



# Is omicron a new serotype

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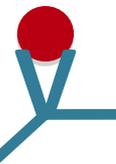


Virus replication as error prone process leads to mutations in genome

High virus replication rate → more mutations

New variants can become dominant, when mutations lead to

- Higher transmission
- Faster replication
- Evasion of pre-existing immunity/ immune escape variants



- Since late 2020: emergence of variants posed an increased risk to global health
- **Wuhan/D614G** (ancestral strain)

## Variants of concern (VOCs):

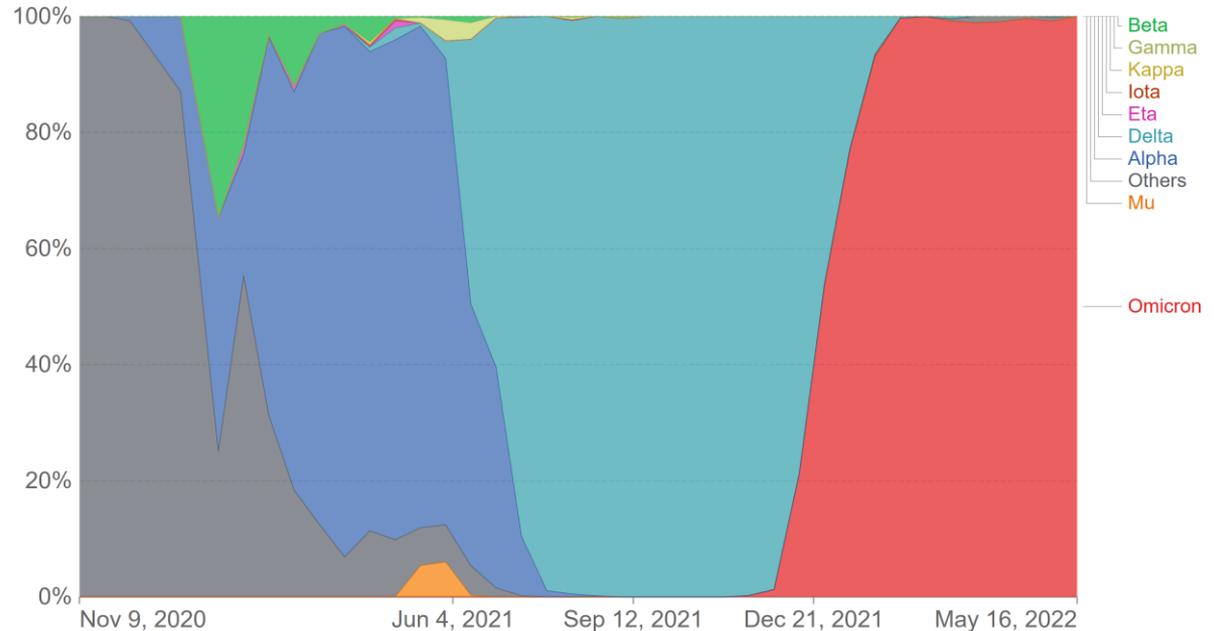
- **Alpha** (B.1.1.7)
- **Beta** (B.1.351)\*
- **Gamma** (P.1) \*
- **Delta** (B.1.617.2)\*
- **Omicron** (B.1.1.529)\*

\*immune escape variants

## SARS-CoV-2 variants in analyzed sequences, Austria

The number of analyzed sequences in the preceding two weeks that correspond to each variant group. This number may not reflect the complete breakdown of cases since only a fraction of all cases are sequenced.

Our World in Data



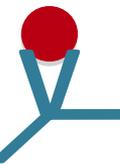
Source: GISAID, via CoVariants.org – Last updated 19 May 2022

OurWorldInData.org/coronavirus • CC BY

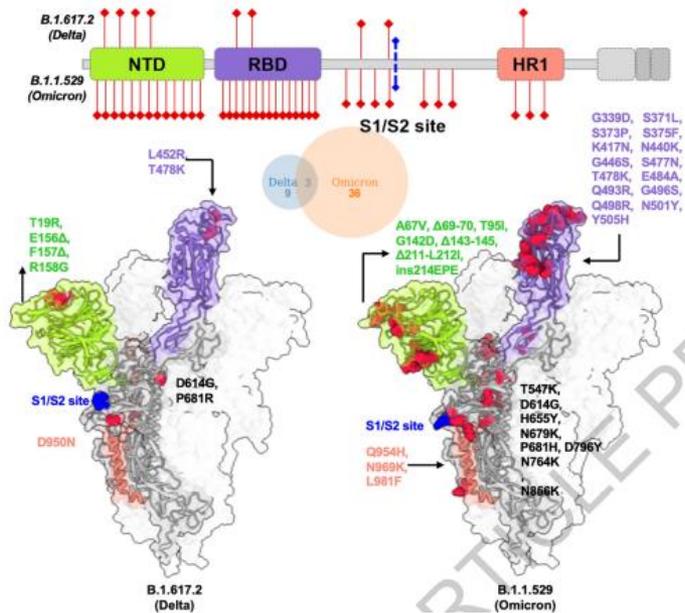
Note: Recently-discovered or actively-monitored variants may be overrepresented, as suspected cases of these variants are likely to be sequenced preferentially or faster than other cases.

Source: OurWorldinData.org (20.05.22)

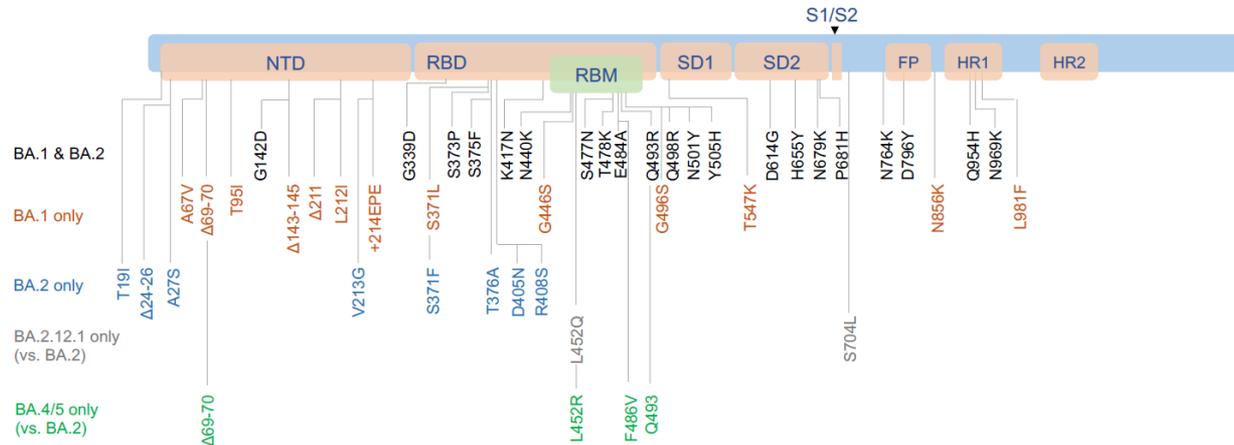
# Omicron – emerging variant of concern



- on 26th Nov. 2021 the WHO classified the omicron variant (B.1.1.529) as new VOC
- 50 mutations -> 32 are located on the spike protein



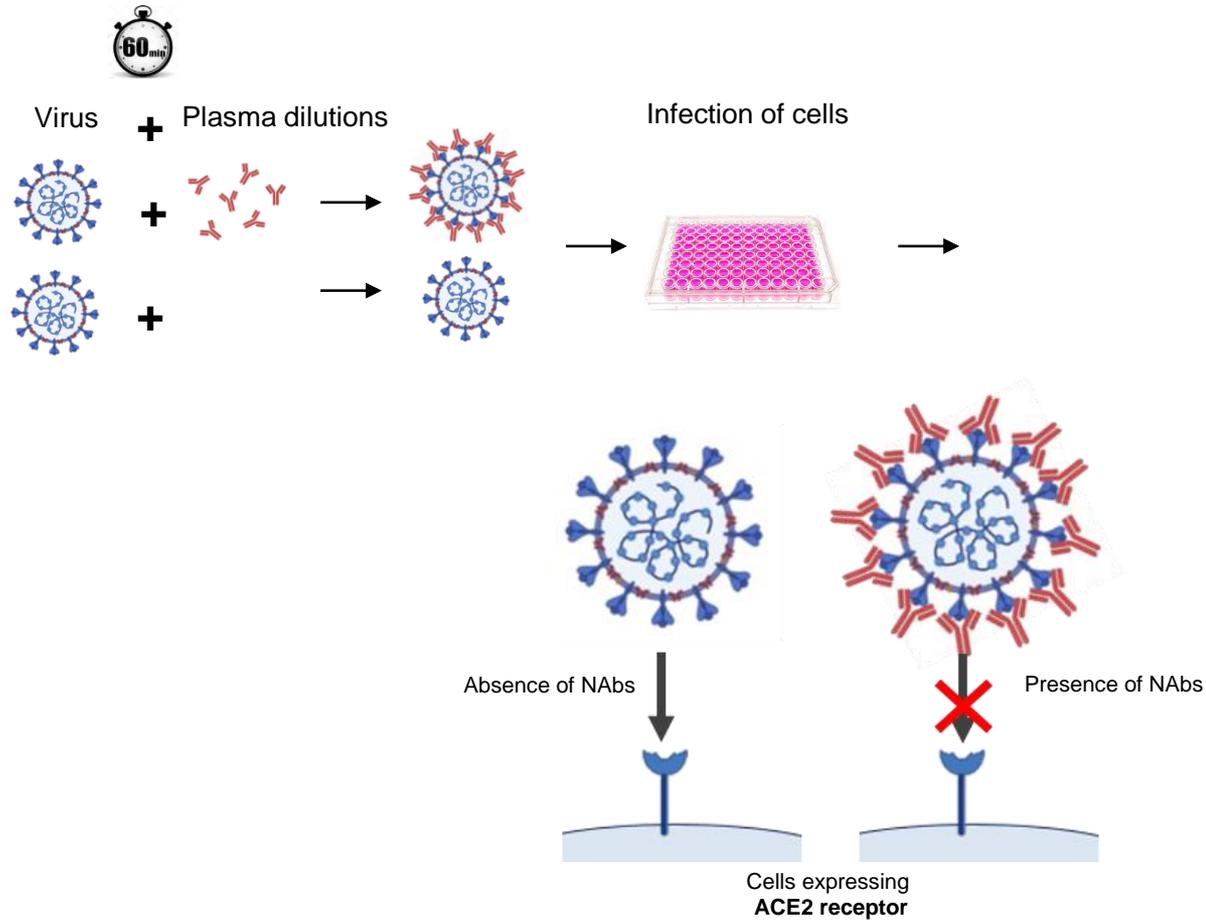
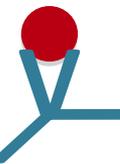
## Omicron sub-variants

