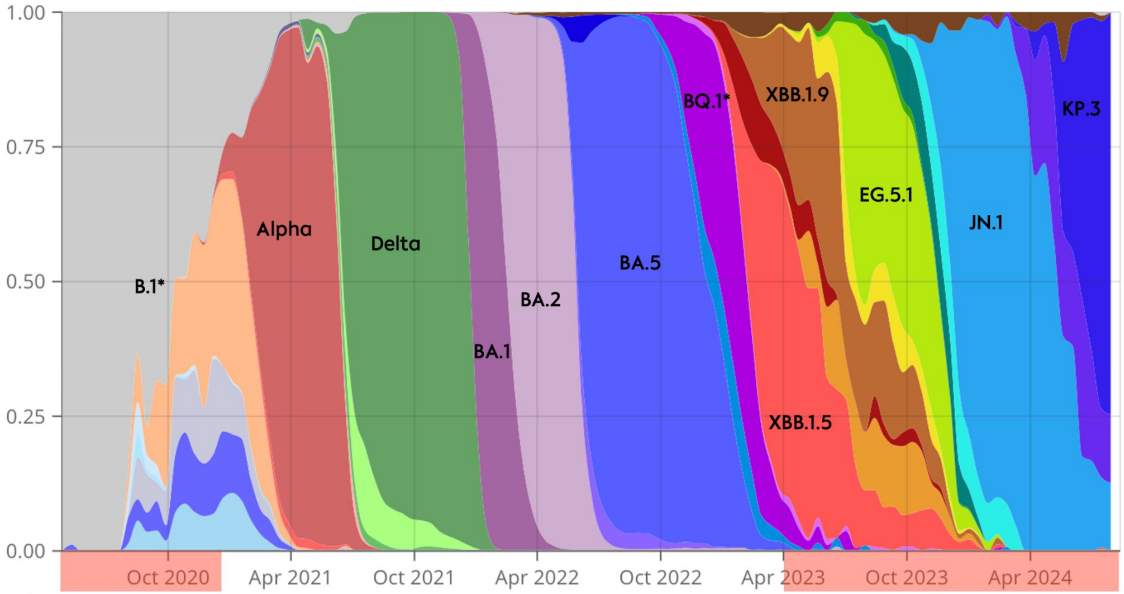
An introduction to antigenic cartography

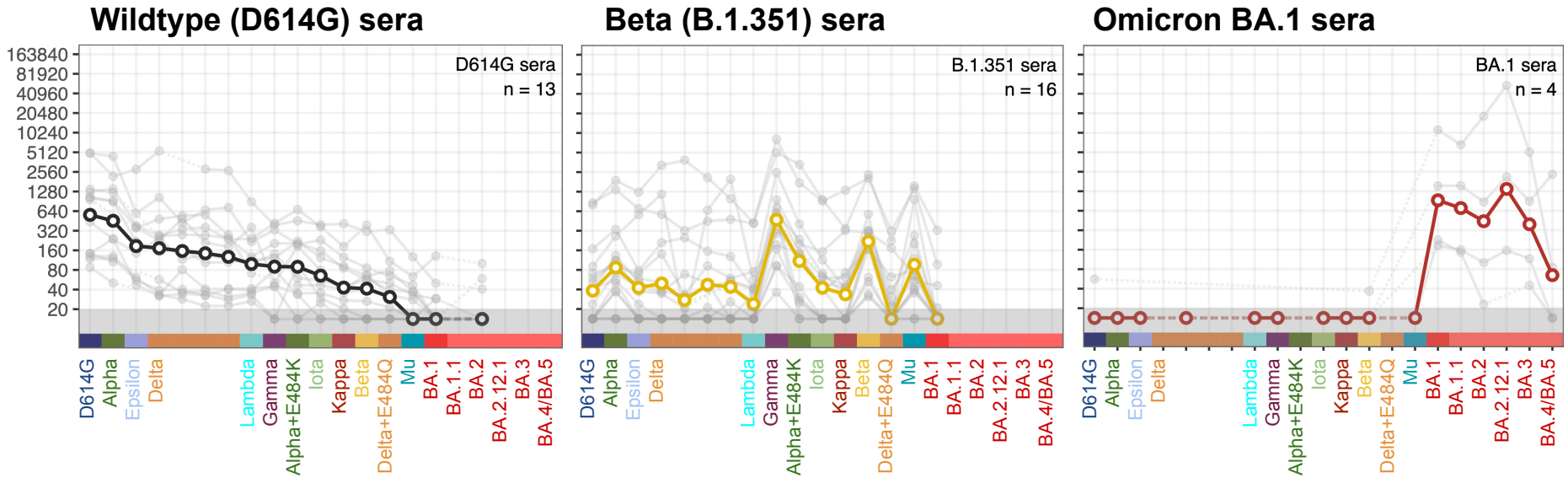
Antigenic variation in SARS-CoV-2

Variant prevalence in Germany based on sequencing data.



From https://covariants.org/per-country?country=Germany, 2024-09-01

Antigenic variation in SARS-CoV-2

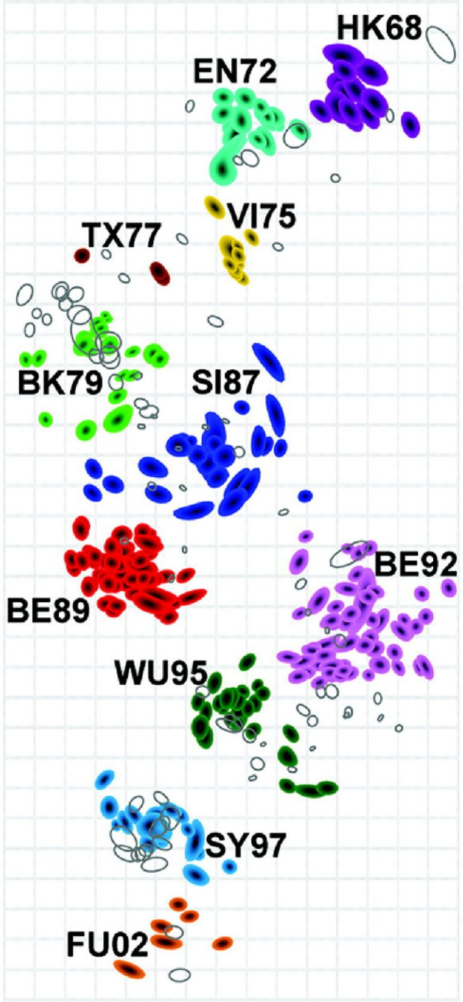


Wilks, Mühlemann, Shen et al., Mapping SARS-CoV-2 antigenic relationships and serological responses, bioRxiv, 2022

Antigenic cartography

A method to visualise antigenic relationships between viruses and sera.

The distance between viruses and sera corresponds to the neutralisation titer.



Antigenic map for Influenza H3N2

Smith, Lapedes et al., Mapping the Antigenic and Genetic Evolution of Influenza Virus, Science, 2004

