



Mapping Immunogenic Regions in SARS-CoV-2 Variants to Understand Vaccine Design Using Bioinformatics Tools



Joanna Sanchez
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Outline

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2. Structure of SARS-CoV 2 and Composition of Spike Glycoprotein

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2. Research goals

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2. Five Variants of Interest
3. Comparison of Five SARS-CoV 2 Variants

Conclusions

1. Looking ahead
2. Conclusions
3. References

Types of vaccines

Images from [here](#)



RNA

[https://www.who.int/news-room/infographics/infographic-vaccine-types](#)



DNA

[https://www.who.int/news-room/infographics/infographic-vaccine-types](#)



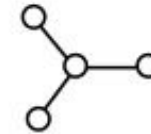
Viral
vector

[https://www.who.int/news-room/infographics/infographic-vaccine-types](#)



Virus-like
particle

[https://www.who.int/news-room/infographics/infographic-vaccine-types](#)



Protein
sub-unit

[https://www.who.int/news-room/infographics/infographic-vaccine-types](#)



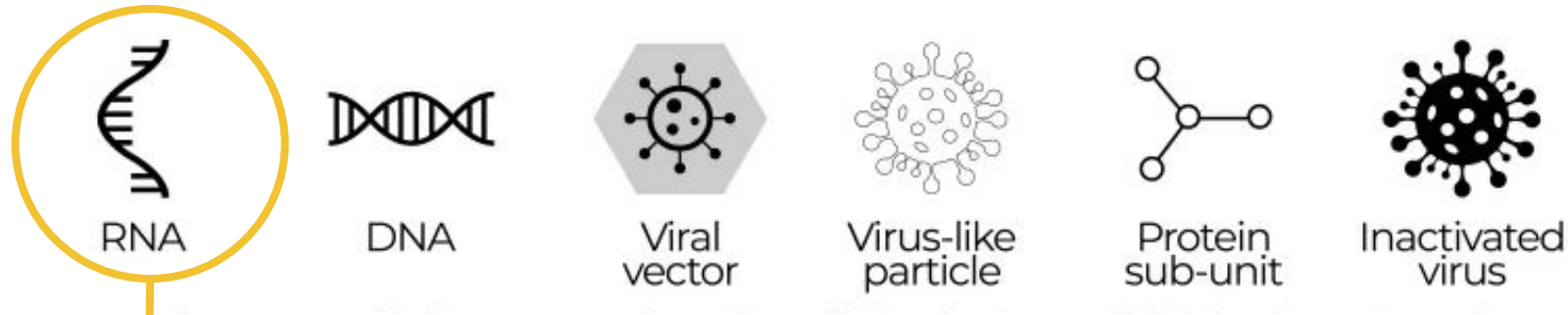
Inactivated
virus

[https://www.who.int/news-room/infographics/infographic-vaccine-types](#)

Why Peptide Based Vaccines?

Types of vaccines

Images from [here](#)



Images from [here](#)

mRNA vaccines: Based on messenger RNA taken from the virus

- Can be produced quickly
- Loose efficacy within a few months post immunization
- Maintained in cold chain storage

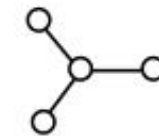
Types of vaccines

Images from [here](#)

RNA

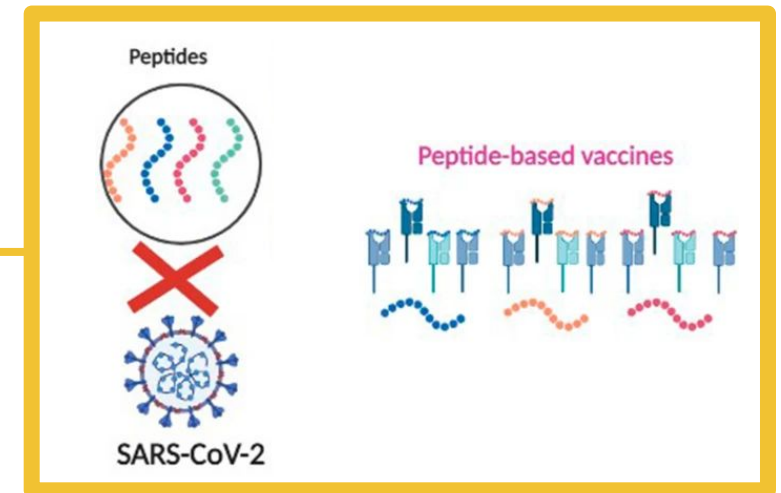


DNA

Viral
vectorVirus-like
particleProtein
sub-unitInactivated
virus

Peptide based vaccines: Based on sequence of immunogenic amino acid

- Greater stability → prolonged efficacy
- No cold chain storage
- Easily be modified and target emerging strains
- Stops anti-inflammatory reactions → help immunocompromised individuals