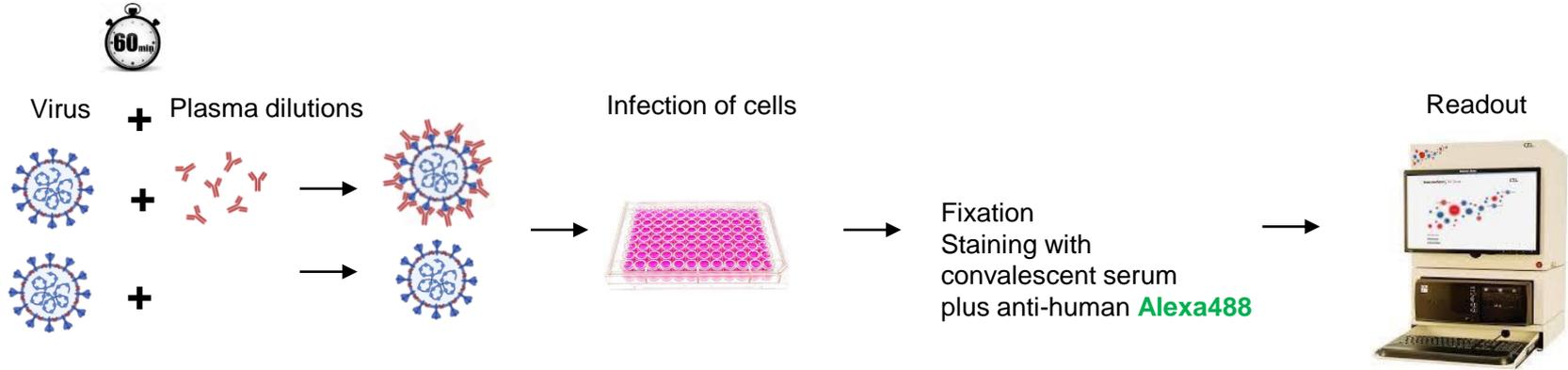
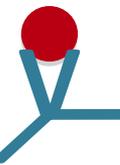




- Omicron variant as immune escape variant
- Analyze neutralization profiles of pre-omicron variants and BA.1 and BA.2 omicron sub-variants
- Perform antigenic cartography
- How do multiple exposures with the same or antigenically different variants influence cross-neutralizing antibodies?

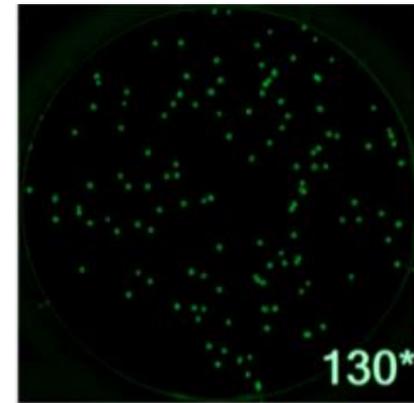
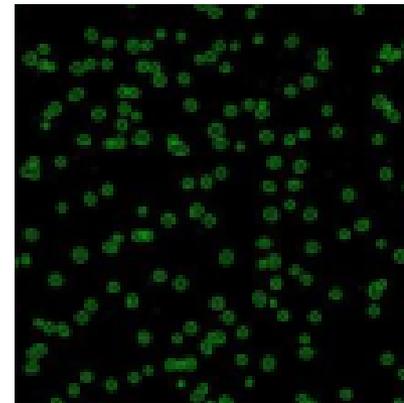
# Principle of neutralization assay

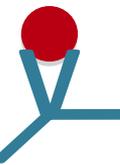




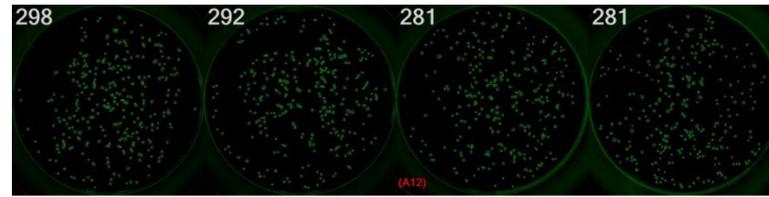
## SARS-CoV-2 variants

- Focus forming assay
- replication competent SARS-CoV-2 isolates

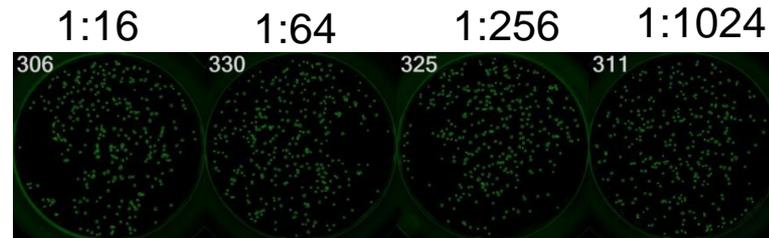




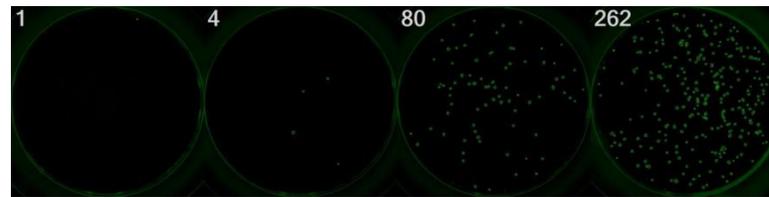
Virus only



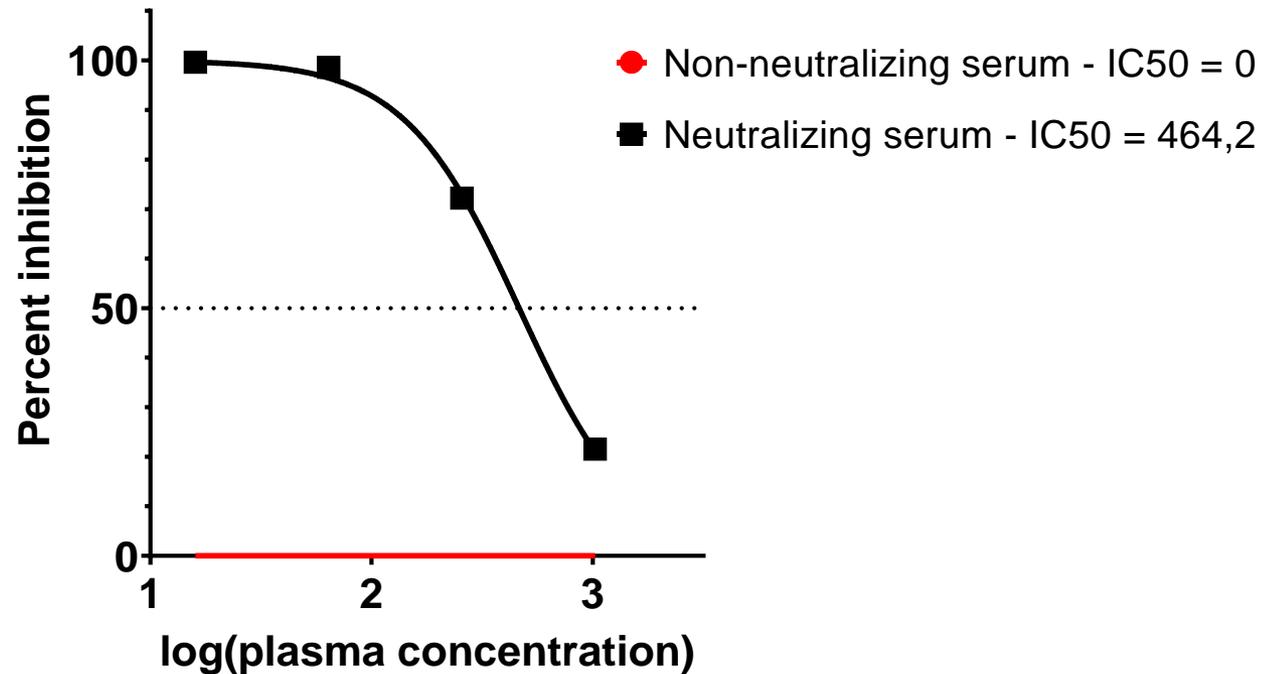
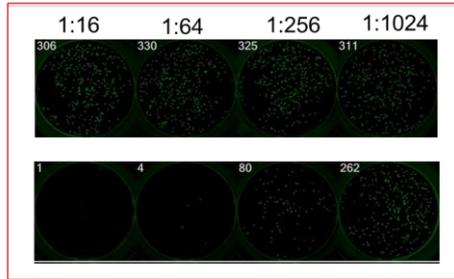
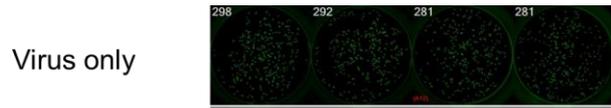
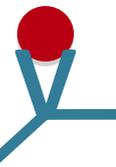
Non-neutralizing serum



Neutralizing serum



# Principle of neutralization assay





## By numbers of exposure (Vaccination or infection)

### **Single exposure**

- Unvaccinated, single infection

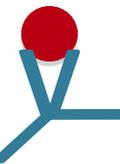
### **Double exposure**

- Two doses of vaccination
- Two subsequent infections with different variants (pre-omicron + omicon)

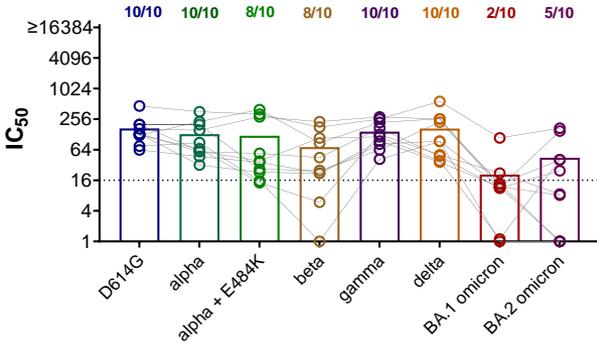
### **Three or more exposures**

- Three doses of vaccination
- Two doses of vaccination + pre-omicron breakthrough
- Two/three doses of vaccination + omicron breakthrough
- Two/three doses of vaccination + pre-omicron breakthrough + omicron breakthrough

