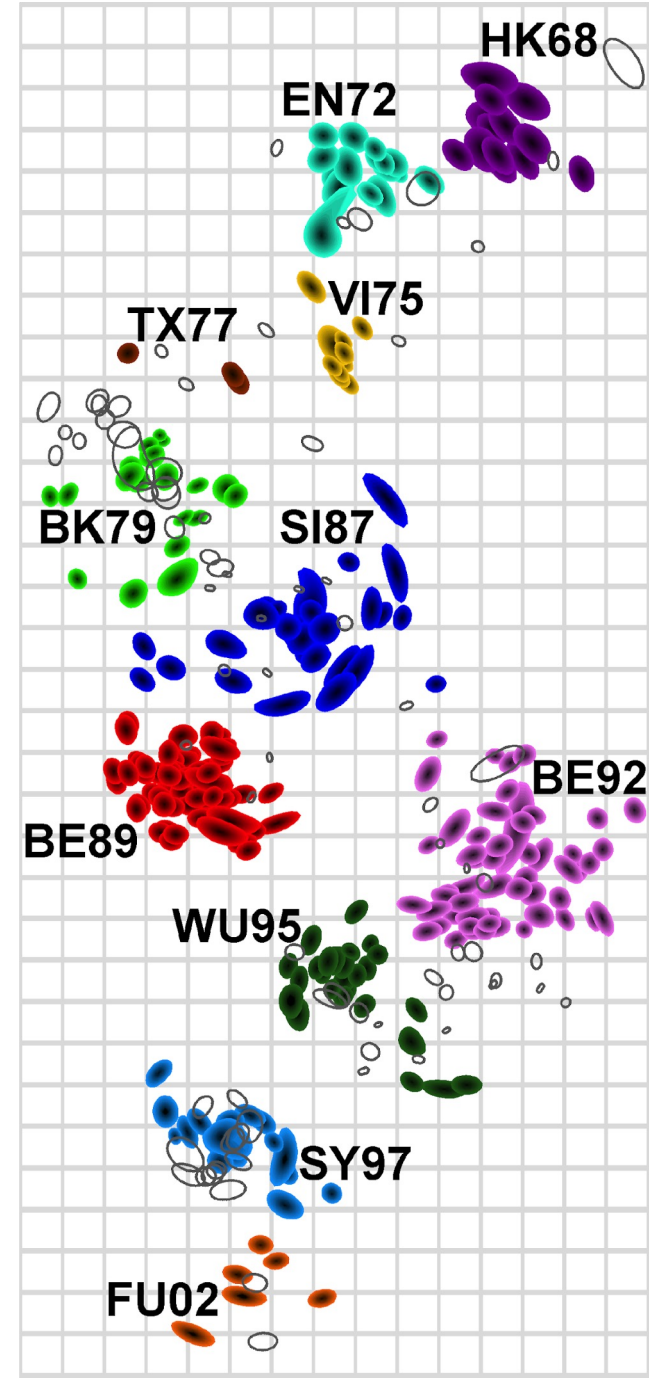
Antigenic map
Influenza A (H3N2) 1968-2004



Smith et al *Science* **305**, 371-376, 2004.

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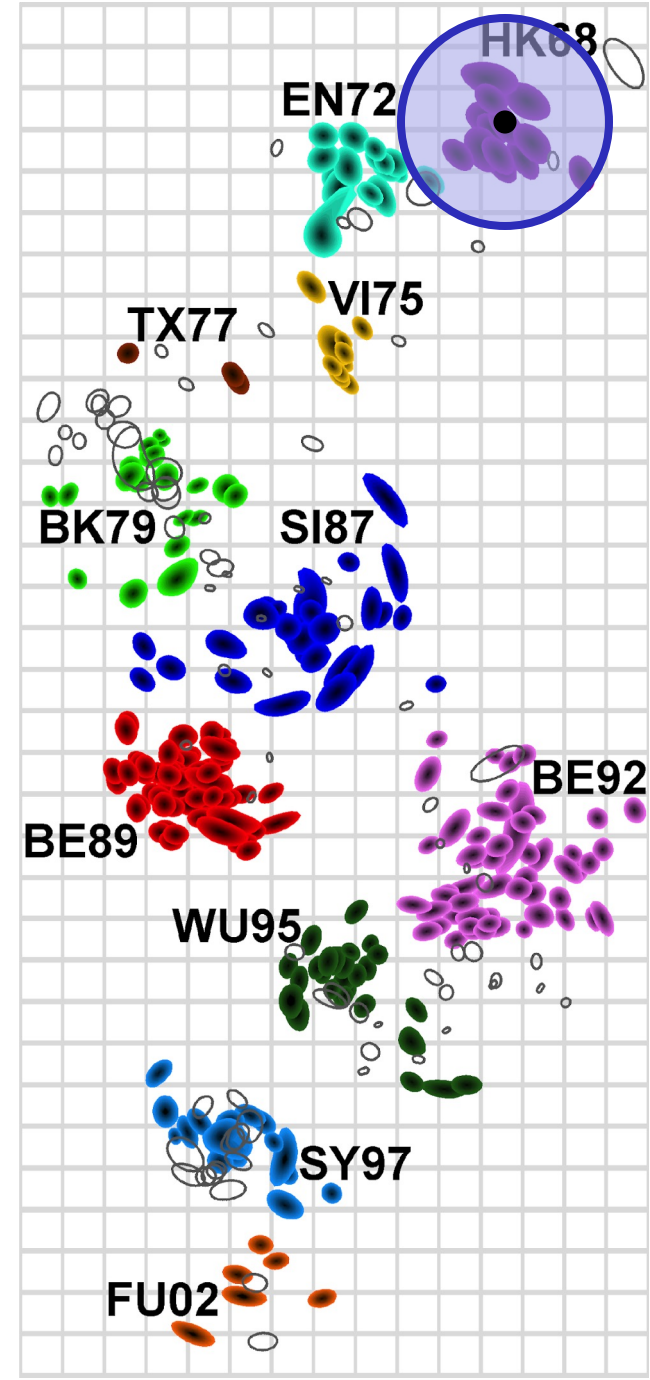

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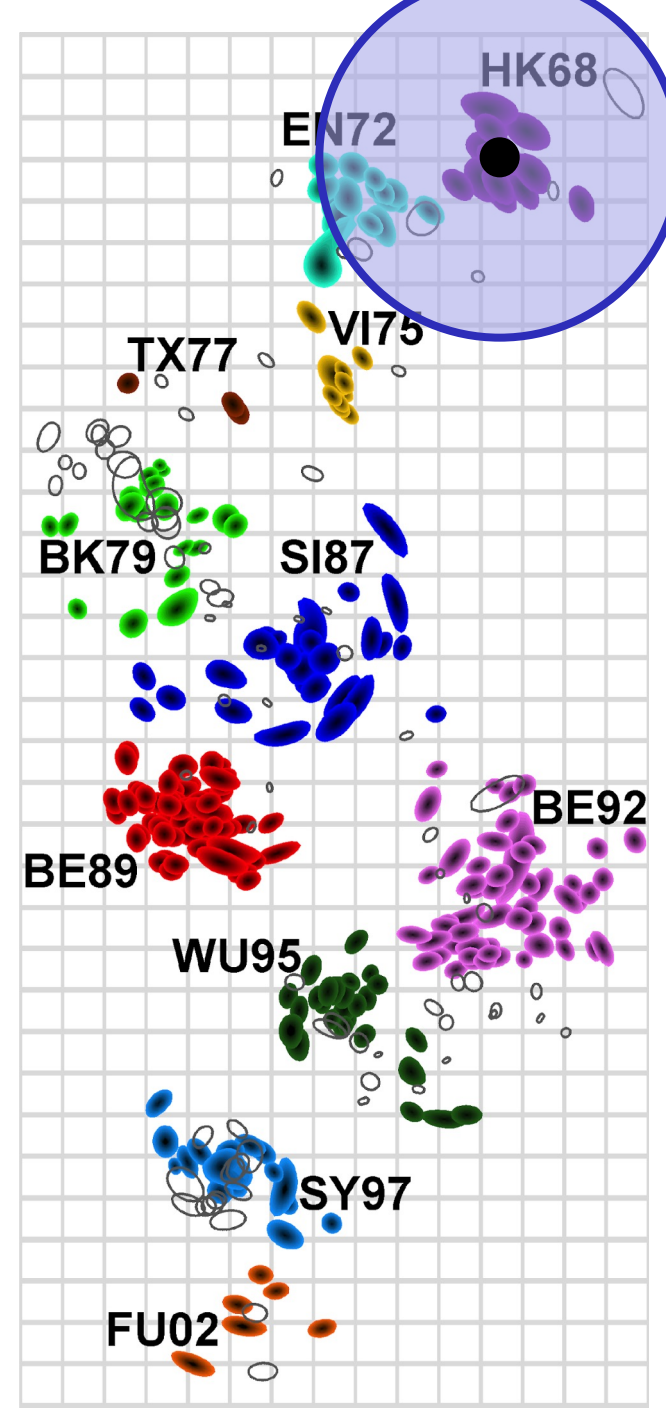

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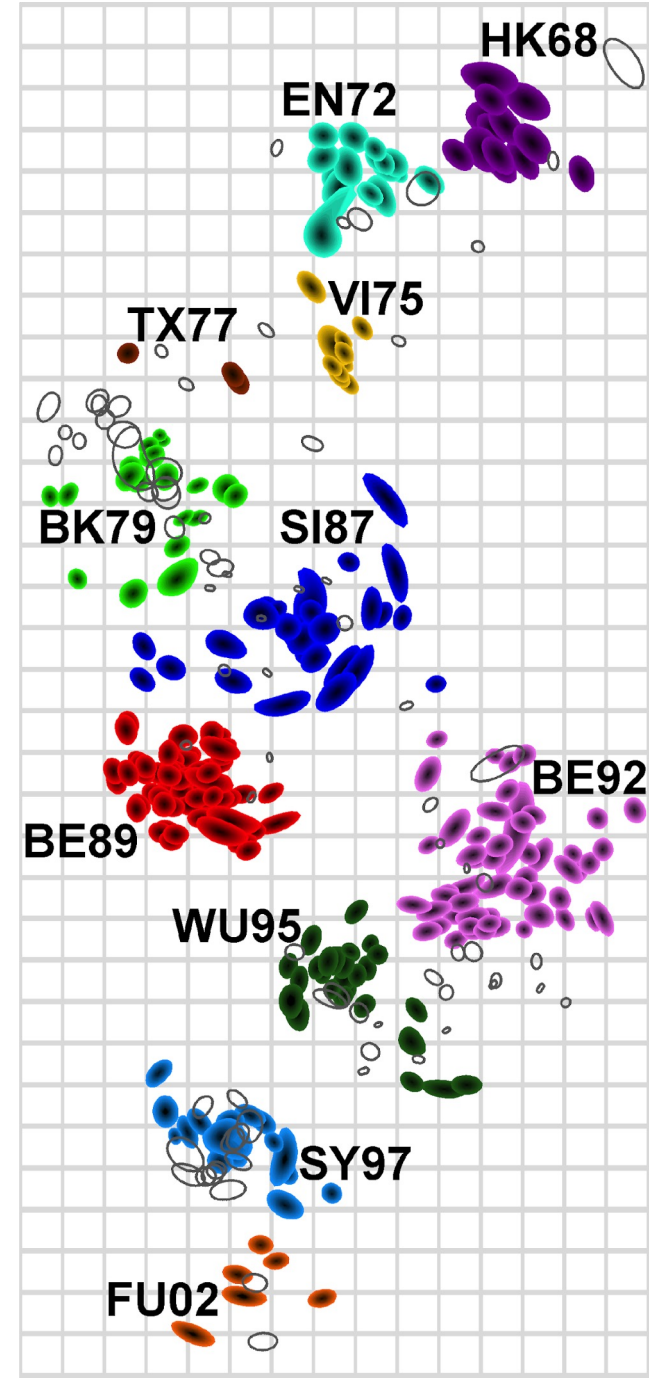

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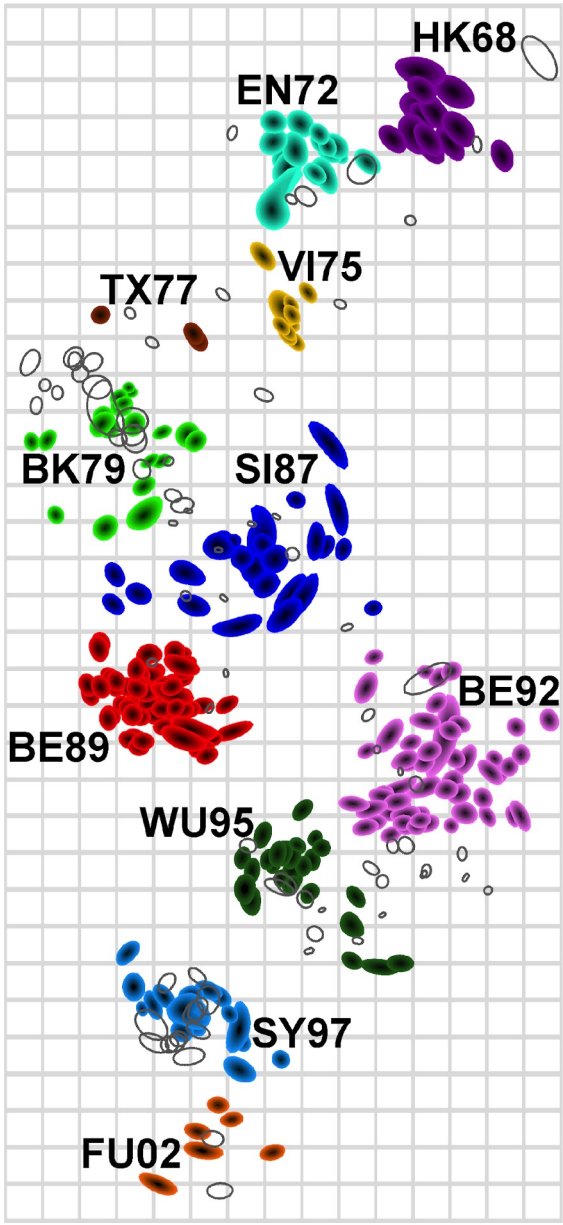
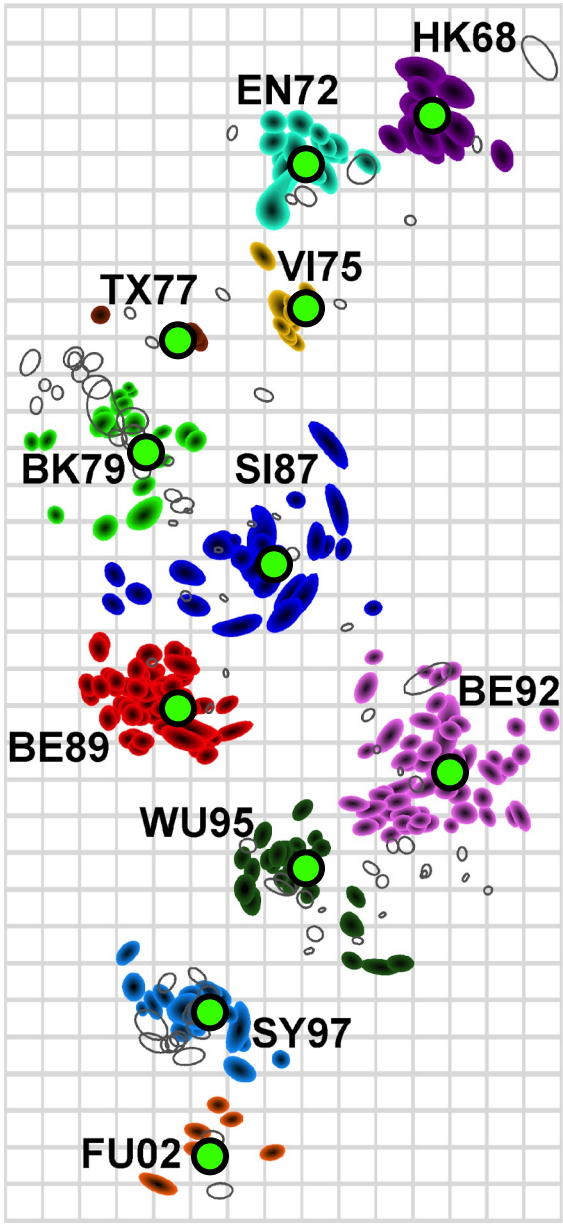
The genetic basis of antigenic change