Introduction

Structure of SARS-CoV 2 and Composition of Spike Glycoprotein

Fig 1

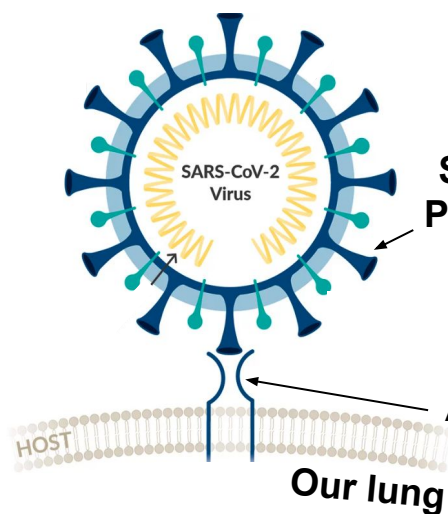


Fig 2

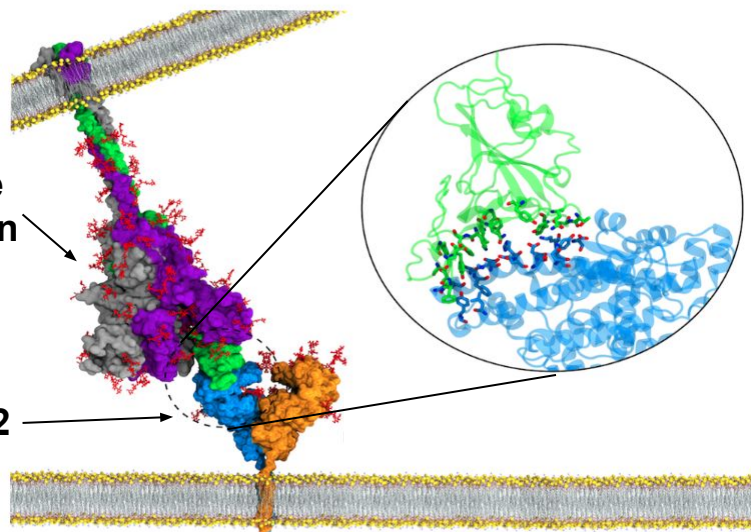
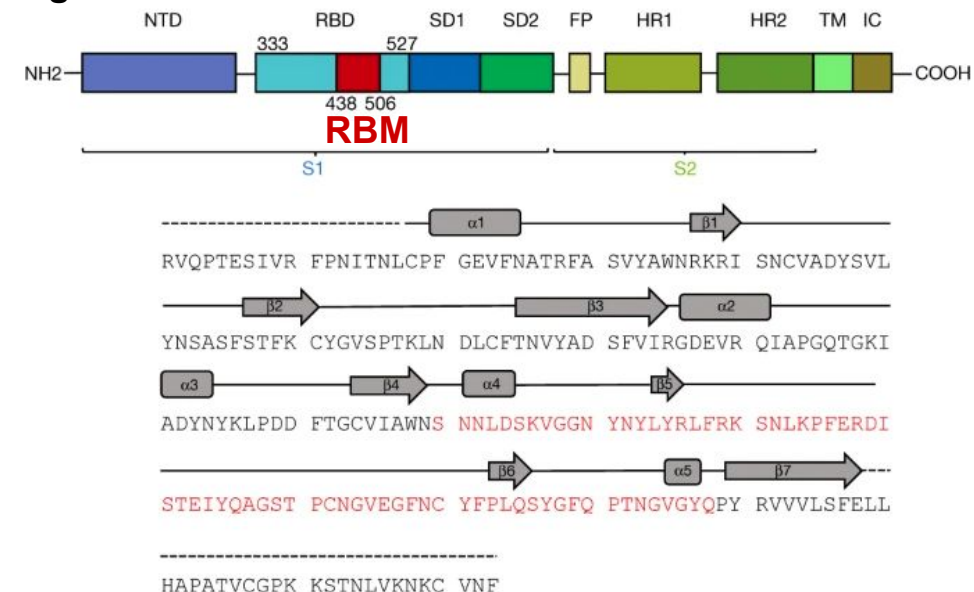
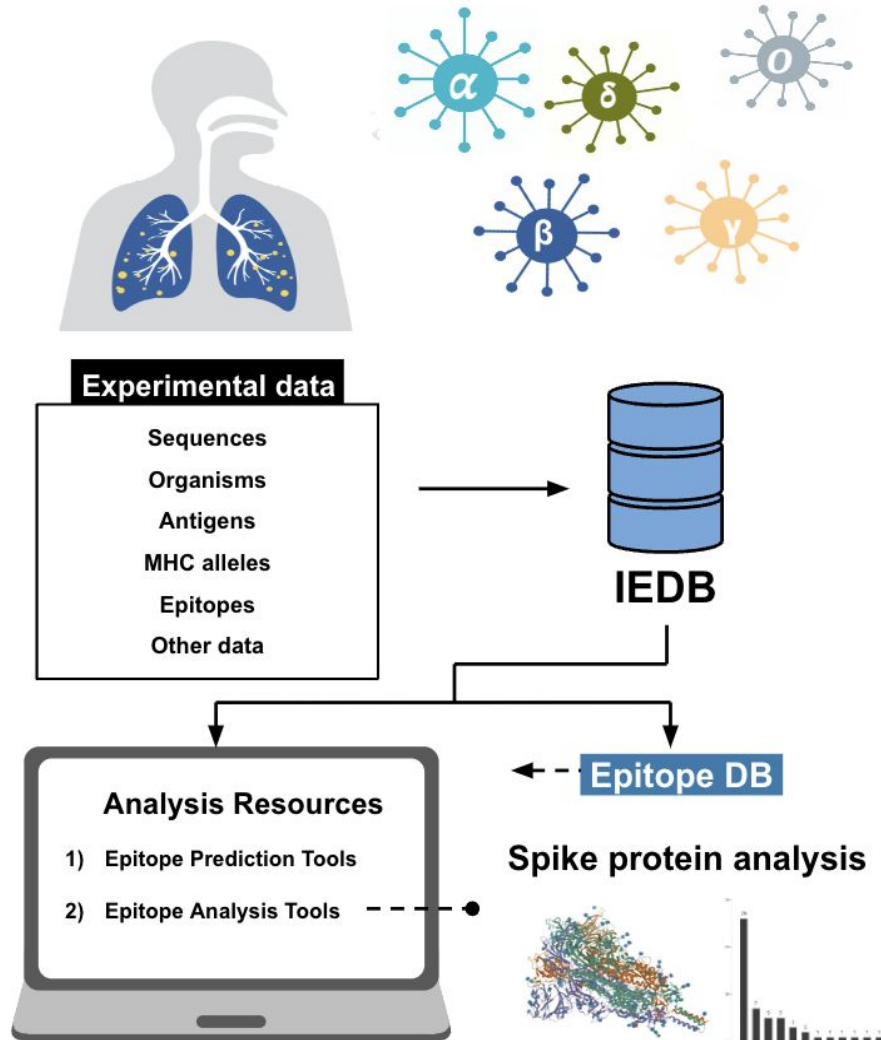