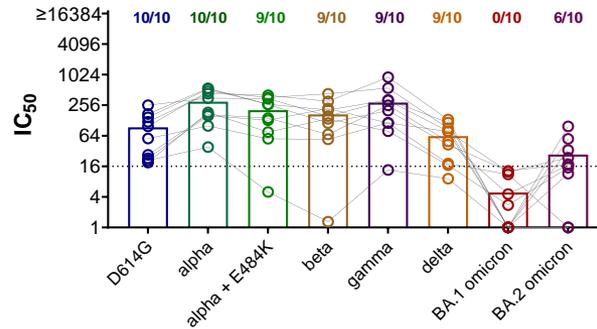
# Single exposure (unvaccinated convalescent)



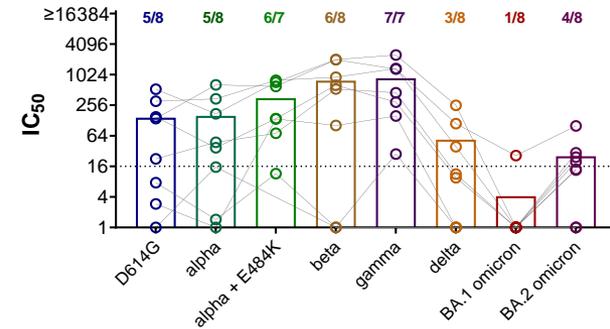
First wave convalescent



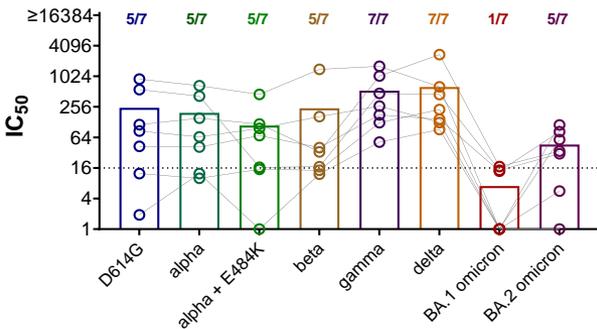
alpha convalescent



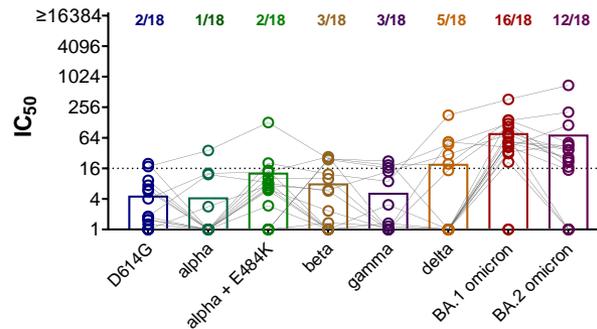
beta convalescent



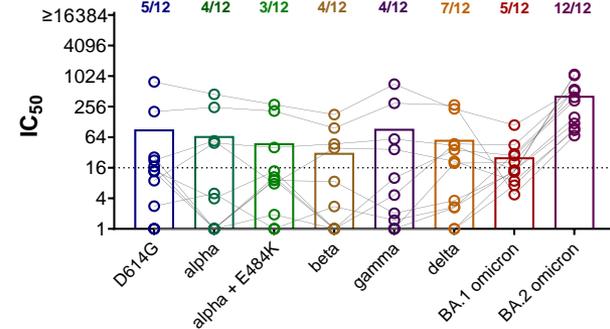
delta convalescent



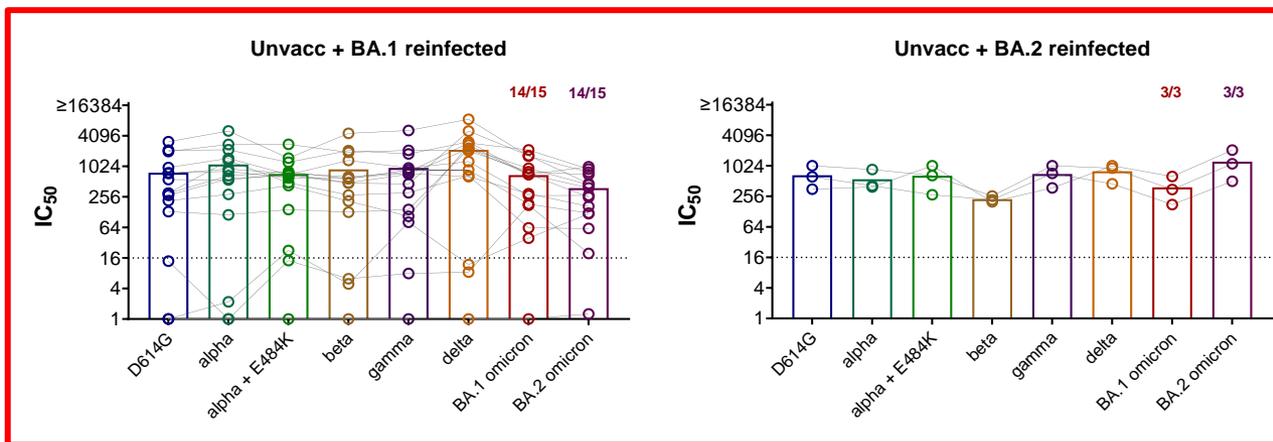
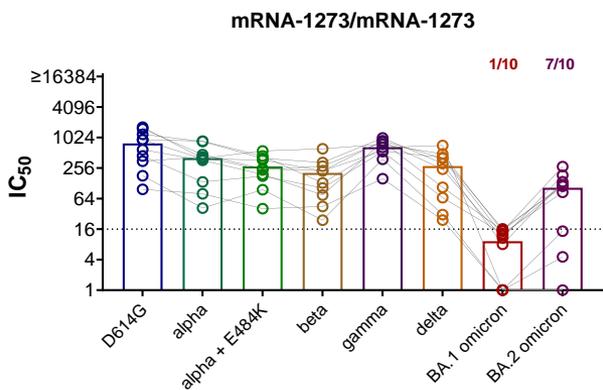
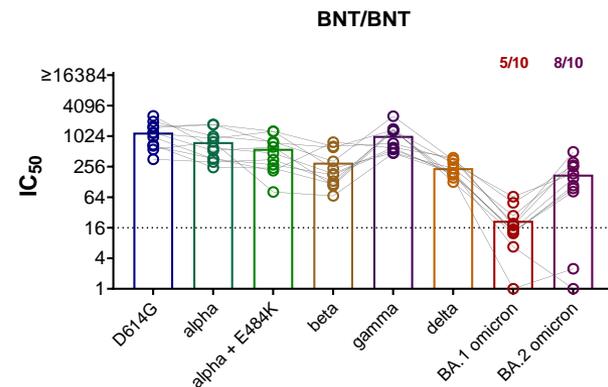
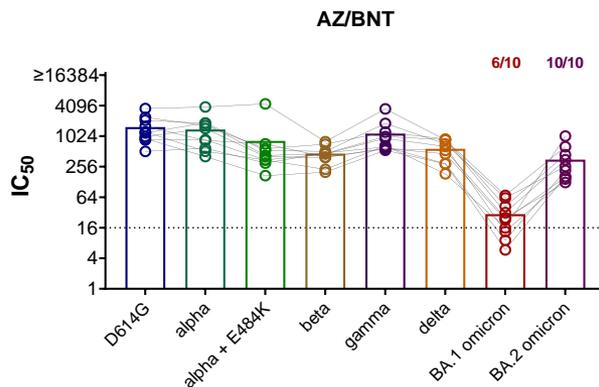
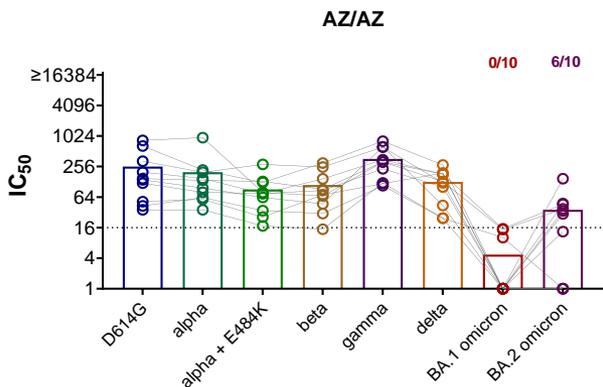
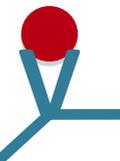
BA.1 omicron convalescent