Cluster transition	Cluster-difference substitutions					
	Site A	Site B	Site C	Site D	Site E	Other
HK68-EN72	T122N G144D	T155Y N188D		R207K		
EN72-VI75	N137S S145N	L164Q Q189K S193D	N53D I278S	F174S R102K I213V I217V I230V		
VI75-TX77	S137Y	G158E Q164L D193N	K50R D53N	S174F K201R V213I V230I	E82K M260I	
TX77-BK79	N133S P143S G146S	K156E N193K T160K Q197R	N53D N54S	D172G V217I V244L	I62K K82E	
BK79-SI87	G124D	Y155H S159Y Q189R				
SI87-BE89	N145K	N193S				
SI87-BE92	S133D	E156K E190D N193S				
BE92-WU95	N145K					
WU95-SY97		K156Q E158K V196A	N276K		K62E	L25I V202I
SY97-FU02	A131T	H155T Q156H	R50G		H75Q E83K	W222R G225D

Smith et al, Science, 2004

The genetic basis of antigenic change



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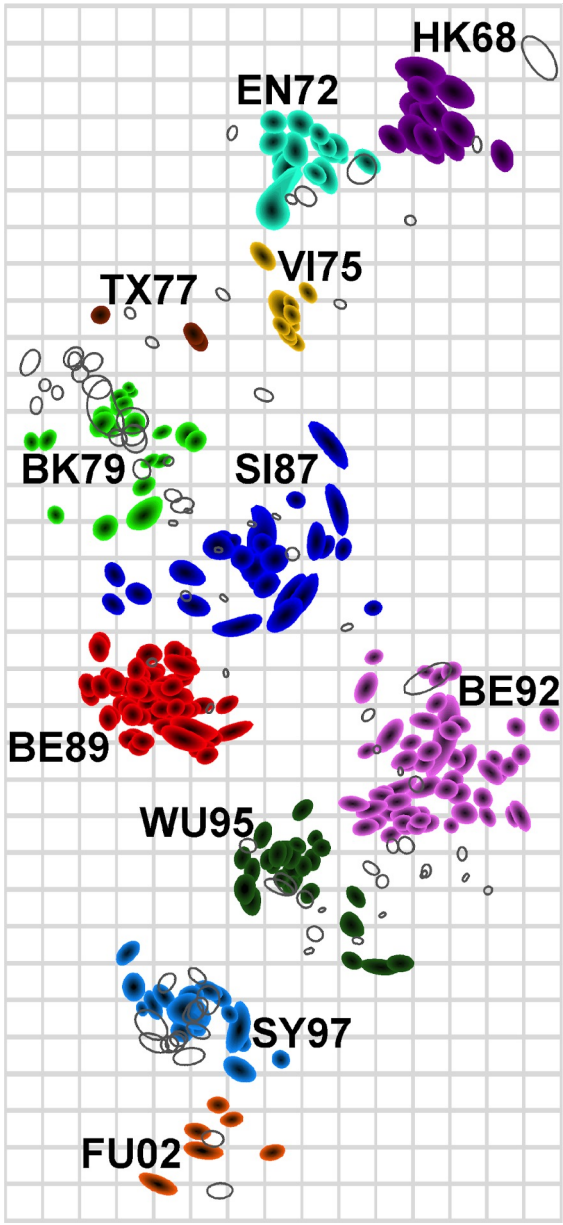

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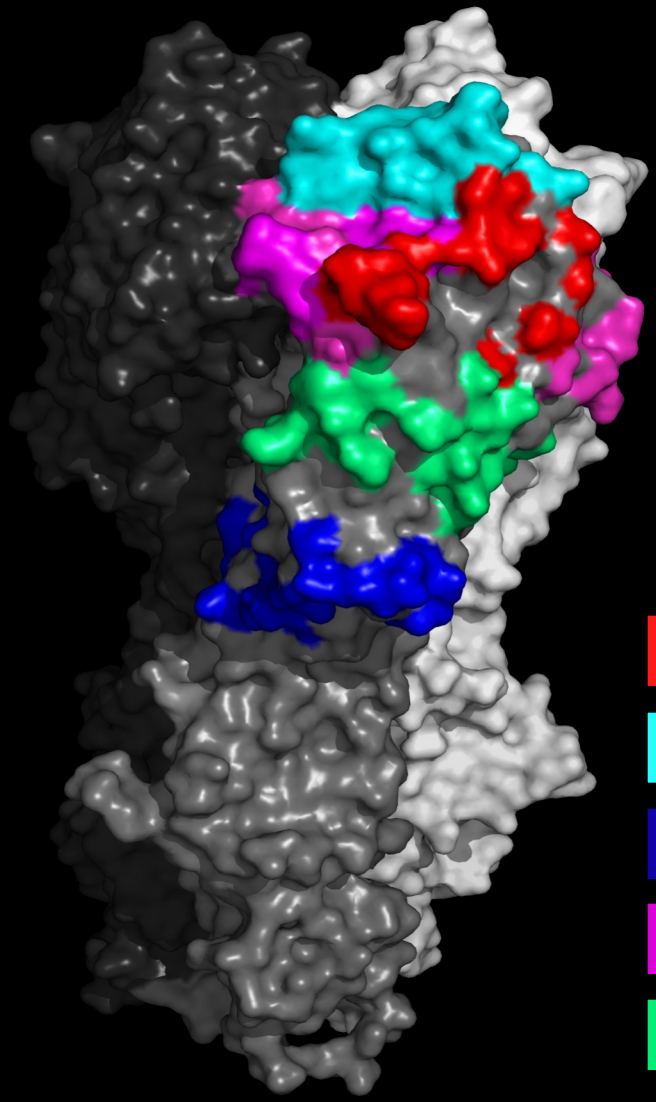
WU95-SY97		K156Q E158K				
SY97-FU02		H155T Q156H				

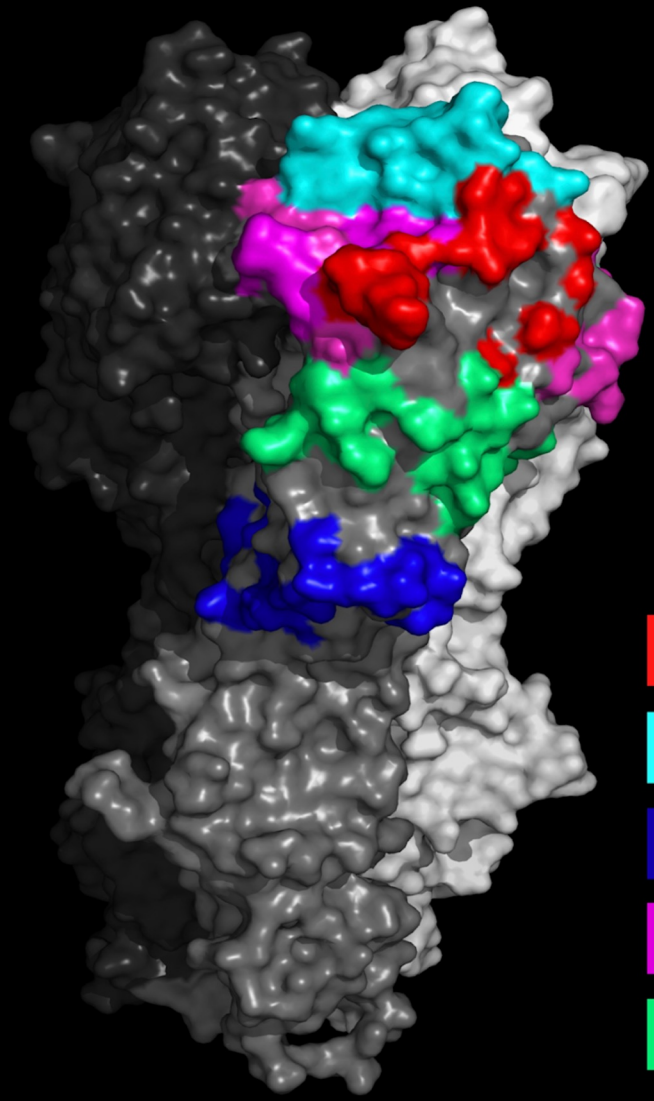
Koel et al, Science, 2013

Hemagglutinin structure



Site A
Site B
Site C
Site D
Site E

Wiley, Wilson, Skehel
Nature, 289, 373-378, 1981



Site A
Site B
Site C
Site D
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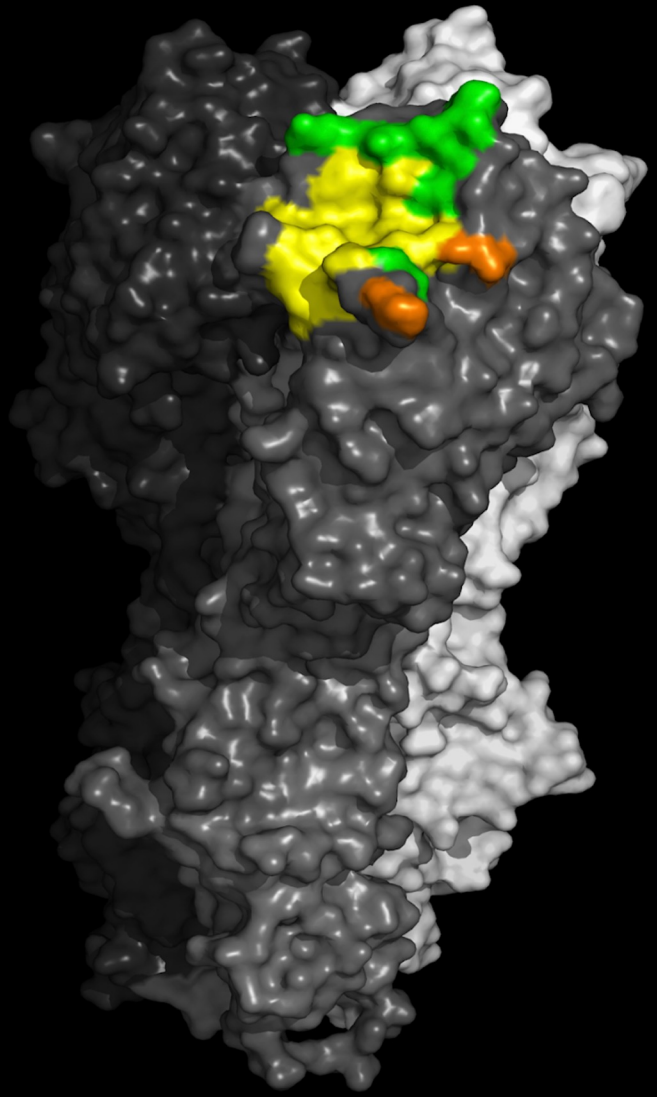
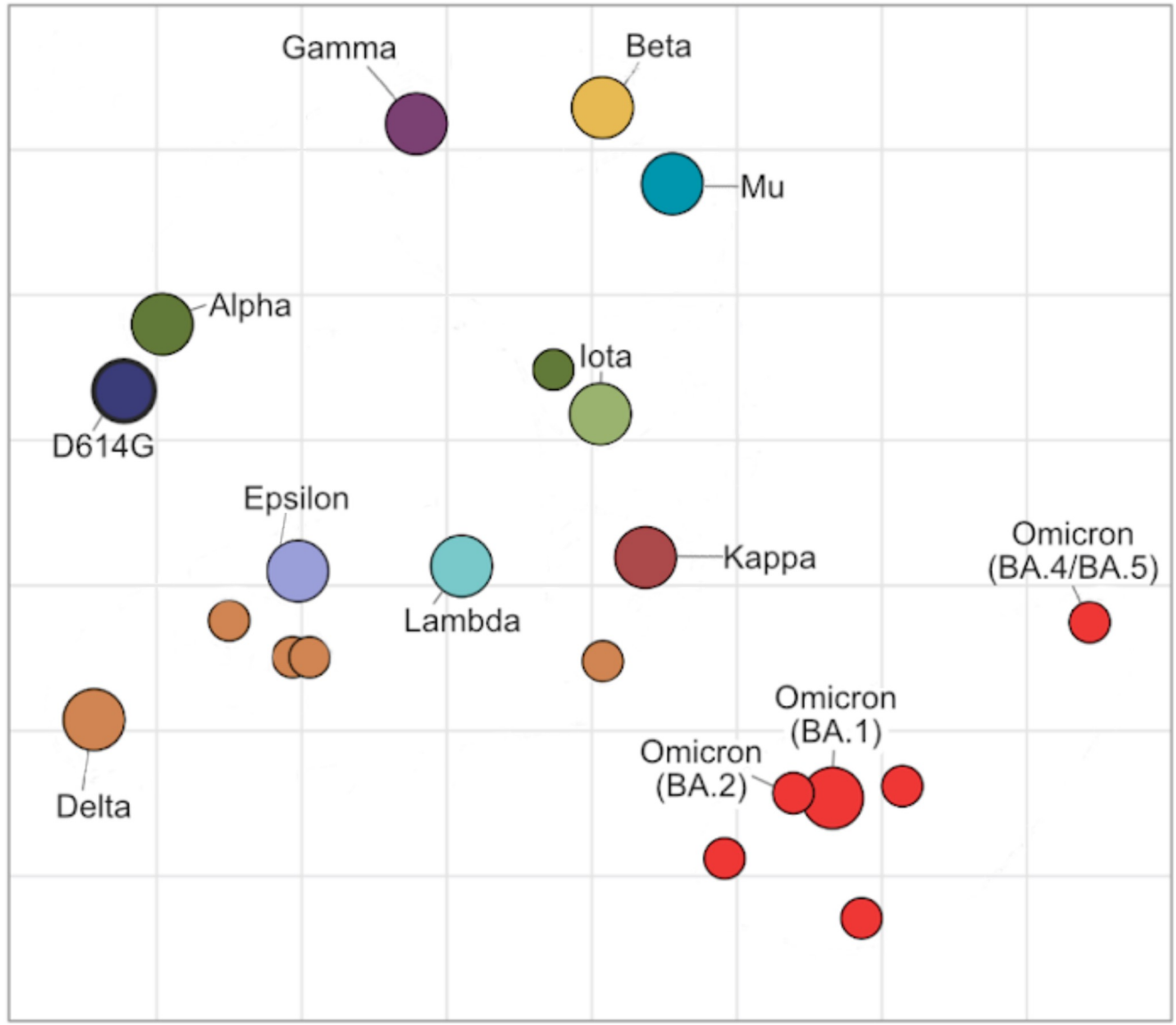
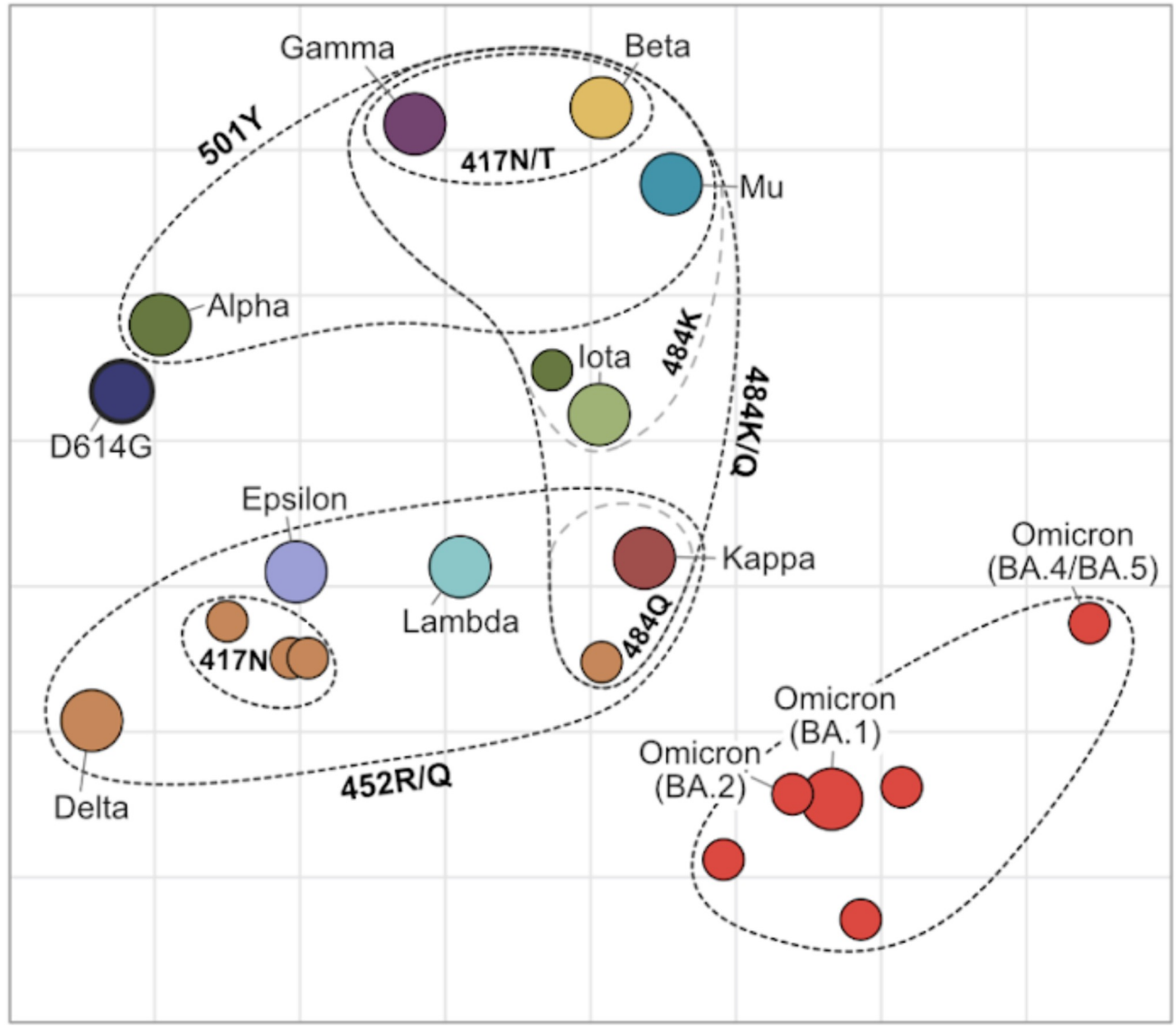


