Vaccines and Related Biological Products Advisory Committee Meeting

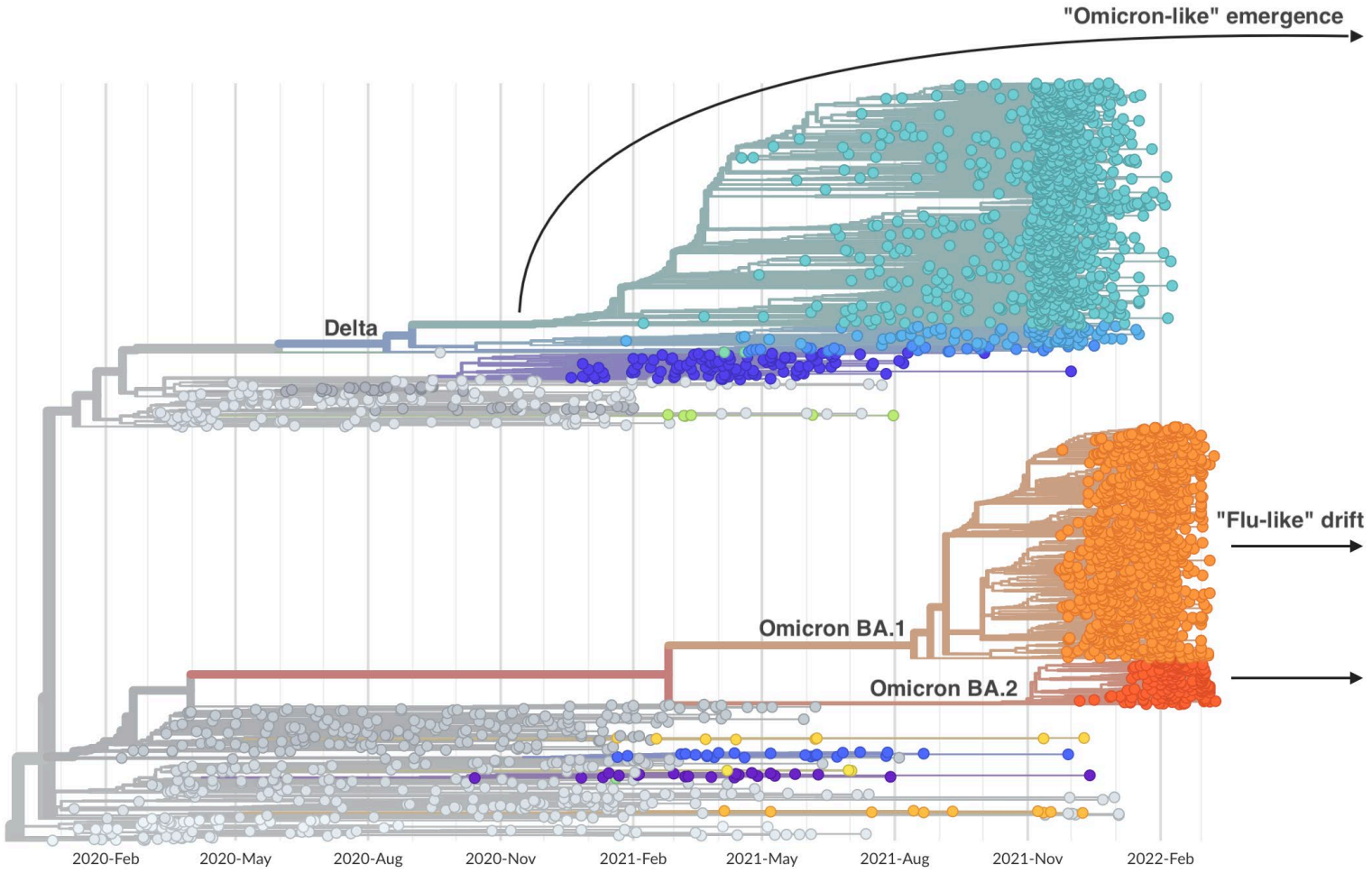
Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

SARS-CoV-2 Antigenic Space

John Beigel
National Institute of Allergy and Infectious Diseases

VRBPAC - April 6, 2022

Given uncertainties of SARS-CoV-2 evolution, picking the next variant to emerge will be challenging

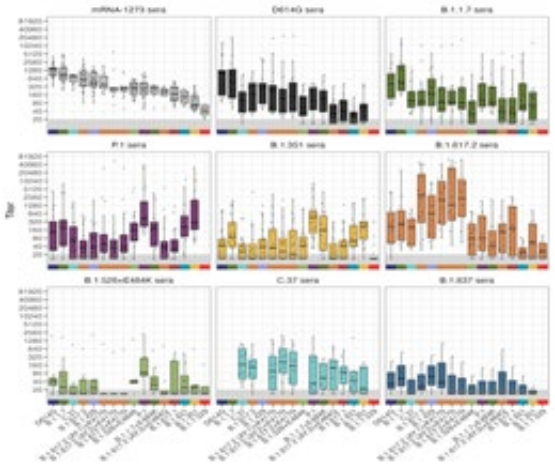


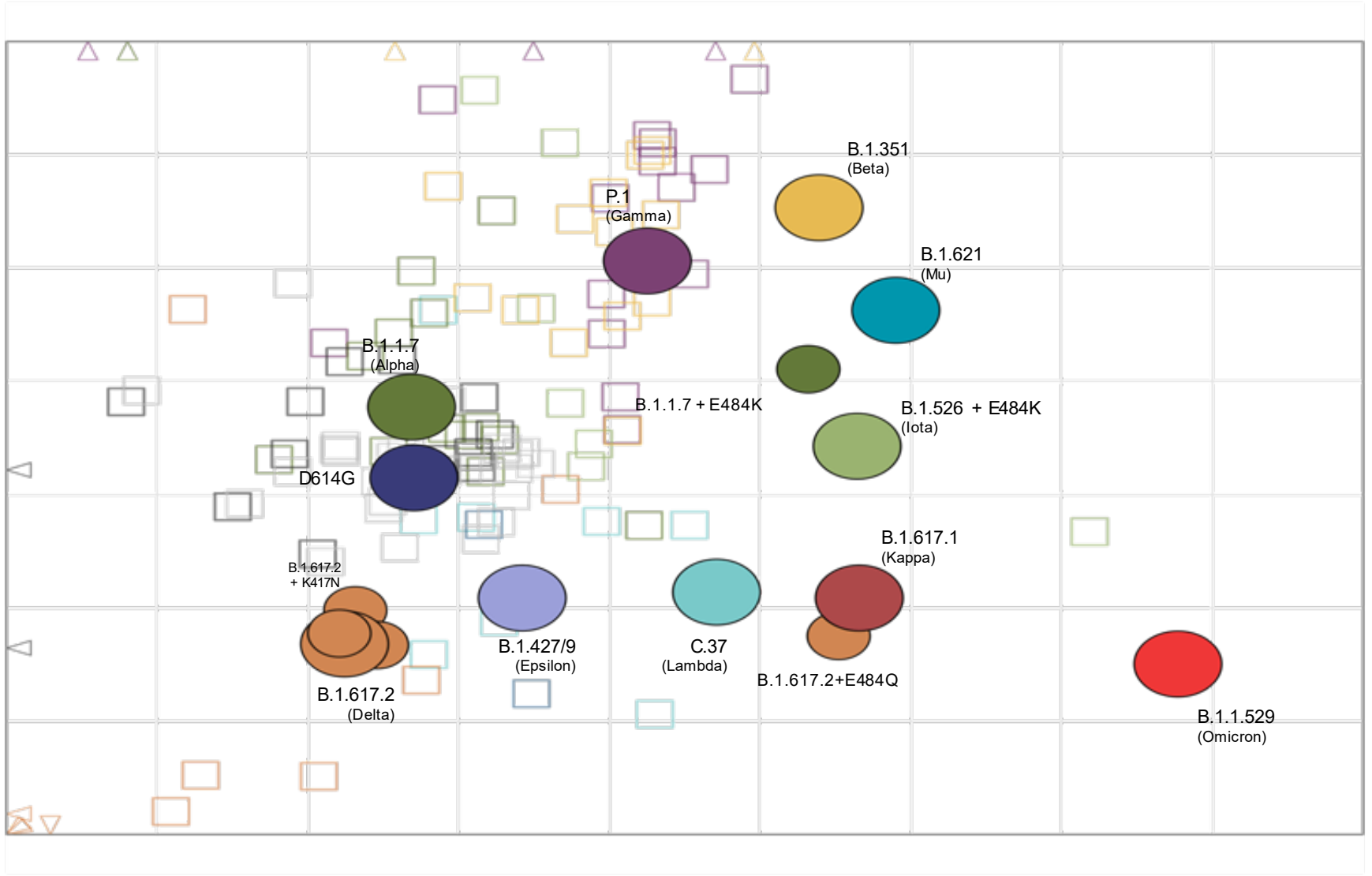
Until we know how SARS-CoV-2 will evolve, we need to be able to react to new strains

Trevor Bedford

Work by NIAID collaborators (SAVE and others) use neutralization assays coupled with antigenic cartography to describe antibody response.

- These maps are visualization tools for neutralization data to help understand antigenic spaces and risks.
- Antigenic cartography and antigenic landscapes are a common tool for strain selection for influenza.

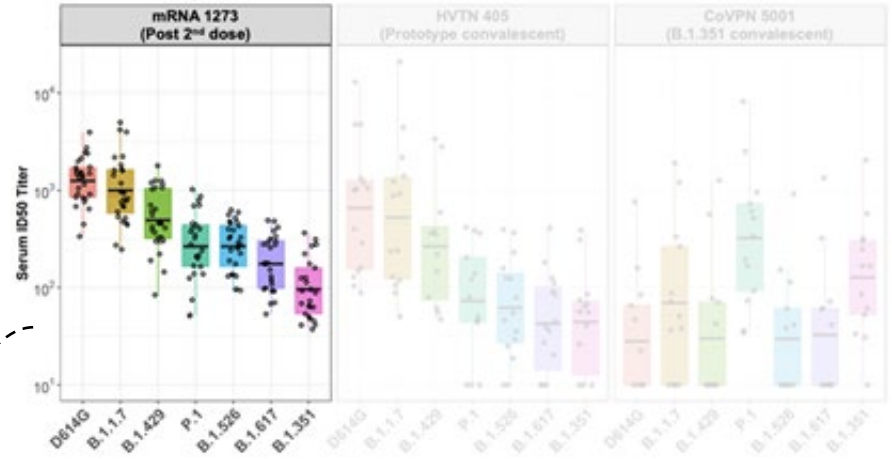




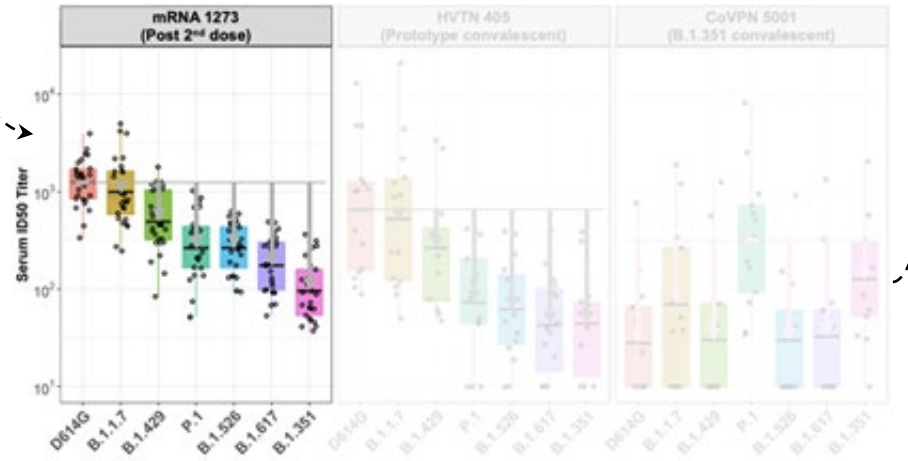
Samuel Wilks & Derek Smith (Cambridge)