Map → Distance table

Map → Distance table

	Berlin	Hamburg	Munich
Berlin	0	300	630
Hamburg		0	750
Munich			0

Distance table → Map

	Berlin	**Hamburg**	**Munich**
Berlin	0	300	630
Hamburg		0	750
Munich			0

Distance table → Map

	Berlin	Hamburg	Munich
Berlin	0	300	630
Hamburg		0	750
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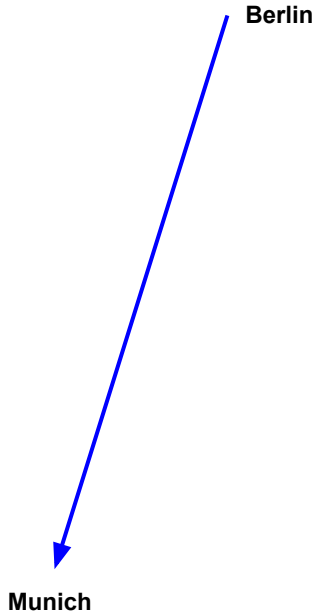
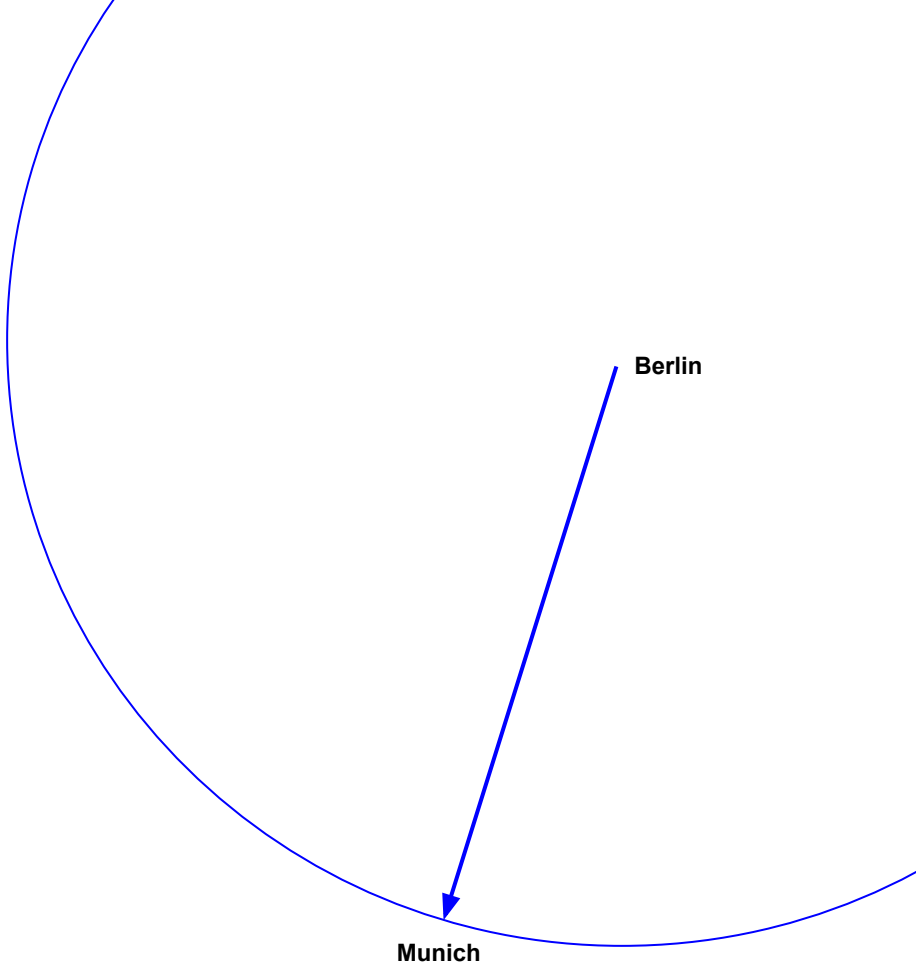


Distance table → Map

	Berlin	Hamburg	Munich
Berlin	0	300	630
Hamburg		0	750
Munich			0



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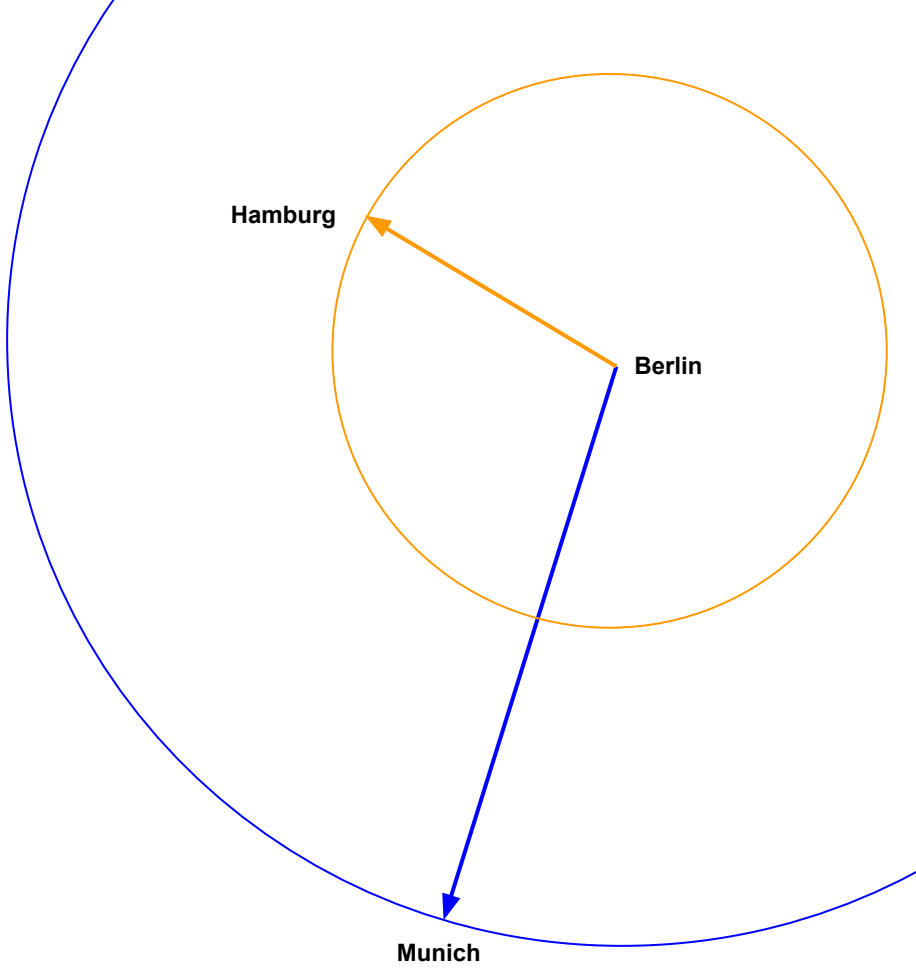

Distance table → Map

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Berlin	0	300	630
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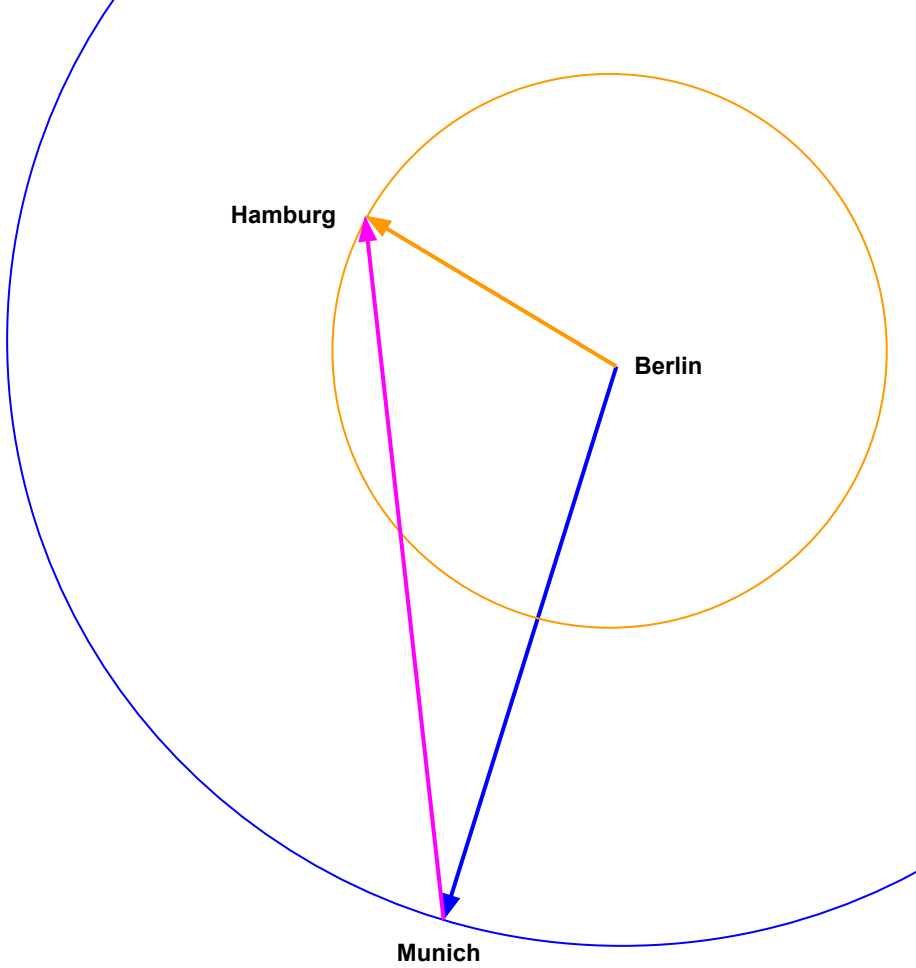
Munich			0



Distance table → Map

	Berlin	Hamburg	Munich
Berlin	0	300	630
Hamburg		0	750
Munich			0

The map is free to rotate, the orientation is only given by convention (e.g., north is always up).