Crucial residue
Accessory residue
RBS

Koel *et al*, **Science**, 2013



Sam Wilks, Barbara Mühelmann, *et al.* Science 2023



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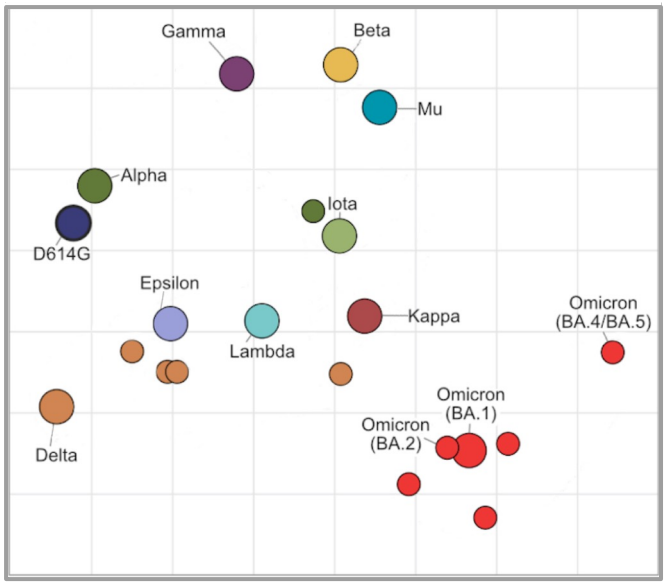
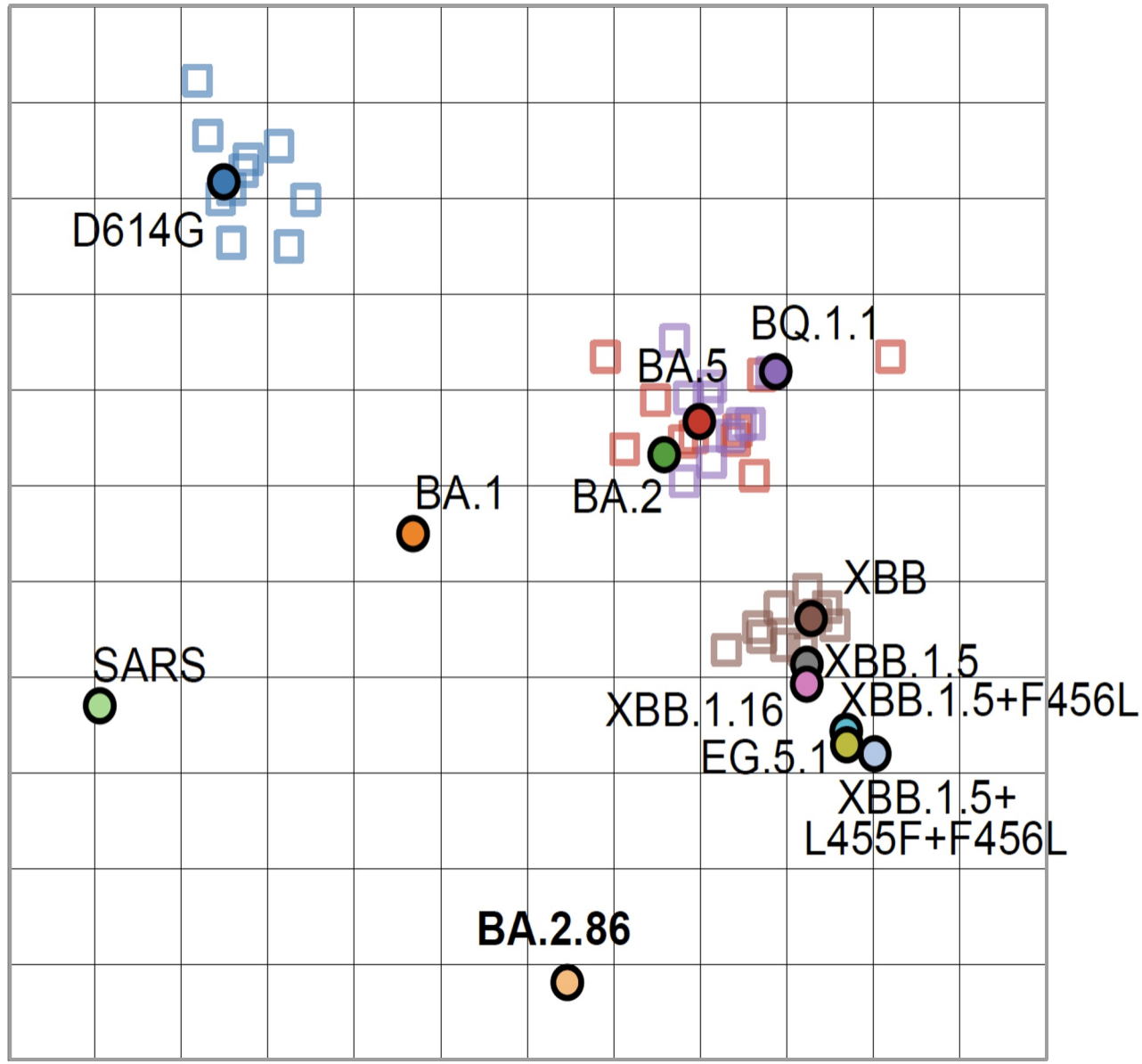
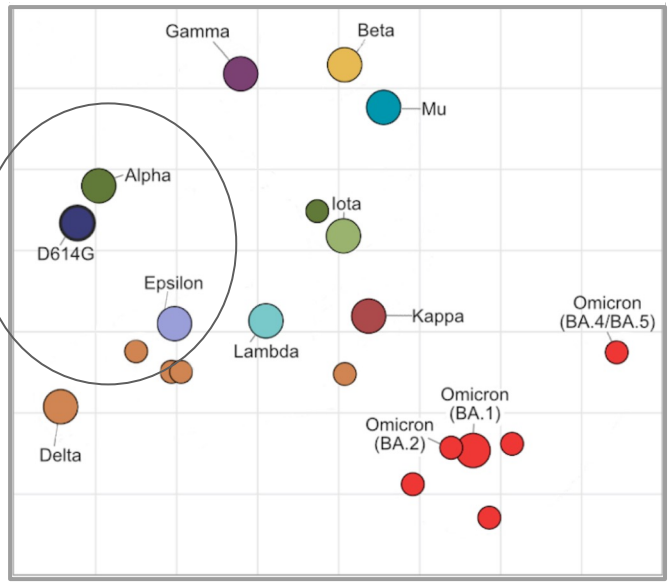
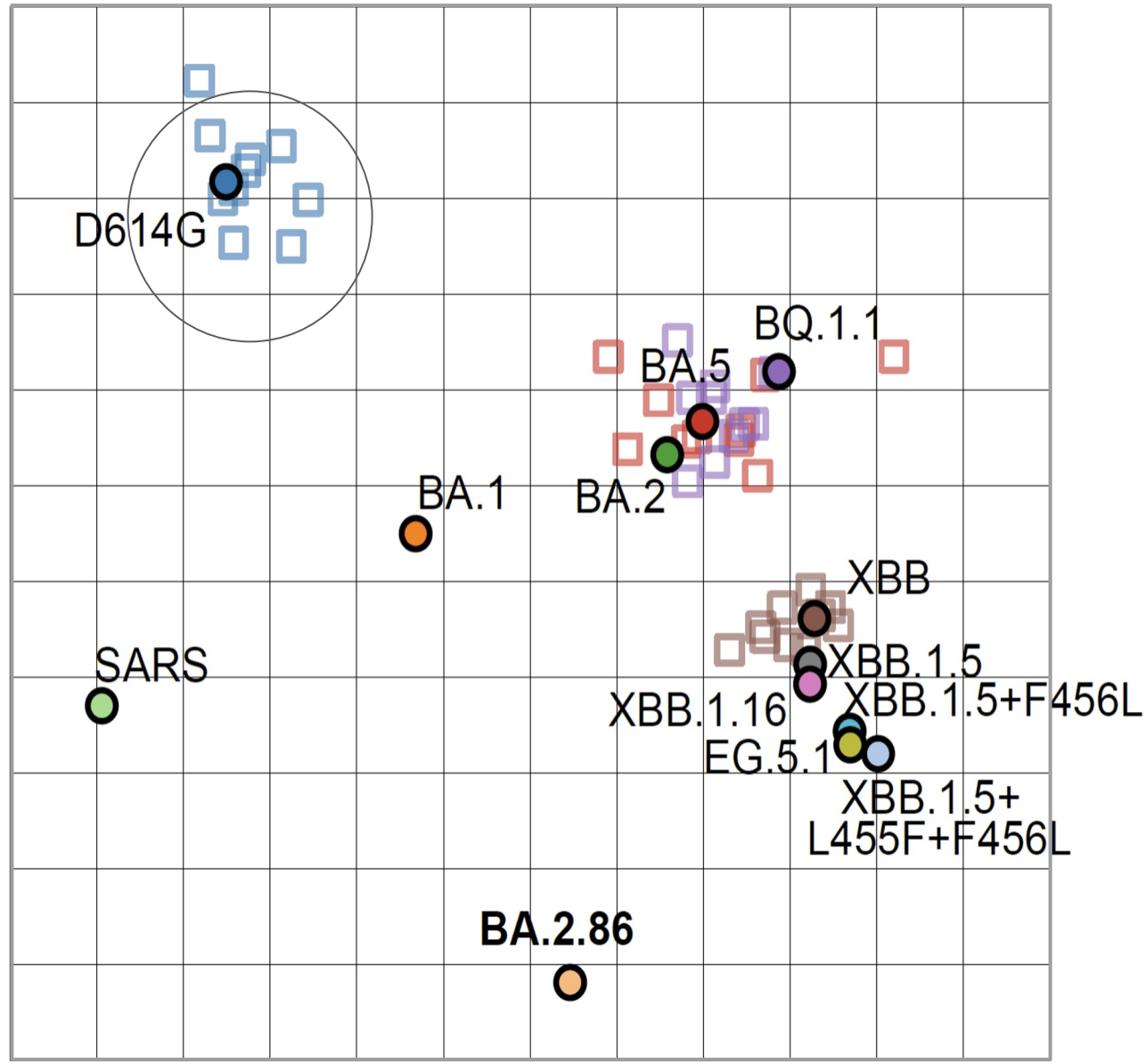




Sijie Yang, Yuanling Yu *et al.* Lancet Infectious Diseases 2023.