PsVNA by Shen & Montefiori (Duke)

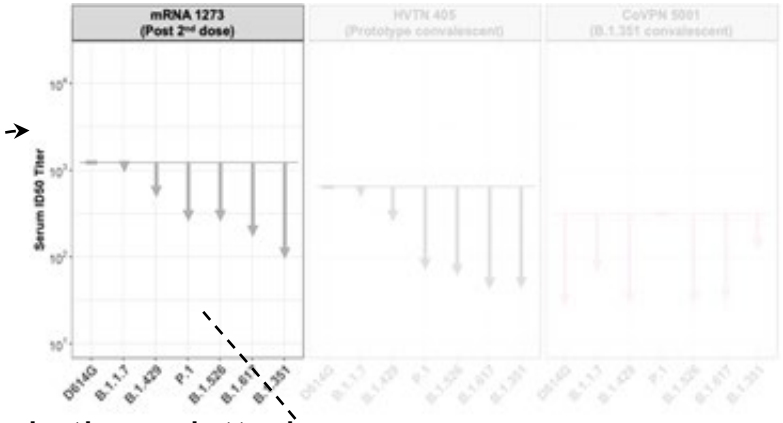
Antigenic cartography



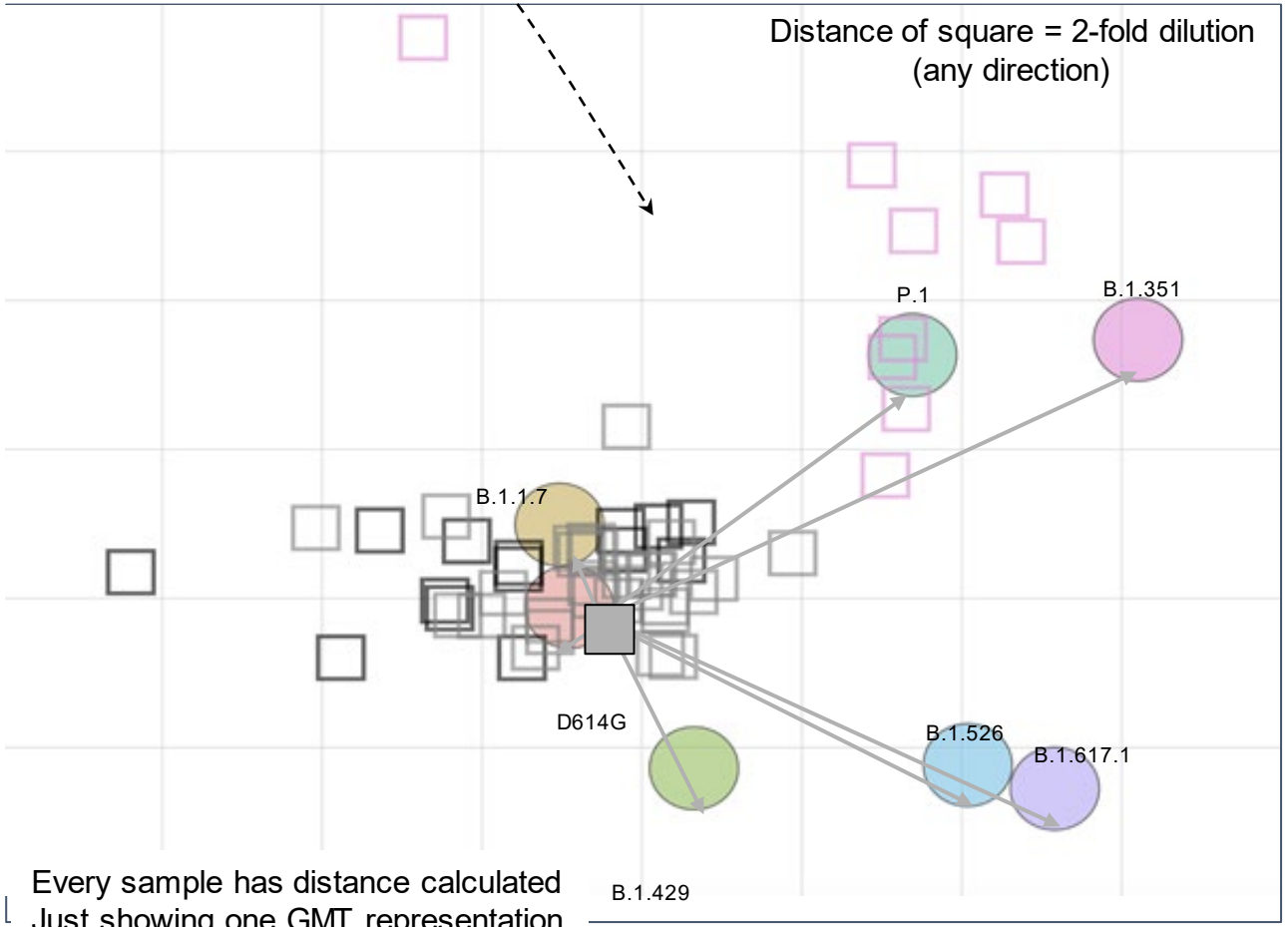
Neutralization titers are determined to multiple strains