BA.2 omicron convalescent



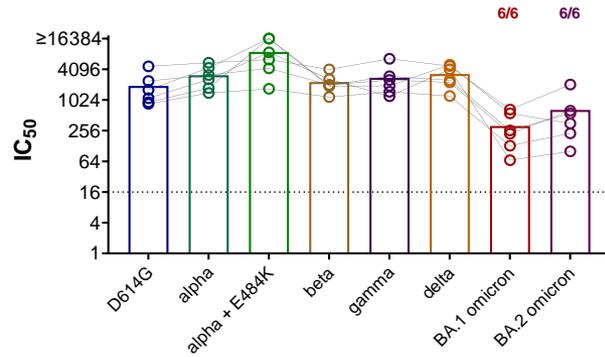
# Double exposure



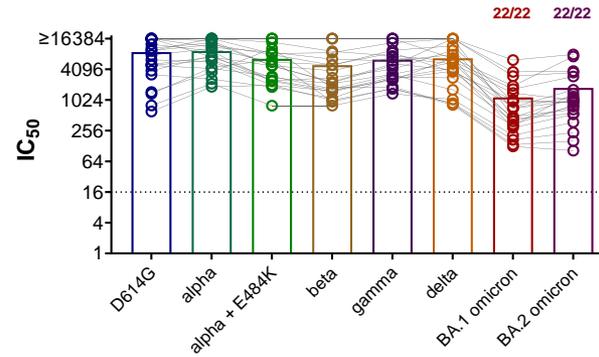
# Three or more exposures



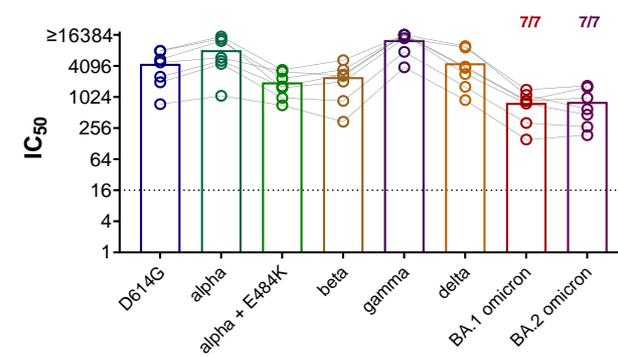
AZ/AZ + delta convalescent



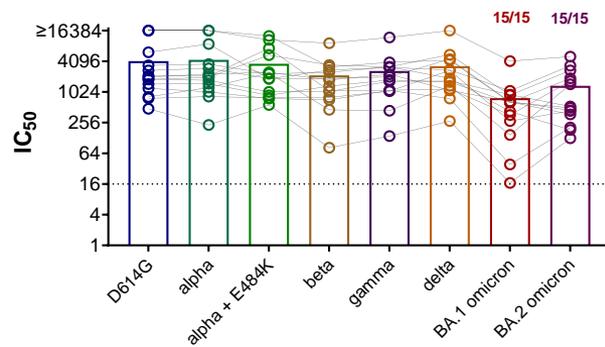
BNT/BNT + delta convalescent



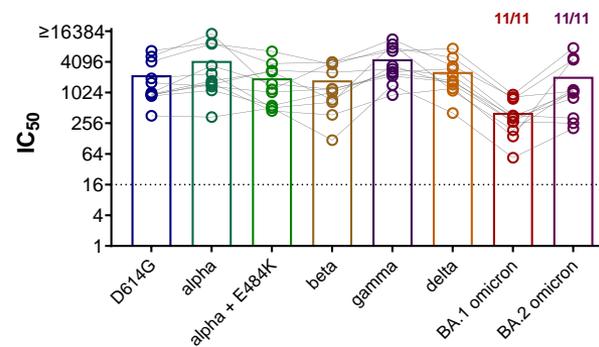
BNT/BNT/BNT



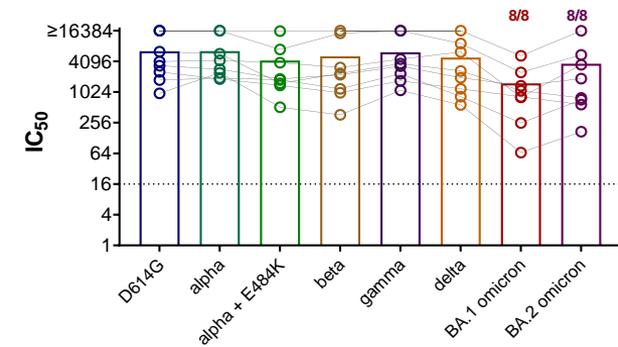
Vacc + BA.1 convalescent



Vacc + BA.1 reinfected

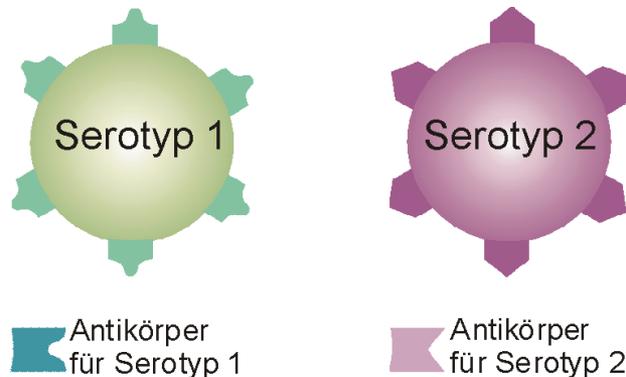


Vacc + BA.2 convalescent

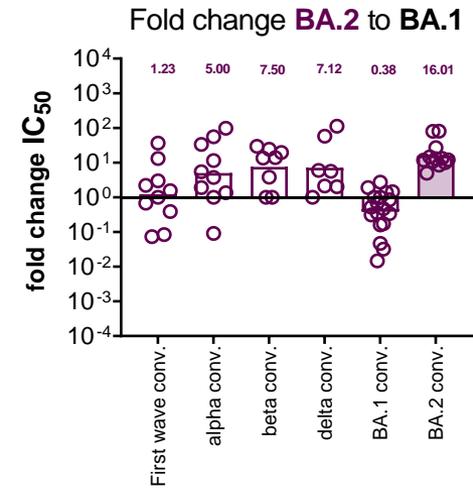
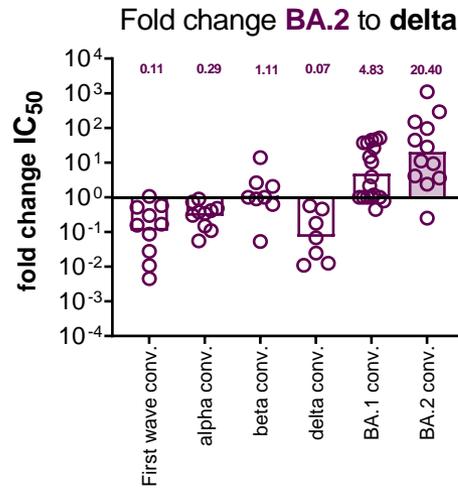
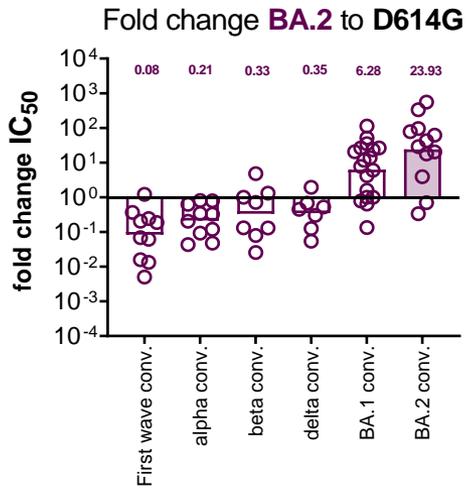
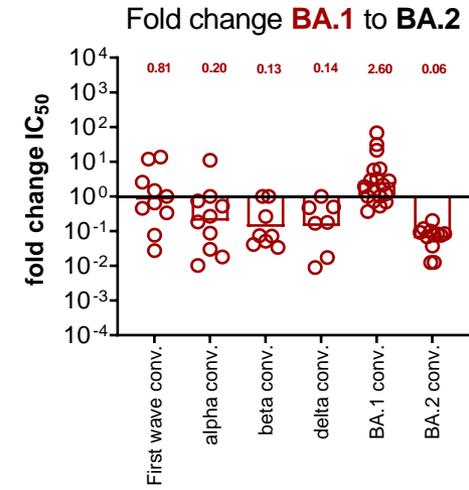
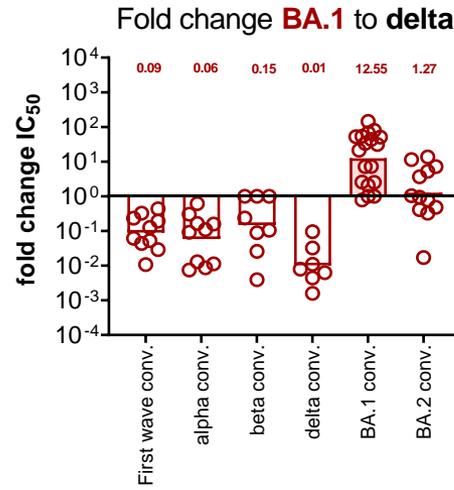
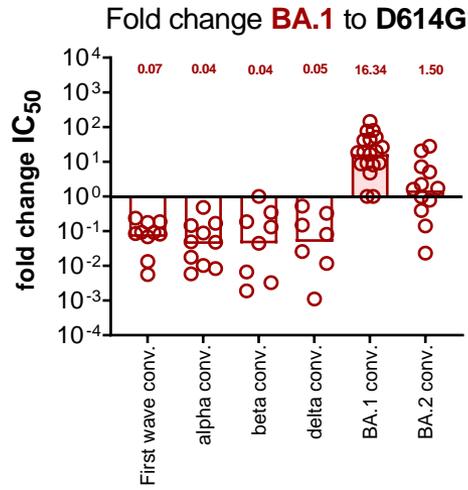




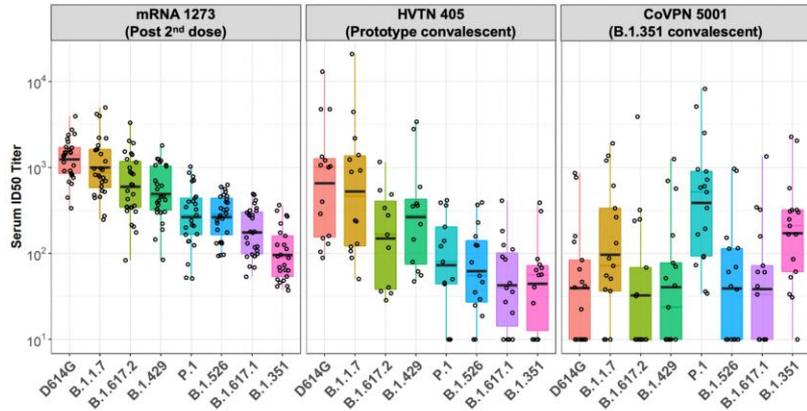
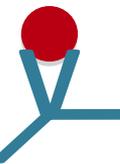
- A serotype is defined as a variation within a microbial species, distinguished by the humoral immune response
- The serotype classification of bacteria or viruses is based on their surface antigens
- Antibodies generated to one serotype do not usually efficiently protect against another serotype