Fig 3



- SARS-CoV-2 virus has Spike-Glycoprotein (left)
- Spike-Glycoprotein binding to host cell receptor ACE2 (middle)
- The linear peptide epitope of SARS-CoV-2 structure (right)
- **Peptide (encoded as sequence of letters):** composed of amino acids
- **Receptor binding motif (RBM):** most immunogenic region

RVQPTESIVR VNF
HAPATVCGPK



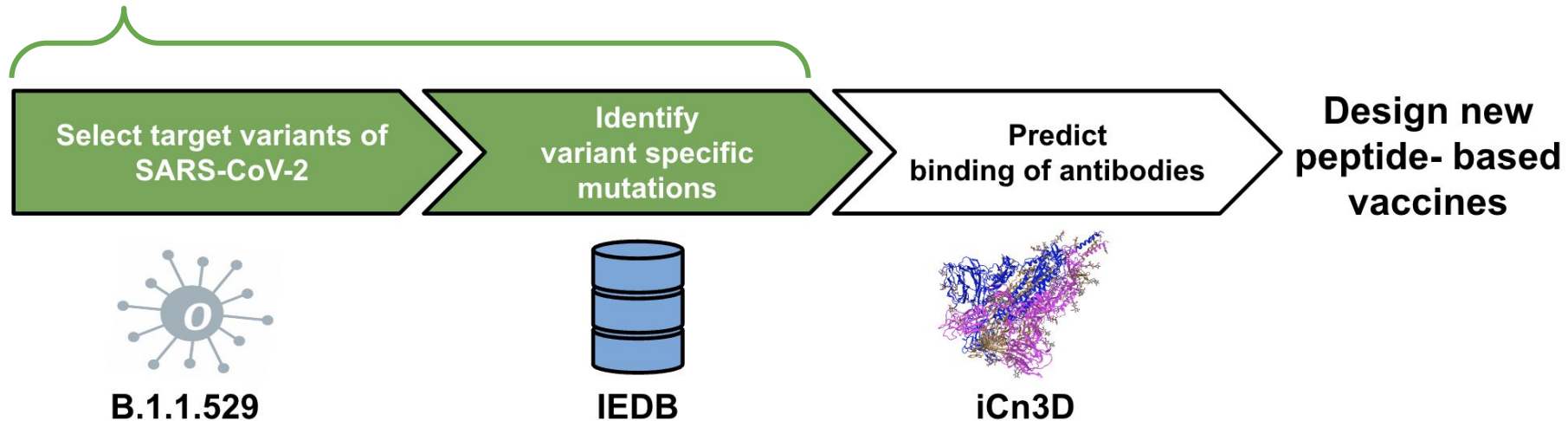
- The IEDB catalogs real experimental data on antibody and T cell epitopes
 - Contains data of humans, non-human primates, and other animal species
 - Other infectious diseases, allergy, autoimmunity and transplantation - ex) SARS-CoV, influenza
- The IEDB also hosts tools
 - Epitope prediction tools
 - Epitope analysis tools

Mapping Immunogenic Regions In Sars-Cov-2 To Understand Vaccine Design Using Bioinformatics

Compare immune evasion of **five different variants** of concern by analysing IEDB data

- Identify immunogenic hotspots of epitope recognition in Spike-Glycoprotein
- Identify conserved epitopes in these different variants

This talk will cover the following two steps



Schematic of procedure to design new peptide-based vaccines

START YOUR SEARCH HERE

Epitope ?

☒ Any
☐ Linear peptide
☐ Discontinuous
☐ Non-peptidic

Assay ?

☐ T Cell
☒ B Cell
☐ MHC Ligand

Outcome: ☒ Positive ☒ Negative

Epitope Source ?

Organism

Antigen

MHC Restriction ?

☒ Any
☐ Class I
☐ Class II
☐ Non-classical

Host ?

☐ Any
☒ Human
☐ Mouse
☐ Non-human primate

Disease ?