Distance (in terms of dilutions) from highest strain is calculated

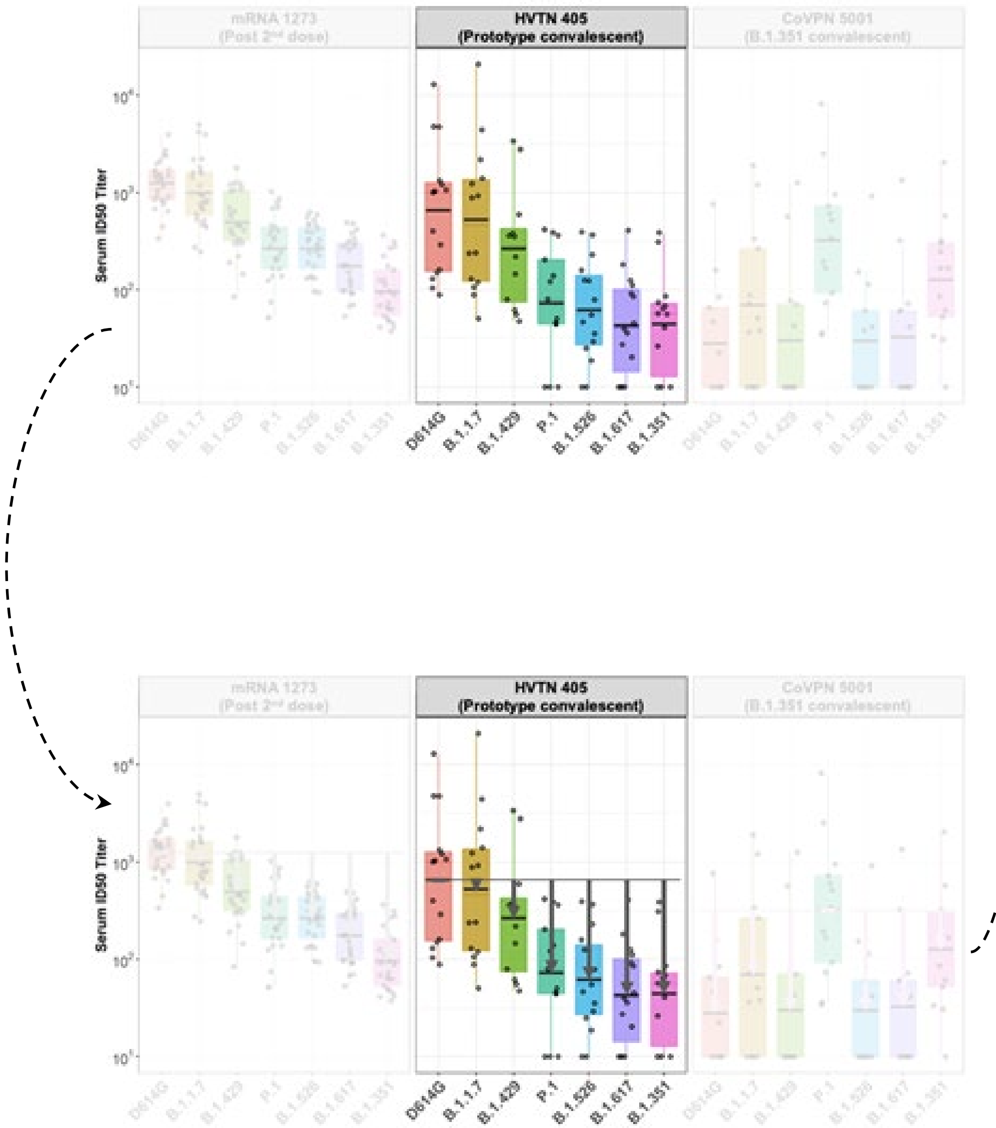


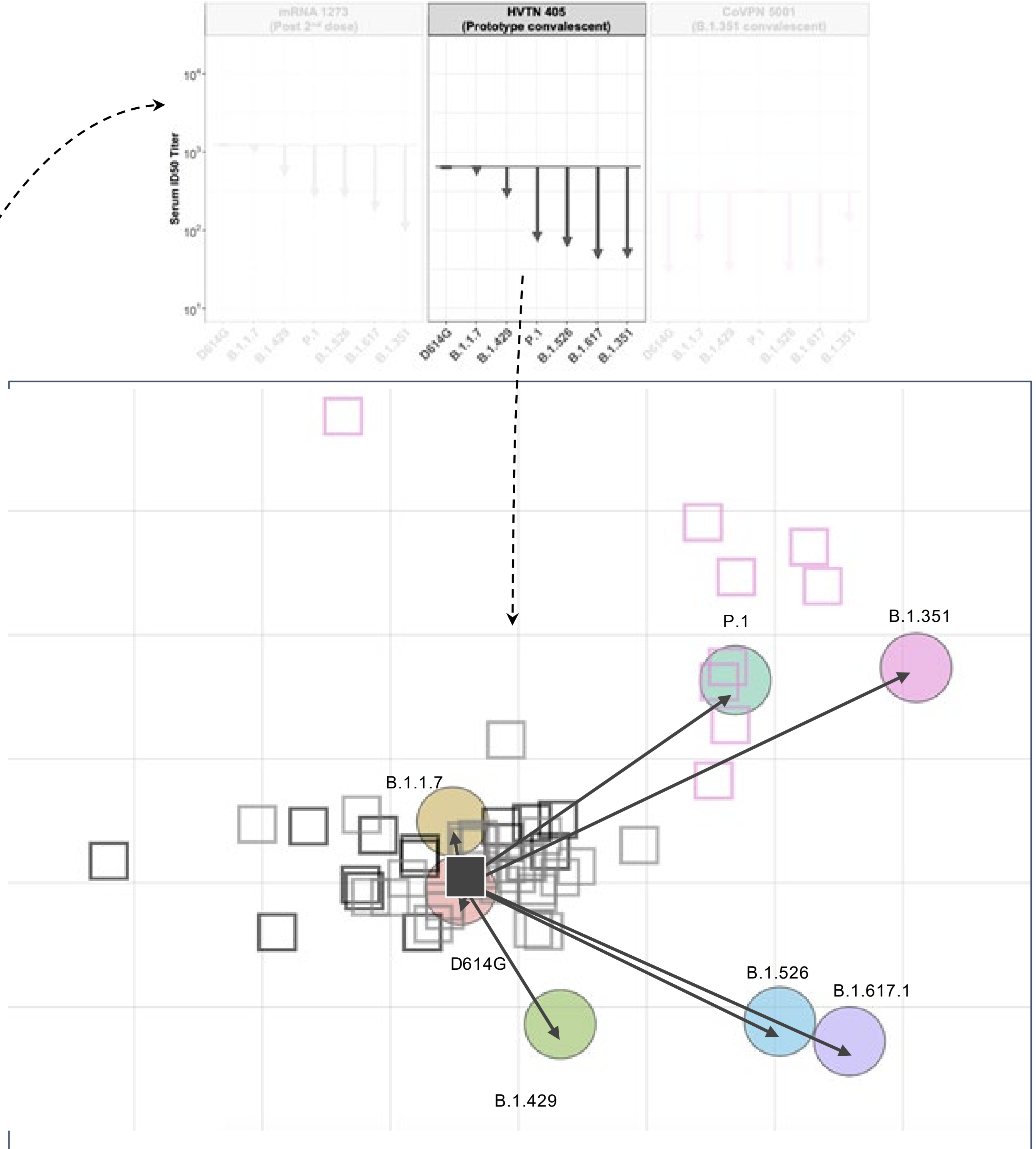
Distance is then plotted on a map



Every sample has distance calculated
Just showing one GMT representation

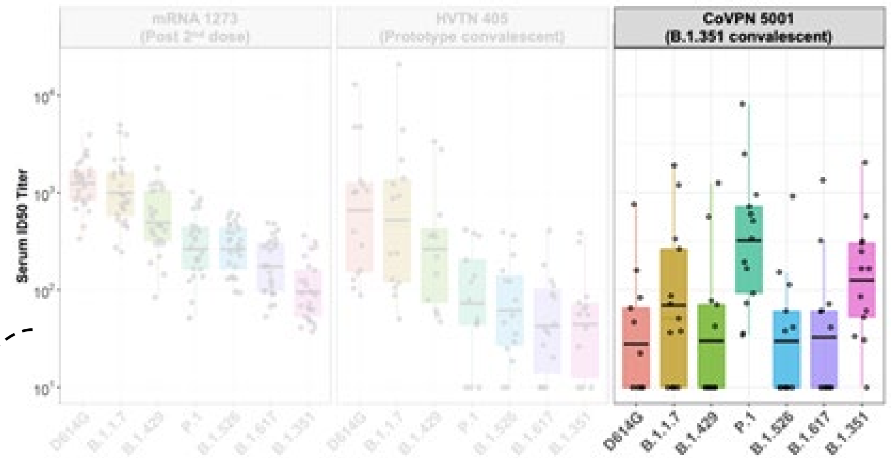
This process is repeated for different groups (in this case convalescent serum)

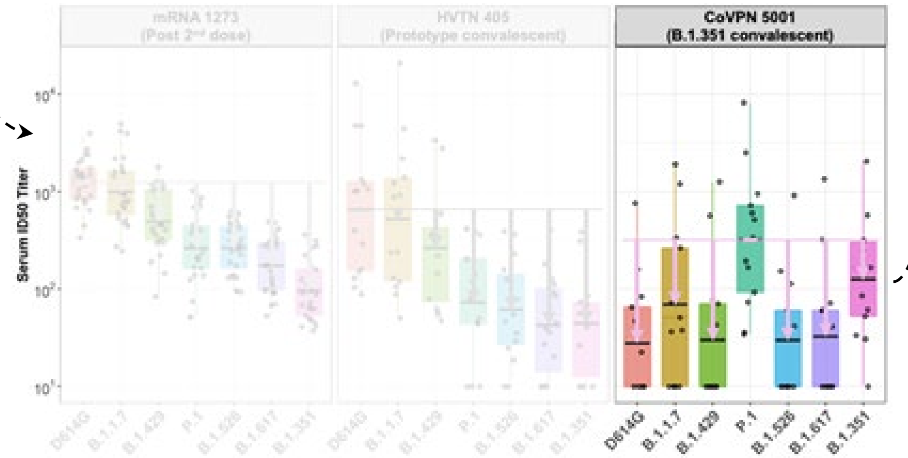


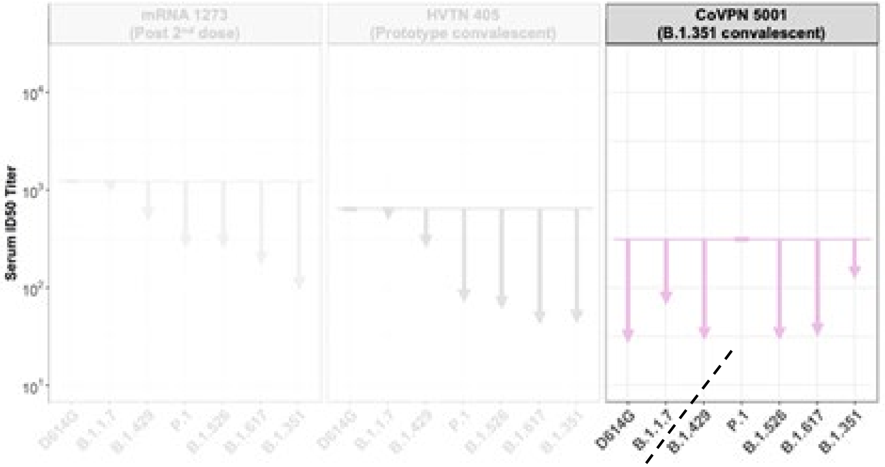


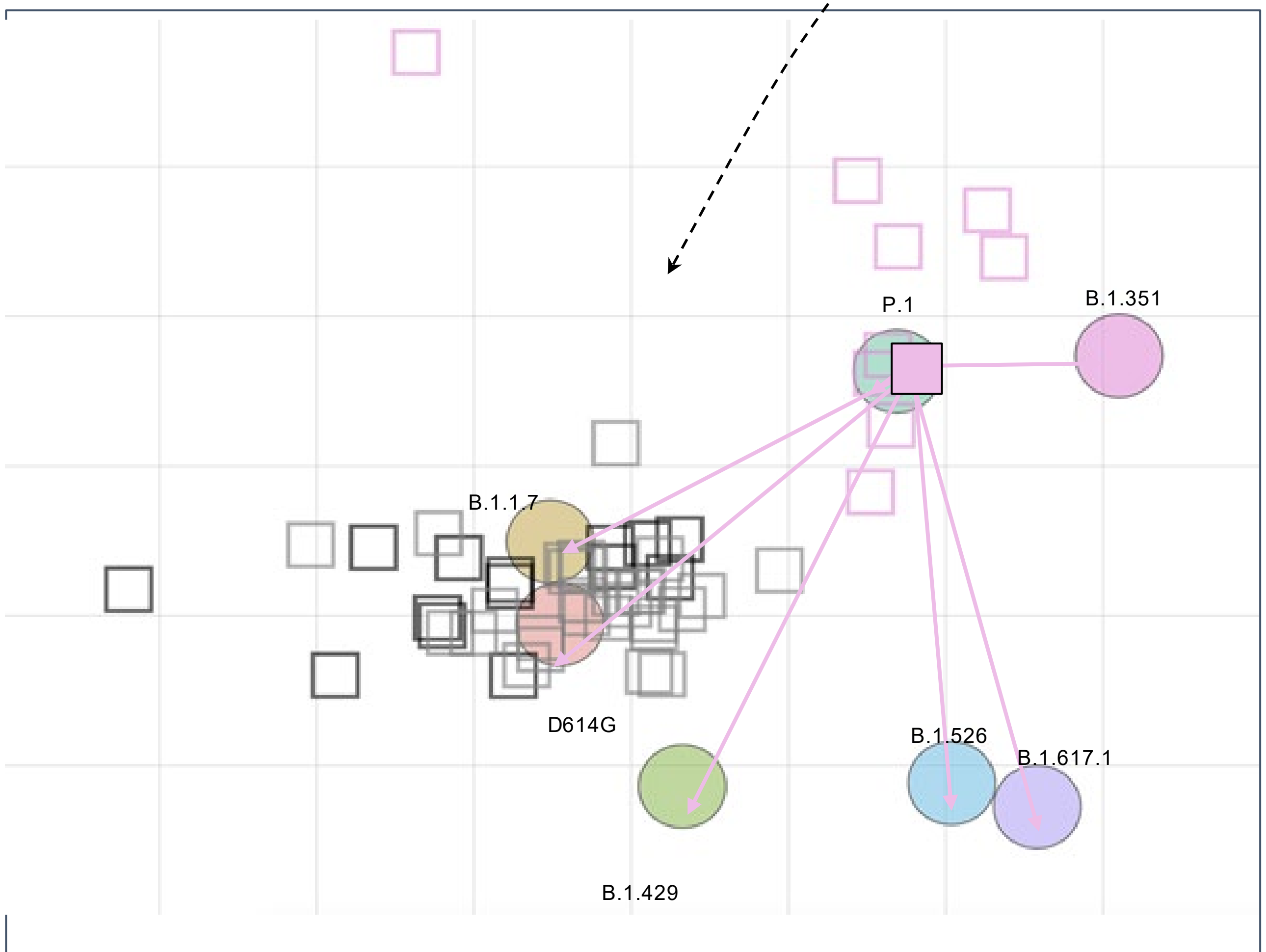
Derek Smith (Cambridge)