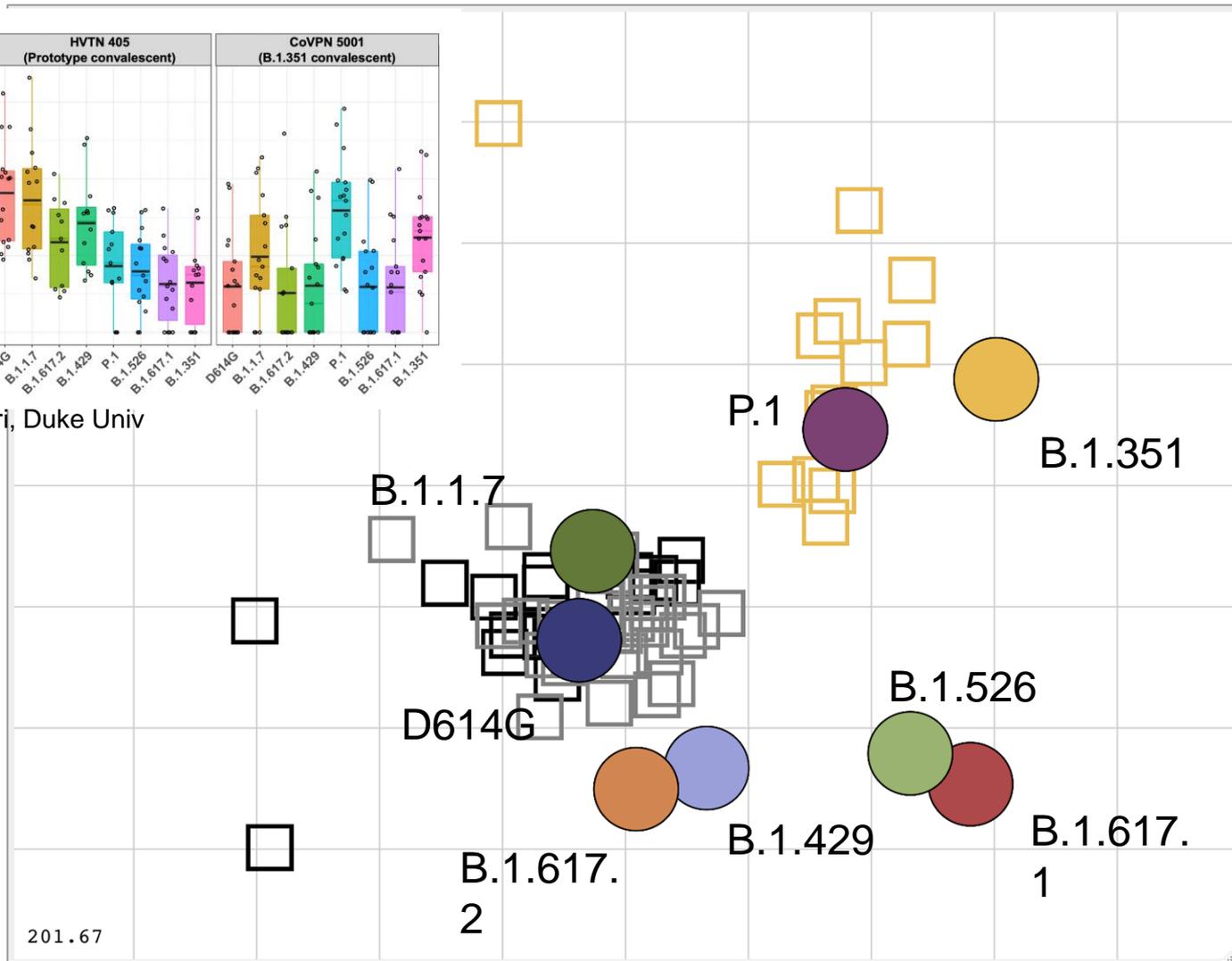
# pre-omicron variants BA.1 and BA.2



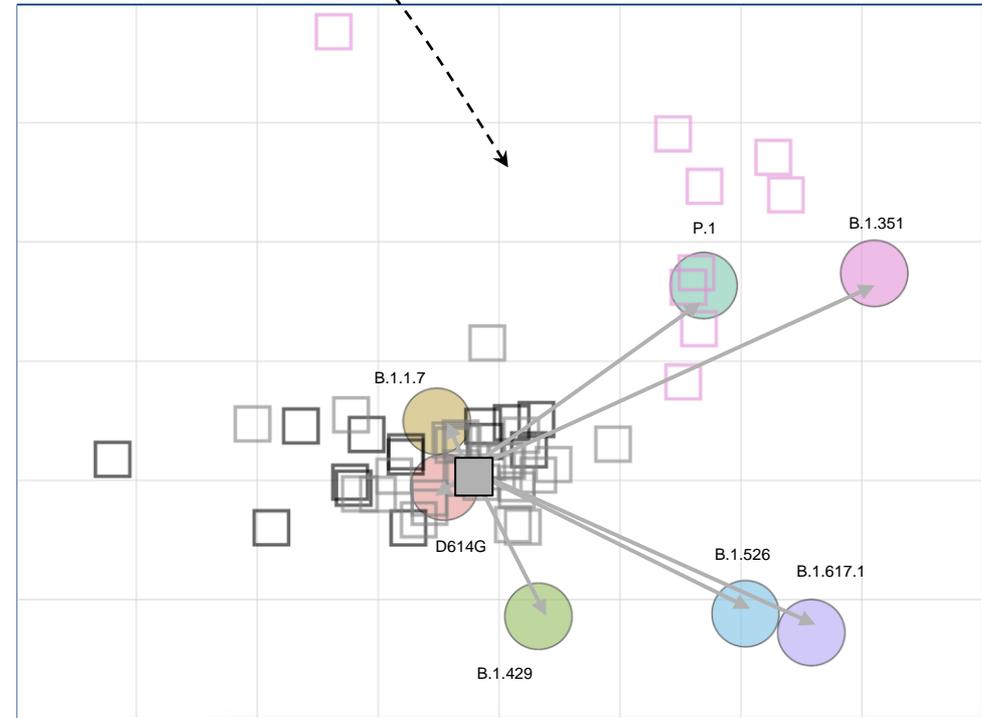
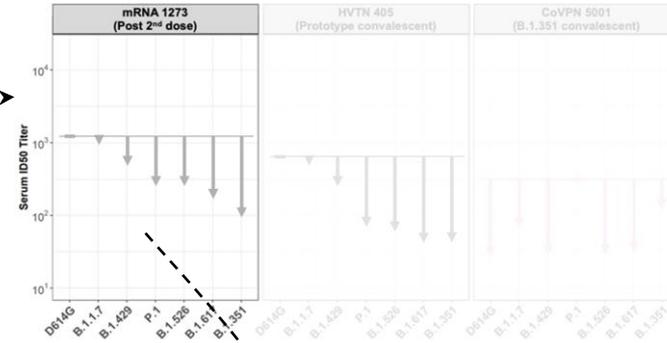
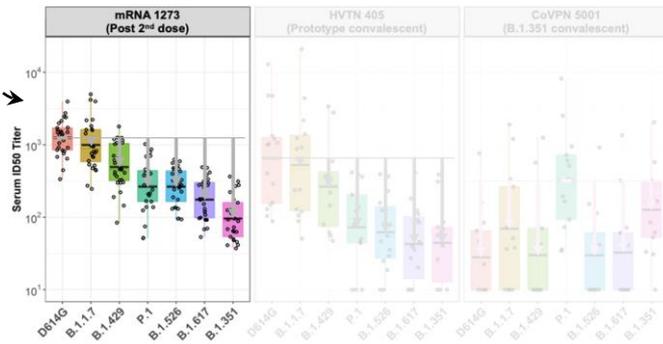
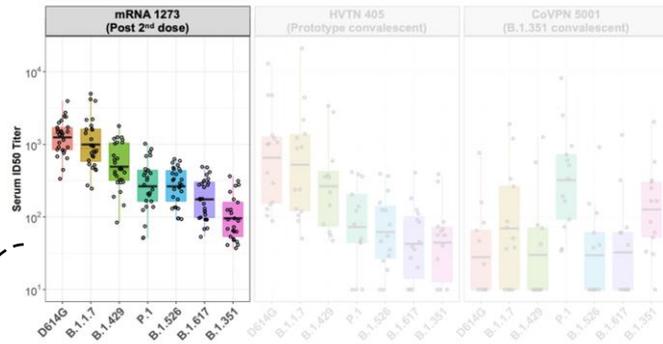
# Construction of antigenic maps



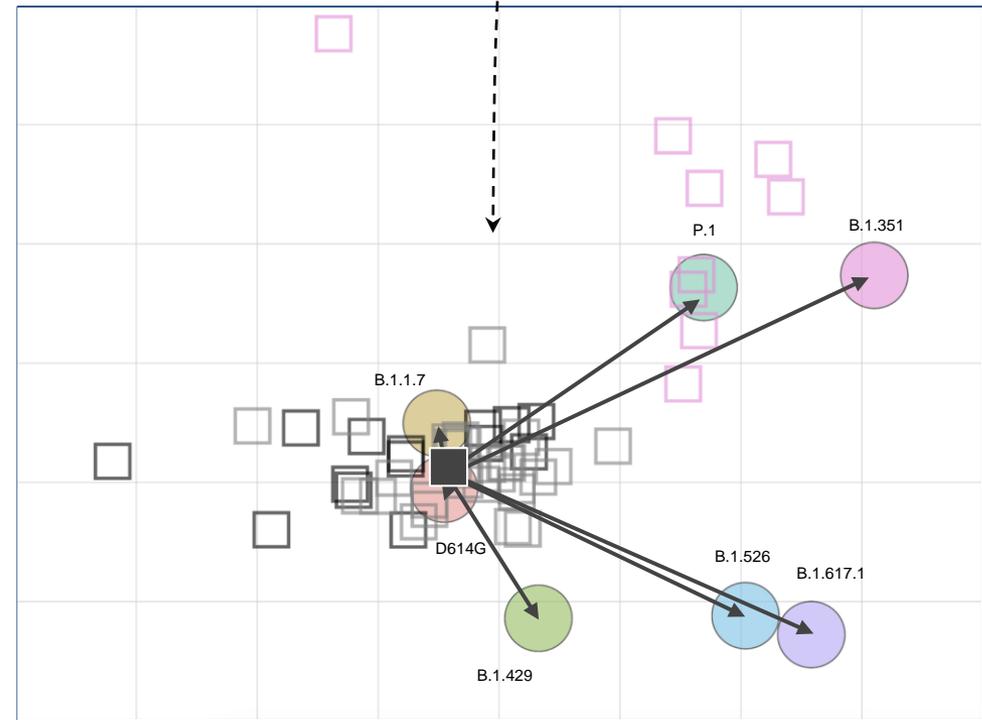
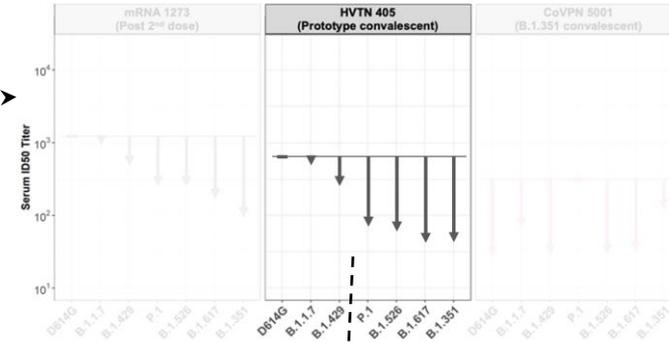
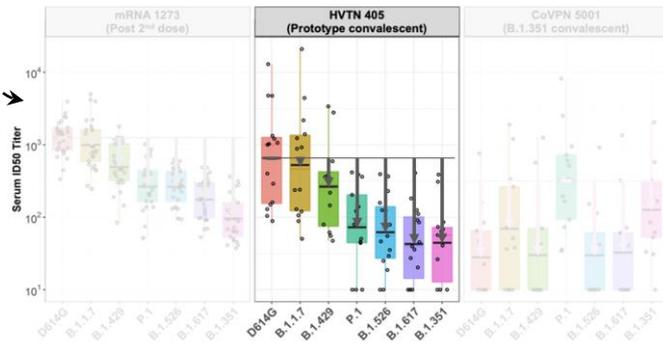
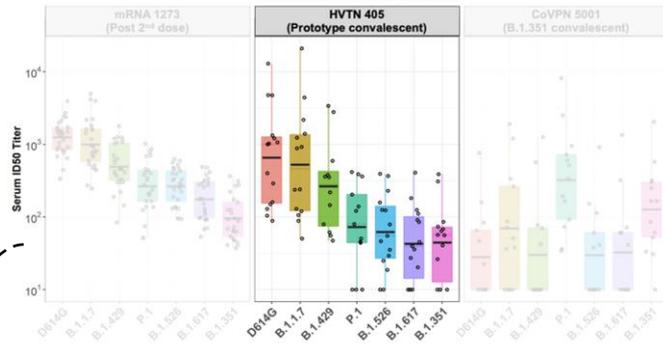
X Shen, DC Montefiori, Duke Univ