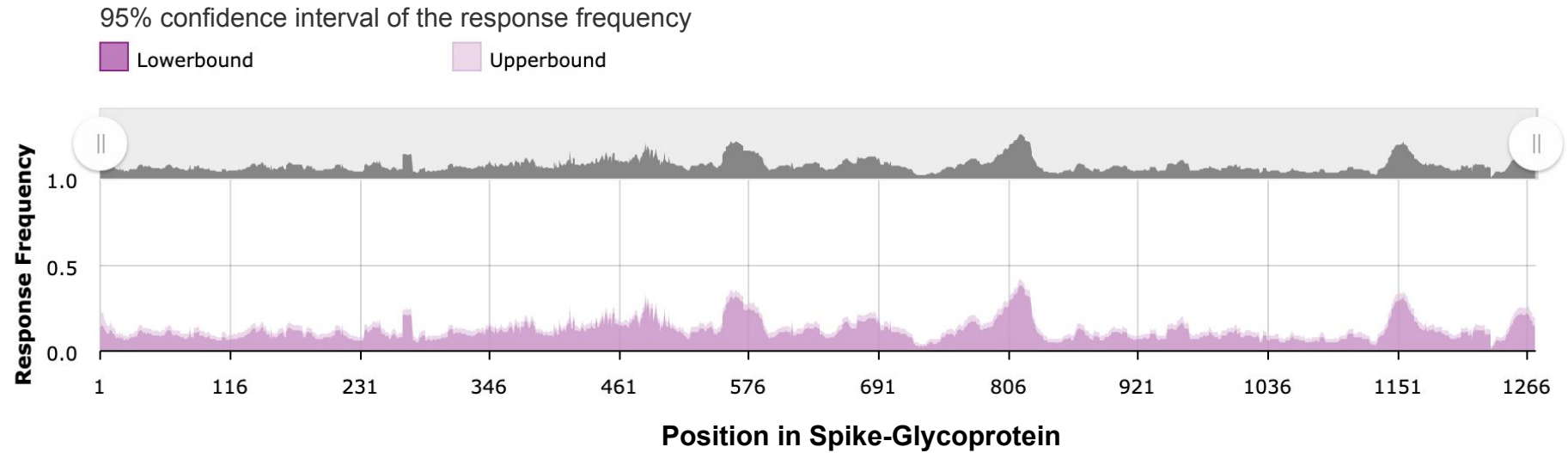
☒ Any
☐ Infectious
☐ Allergic
☐ Autoimmune

- The IEDB data can be filtered
- Our study was focused on the following selections
 - Any epitope
 - Epitope source: **SARS-CoV2**
 - Host: **Human**
 - Assay: **B cell**
 - MHC restriction: Any
 - Disease: Any

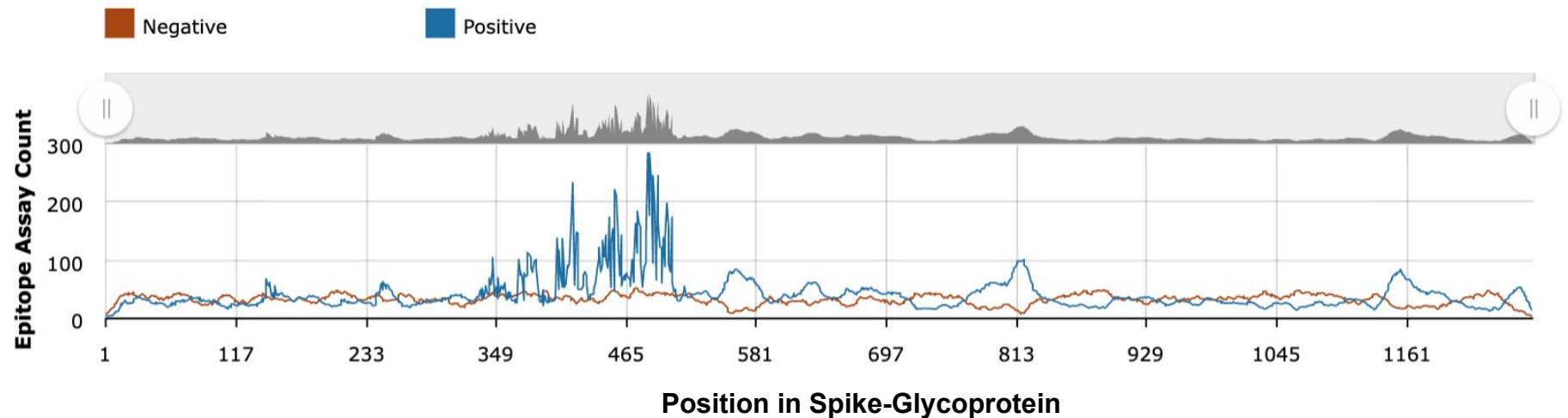
Results

Immunome Browser

The number of positively
responded individuals
relative to the total
number of people tested