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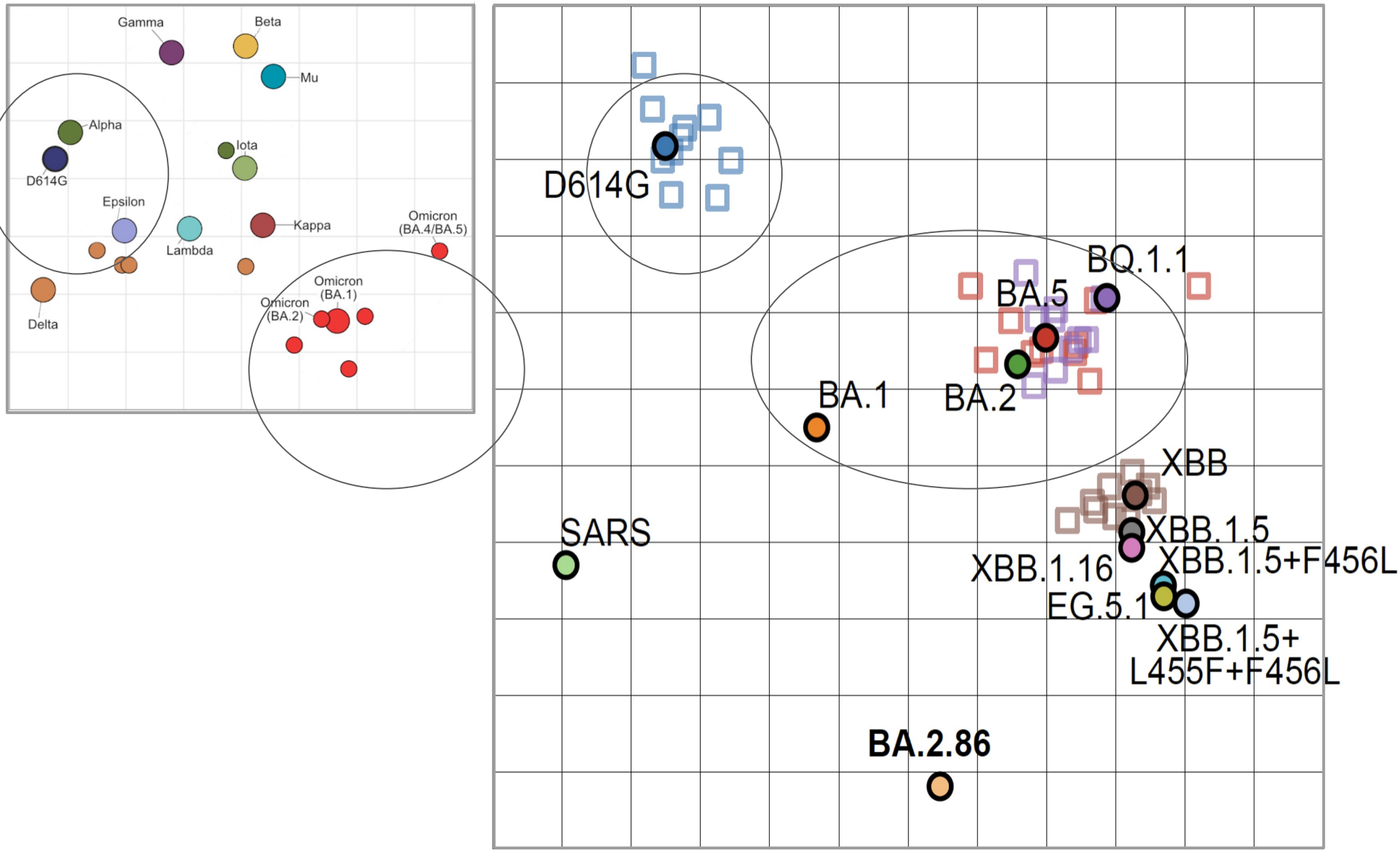

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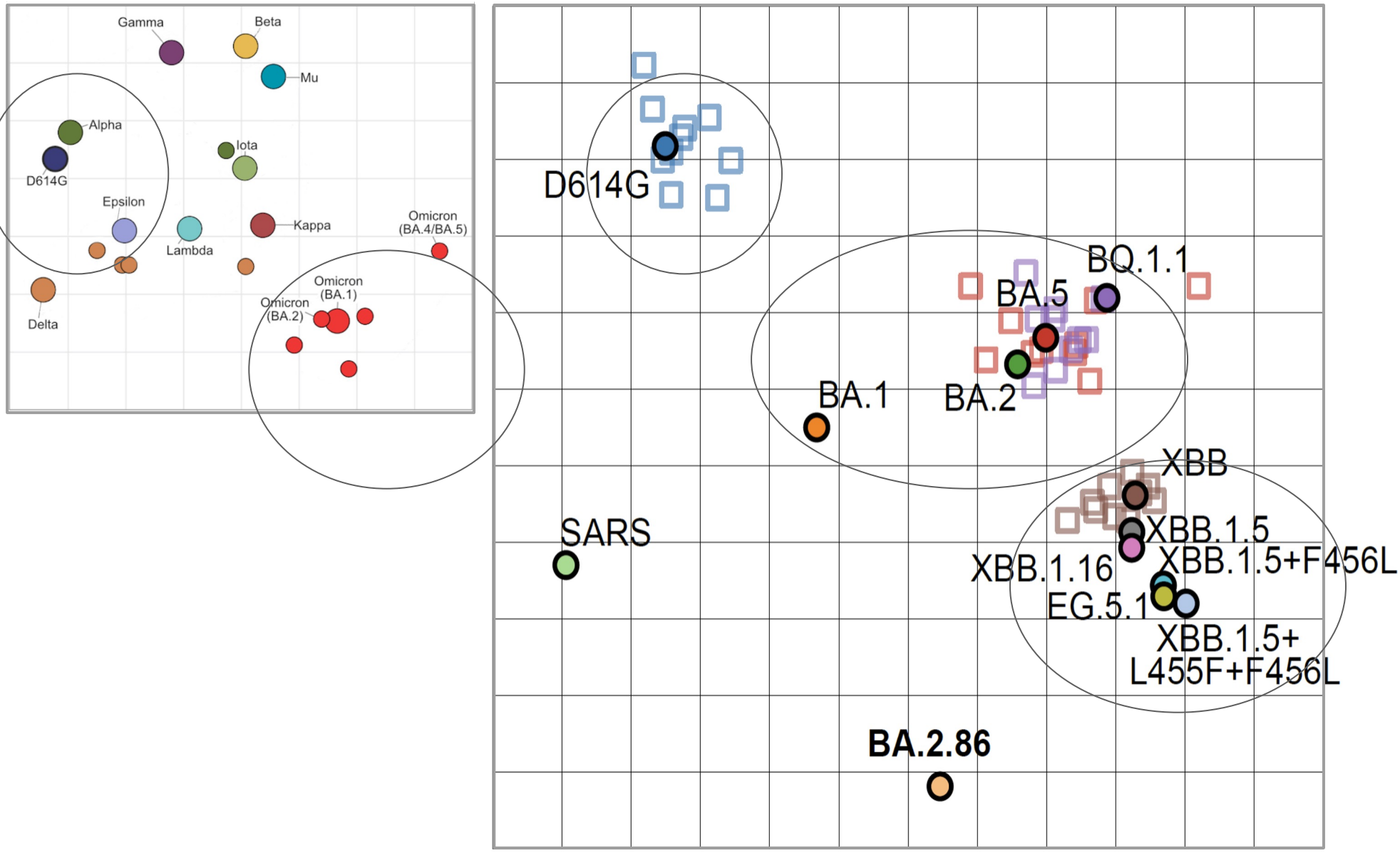

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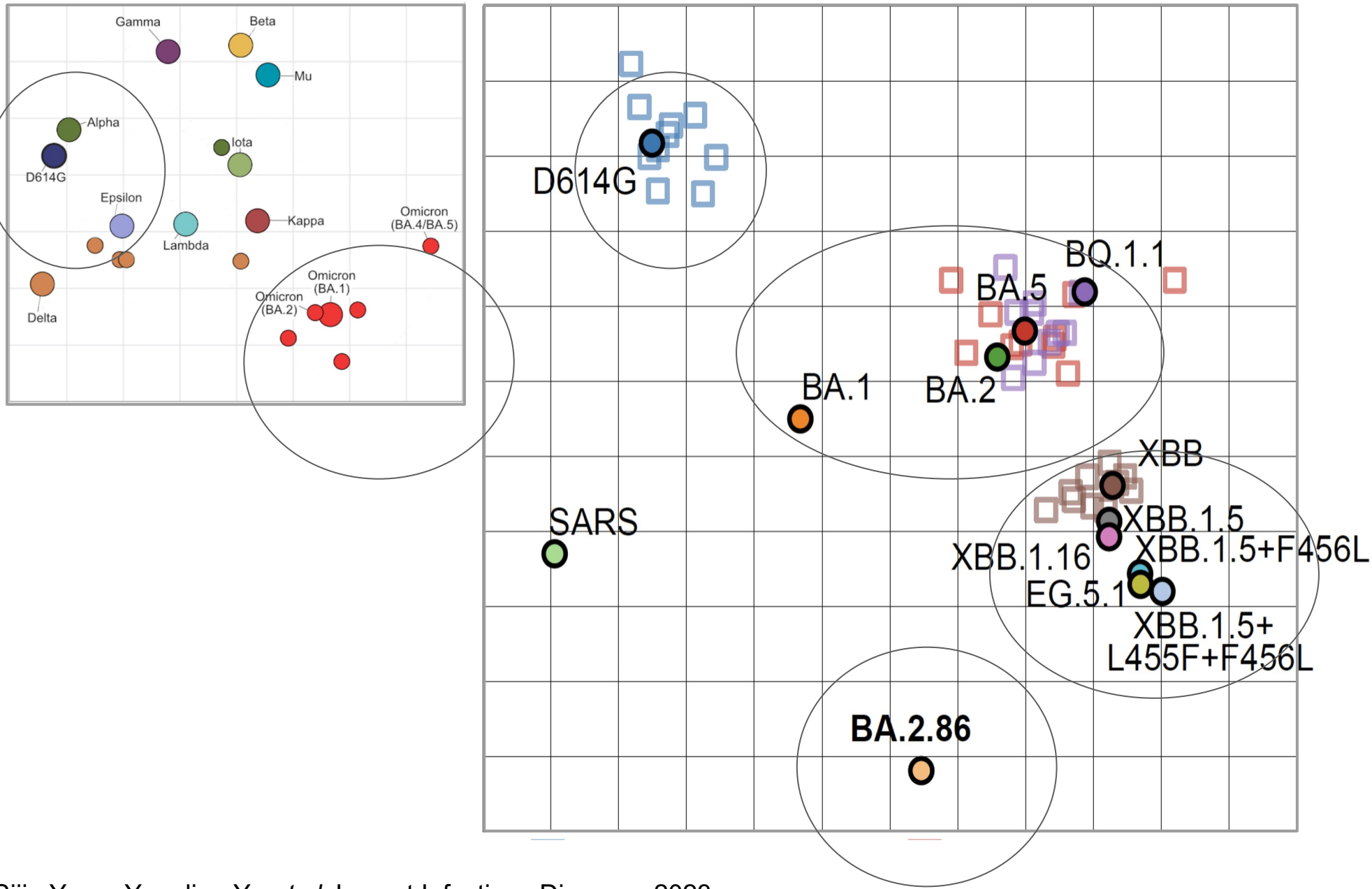

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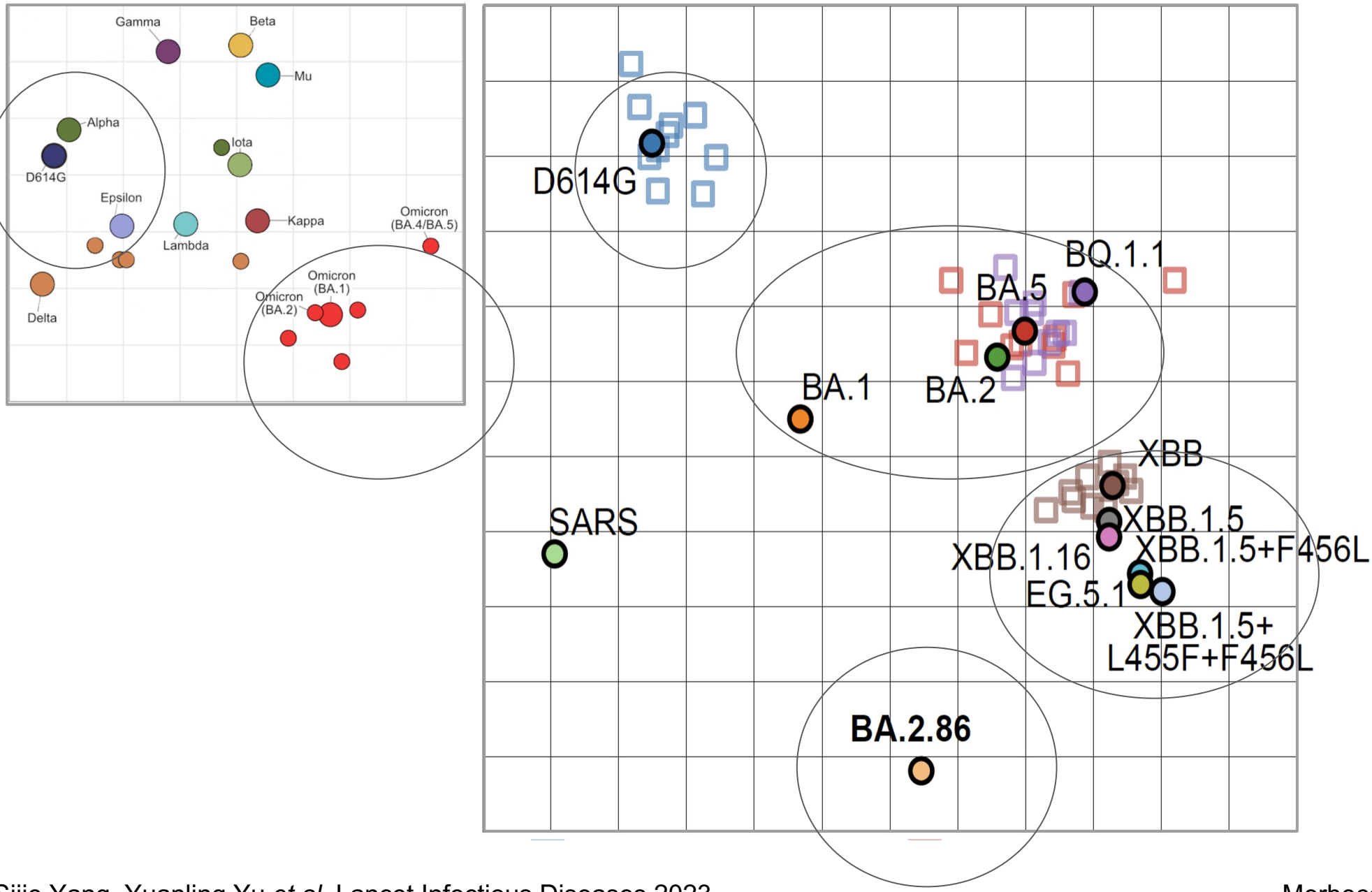
Gamma
Beta
Mu
Alpha
D614G
Iota
Epsilon
Kappa
Lambda
Omicron (BA.4/BA.5)
Omicron (BA.1)
Omicron (BA.2)
Delta
D614G
BQ.1.1
BA.5
BA.1
BA.2
XBB
XBB.1.5
XBB.1.16
XBB.1.5+F456L
EG.5.1
XBB.1.5+ L455F+F456L
SARS
BA.2.86