And further repeated as needed



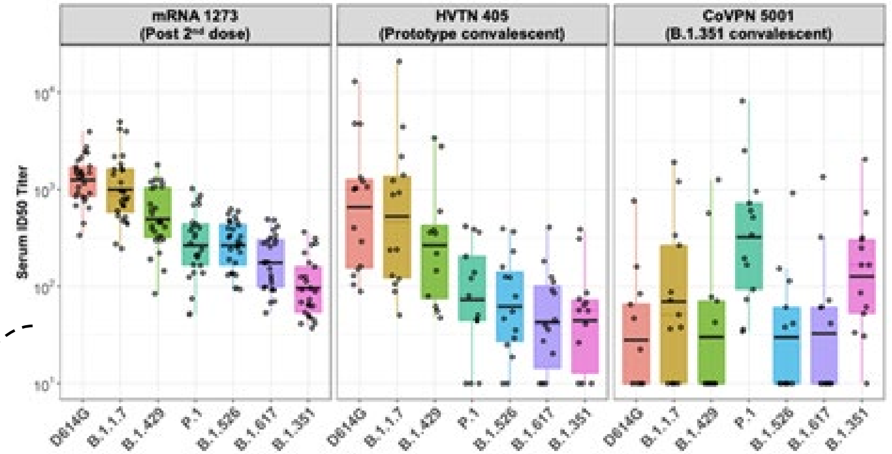


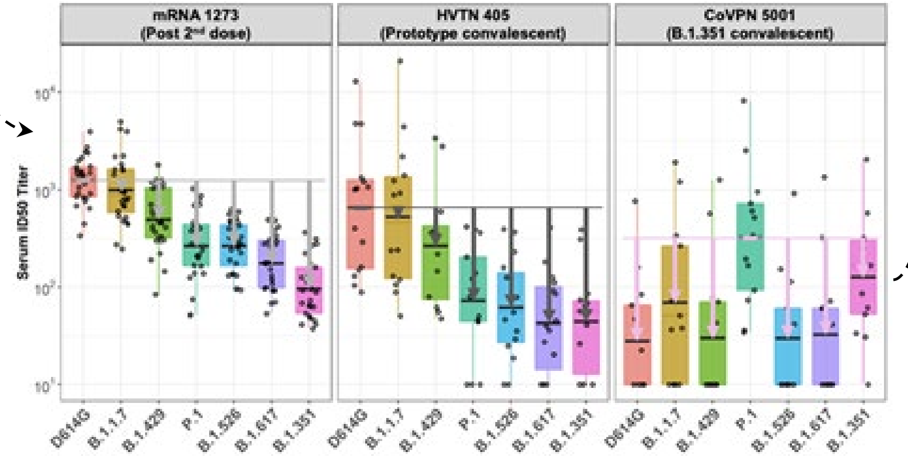


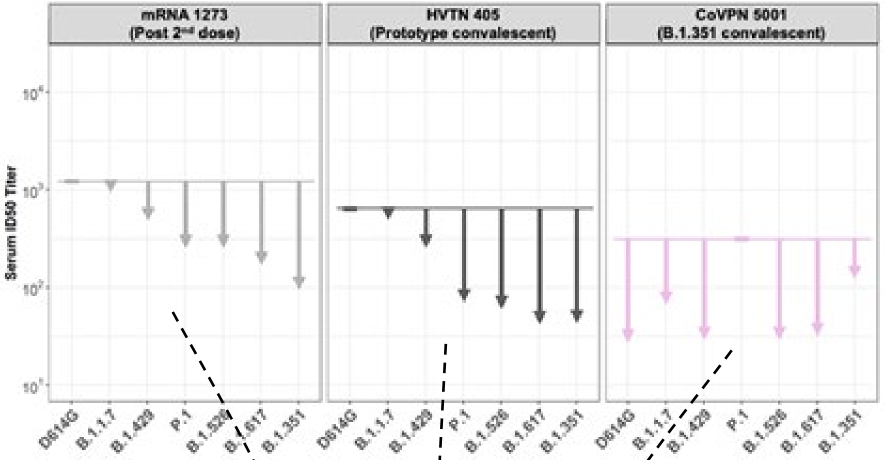


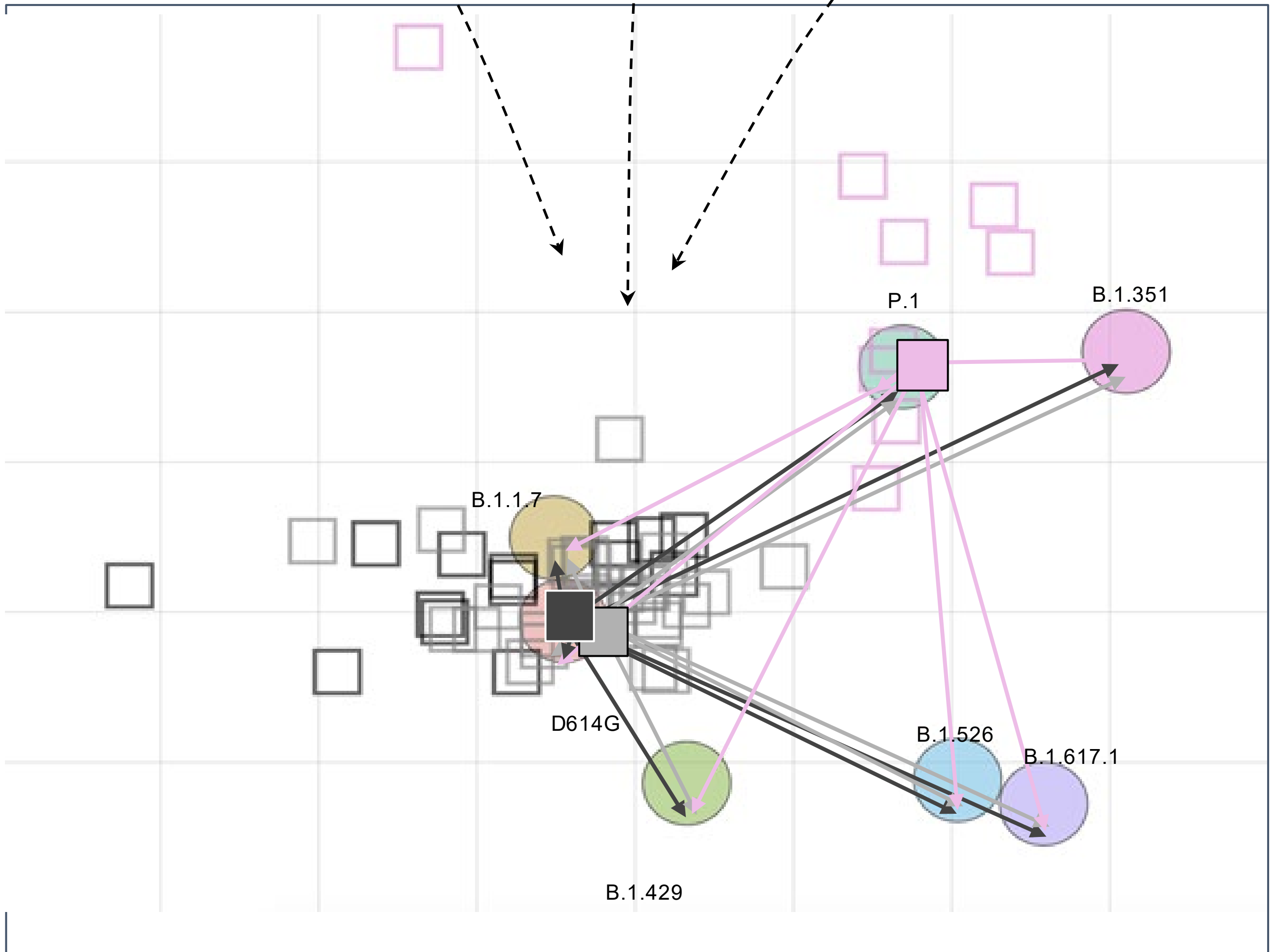
Derek Smith (Cambridge)

Taken together, it shows a detailed map of how groups and antigens cluster





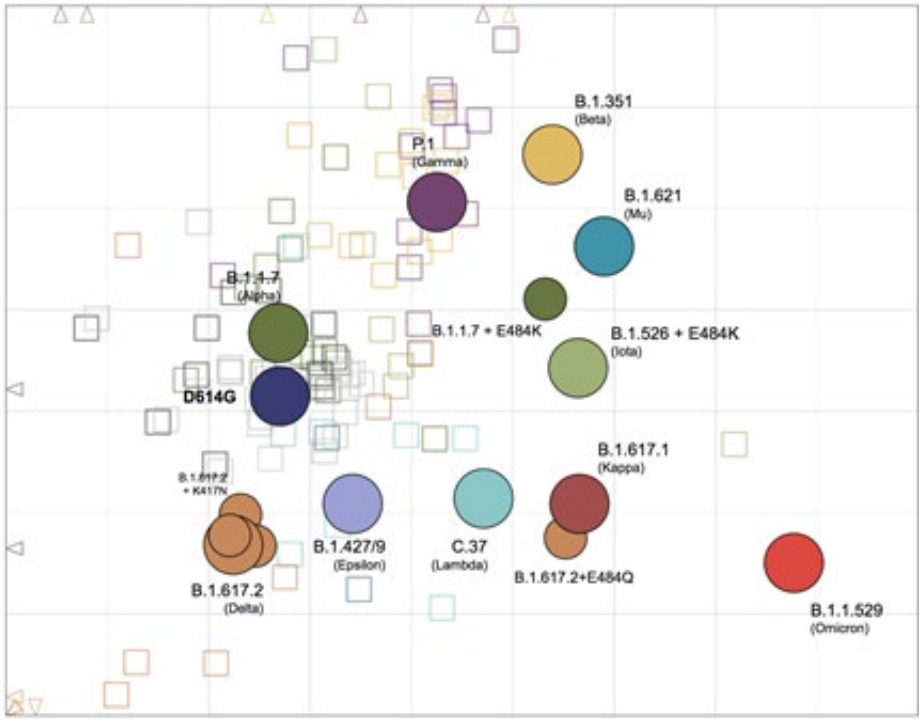


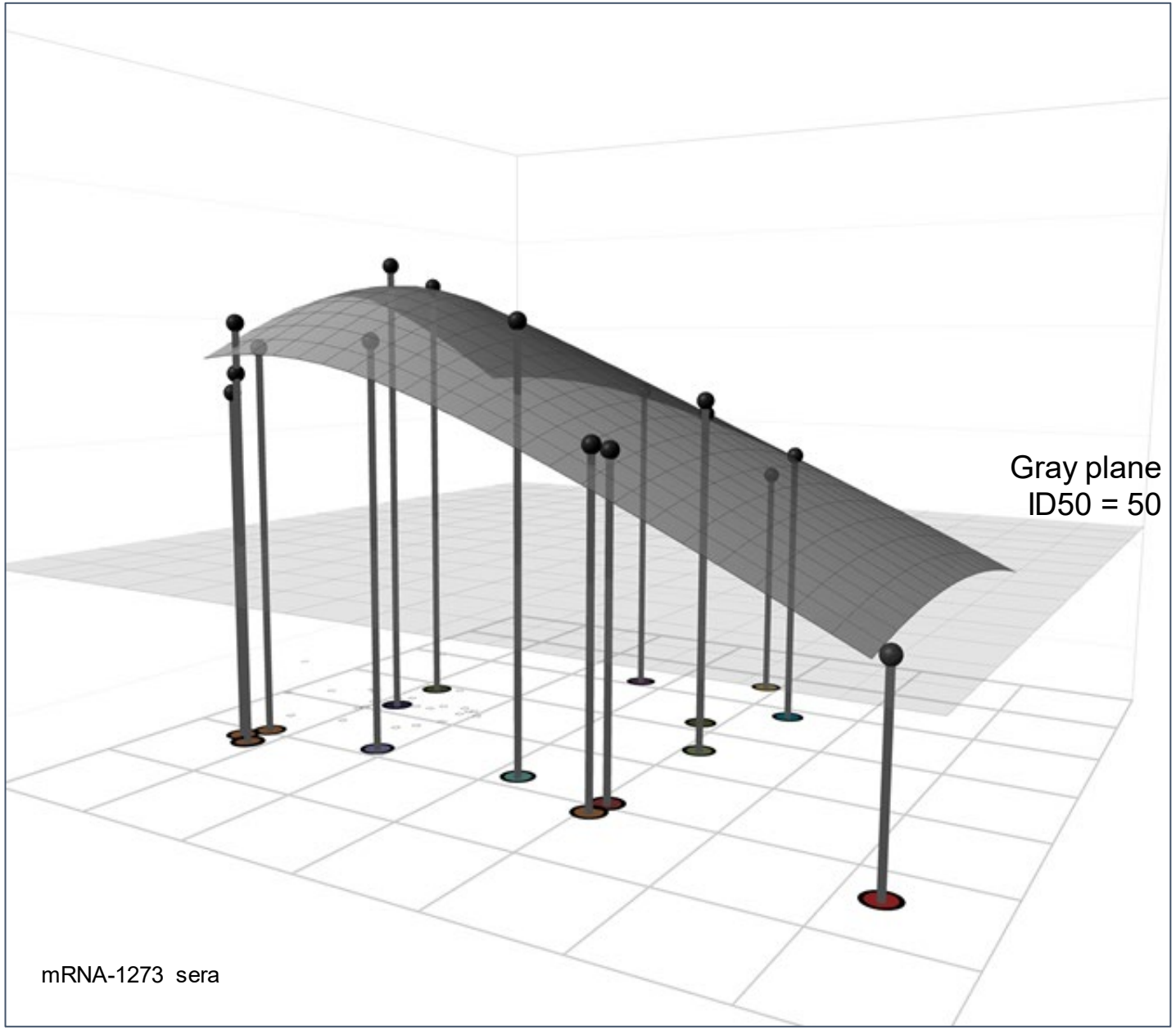


Derek Smith (Cambridge)

Map only reflects relative distance (dilutions) of antigens and serum

Landscape shows titers across variants in the map and shows areas of vulnerability