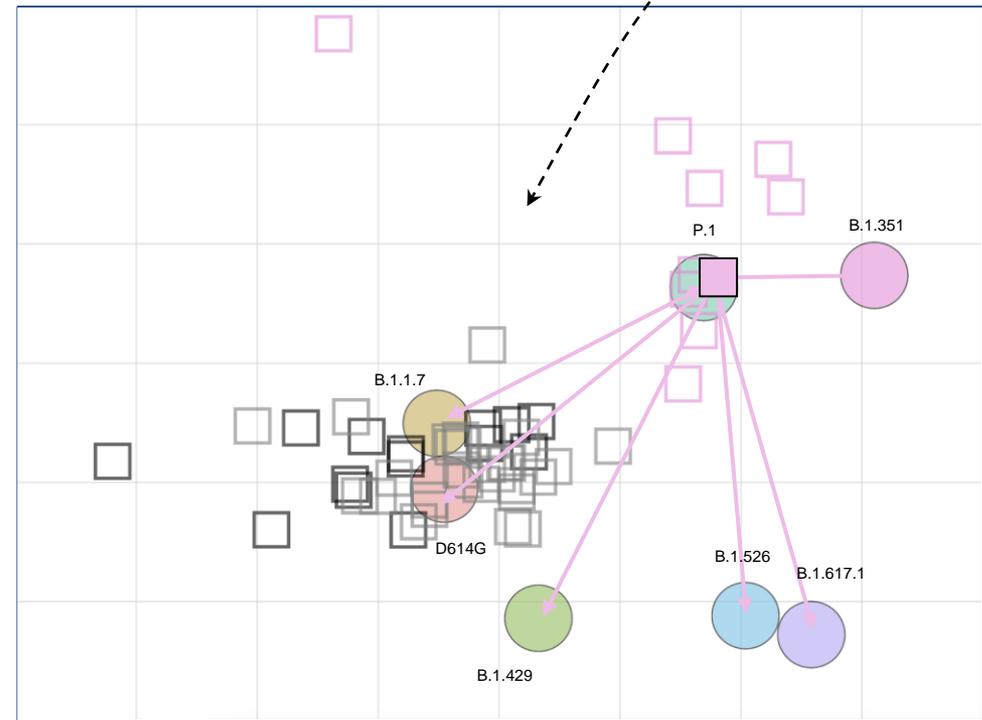
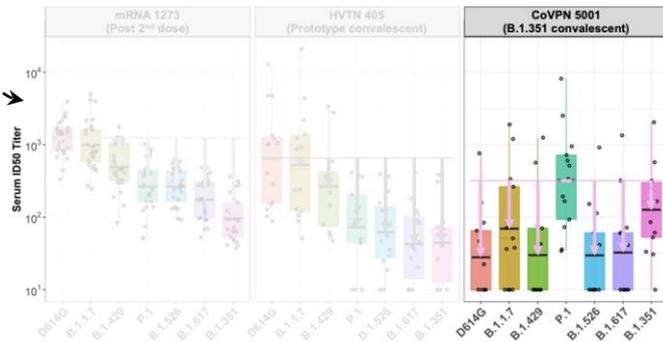
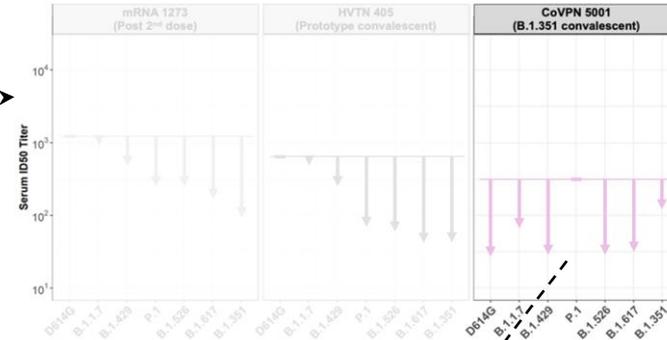
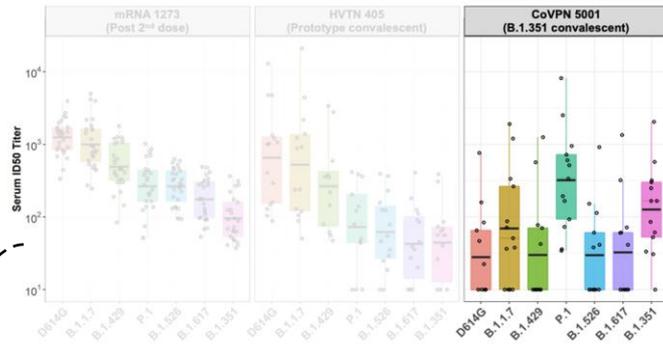
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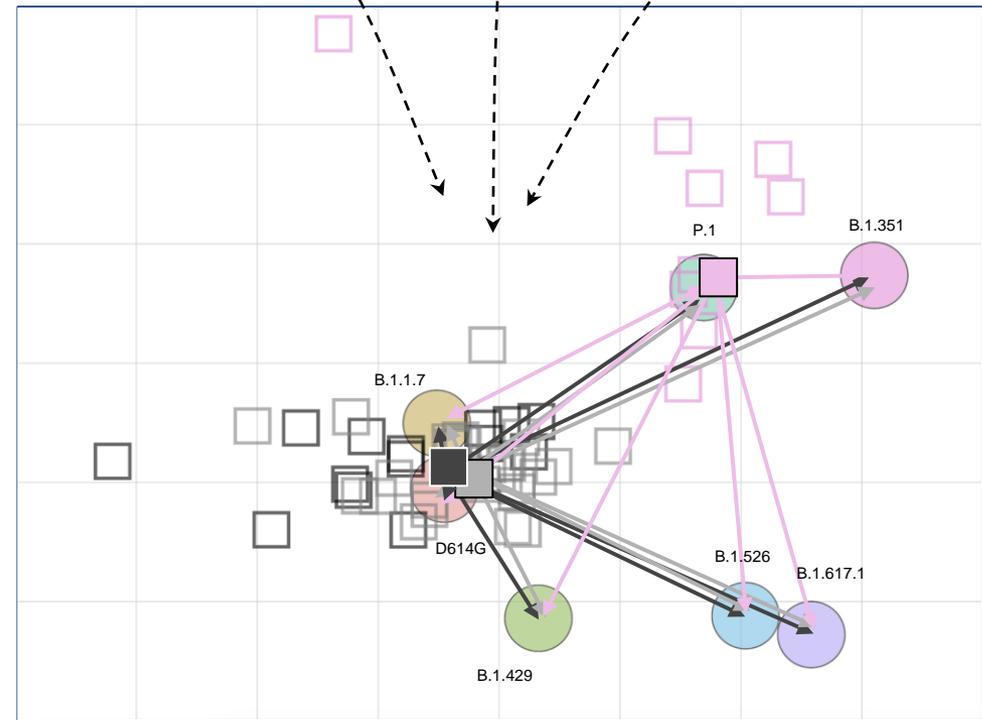
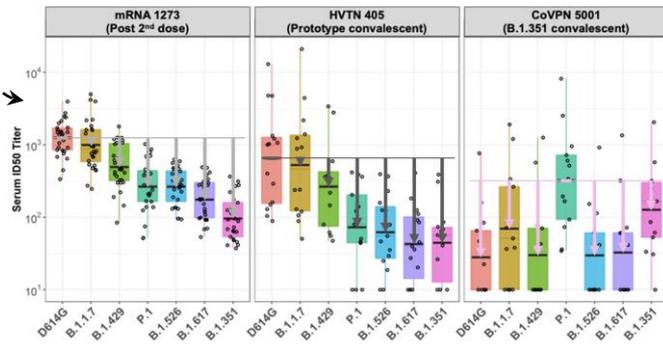
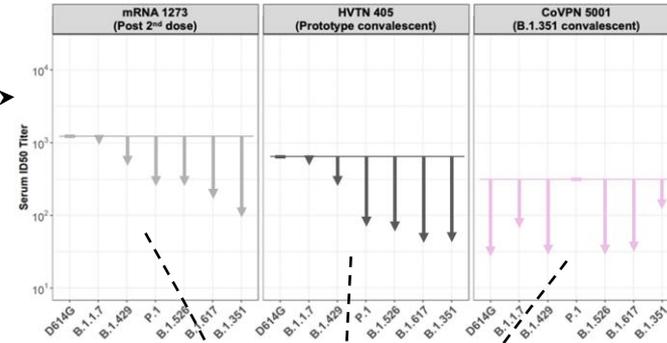
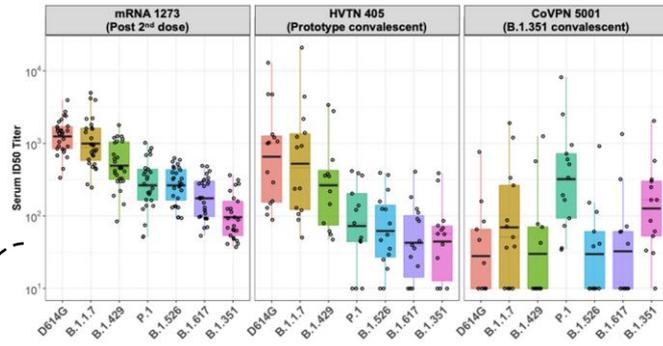
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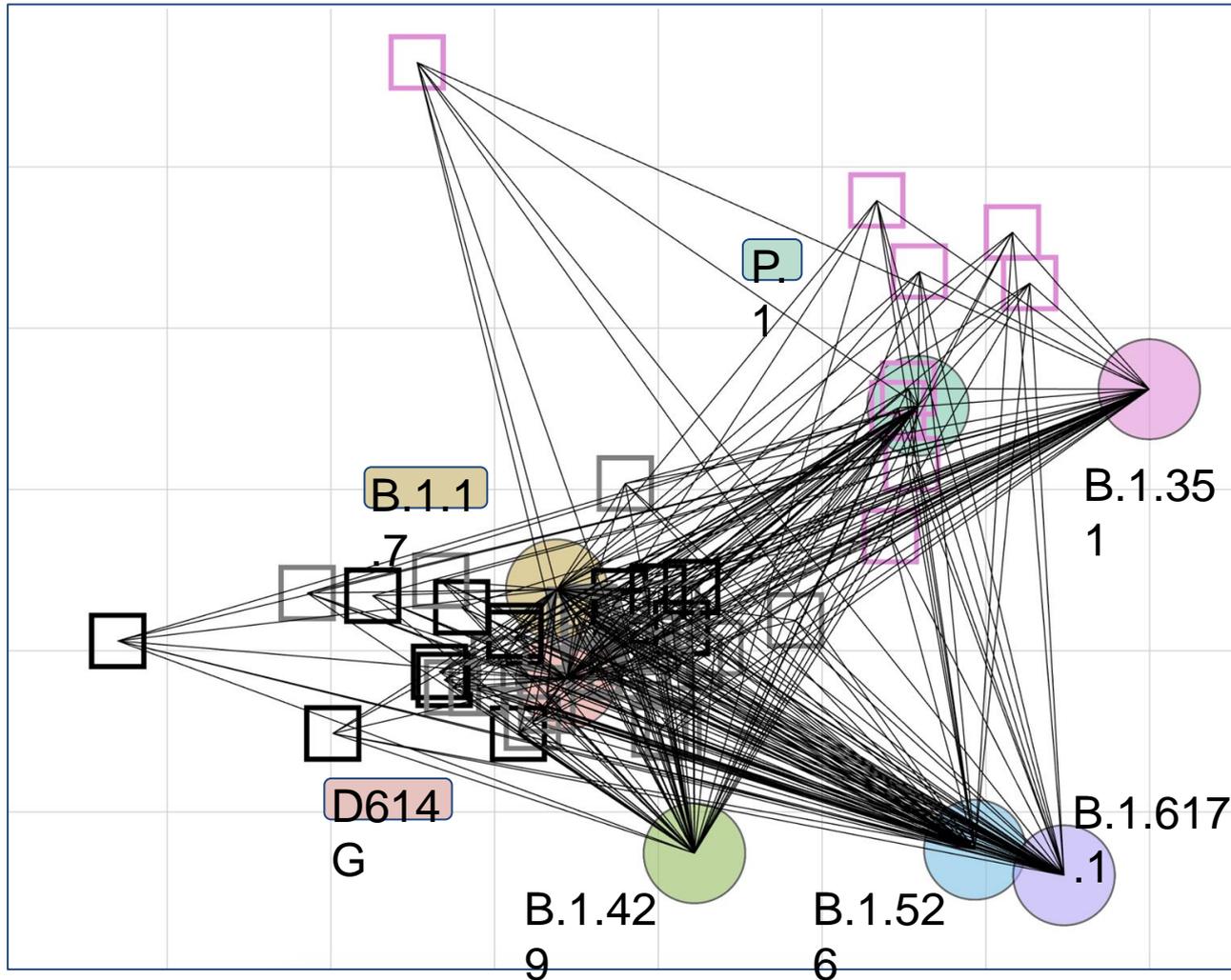
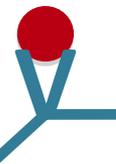
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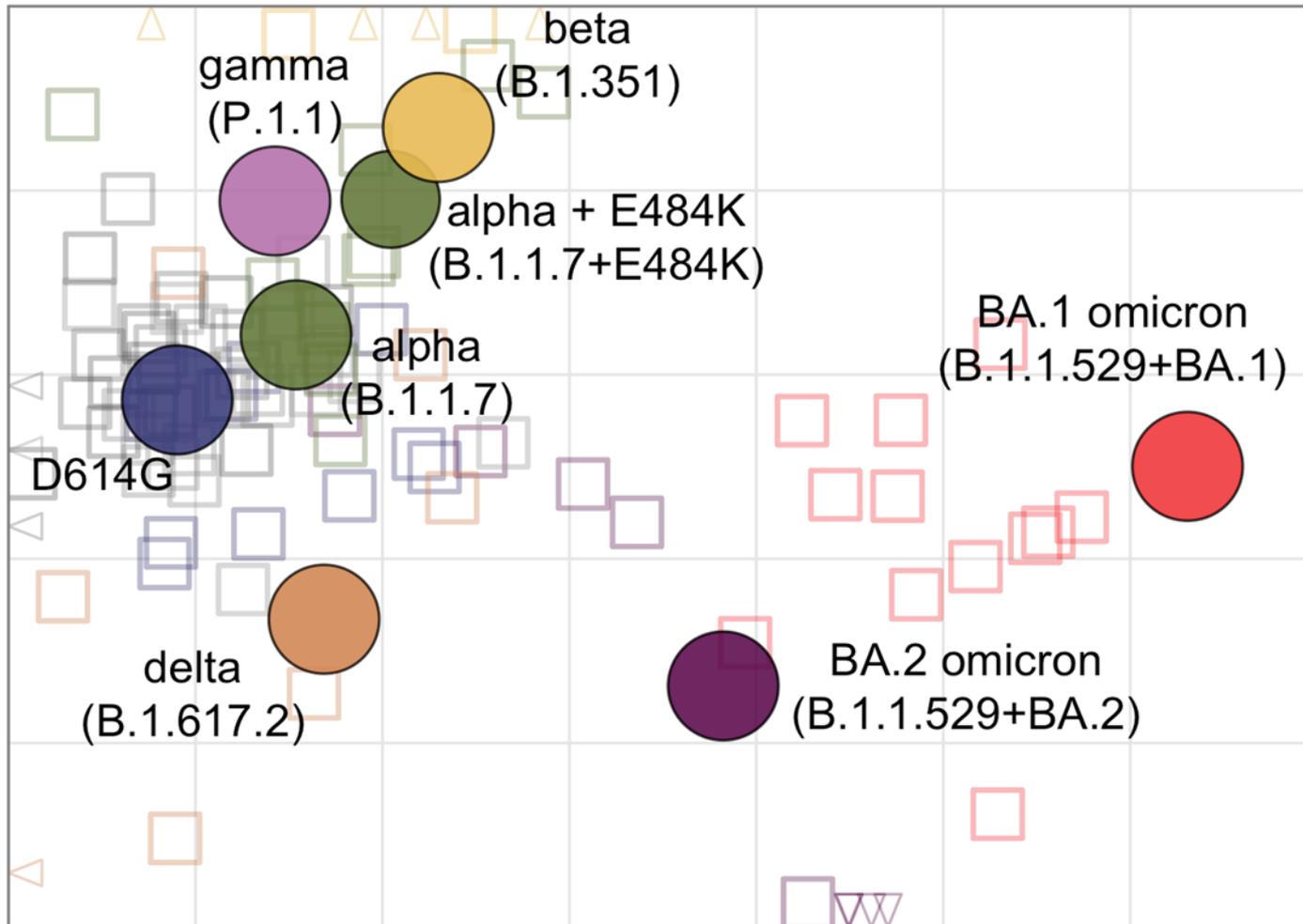
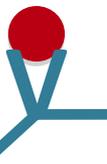