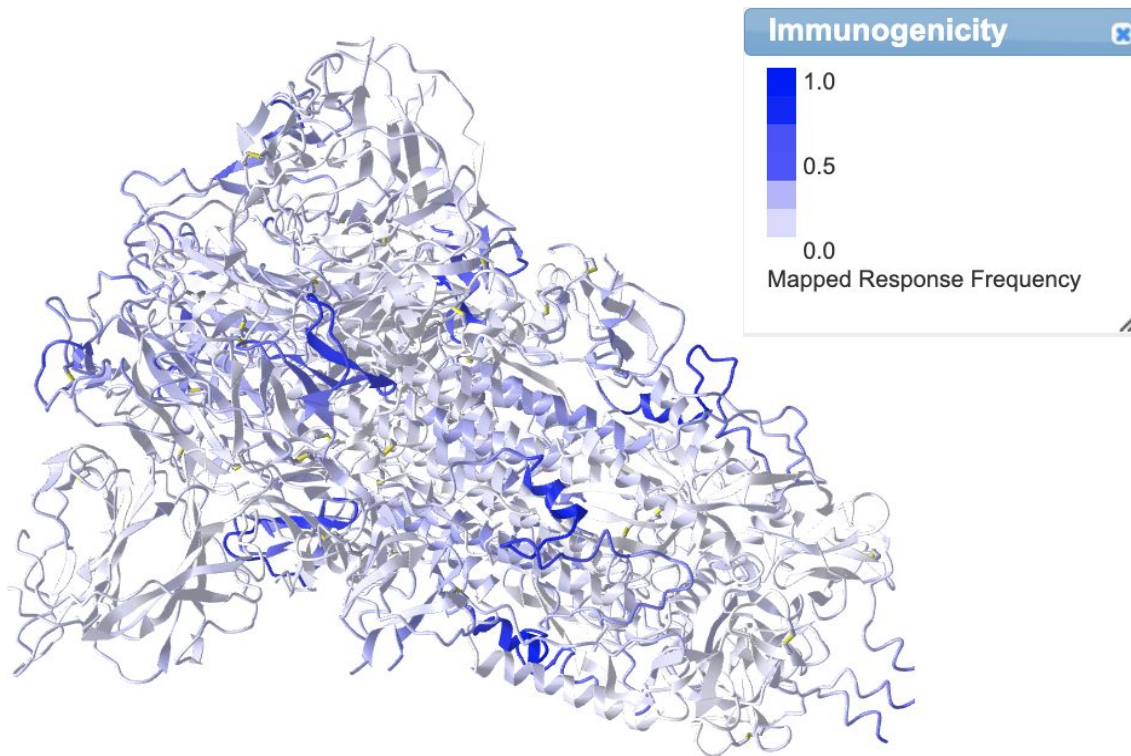


The number of positive
and negative assays



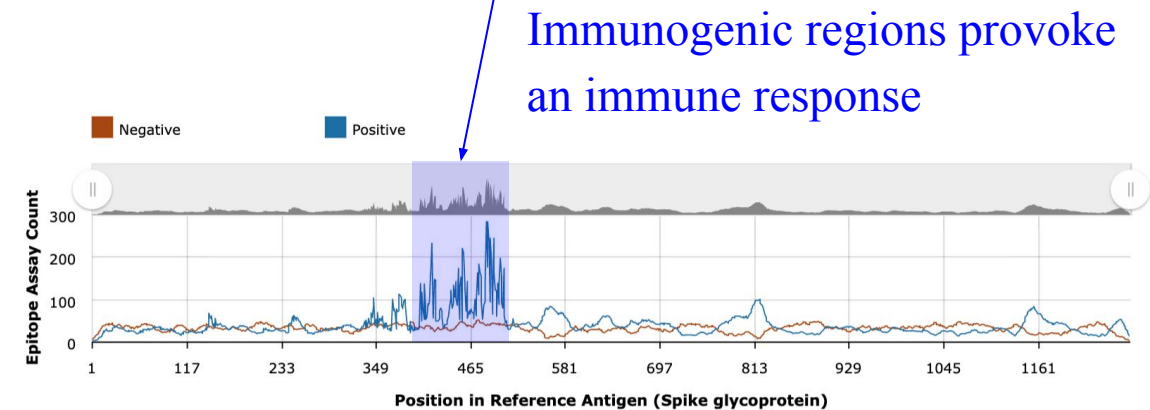
Results

Positions in Spike-Glycoprotein



**Spike-Glycoprotein of SARS-CoV 2
(with selected filter)**

- 3D images are normalized such that maximum value = 1 and minimum value = 0
- The more immunogenic regions, the more darker blue



The immunogenicity hotspots were found in the residue range of 400 - 550, corresponds to the receptor binding domain

Results

SARS-CoV 2 Variants of Interest



Alpha (B.1.1.7)

Primitive determination: September 2020

First origin: United Kingdom



Beta (B.1.351)

Primitive determination: October 2020

First origin: South Africa



Gamma (P.1)

Primitive determination: January 2021

First origin: Brazil/ Japan



Delta (B.1.617.2)