Distance table → Map

	Berlin	Hamburg	Munich
Berlin	0	300	630
Hamburg		0	750
Munich			0

The map is free to rotate, the orientation is only given by convention (e.g., north is always up).

Making an antigenic map

Titer table

	Sr-LE	Sr-BN	Sr-JO	Sr-BE	Sr-HK
Ag-LE	640	40	20	<10	<10
Ag-BN	320	1280	20	<10	40
Ag-JO	20	10	1280	20	10
Ag-BE	10	10	160	320	80
Ag-HK	10	10	10	160	320

$$log_2\left(\frac{\text{Titer}}{10}\right)$$

Log titer table

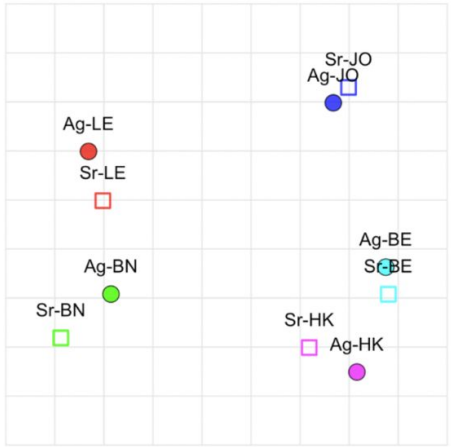
	Sr-LE	Sr-BN	Sr-JO	Sr-BE	Sr-HK
Ag-LE	6	2	1	<0	<0
Ag-BN	5	7	1	<0	2
Ag-JO	1	0	7	1	0
Ag-BE	0	0	4	5	3
Ag-HK	0	0	0	4	5

	Sr-LE	Sr-BN	Sr-JO	Sr-BE	Sr-HK
Column base	6	7	7	5	5

Distance = Column base - log titer

Distance table

	Sr-LE	Sr-BN	Sr-JO	Sr-BE	Sr-HK
Ag-LE	0	5	6	>5	>5
Ag-BN	1	0	6	>5	3
Ag-JO	5	7	0	4	5
Ag-BE	6	7	3	0	2
Ag-HK	6	7	7	1	0



1 grid square = 1 two-fold serum dilution in the assay

Wilks, An introduction to antigenic cartography
https://acorg.github.io/Racmacs/articles/intro-to-antigenic-cartography.html

Applying antigenic cartography to SARS-CoV-2 neutralisation data

A antigenic map from human first infection sera

In collaboration with Sam Wilks and Derek Smith (Cambridge), and Shaunna Shen and David Montefiori (Duke).

14 groups of sera titrated against 21 variants.

Sera:

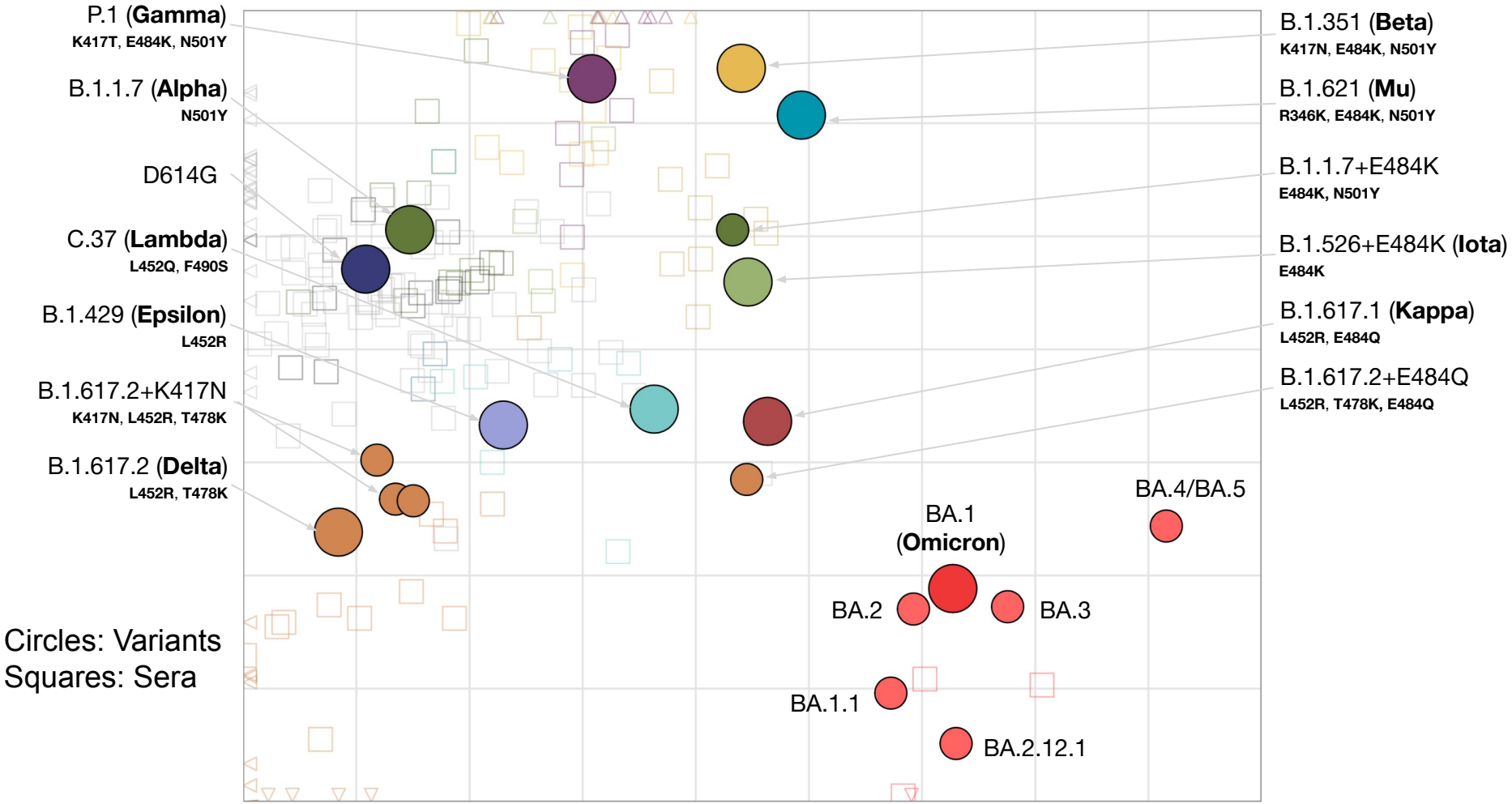
- Post infection sera of individuals infected with wild type (D614G), Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), Lambda (C.37), Iota (B.1.526+E484K), B.1.637, Omicron BA.1, Omicron BA.2.
- Post vaccination sera 4 weeks post-second dose, 6 months post-second dose, 4 weeks post 3rd dose with mRNA-1273. Post vaccination sera 4 weeks post second dose of mRNA-1273.351