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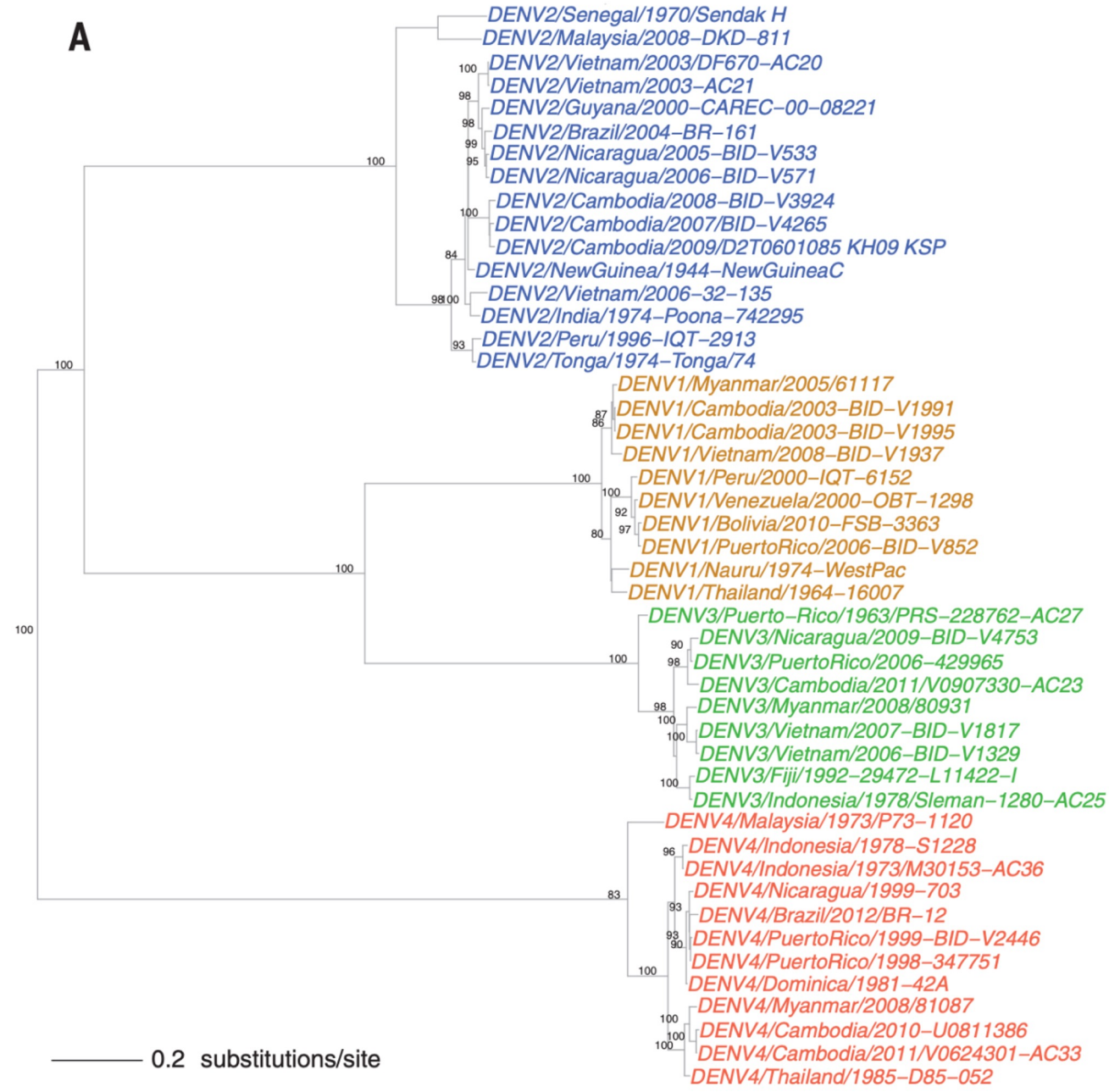
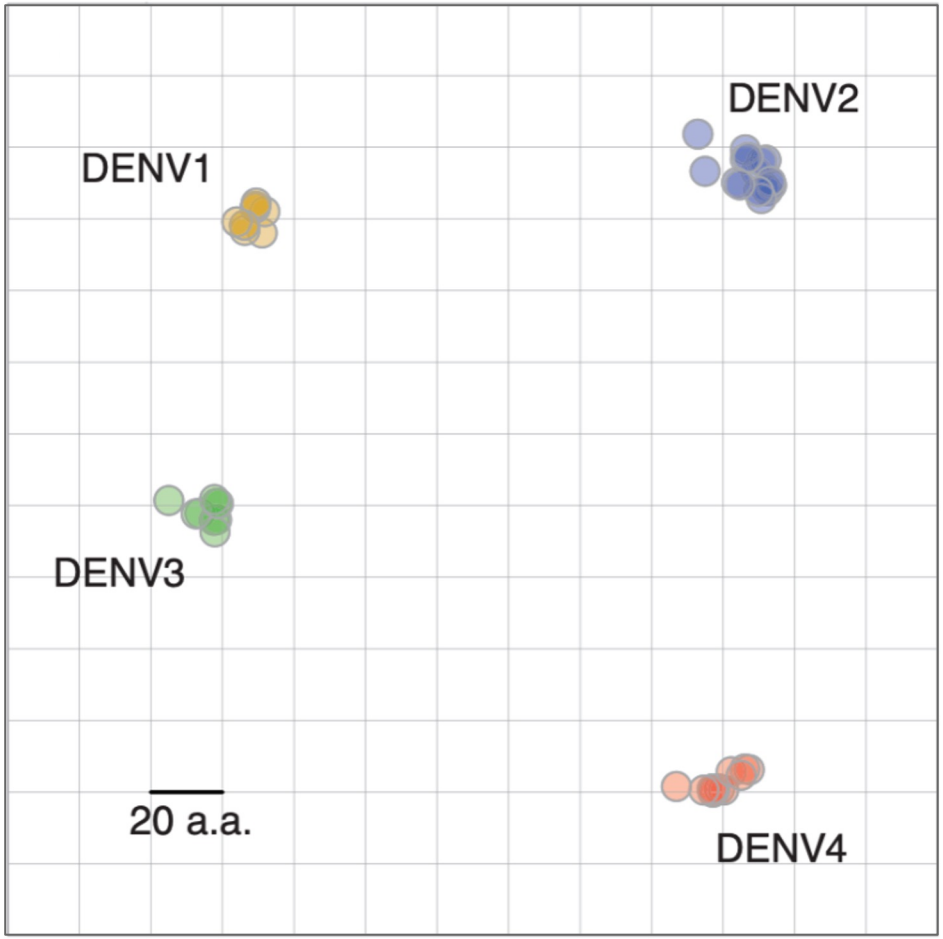
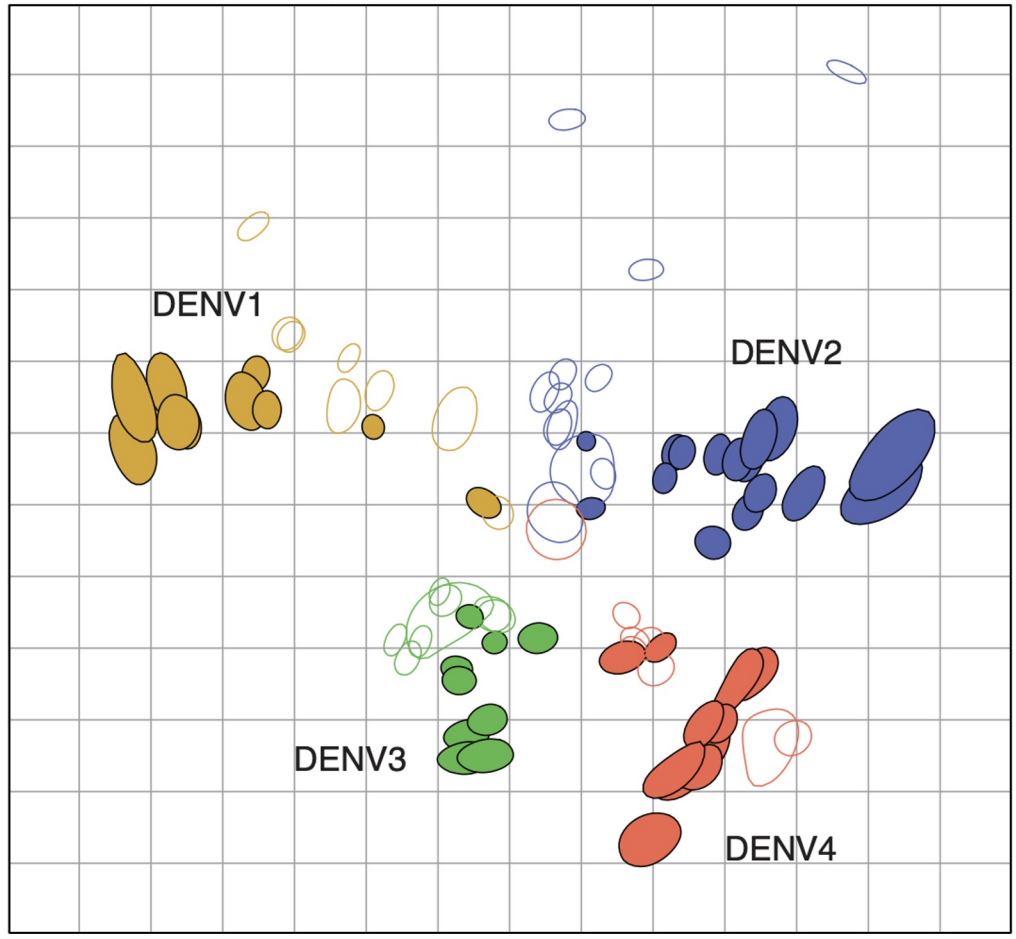


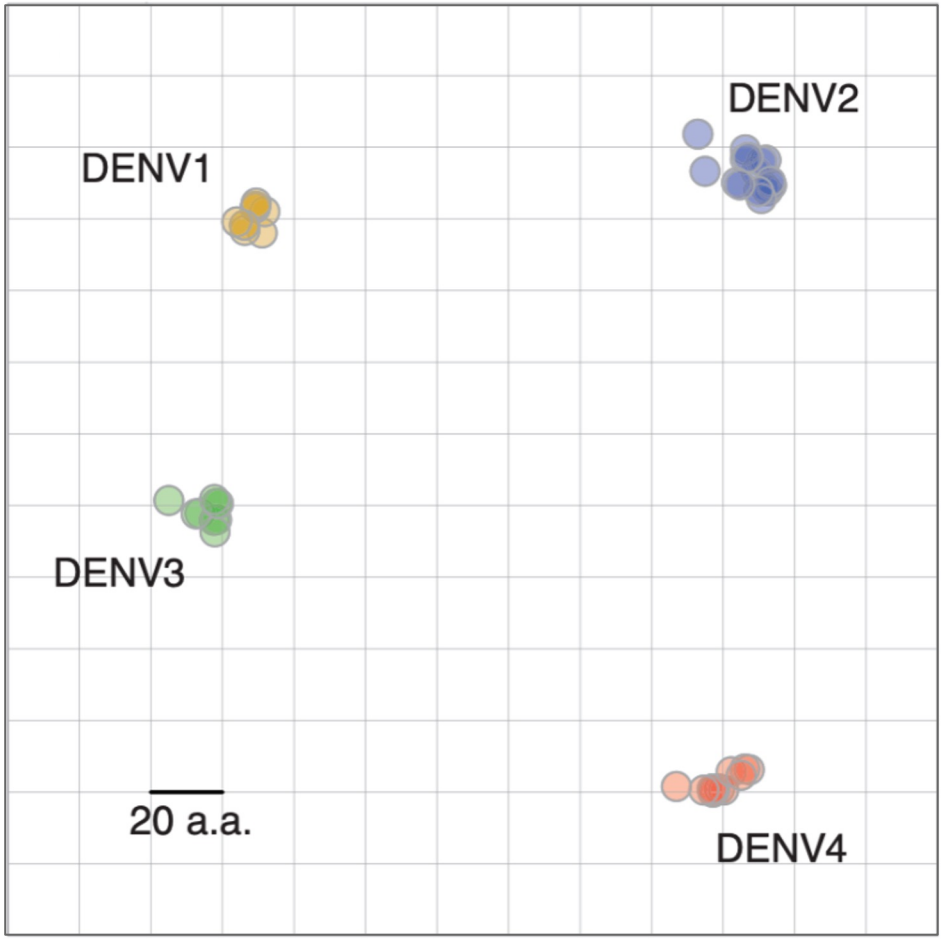
Fig. 1. Genetic analyses of the DENV panel (*n* = 47). (**A**) Phylogenetic tree showing the evolutionary relationships of DENV E gene sequences. Sequences were aligned with MAFFT, and a maximum likelihood tree was estimated using a general time-reversible model, accounting for both among-site rate variation and invariant sites (GTR+Γ_4+I). Bootstrap support values of at least 75% are shown. (**B**) Amino acid map of DENV E protein sequences (493 to 495 amino acids in length). The total amino acid differences between pairs of E sequences correspond to distances between points on the geometric display.