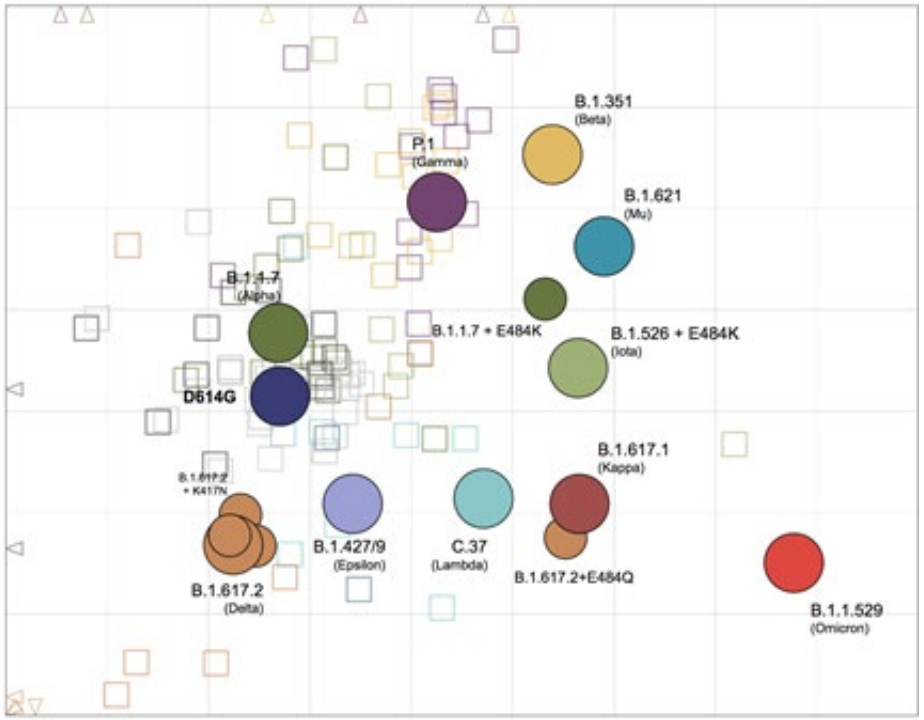


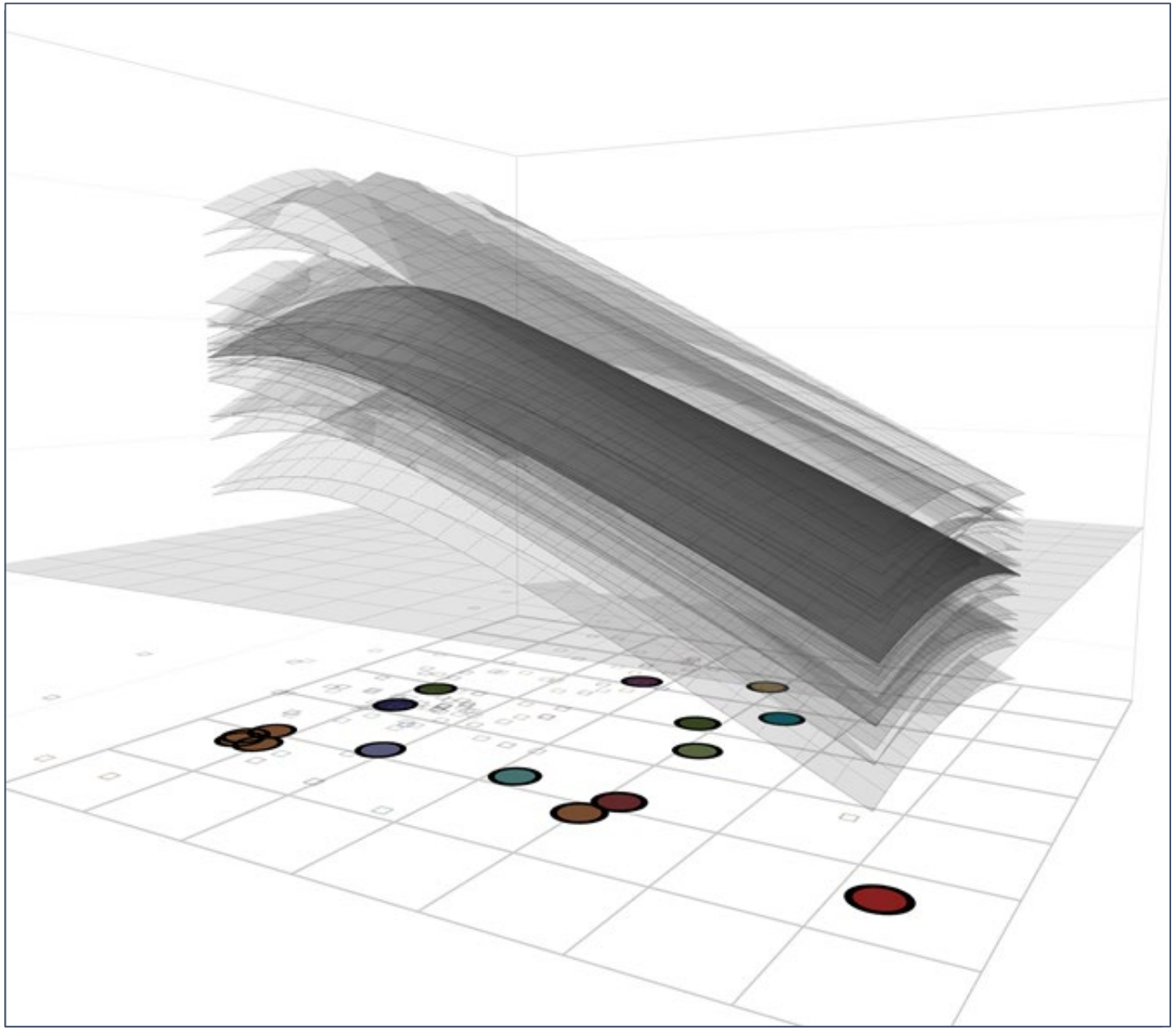


Derek Smith (Cambridge)

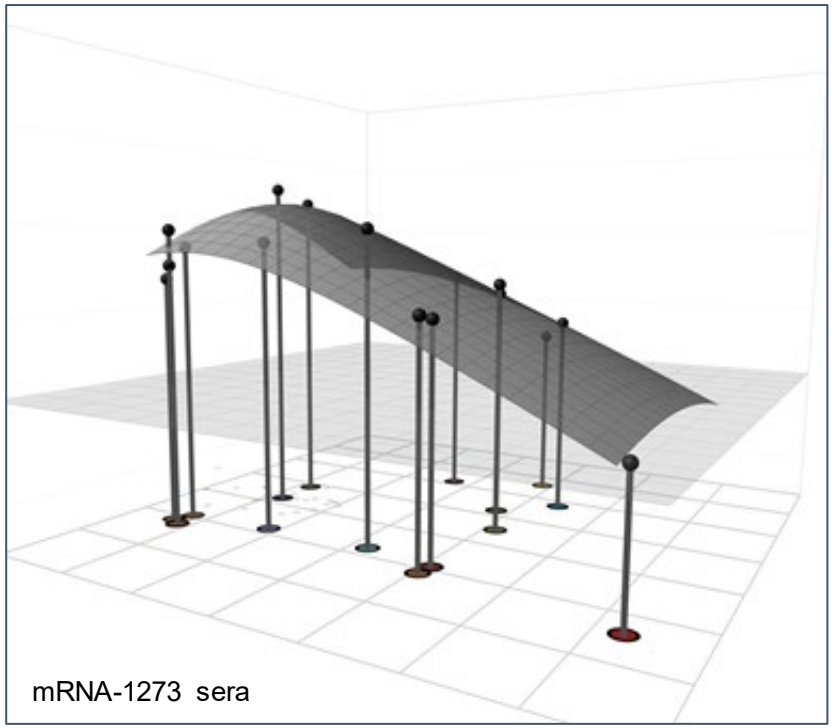
Landscapes are individual

- Consolidated to GMT to understand cohorts
- Landscapes change over time

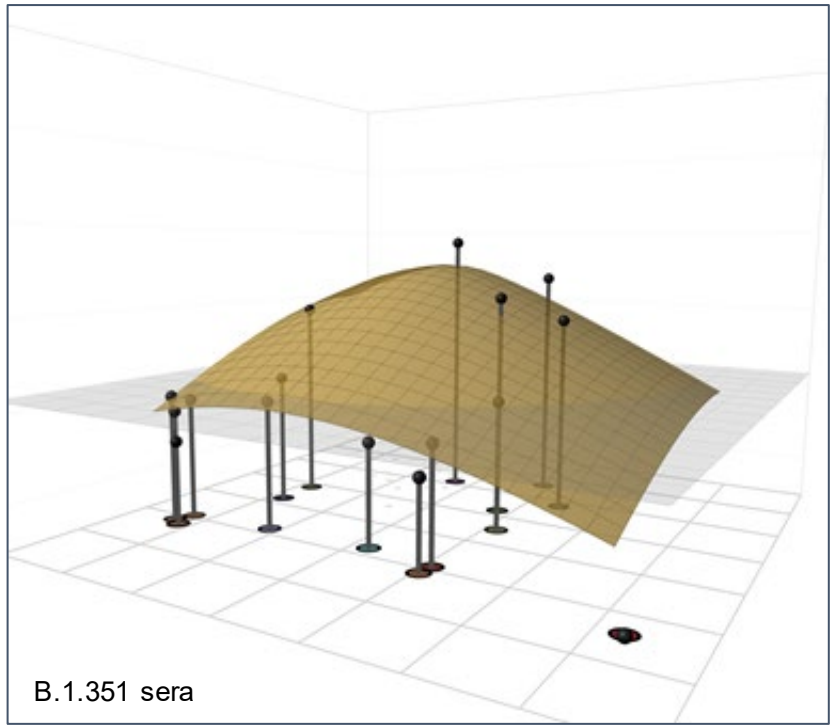




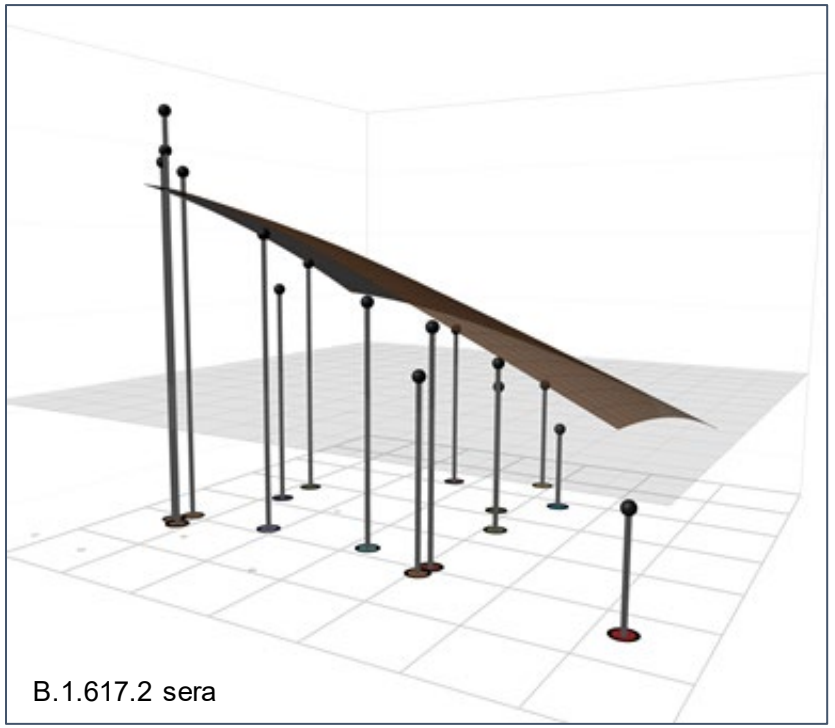
Infection by different strains give different antigenic landscapes