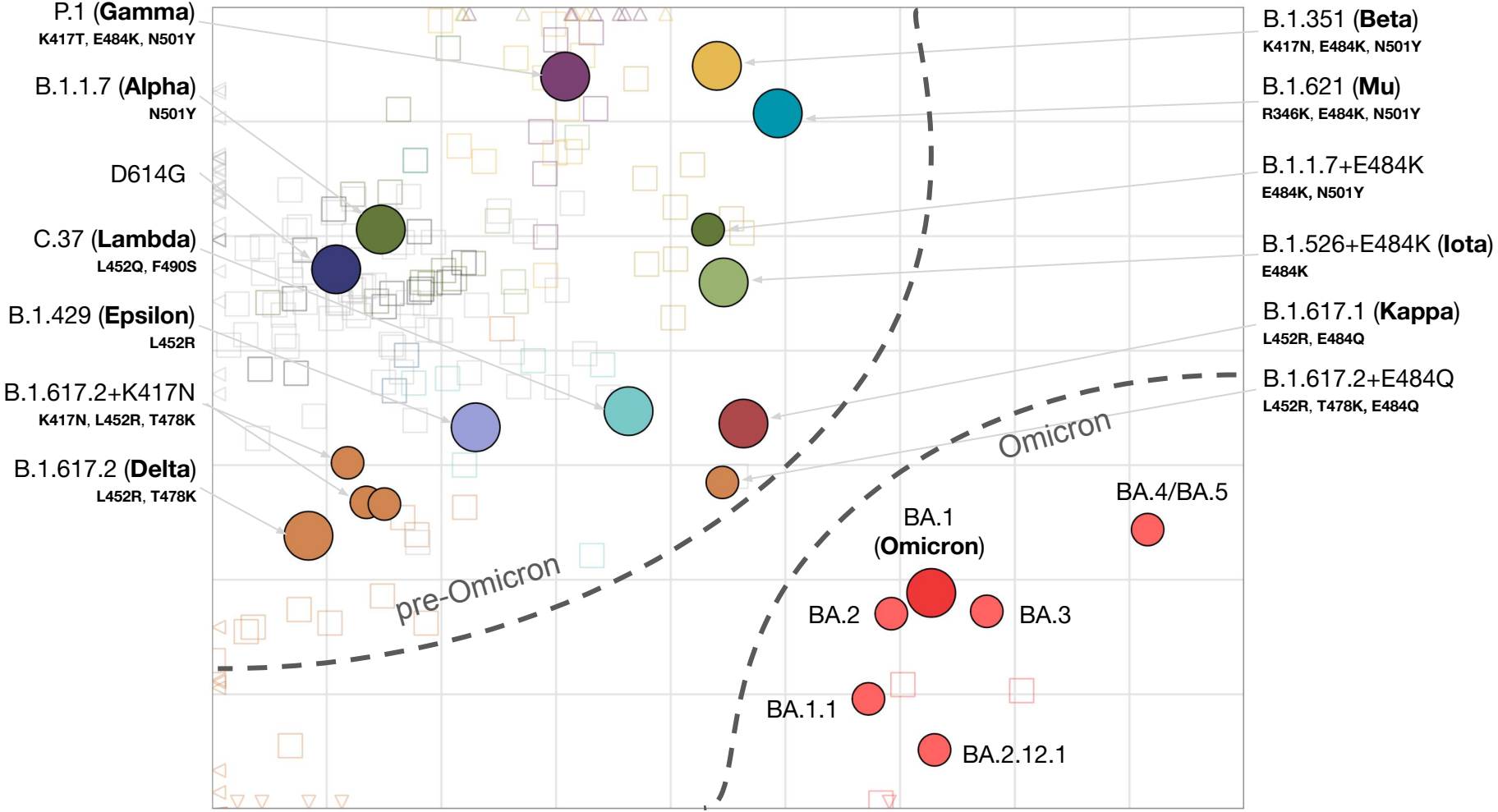
Variants:

D614G, Epsilon (B.1.429), Alpha (B.1.1.7), Alpha+E484K, Beta (B.1.351), Gamma (P.1), Mu (B.1.621),Iota (B.1.526+E484K), Kappa (B.1.617.1), Delta (B.1.617.2), Delta+K417N, Delta+E484Q, Lambda (C.37), BA.1, BA.1.1, BA.2, BA.2.12.1, BA.3, BA.4/BA.5

Lentivirus pseudotype neutralisation assay on 293T/ACE2 cells.

Wilks, Mühlemann, Shen et al., Mapping SARS-CoV-2 antigenic relationships and serological responses, bioRxiv, 2022