# Construction of antigenic maps



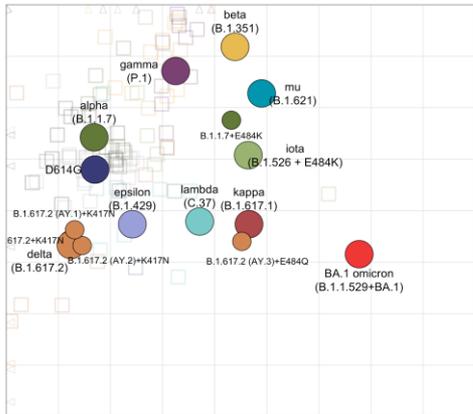
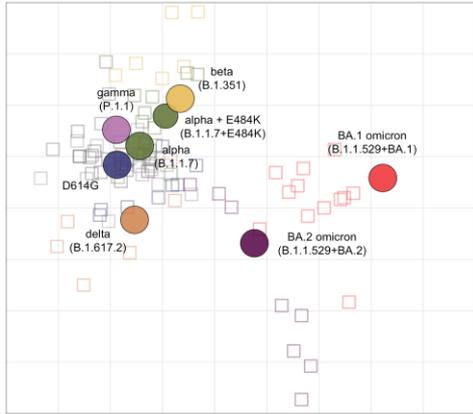
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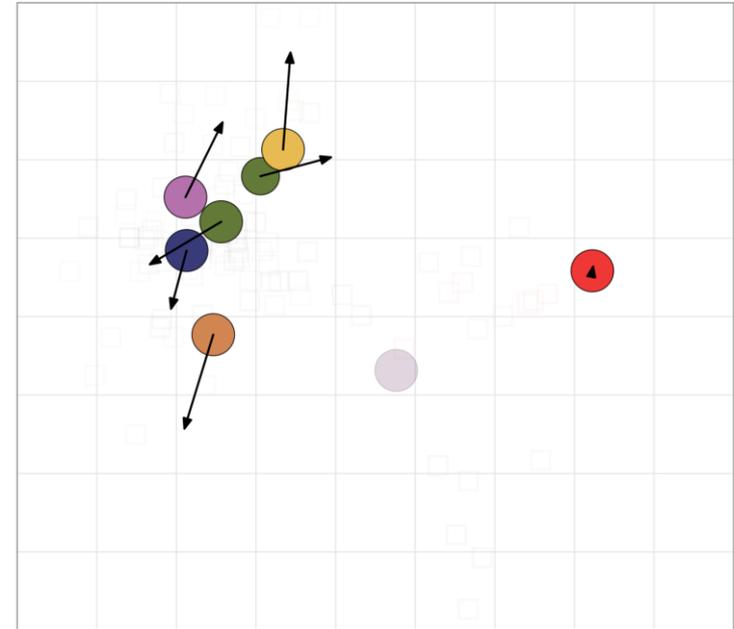


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Derek Smith

# Comparison to Duke map



Arrows point to position of variant in Wilks *et al.* map



Map topology corresponds well.

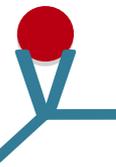
Both maps show similar range of escape of BA.1 from D614G.

High P.1 titers in Kimpel's vaccine, B.1.617.2 sera explain different position of P.1.