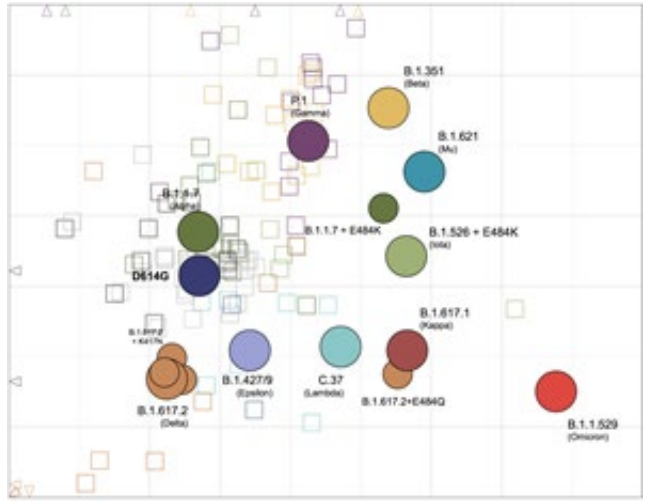
mRNA-1273 sera



B.1.351 sera

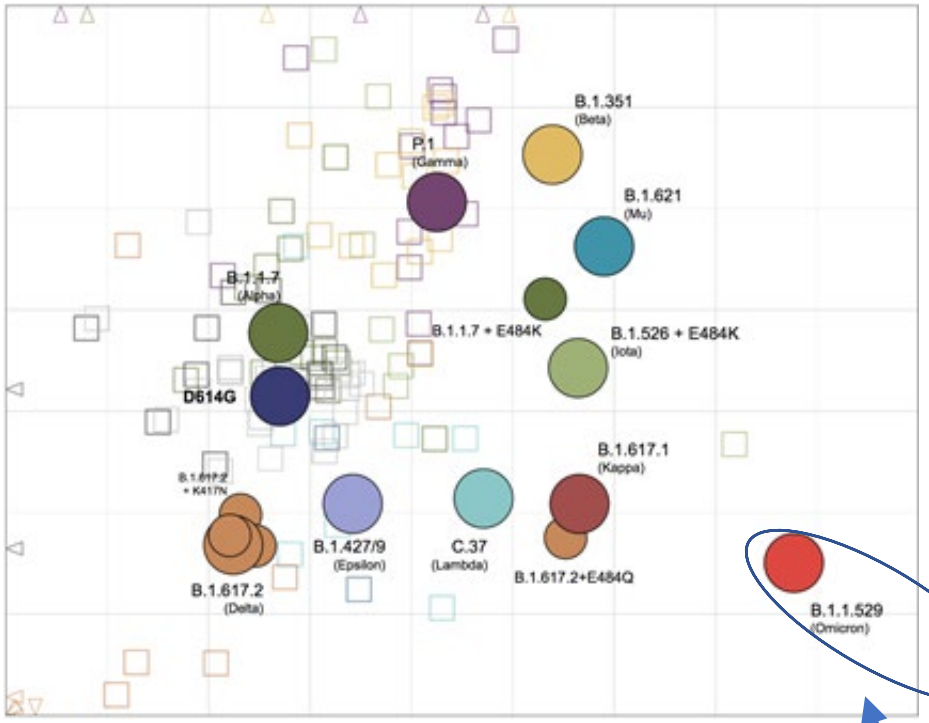


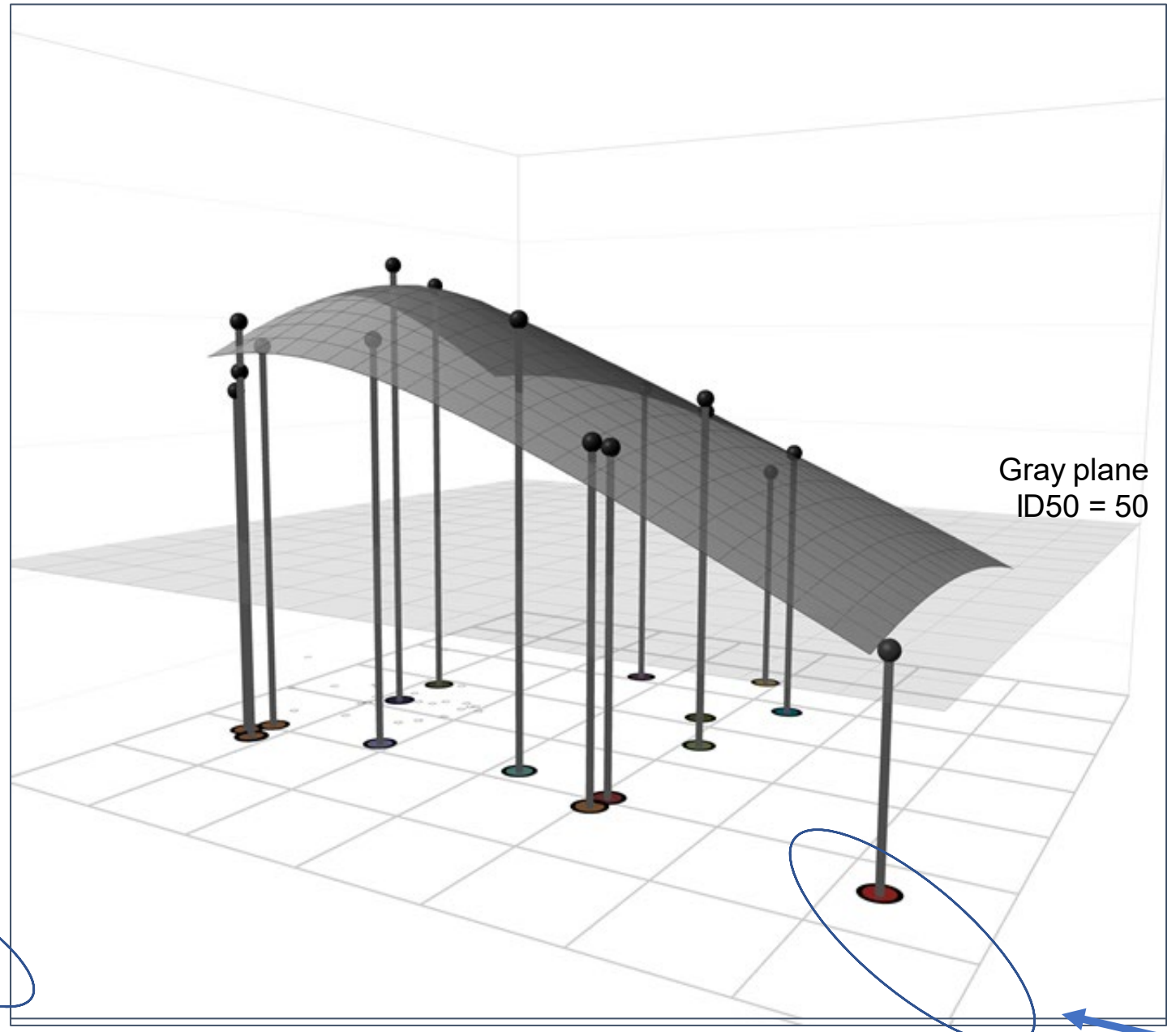
B.1.617.2 sera



Derek Smith (Cambridge)

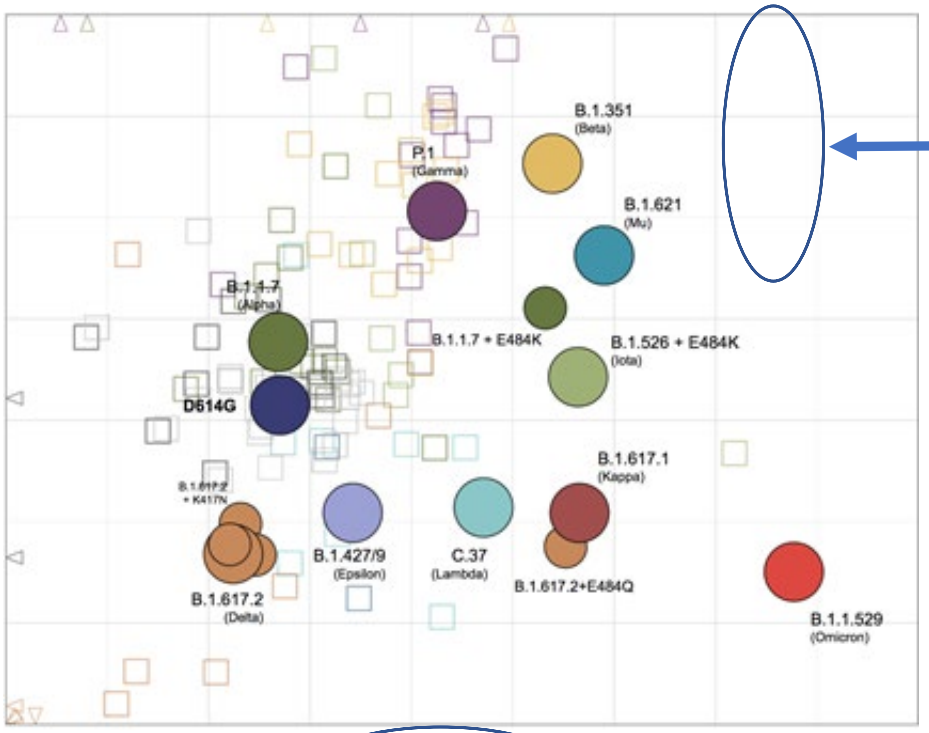
Targeting Omicron
-assumes an Omicron recurrence, or drift from Omicron