P.1 (Gamma)
K417T, E484K, N501Y
B.1.1.7 (Alpha)
N501Y
D614G
C.37 (Lambda)
L452Q, F490S
B.1.429 (Epsilon)
L452R
B.1.617.2+K417N
K417N, L452R, T478K
B.1.617.2 (Delta)
L452R, T478K
B.1.351 (Beta)
K417N, E484K, N501Y
B.1.621 (Mu)
R346K, E484K, N501Y
B.1.1.7+E484K
E484K, N501Y
B.1.526+E484K (Iota)
E484K
B.1.617.1 (Kappa)
L452R, E484Q
B.1.617.2+E484Q
L452R, T478K, E484Q
BA.4/BA.5
BA.1
(Omicron)
BA.2
BA.3
BA.1.1
BA.2.12.1
Circles: Variants
Squares: Sera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L452R, T478K, E484Q
pre-Omicron
Omicron
BA.1
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BA.2
BA.3
BA.4/BA.5
BA.1.1
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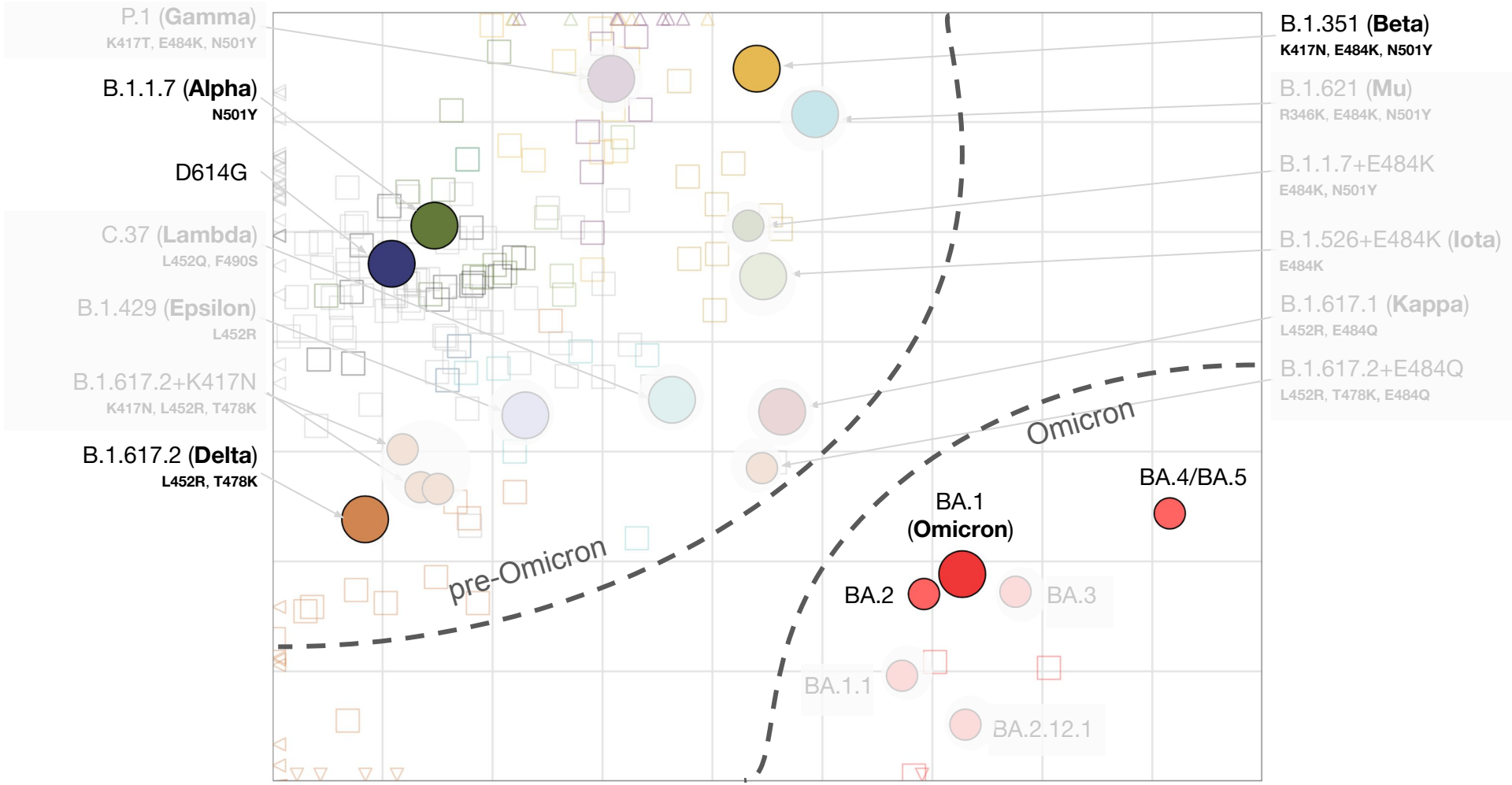
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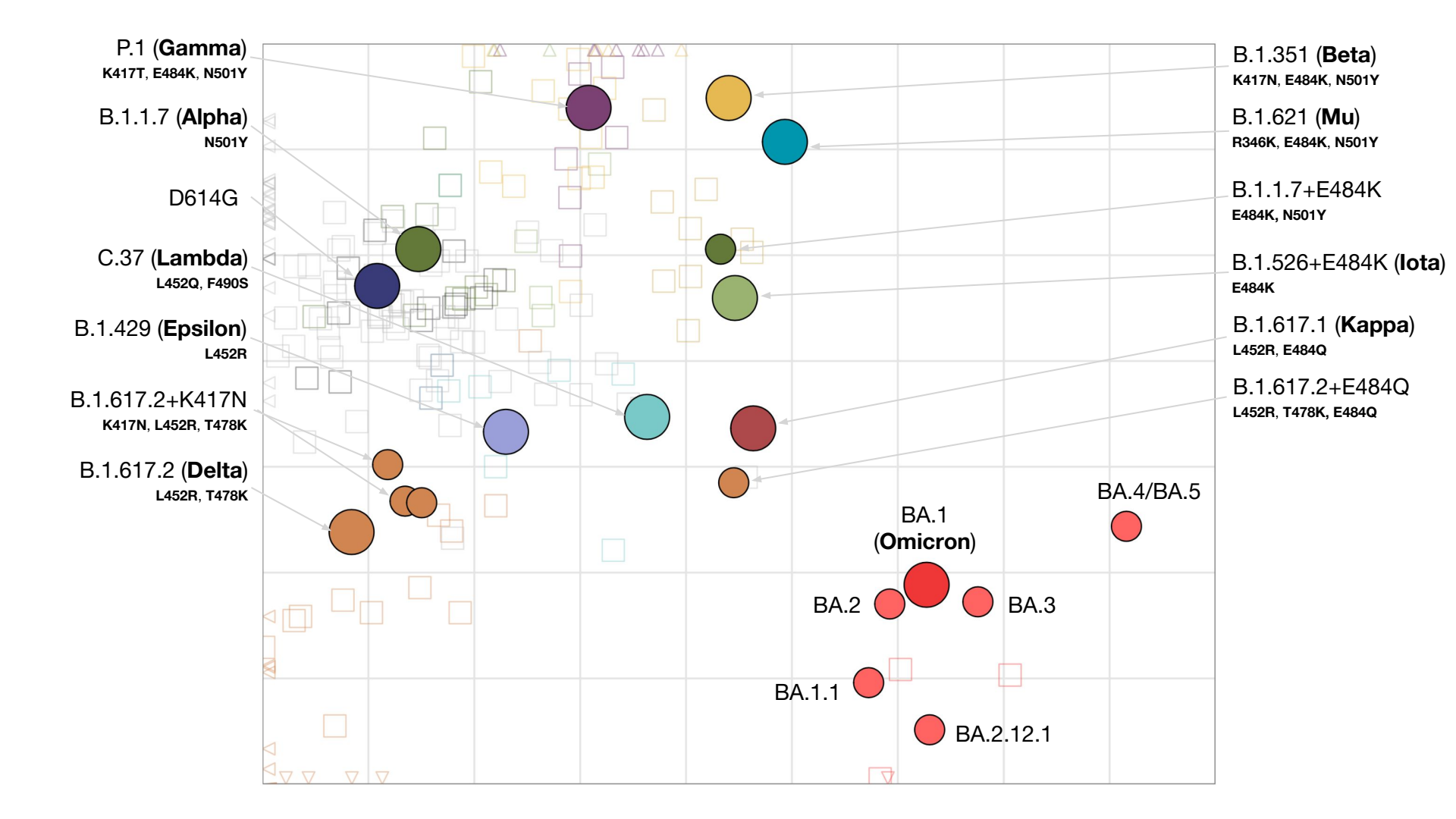