Katzelnick *et al* 2015 Science





Katzelnick *et al* 2015 Science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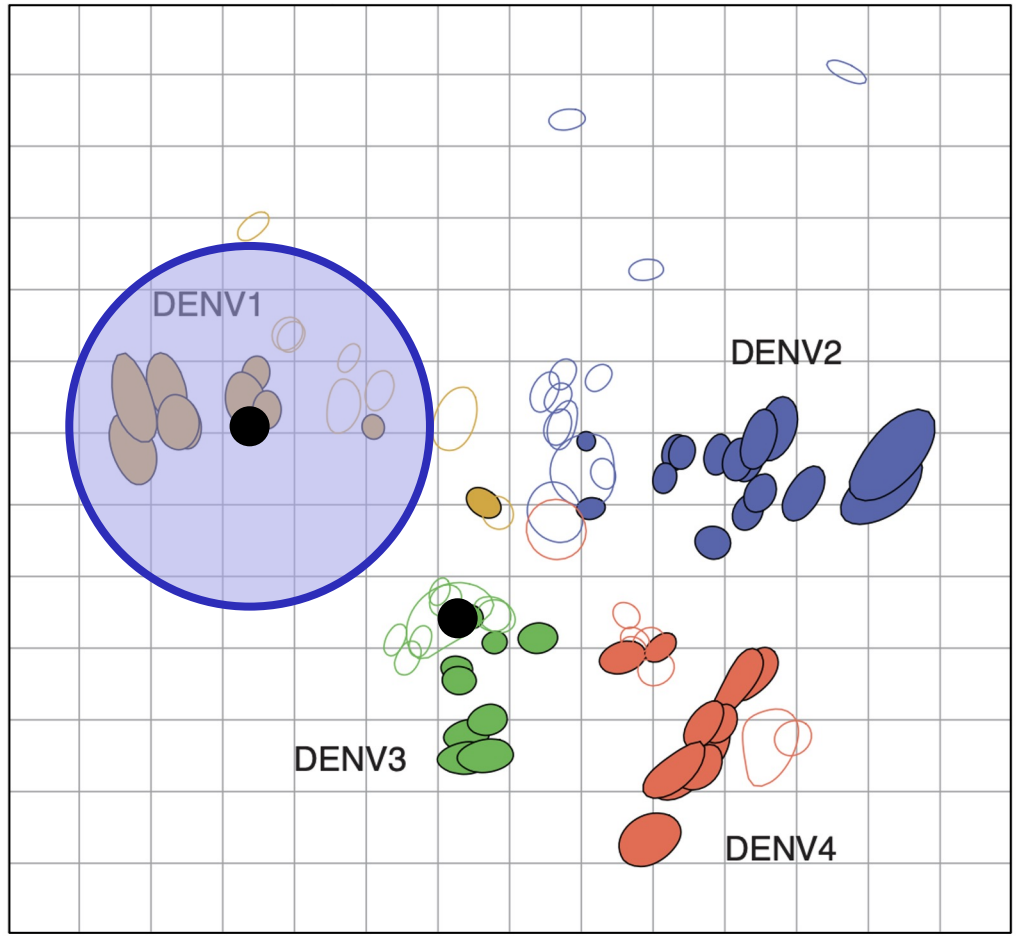
DENV1
DENV3
20 a.a.
DENV4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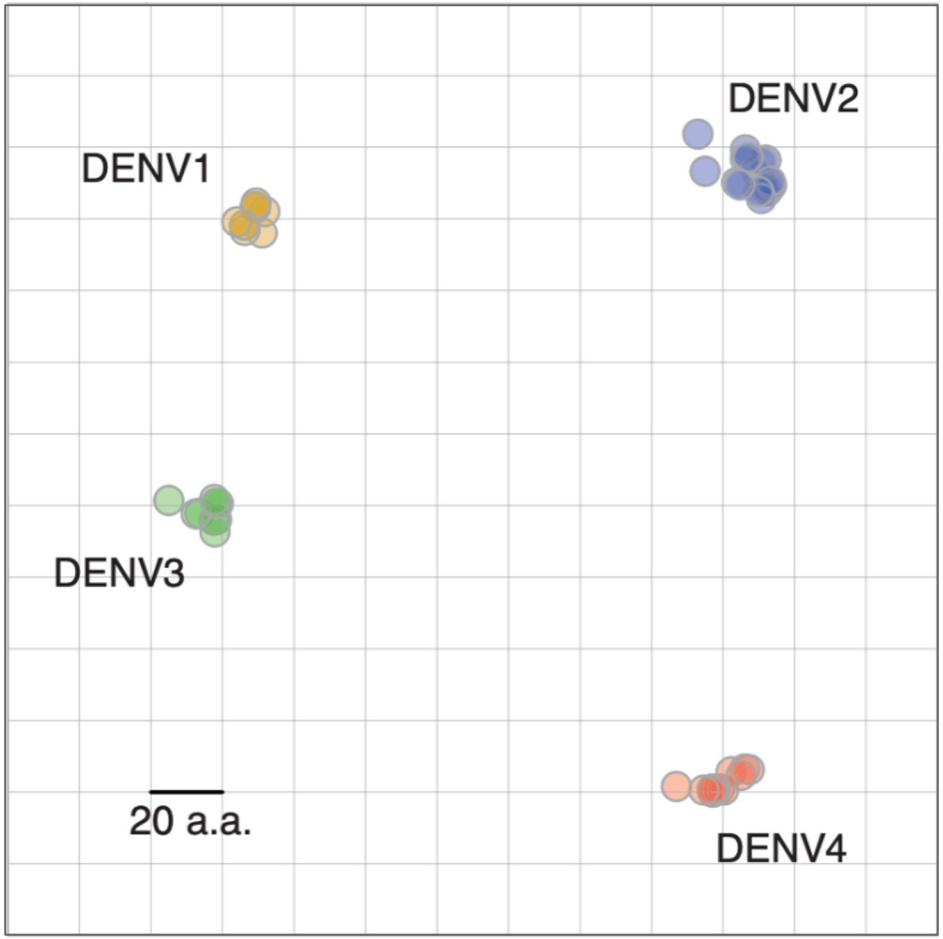
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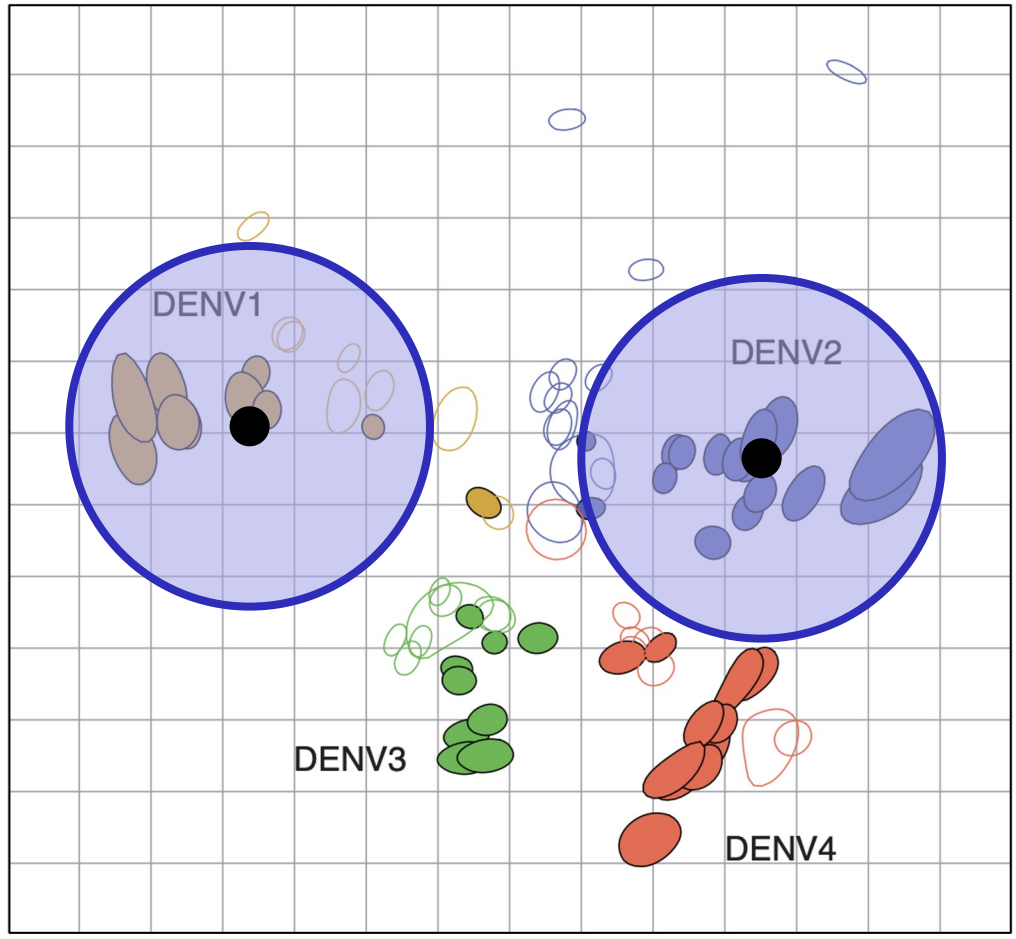
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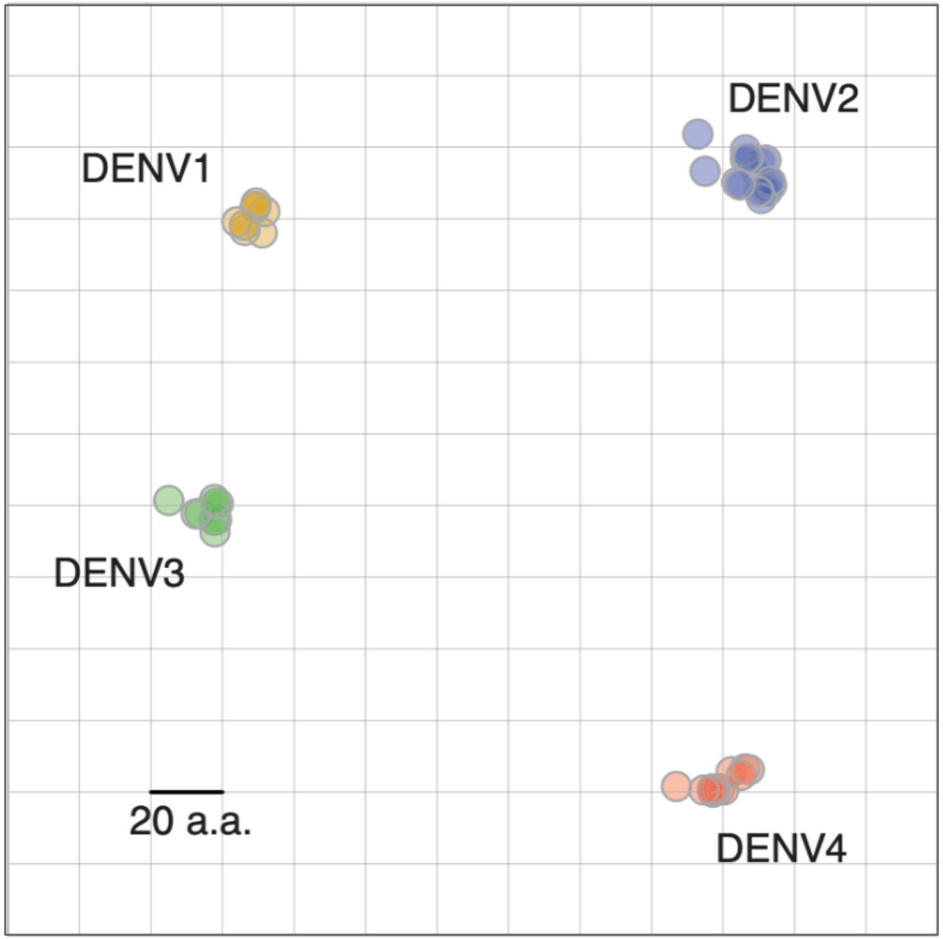
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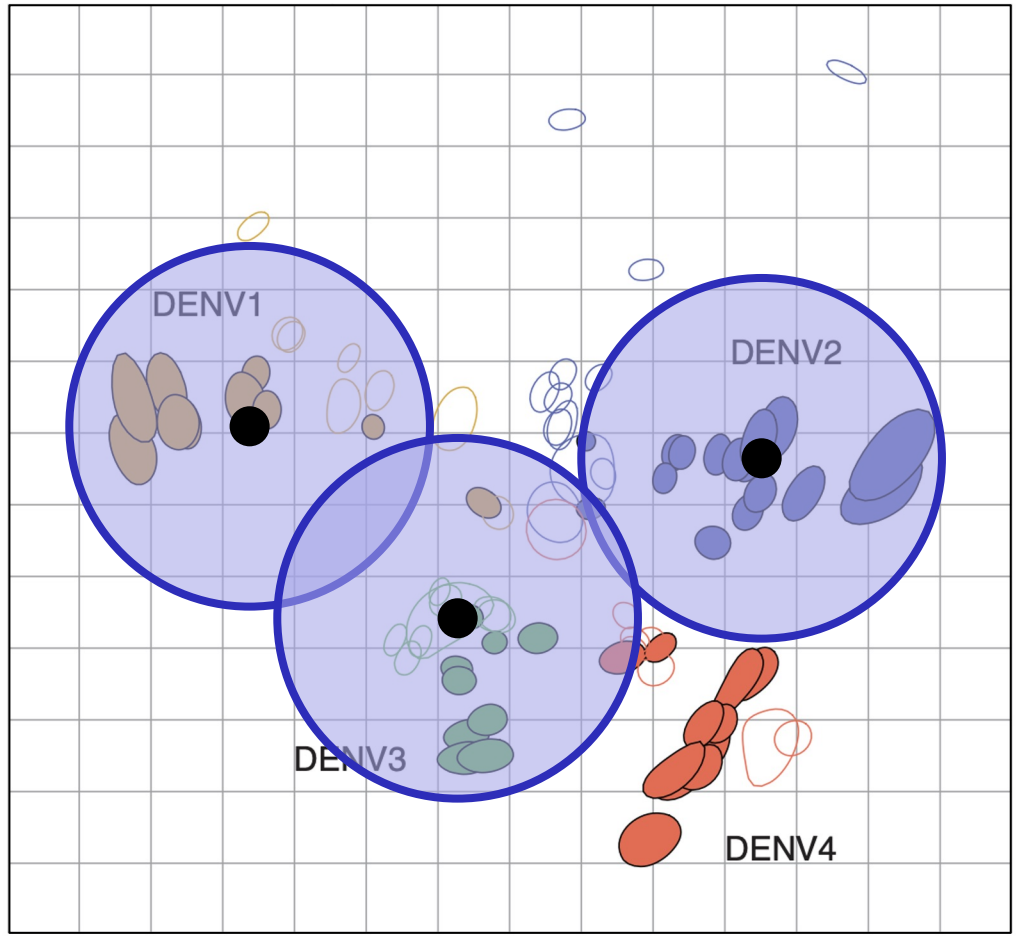
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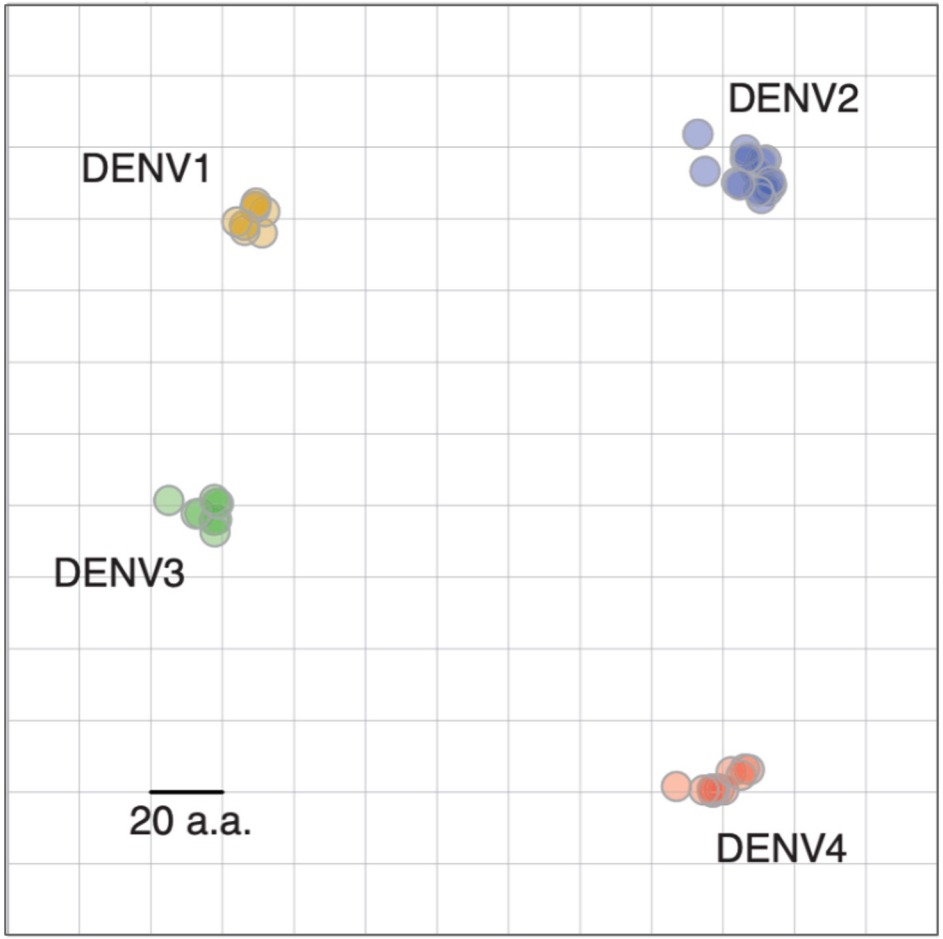
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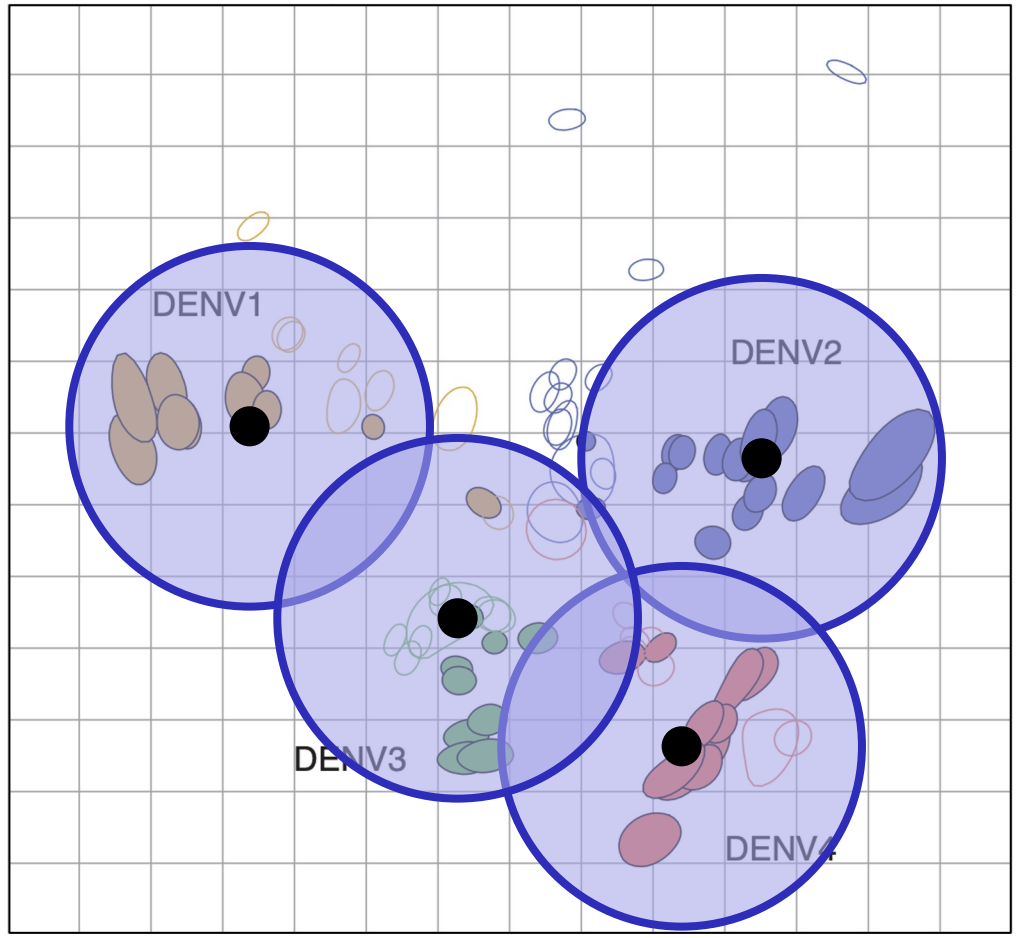
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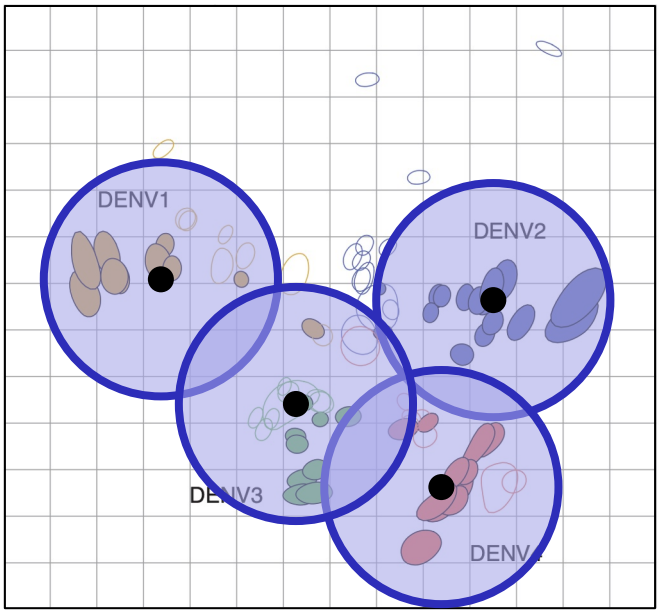
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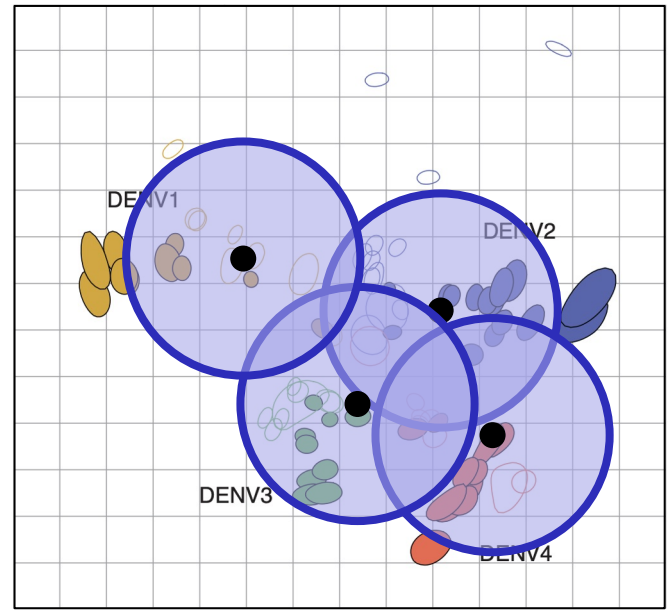
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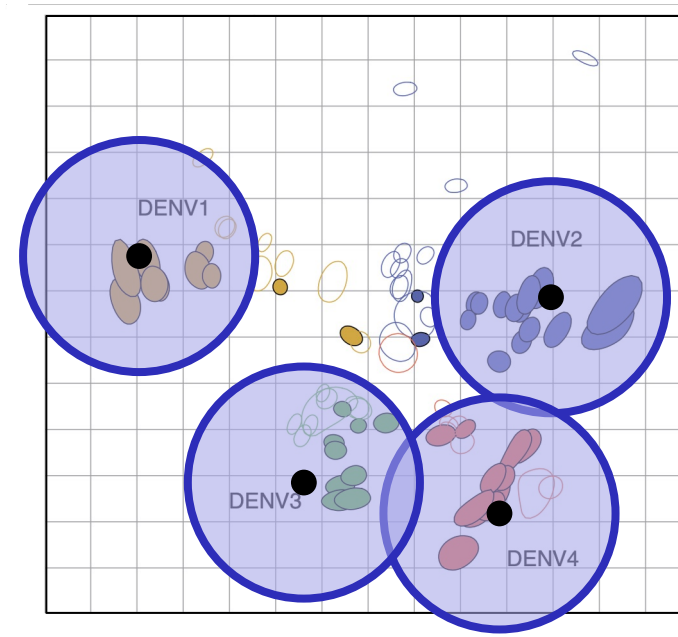
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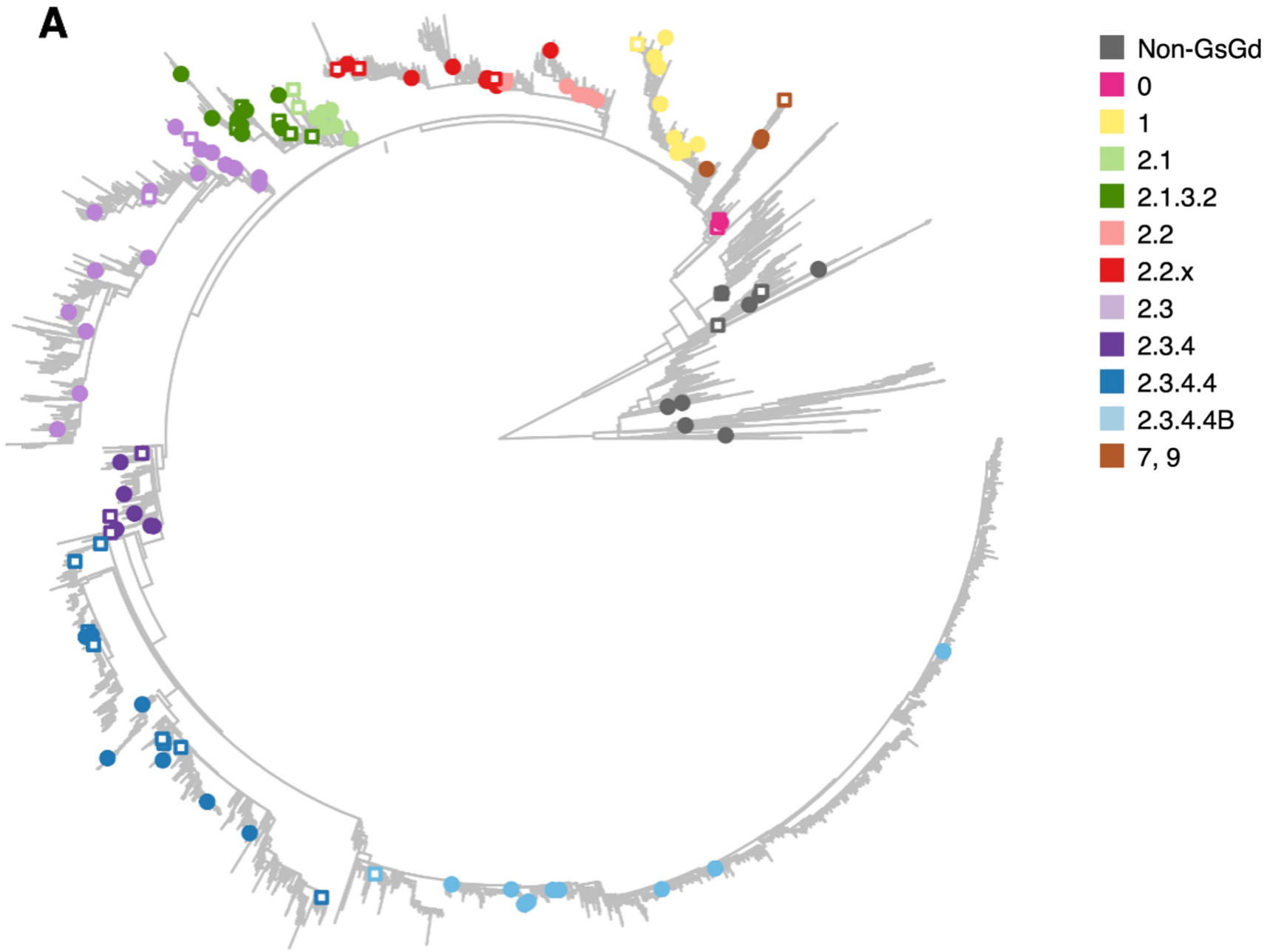
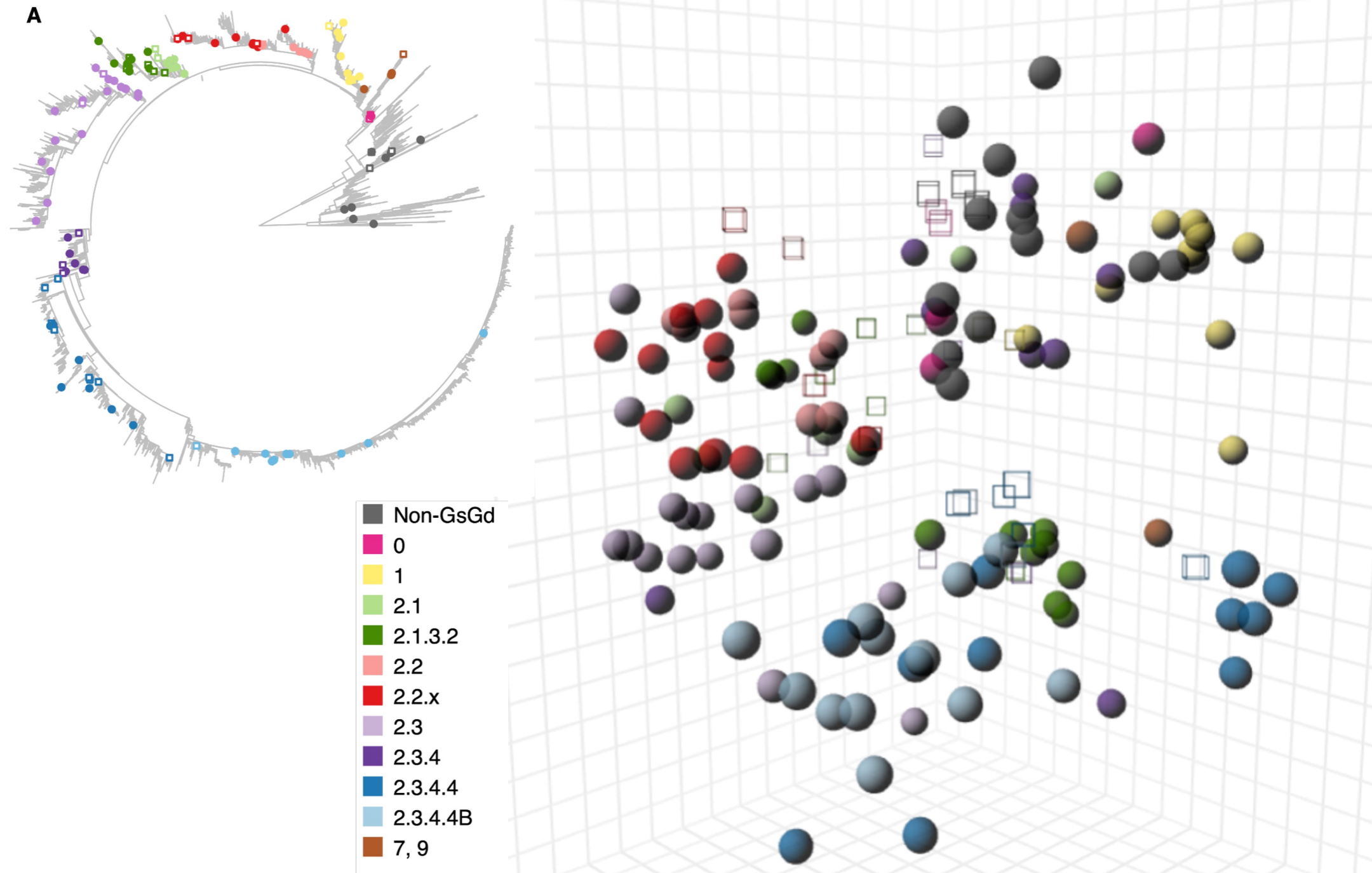