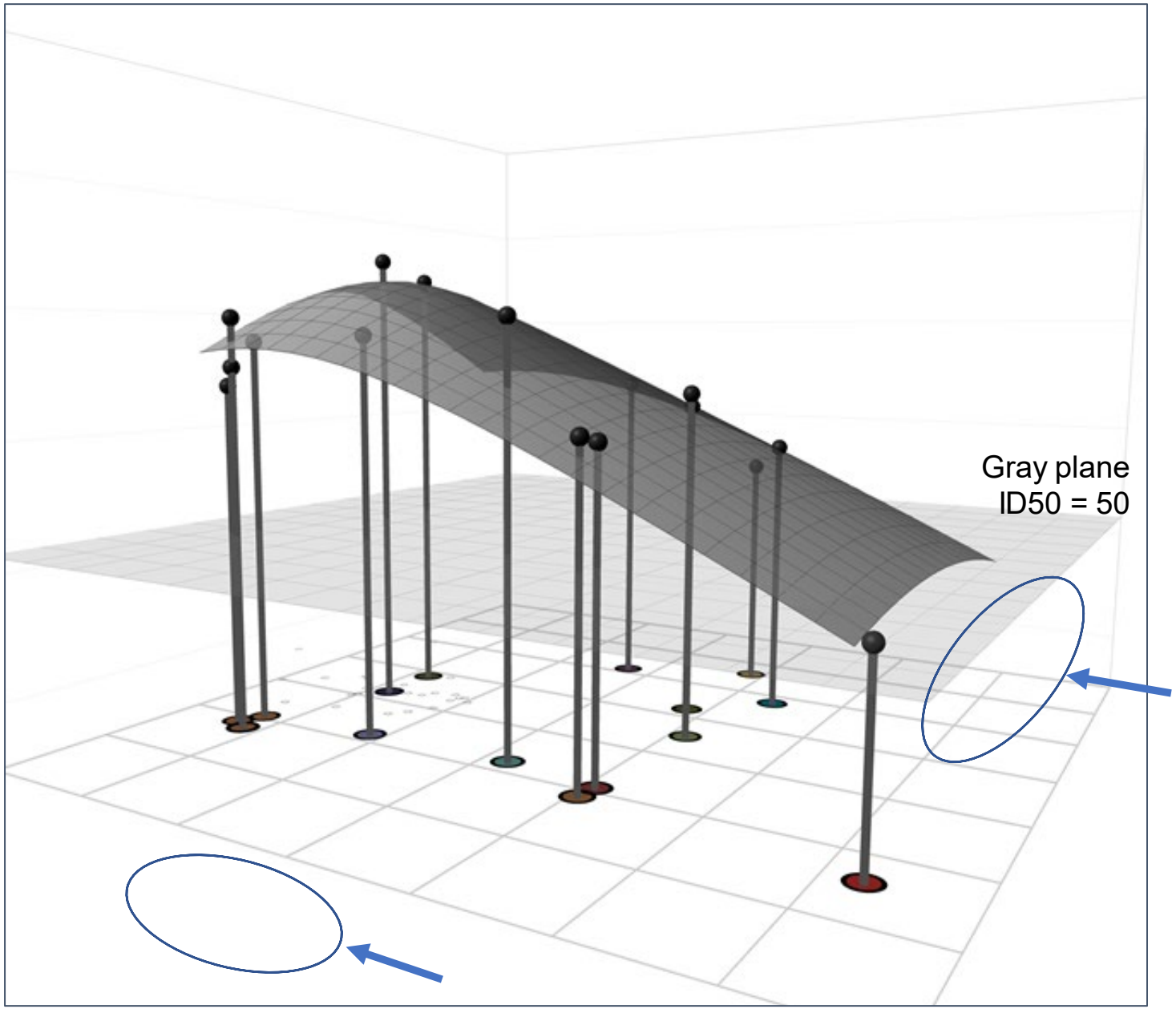




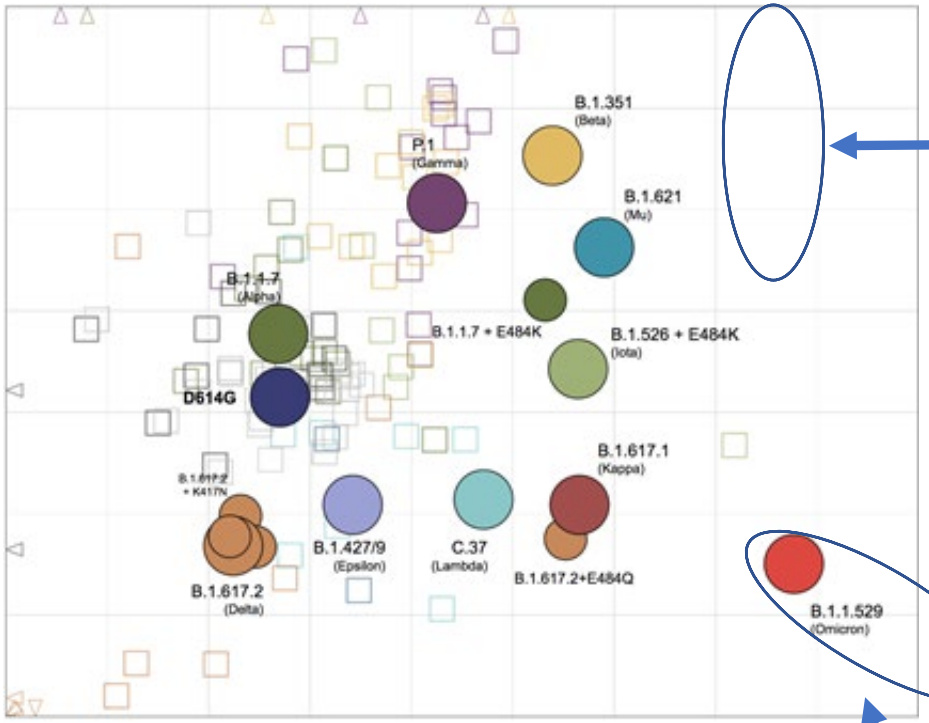
There may be other antigenic areas where the next variant may occur

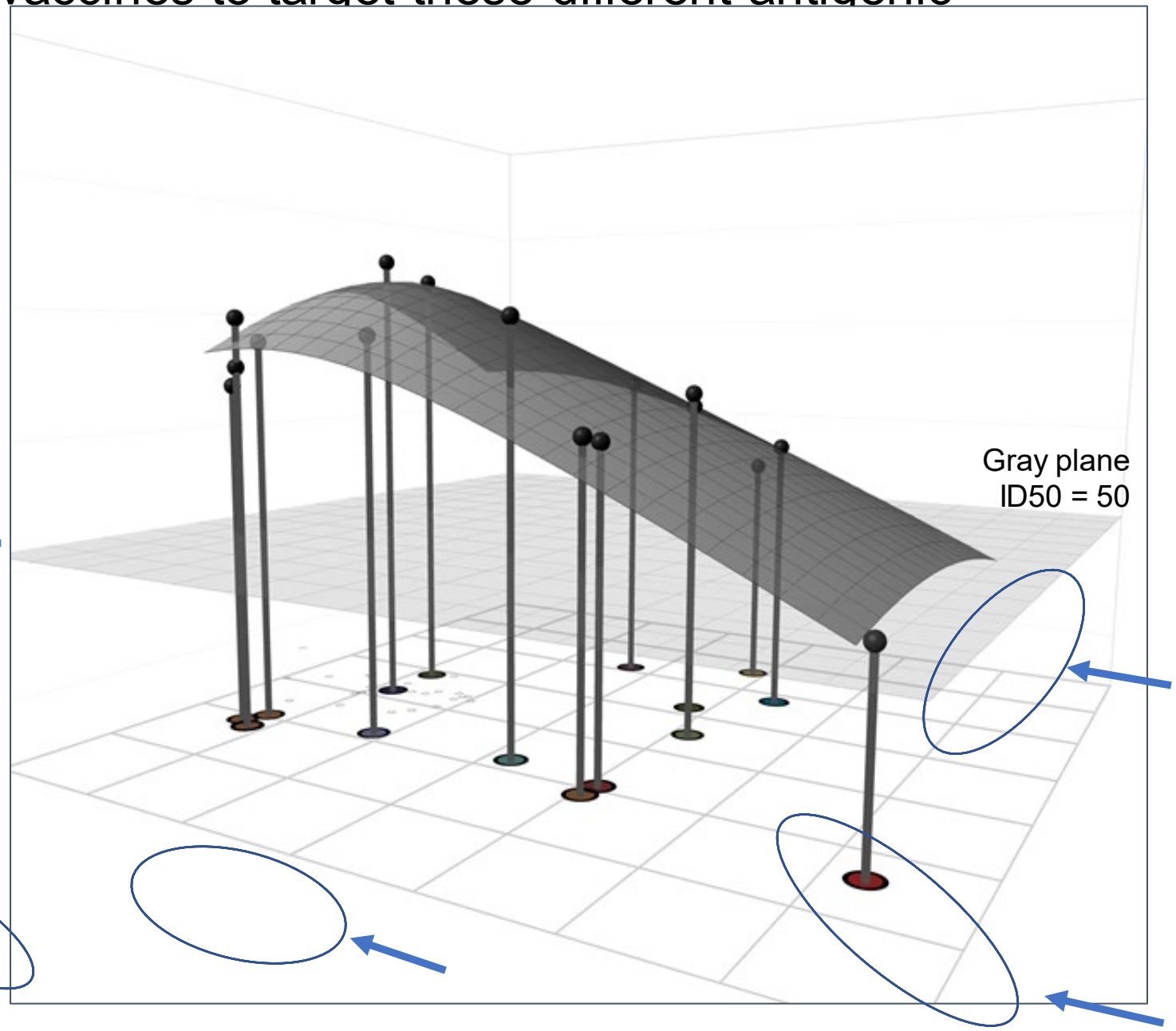
e.g., near beta or near delta
(distant from D614G and Omicron)





How do we use available variant vaccines to target these different antigenic spaces?





NIH COVAIL Trial

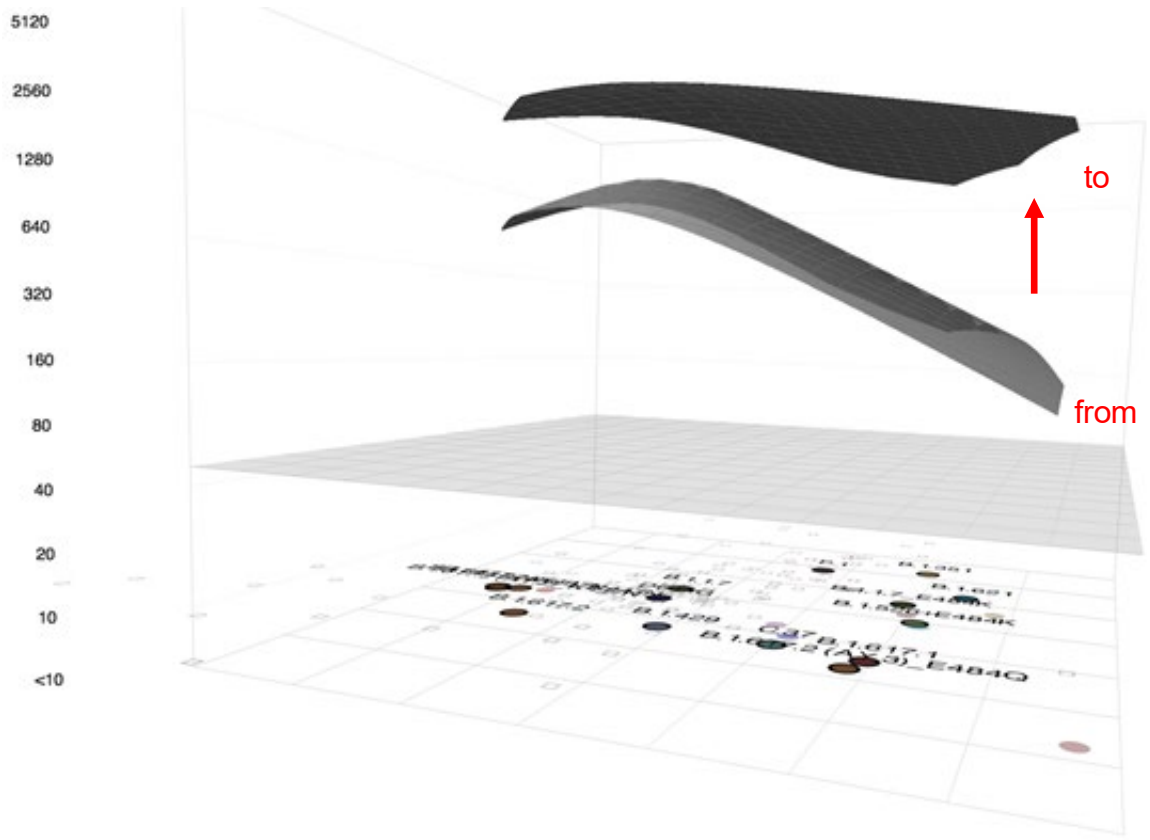
- Population:
  - Any COVID-19 primary vaccine and boost
  - Homologous or heterologous
- Two age strata:
  - 18-64 years
  - ≥ 65 years (>45% in ≥ 65 years).
- Two infection strata:
  - Confirmed prior COVID-19 (>35%)
  - No known history of prior infection.
- Primary endpoint:
  - Humoral immune responses
    - PsVNA and binding
  - D614G, beta, delta, omicron
- 24 sites
  - Began enrollment last week