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L452R, E484Q
B.1.617.2+E484Q
L452R, T478K, E484Q
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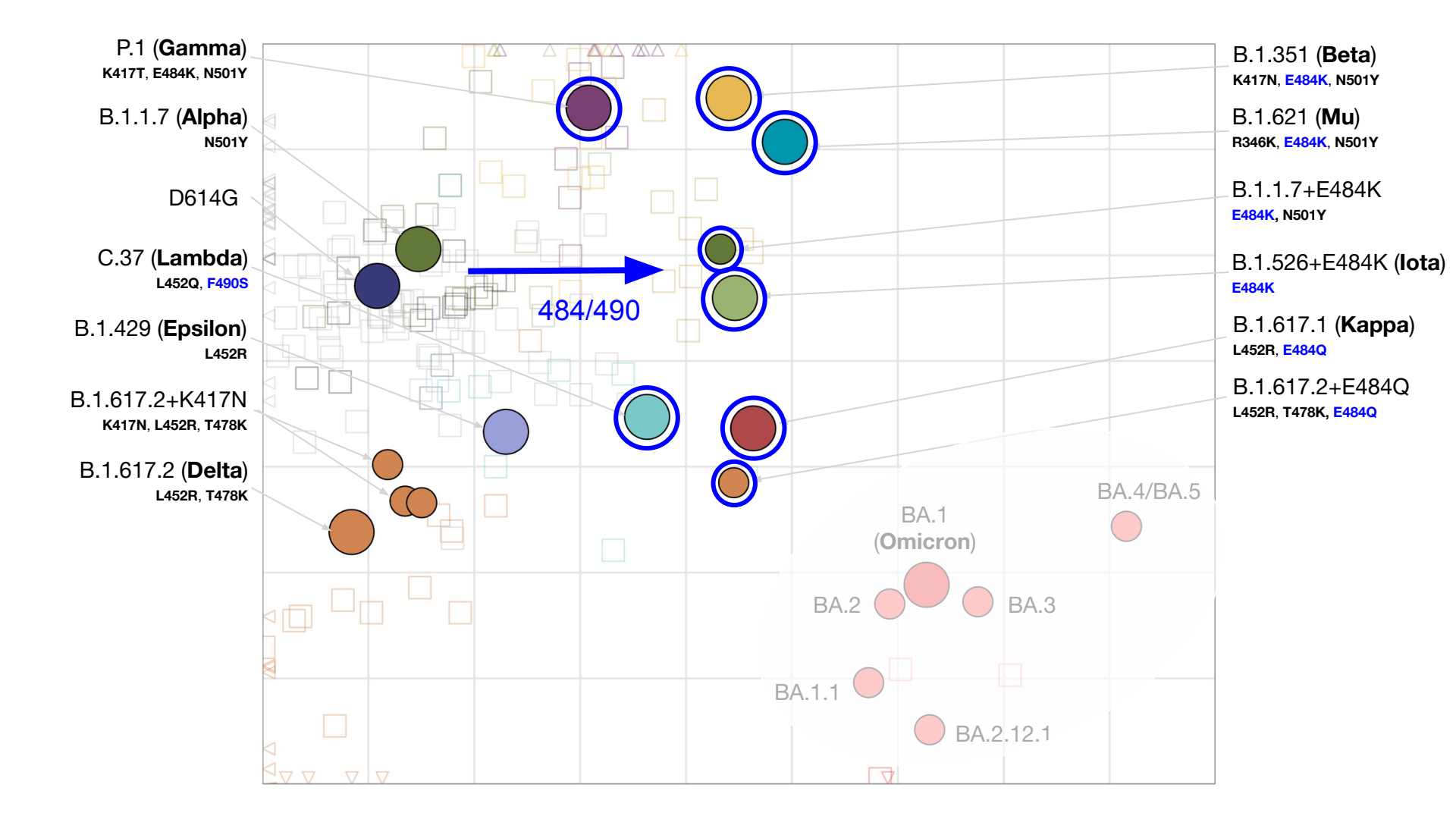
(Omicron)
BA.2
BA.3
BA.1.1
BA.2.12.1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L452R, E484Q
B.1.617.2+E484Q
L452R, T478K, E484Q
BA.1
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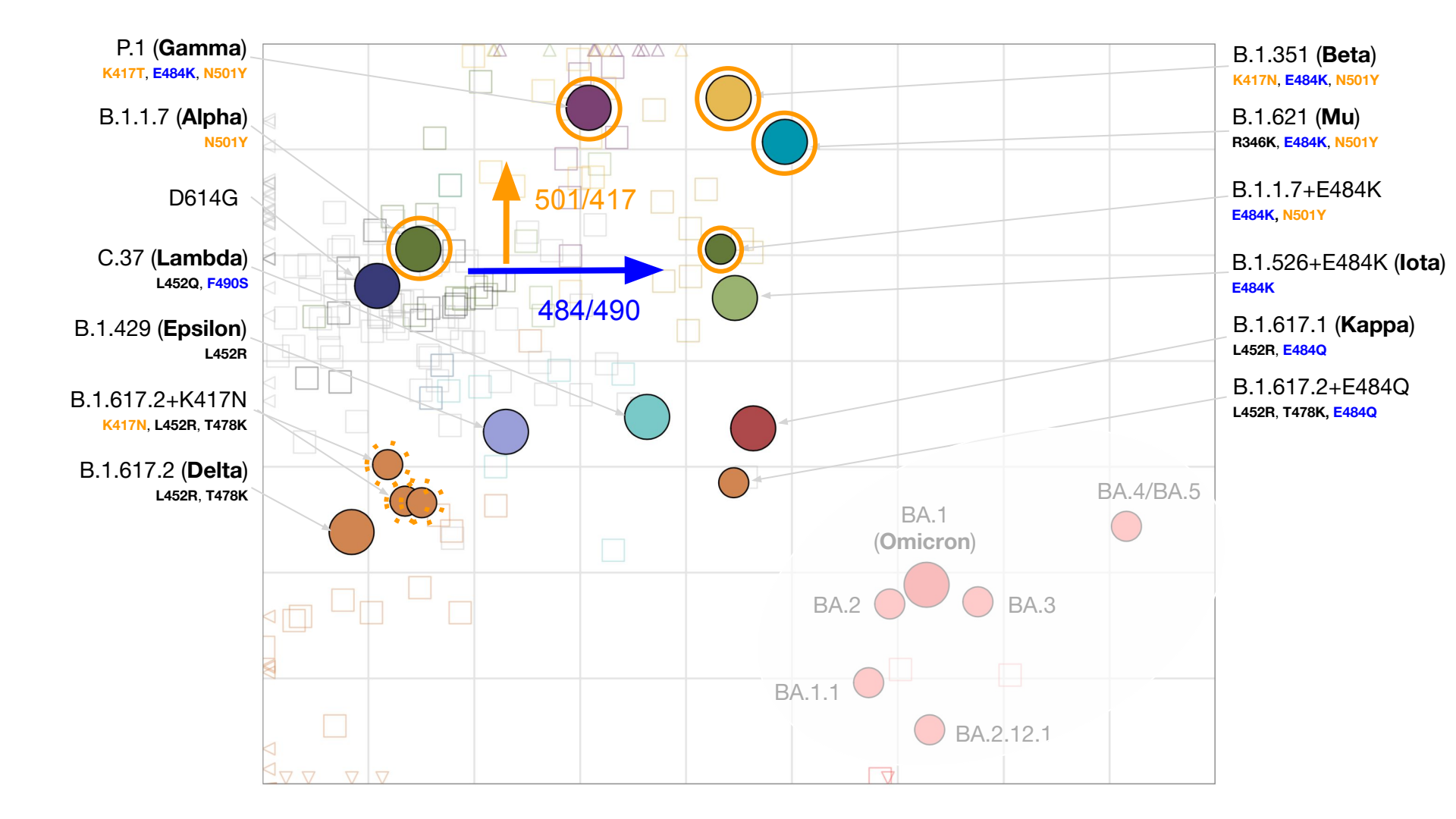
BA.2
BA.3
BA.1.1
BA.2.12.1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L452R, T478K, E484Q
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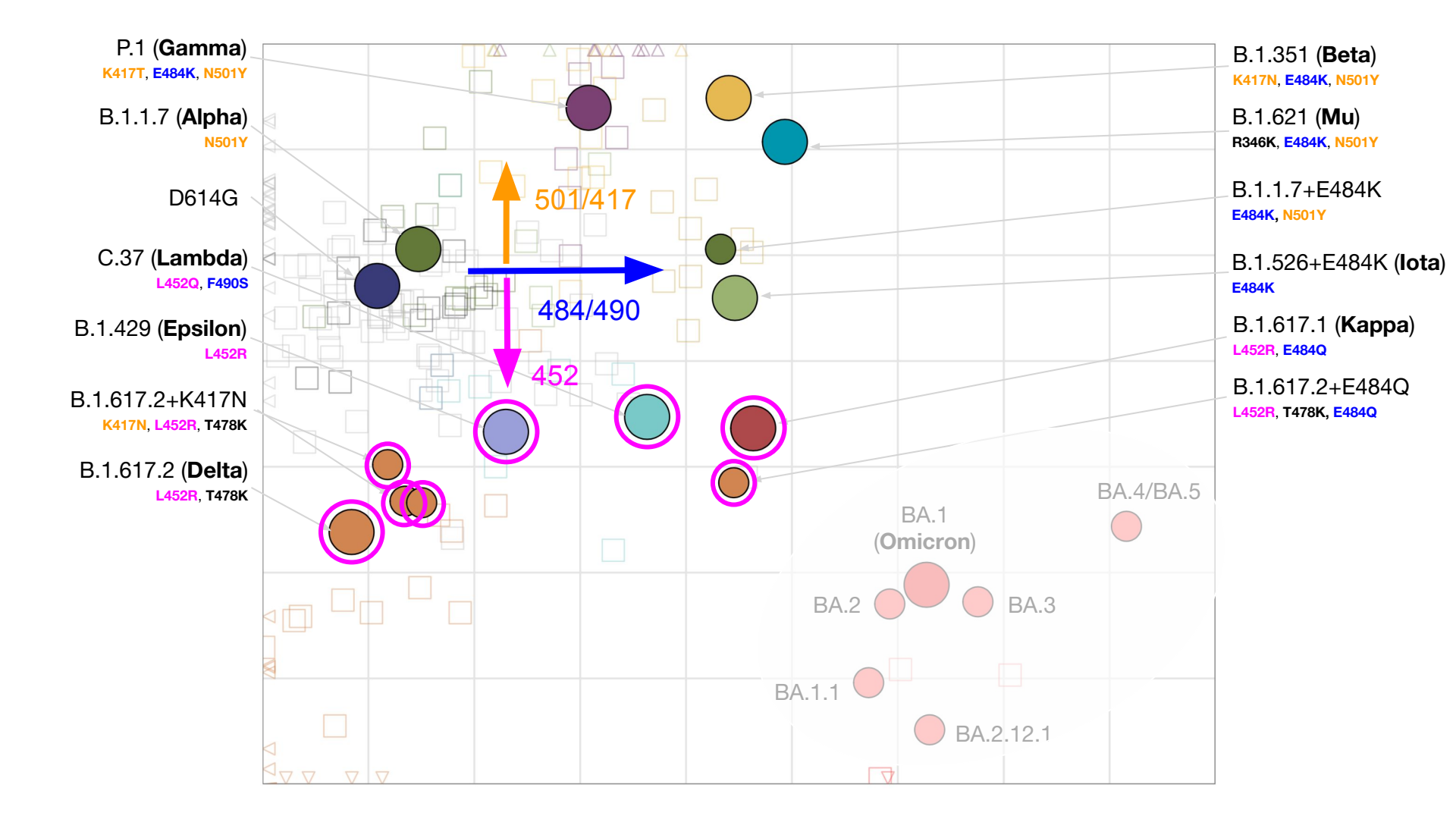
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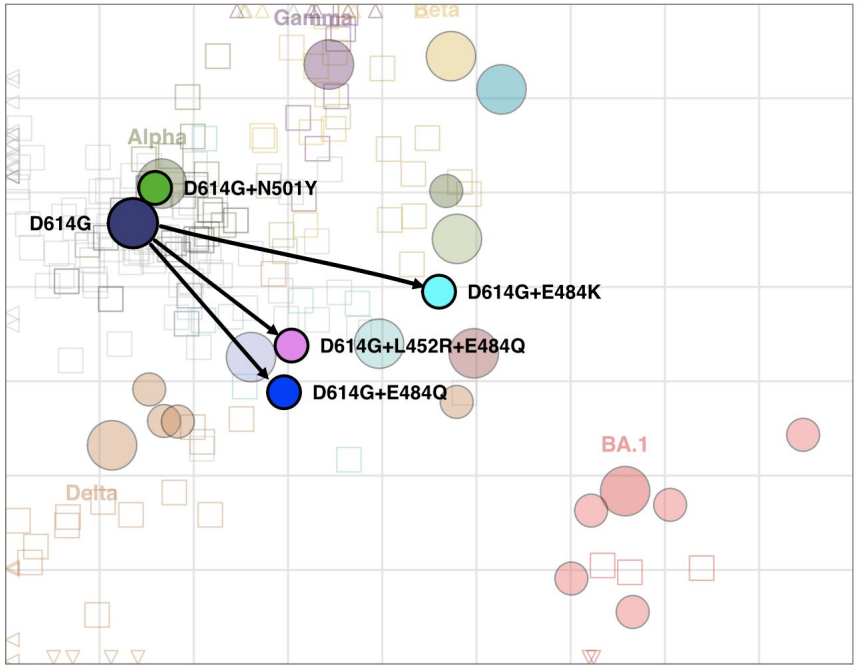
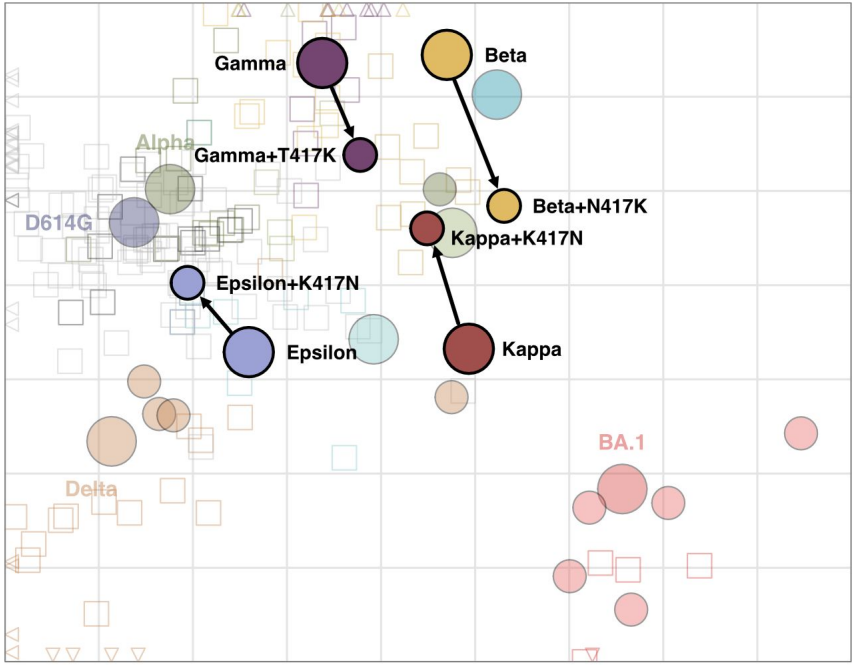
B.1.617.2+E484Q
L452R, T478K, E484Q
501/417
484/490
452
BA.1
(Omicron)
BA.4/BA.5
BA.2
BA.3
BA.1.1
BA.2.12.1