Adinda Kok, Ron Fouchier, Mathilde Richard Erasmus Medical Center, Rotterdam.



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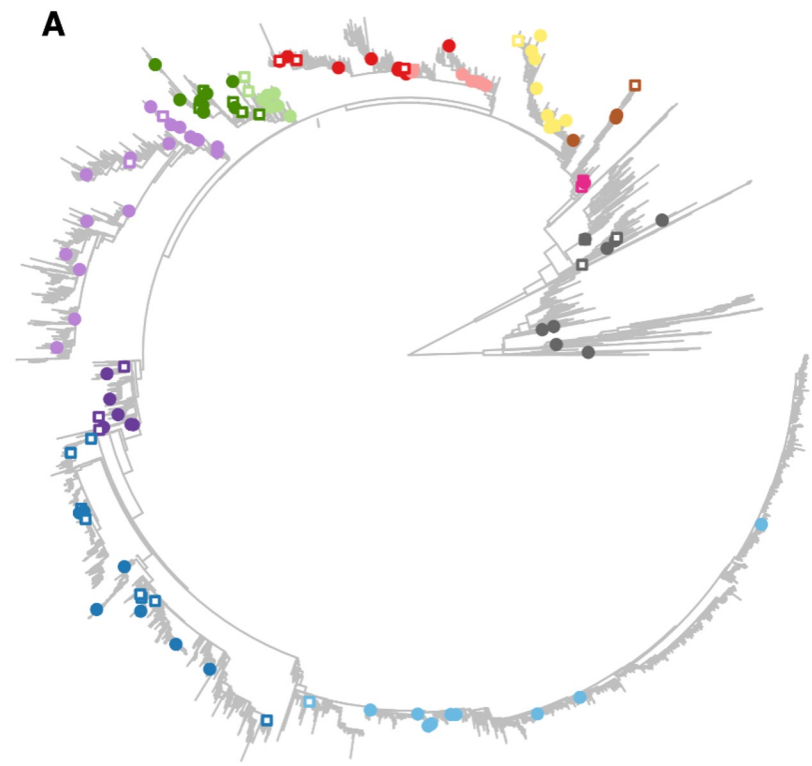