Primitive determination: October 2020

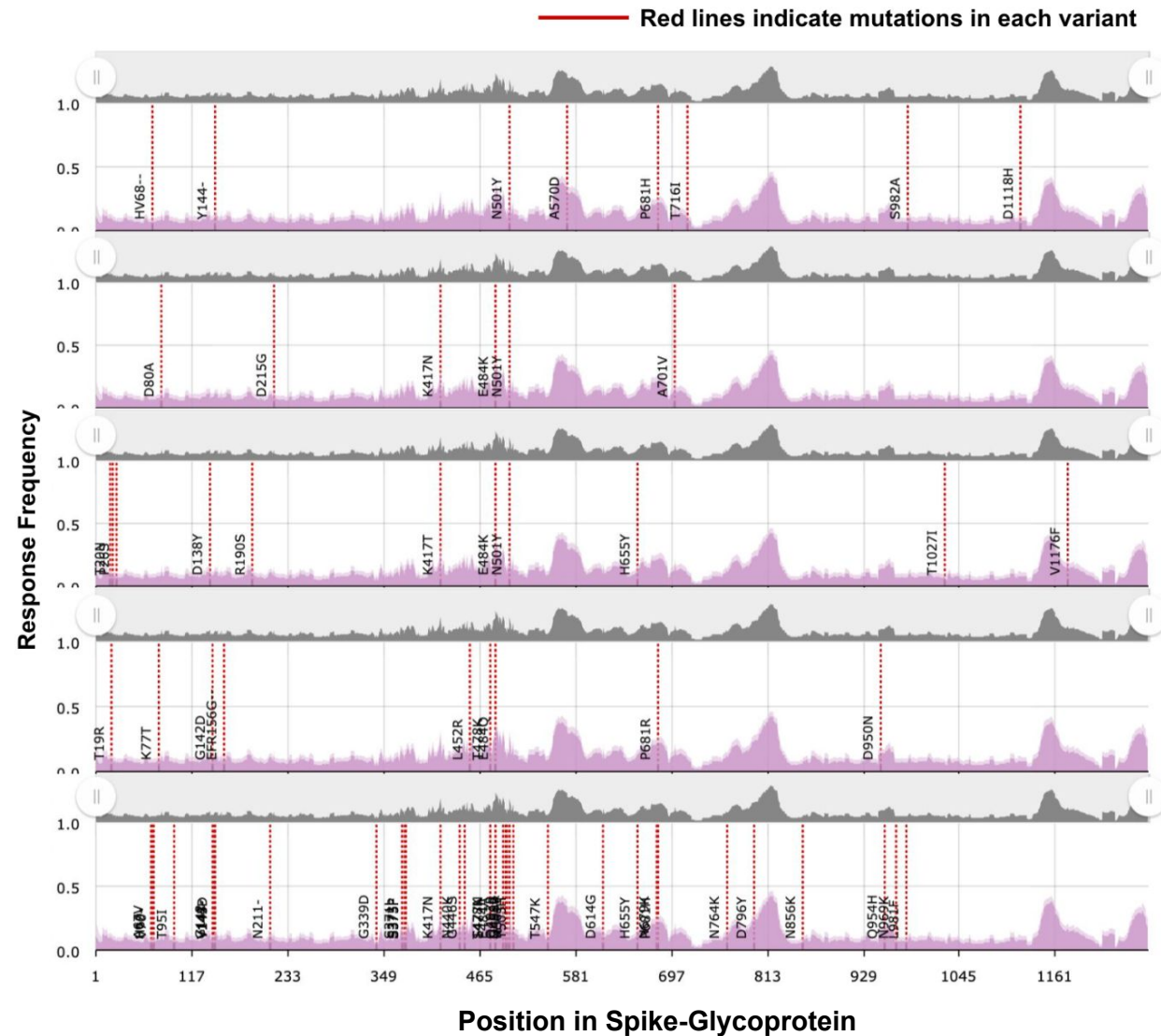
First origin: India



Omicron (B.1.1.529)

Primitive determination: November 2021

First origin: South Africa



Results

SARS-CoV 2 Variants of Interest



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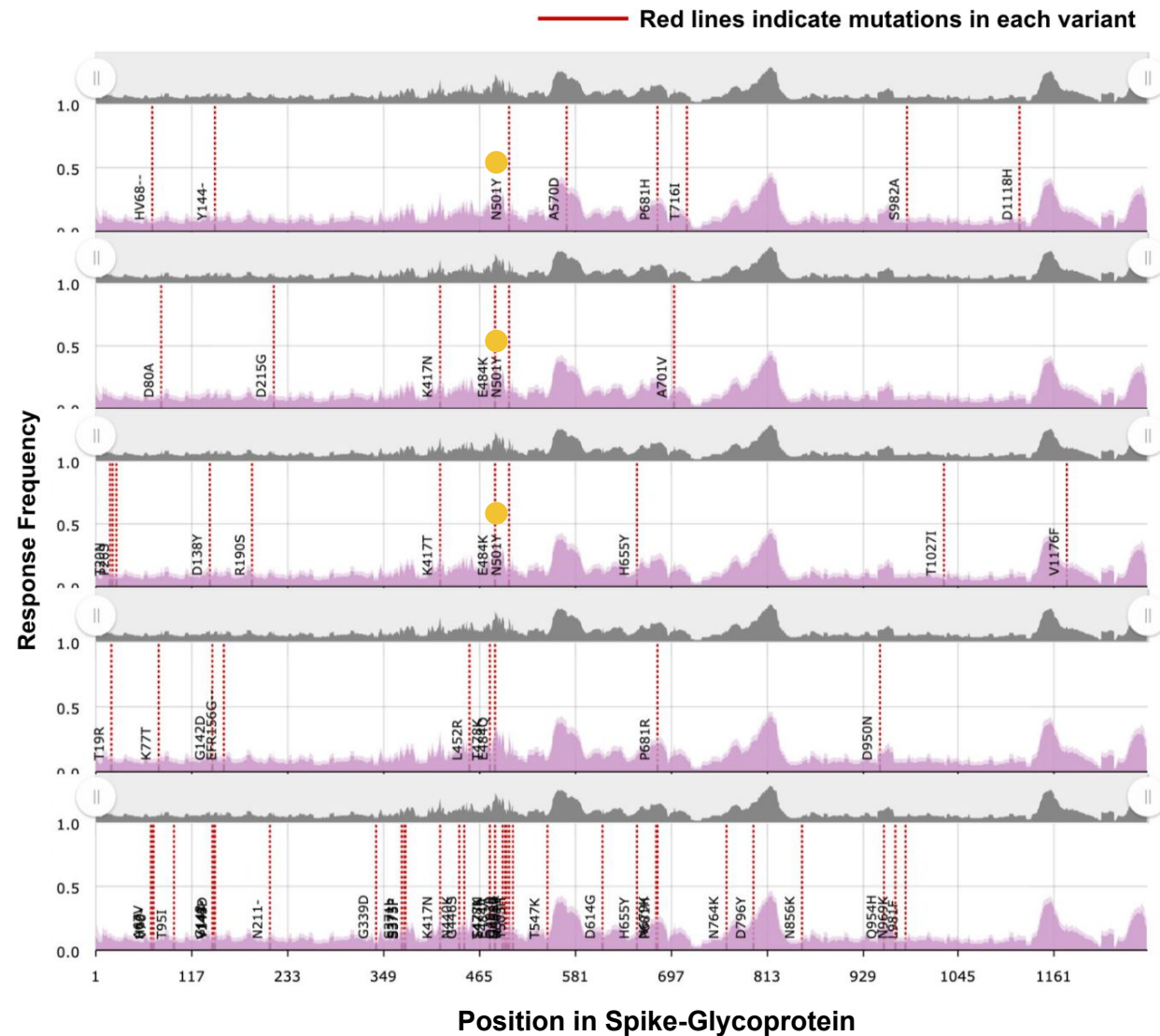
First origin: India