Molecular basis of antigenic map topology

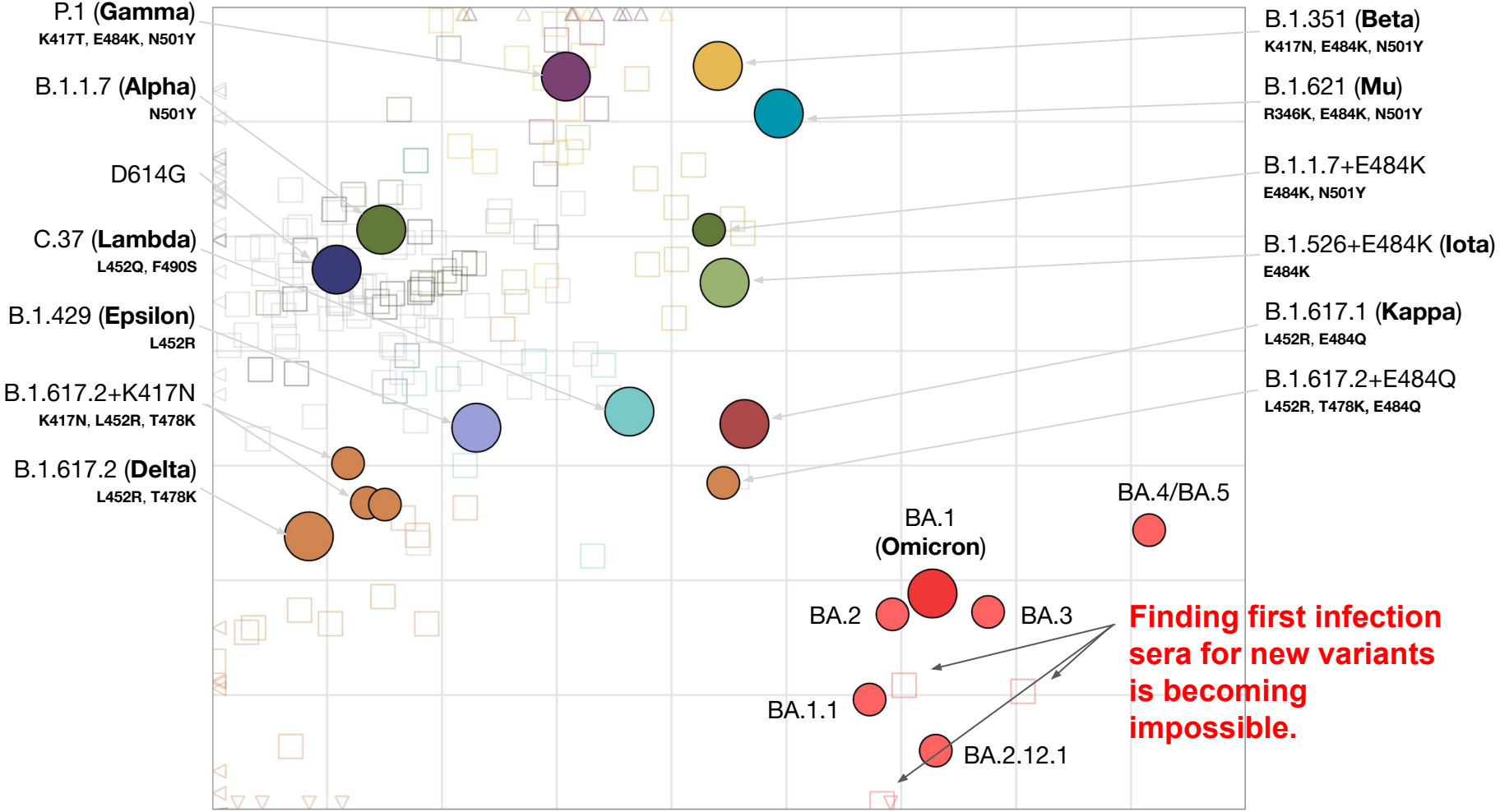
Effect of substitutions at positions 484, 501, 452



Effect of substitutions at position 417



Mutants were only titrated against D614G and Beta sera.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L452R, T478K, E484Q
BA.4/BA.5
BA.1
(Omicron)
BA.2
BA.3
BA.1.1
BA.2.12.1
Finding first infection sera for new variants is becoming impossible.