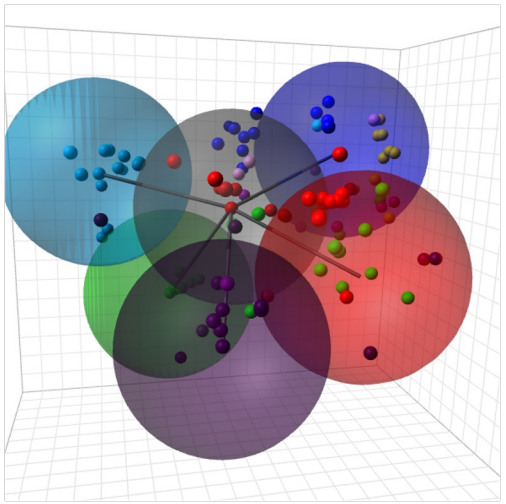

Non-GsGd
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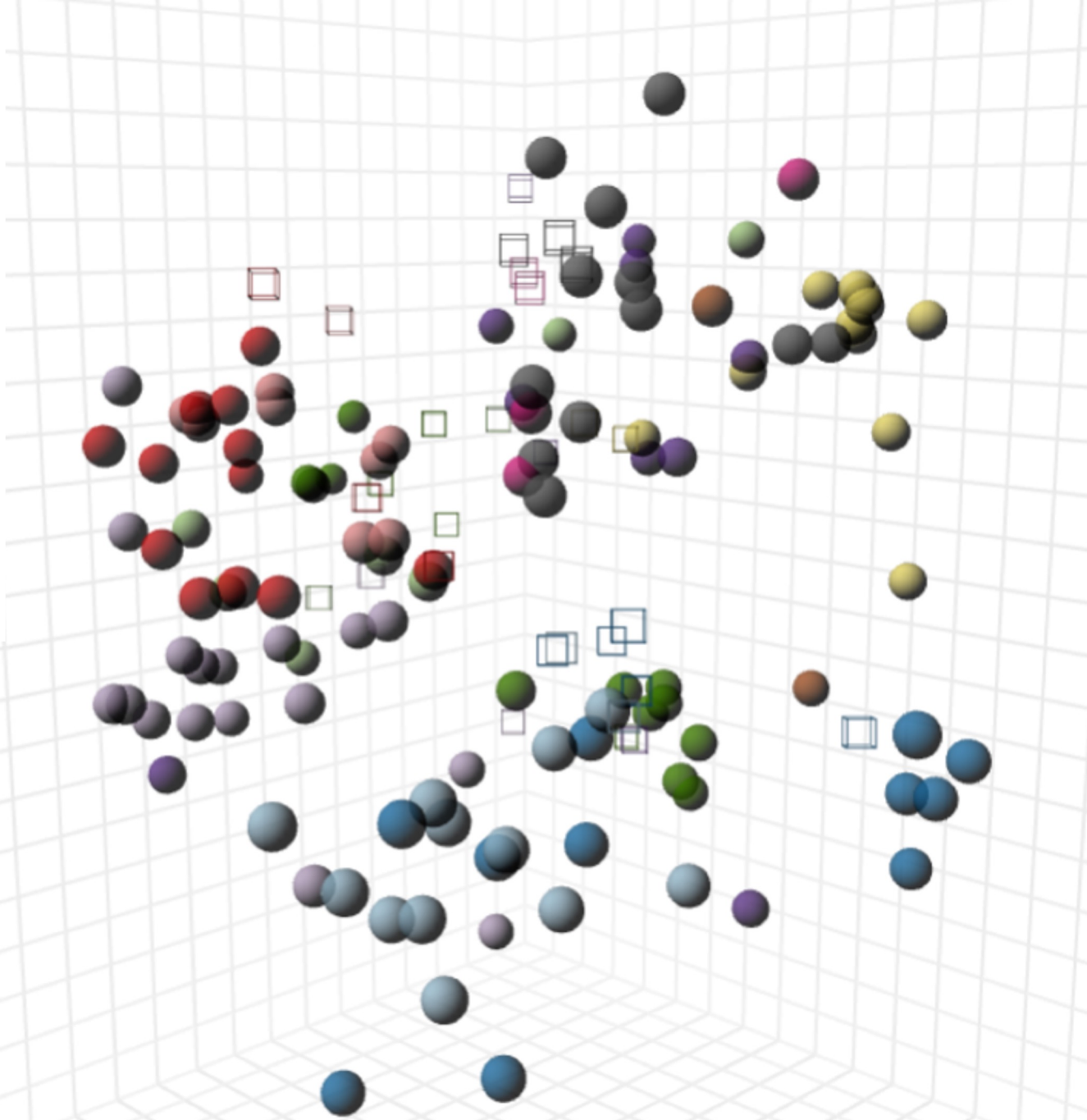
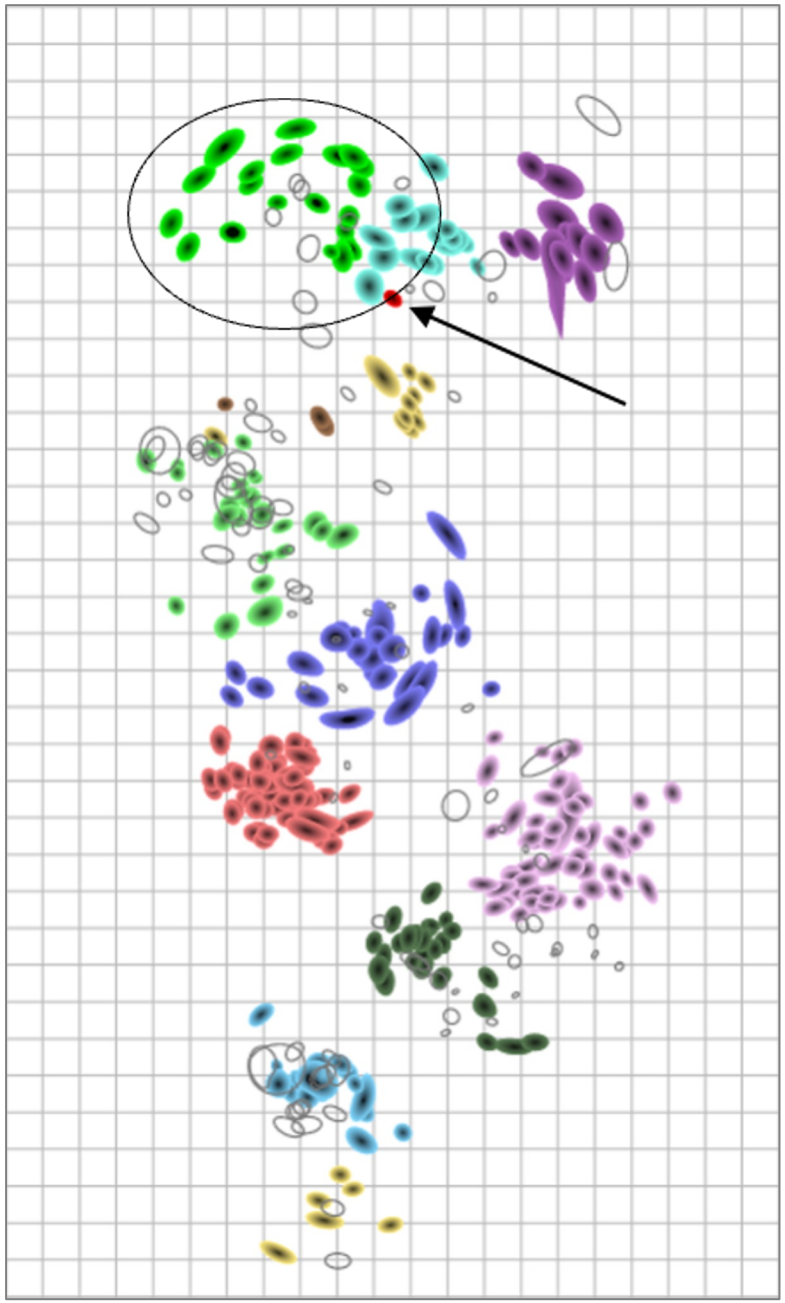
2.2
2.2.x
2.3
2.3.4
2.3.4.4
2.3.4.4B
7, 9



Adinda Kok, Ron Fouchier, Mathilde Richard Erasmus Medical Center, Rotterdam.

Human seasonal and Eurasian swine H3 influenza



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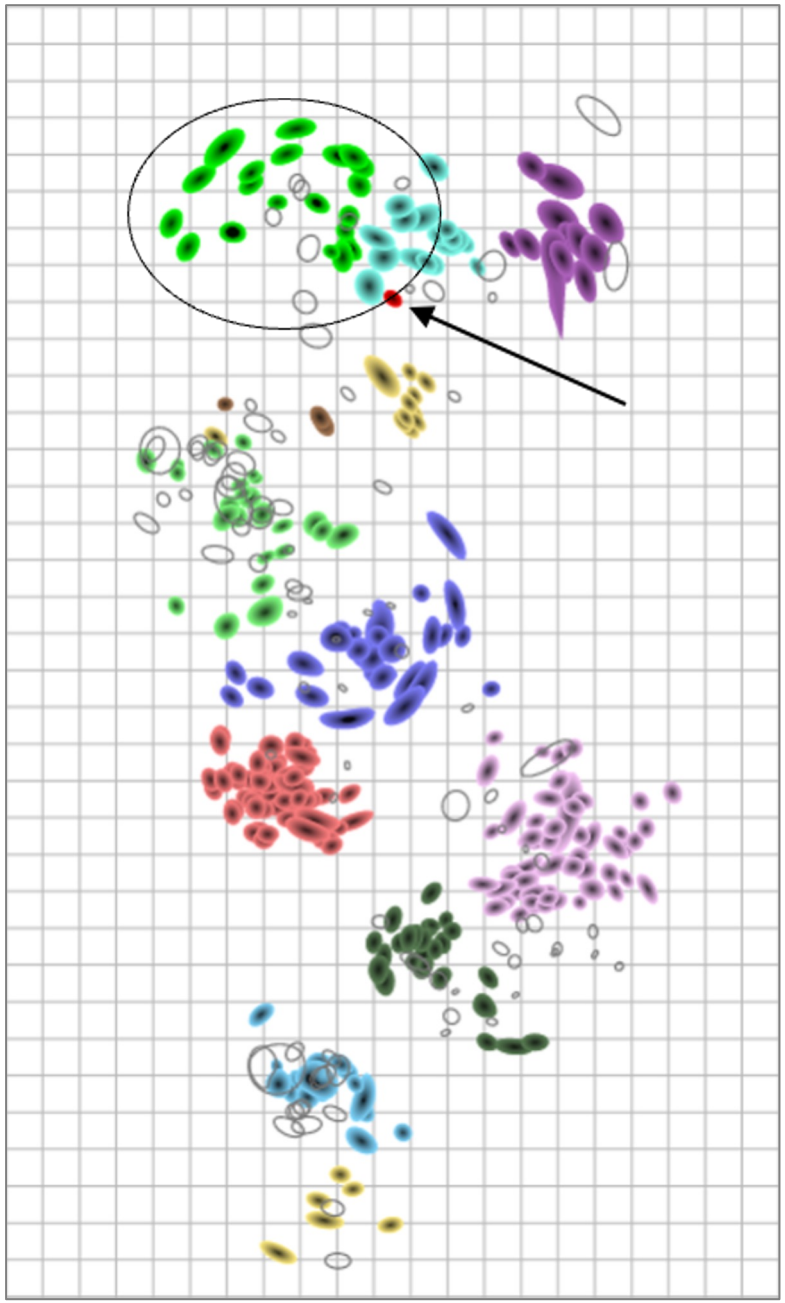
Human seasonal and Eurasian swine H3 influenza



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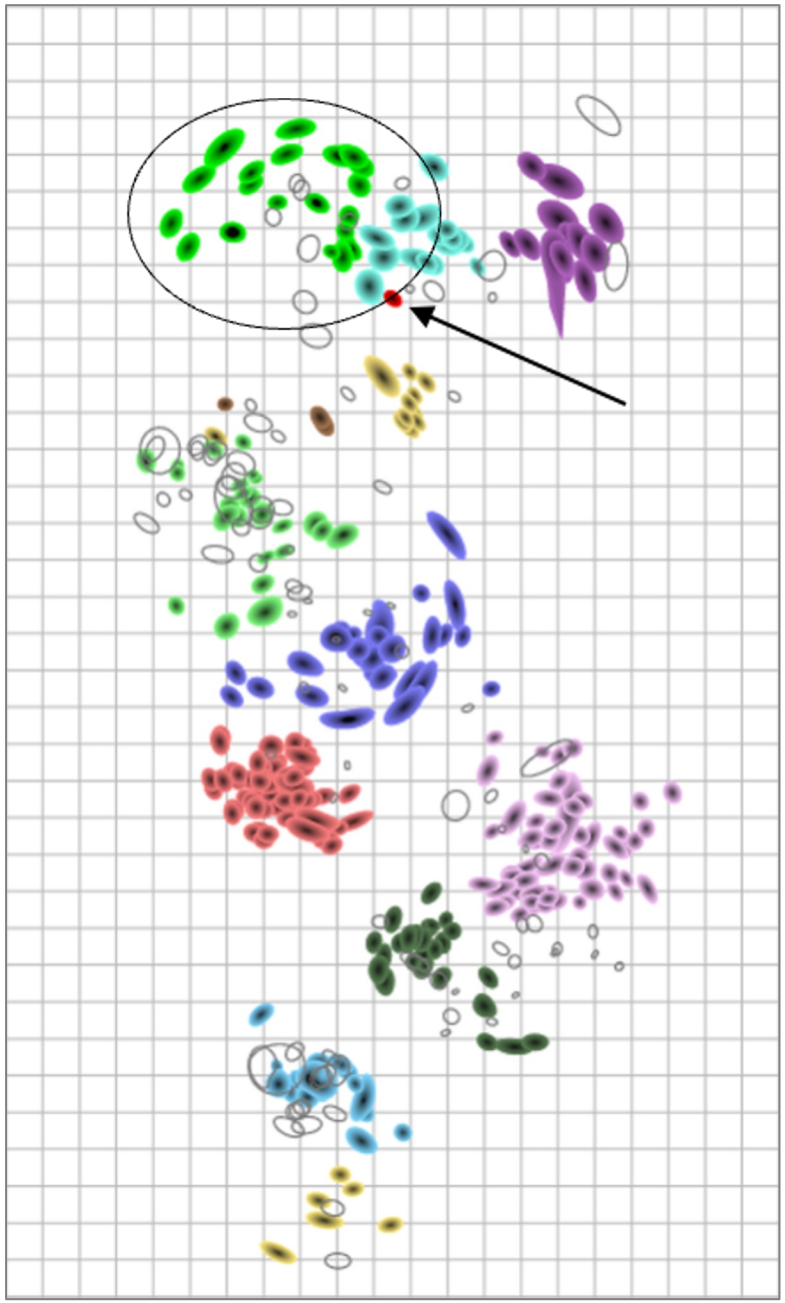
Human seasonal and Eurasian swine H3 influenza



Vaccination and Tavis

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Summary

The importance of the antigenic phenotype for vaccine strain selection

(Richard “Aggregation of phenotypic data”, here antigenic cartography)

A small subset of aa substs can cause the majority of antigenic change

(Influenza and SARS-CoV-2)

Sometimes substantial genetic divergence can cause little antigenic change

(Dengue virus, H5 influenza virus, and sometimes swine influenza viruses)

Summary

The importance of the antigenic phenotype for vaccine strain selection

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(Influenza and SARS-CoV-2)

Sometimes substantial genetic divergence can cause little antigenic change

(Dengue virus, H5 influenza virus, and sometimes swine influenza viruses)

An indication of antigenic difference in classification is useful for some stakeholders

(For a while in human seasonal influenza viruses we used a “.” to indicate phenotypic change 3C3.2a)


Ana Mosterín


Antonia Netzl


Barbara Mühlemann


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Poppy Roth


Sam Turner

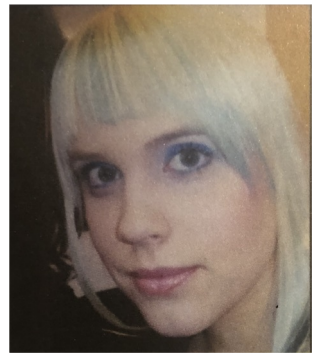

Sam Wilks


Sarah James


Sina Türeli


Terry Jones


Ron Fouchier


Mathilde Richard


Yoshi Kawaoka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Swine Influenza

Jan de Jong

H5 Influenza

Adinda Kok
Matilde Richard
Ron Fouchier

SARS-CoV-2

Shaunna Shen
David Montefiori

Dengue

Leah Katzelnick
Steve Whitehead

Influenza surveillance

WHO GISRS
- US CDC
  - Dave Wentworth
  - Becky Garten
- Australia VIDRL
  - Malet Aban
  - Ian Barr
- UK Crick Institute
  - Nicola Lewis
  - John McCauley
- Japan NIID
  - Shinji Watanabe
  - Hideki Hasegawa
- China CDC
  - Dayan Wang