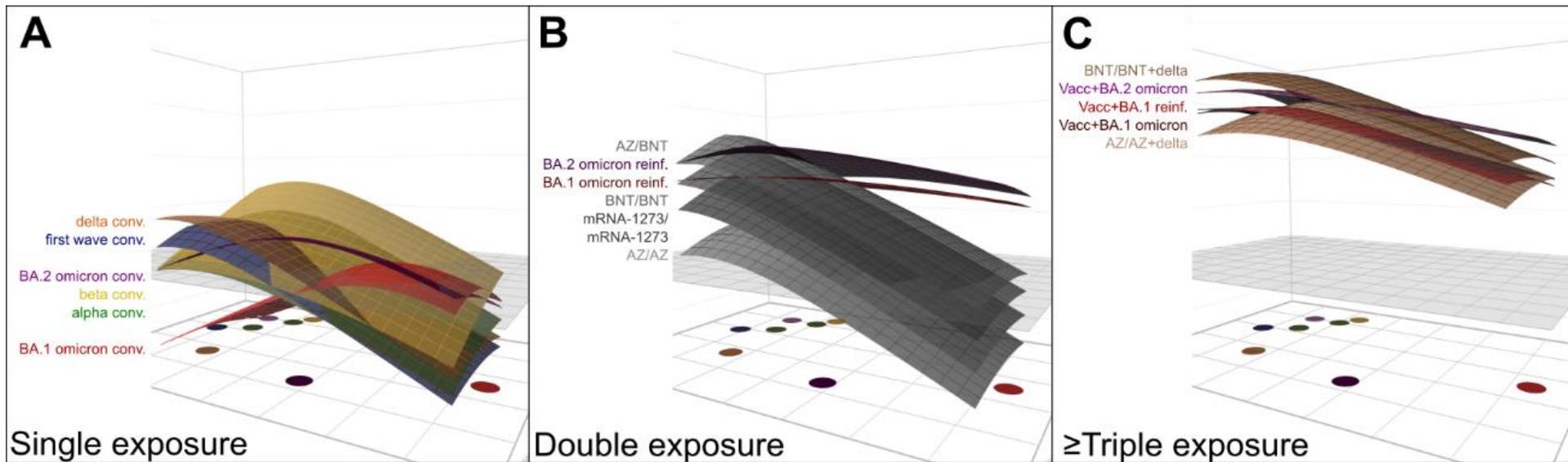
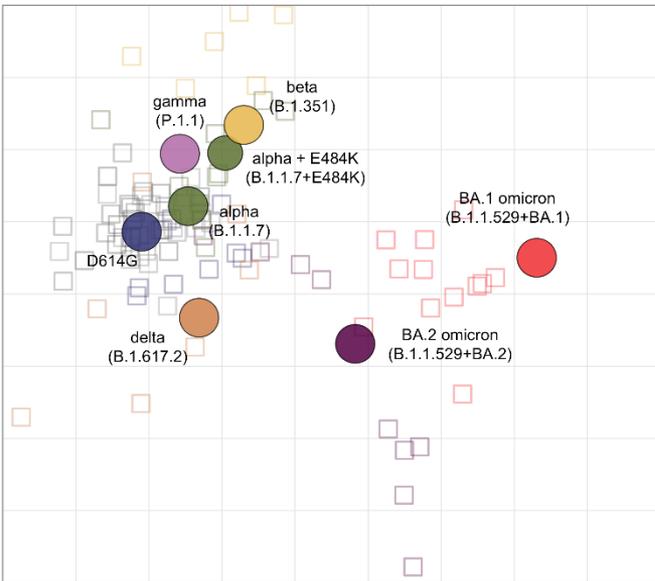
Generally higher degree of cross-neutralization in non-Omicron sera explains smaller spread of non-Omicron variants.

Map from Wilks *et al.*, 2022, bioRxiv, <http://doi.org/10.1101/2022.01.28.477987>

# Antibody landscapes



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- Pre-omicron variants, BA.1 omicron and BA.2 omicron represent three antigenically distinct clusters and single infection with a virus from one of the three groups in naive individuals induces only poor cross neutralizing antibodies against the two other clusters
- BA.2 omicron is antigenically closer to pre-omicron variants compared to BA.1
- Multiple exposures increase cross-neutralizing antibodies even against non-exposed variants
- Two exposures to antigenically distinct variants or three to antigenically related variants induce good neutralizing antibody titers against the current antigenic space
- New omicron sub-variants BA.4/BA.5 and BA.2.12.1 emerge
- Good news: T cell responses are more conserved across variants



Medical University of Innsbruck  
Institute of Virology

Dorothee von Laer

**Annika Rössler**

Albert Falch

Eva Hochmuth

Evelyn Peer

Lisa-Maria Raschbichler

Bianca Neurauter

Lydia Riepler

David Bante

Lukas Perro

Stephan Amstler

Andreas Aufschnaiter

Luiza Hoch

Helena Schäfer

Wegene Borena

Barbara Falkensammer

Tyrolpath Obrist Brunhuber GmbH

Ludwig Knabl

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University of Cambridge

Derek Smith

**Antonia Netzl**

Samuel Wilks

Icahn School of Medicine at Mount Sinai

Florian Krammer

Viviana Simon

Ludwig Maximilians University Munich

Oliver T. Keppler

Marcel Stern

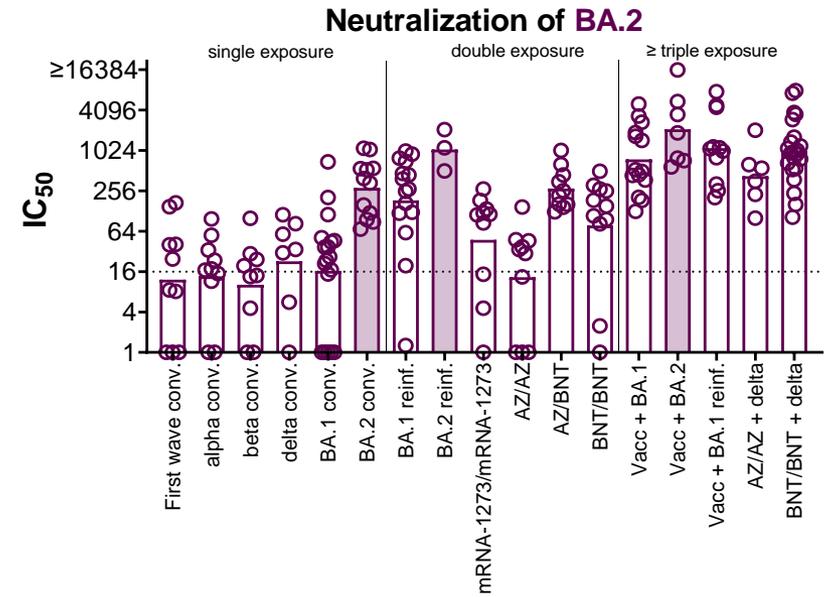
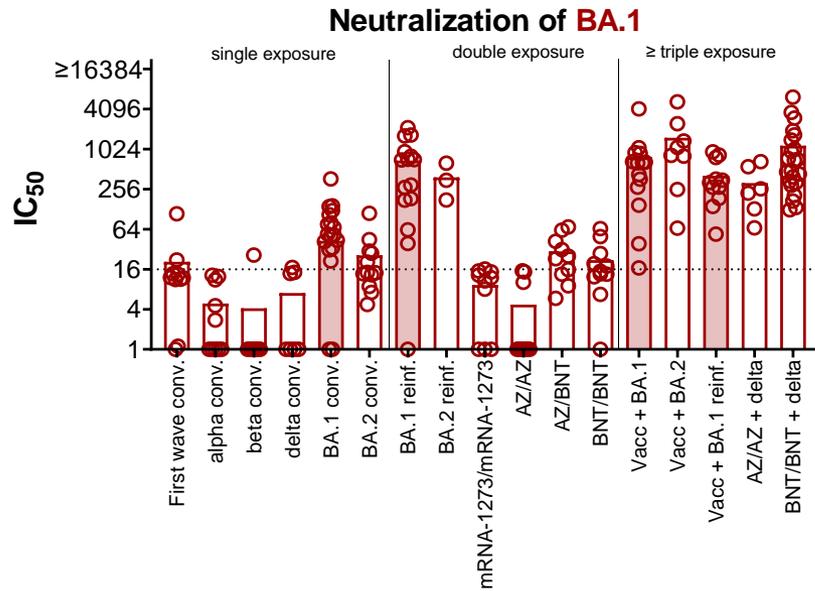






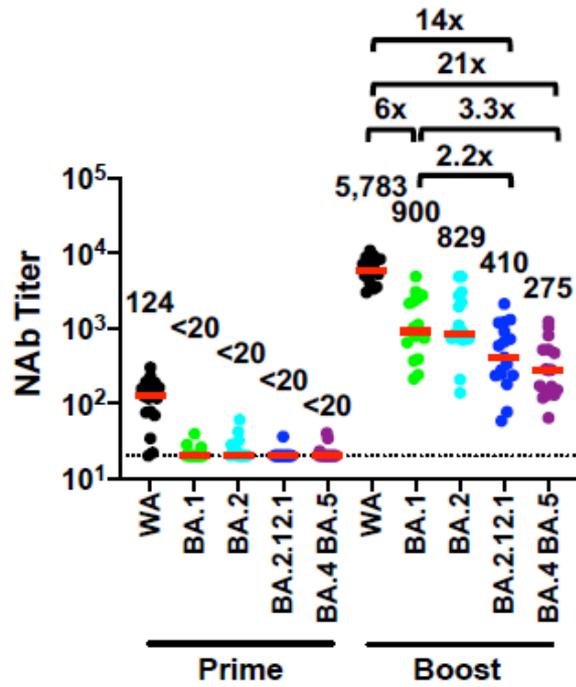
- D614G: Isolate B86.2, GISAID ID EPI\_ISL\_3305837
- B.1.1.7 (Alpha): isolate C69.1, GISAID ID EPI\_ISL\_3277382
- B.1.1.7-E484K (Alpha-E484K): isolate C79.2, GISAID ID EPI\_ISL\_3277383
- B.1.351 (Beta): isolate C24.1, GISAID ID EPI\_ISL\_1123262
- P1.1 (Gamma): isolate hCoV-19/Germany/BY-MVP-000005870/2021, GISAID ID EPI\_ISL\_2095177
- B.1.617.2 (Delta): isolate SARS-CoV-2-hCoV-19/USA/NY-MSHSPSP-PV29995/2021, GISAID ID EPI\_ISL\_2290769
- BA.1 (Omicron): isolate E16.1, GISAID ID EPI\_ISL\_6902053
- BA.2 (Omicron): isolate E65.1, GISAID ID EPI\_ISL\_12486408

# Neutralization of BA.1 vs. BA.2





**B**



**C**