First stage

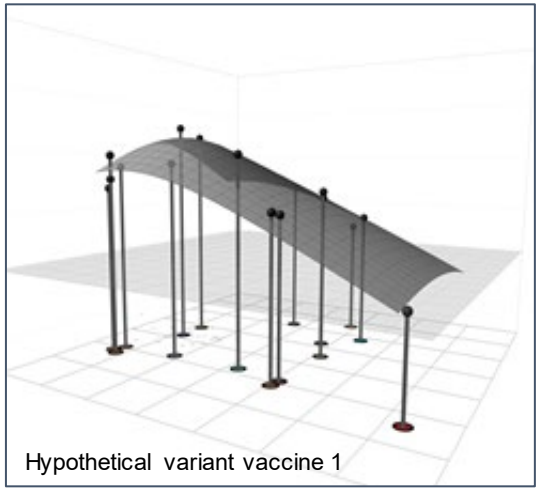
Arms	Sample Size	Vaccine Candidate	Interval (weeks)	Timing of First Dose	Second Dose	
1	100	Prototype	≥16	D1		Moderna
2	100	Beta + Omicron	≥16	D1		
3	100	Beta + Omicron	≥16	D1	D56	
4	100	Delta + Omicron	≥16	D1		
5	100	Omicron	≥16	D1		
6	100	Omicron + Prototype	≥16	D1		

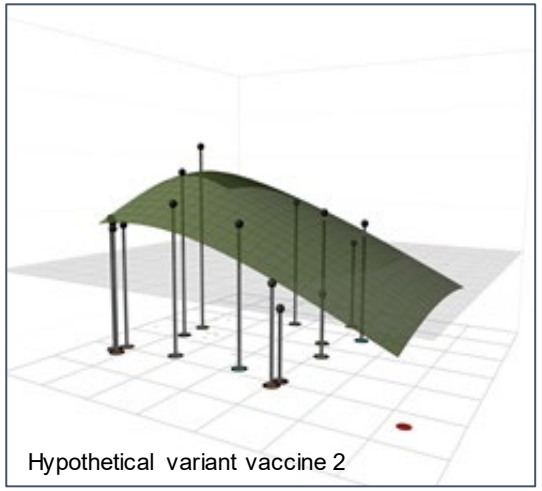
https://clinicaltrials.gov/ct2/show/NCT05289037

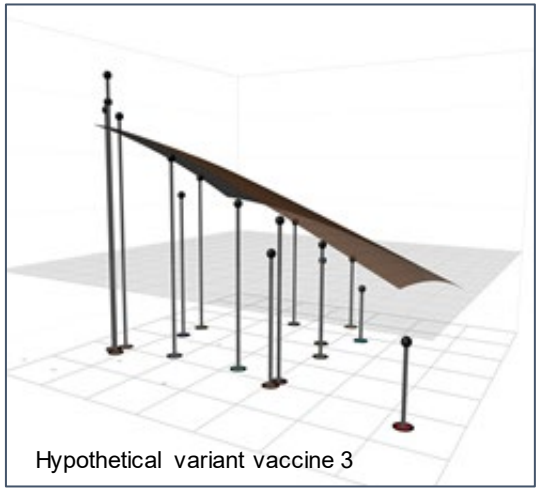
Early responses for nay given variant vaccine may increase titers across landscape

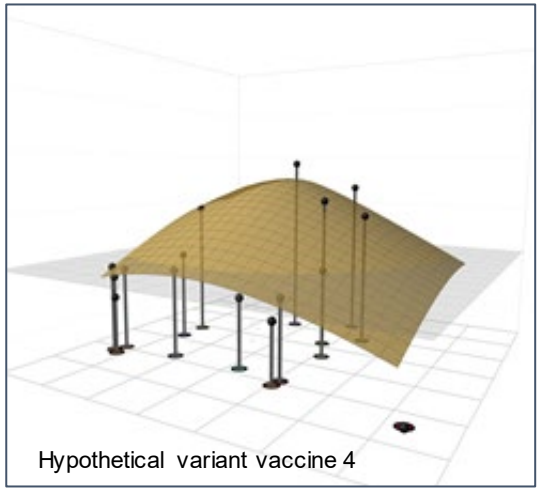


Later timepoints may show differential responses



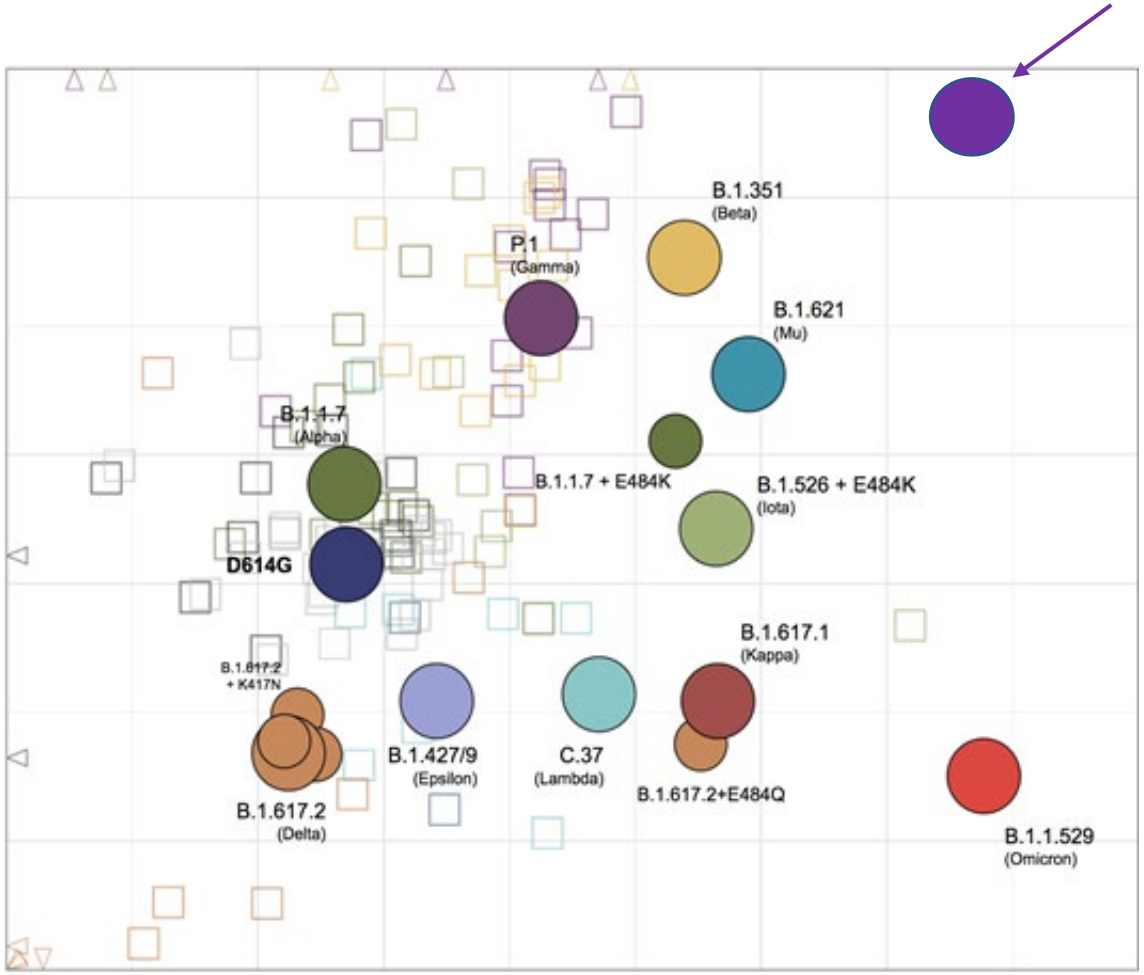


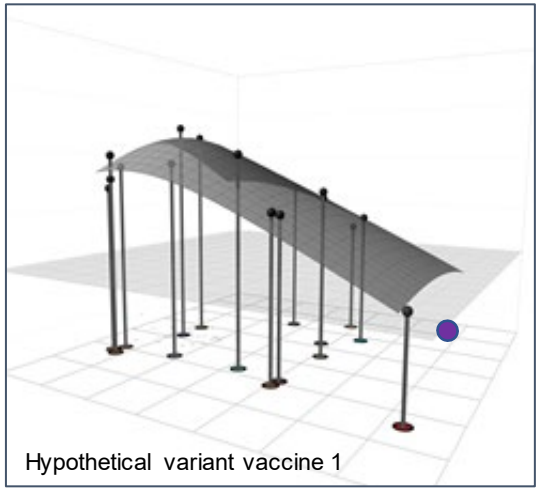


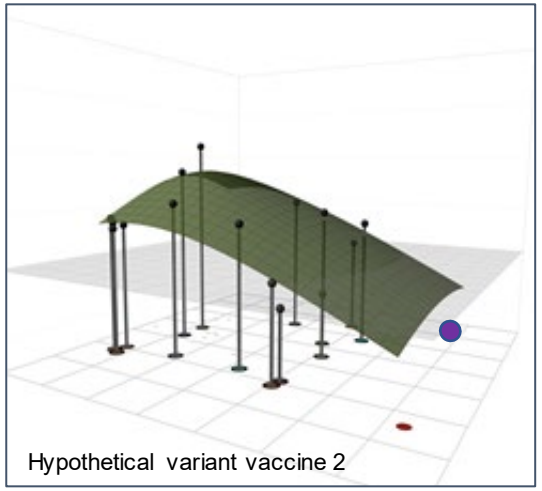


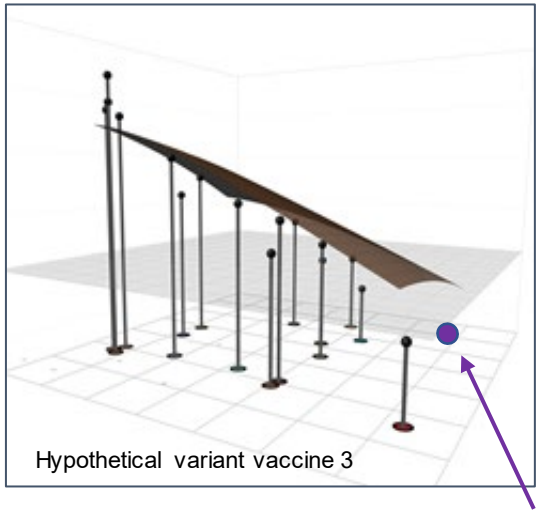
If (when) a new variant emerges, we can test serum to the new antigen

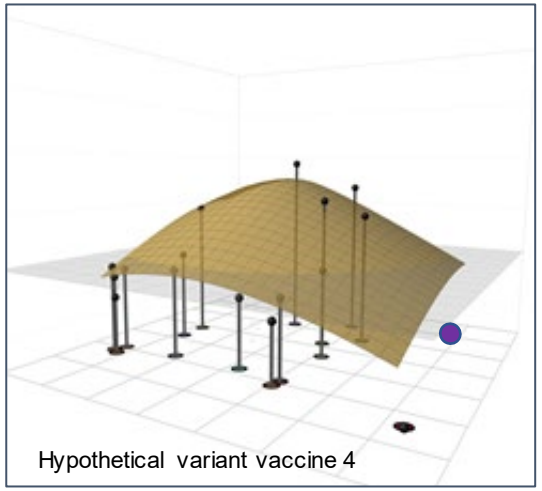
- will inform of vaccine options to use with previously tested variant vaccines











Conclusion

- There is likely to be continued evolution of the SARS-CoV-2 virus.
  - Evolution within Omicron BA.2, or
  - Another Omicron-like emergence event

- Ideally we learn to pick vaccine strains based on anticipated evolution.

- We also need to understand how to use available vaccines (prototype and variant) to modify antibody responses and target different antigenic spaces.