Omicron (B.1.1.529)

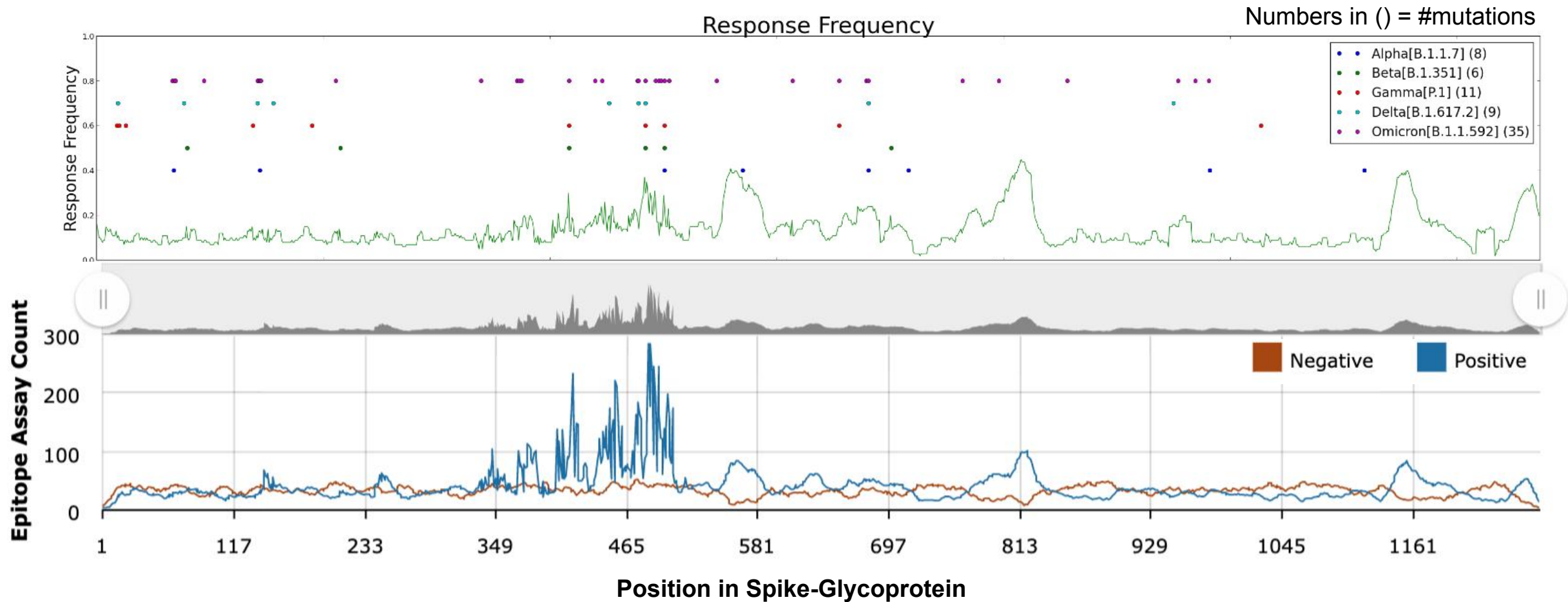
Primitive determination: November 2021

First origin: South Africa



Results

Comparison of Five SARS-CoV 2 Variants

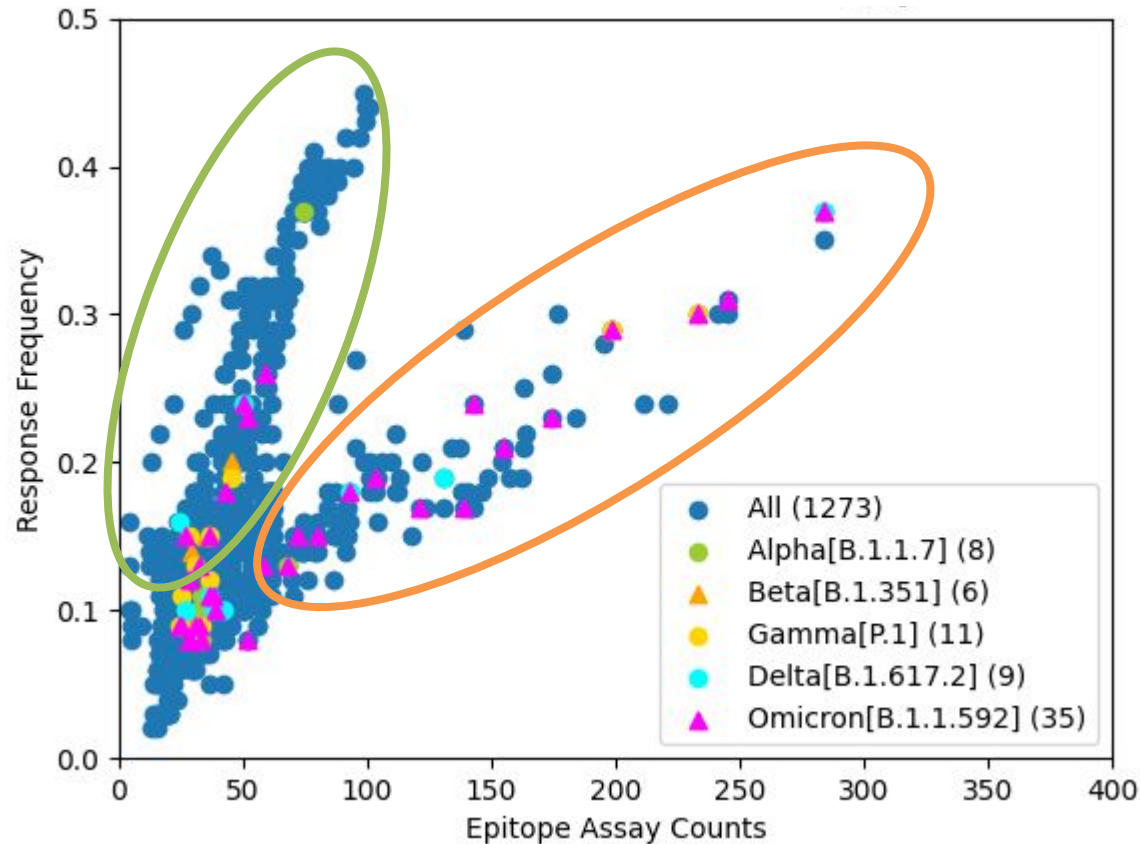


Among, all five variants **omicron** has the most immunogenic regions (35) → **highly transmissible**

Results

Epitope Assay Counts vs Response Frequency

With respect to smaller counts,
more frequently responded



With respect to larger counts,
less frequently responded 🐱

- Data from IDEB was analyzed to study correlation between epitope assay counts and response frequency

We see two trends:

- Smaller counts with respect to response more frequently responded
- Larger count with respect to response less frequently responded
- Many mutations in **Omicron** follows the larger count trend within respect to higher response frequency

Conclusions

Looking Ahead

All positions in the Spike-Glycoprotein, where omicron has shared mutations with other variants

Position	142	144	417	478	484	501	655	681
Alpha		o				o		o
Beta					o	o		
Gamma			o		o	o	o	
Delta	o		o	o	o			o
Omicron	o	o	o	o	o	o	o	o

Emerging potential hotspots for future vaccines

- We hypothesize positions with a high degree of overlap (green) as emerging potential hotspots for immune evasion and target for new peptide-based vaccines