An antigenic map made from hamster data

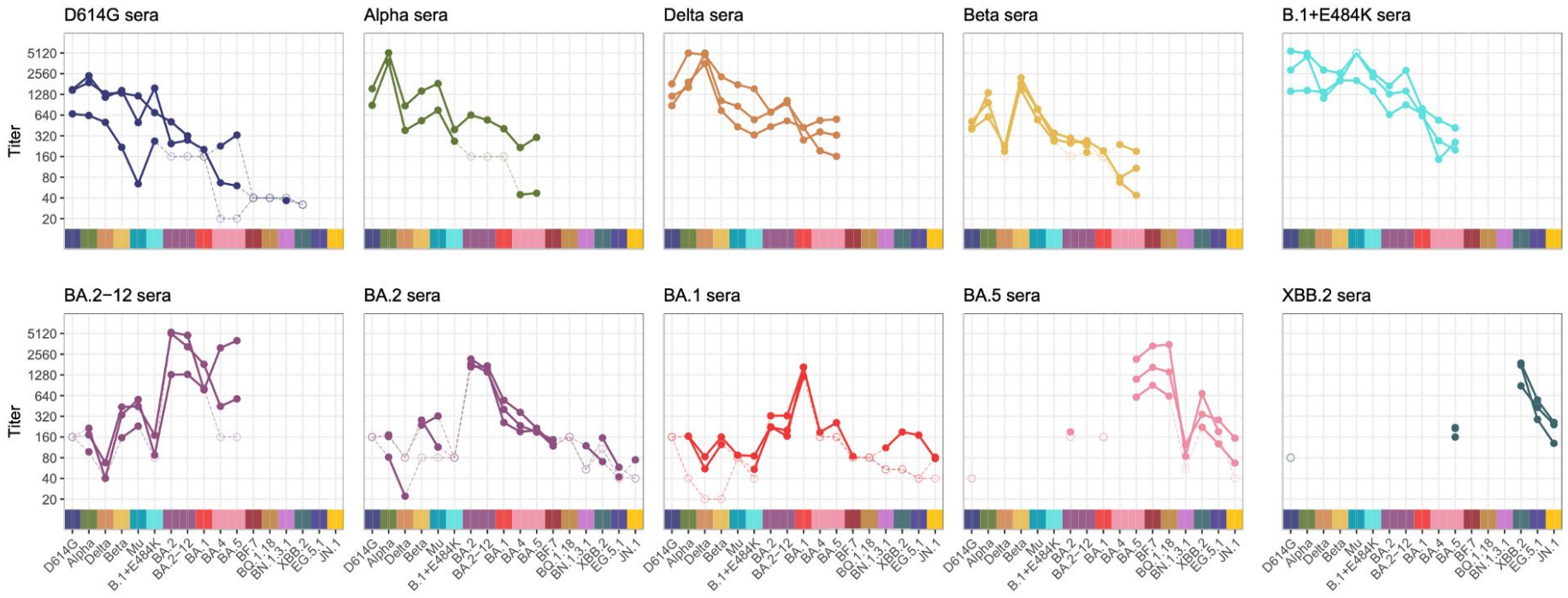
An antigenic map made from hamster sera

- 9 groups of hamster sera titrated against up to 16 variants.
- Hamsters were infected twice, four weeks apart.
- Plaque reduction neutralization test on VeroE6 cells.

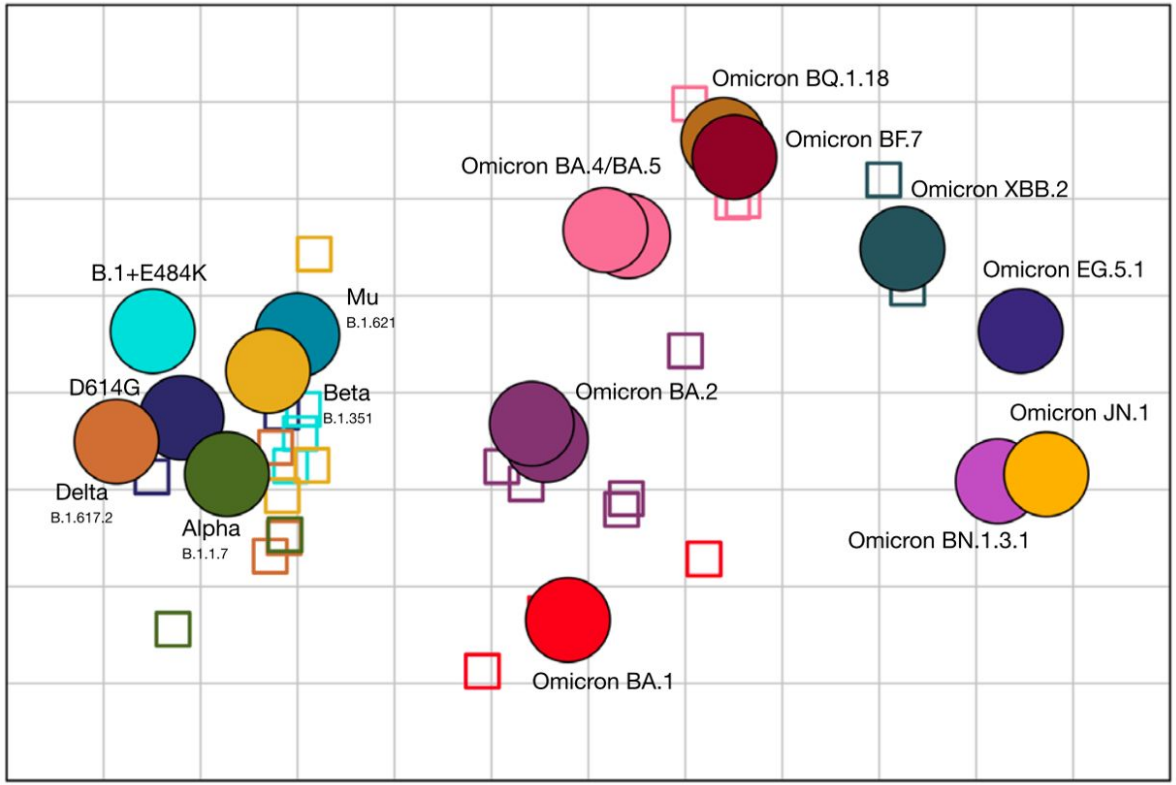
Sera:
D614G, Alpha, Delta, Beta, B.1+E484K, BA.1, BA.2, BA.5, XBB.2

Variants:
D614G, Alpha, Delta, B.1+E484K, Beta, Mu, BA.2, BA.1, BA.4, BA.5, BF.7, BQ.1.18, BN.1.3.1, XBB.2, EG.5.1, JN.1

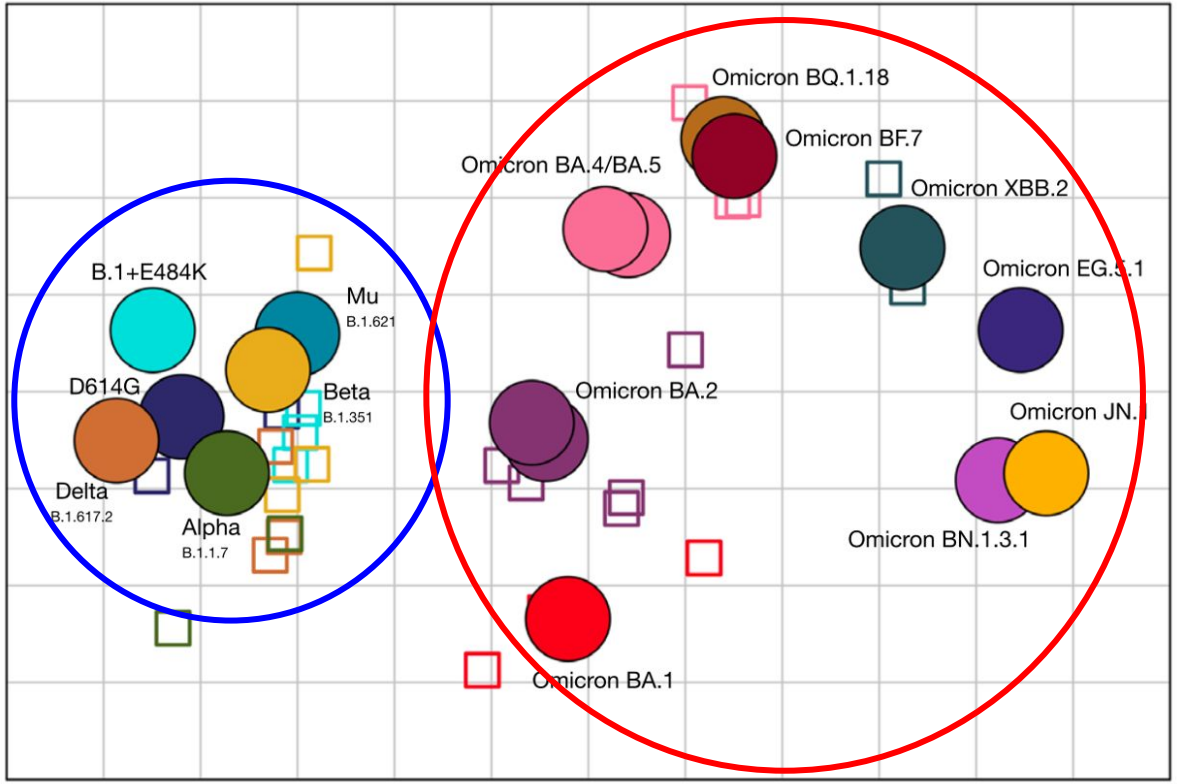
Titerplot


D614G sera
Alpha sera
Delta sera
Beta sera
B.1+E484K sera
BA.2−12 sera
BA.2 sera
BA.1 sera
BA.5 sera
XBB.2 sera
Titer
5120
2560
1280
640
320
160
80
40
20
D614G
Alpha
Delta
Beta
Mu
B.1+E484K
BA.2
BA.2−12
BA.1
BA.4
BA.5
BF.7
BQ.1.18
BN.1.3.1
XBB.2
EG.5.1
JN.1

Antigenic map



Antigenic map



Tighter clustering of pre-Omicron variants, Omicron variants are further apart compared to human map.

Your turn!