- We can use the visualization software like iCn3D to localize the mutations on the 3D structure of the Spike-Glycoprotein
- Using prediction tools in IEDB, we can predict the binding of antibodies that can neutralize the immune evasion of the variants
- This prediction can be utilized in the biopharma industry for future iterations of vaccine development

Conclusions

Summary

- Five different SARS-CoV 2 variants were compared using IEDB
- Omicron has the most immunogenic regions
- Conserved mutation between Omicron and other variants was observed
- Emerging potential hotspots for immune evasion and target for new peptide-based vaccines was identified

Thank you!

Conclusions

References

- [1] Vita R, Mahajan S, Overton JA, Dhanda SK, Martini S, Cantrell JR, Wheeler DK, Sette A, Peters B. The Immune Epitope Database (IEDB): 2018 update. *Nucleic Acids Res.* 2018 Oct 24. doi: 10.1093/nar/gky1006. PMID: 30357391; PMCID: PMC6324067
- [2] Motozono, C., Toyoda, M., Zahradnik, J. et al. (2021). SARS-CoV-2 spike L452R variant evades cellular immunity and increases infectivity. *Cell Host & Microbe*, 29(7), 1124-1136.e11.
<https://doi.org/10.1016/j.chom.2021.06.006>
- [3] Taka, E., Yilmaz, S. Z., Golcuk, M. et al. (2021). Critical Interactions Between the SARS-CoV-2 Spike Glycoprotein and the Human ACE2 Receptor. *The Journal of Physical Chemistry B* 2021 125 (21), 5537-5548 DOI: 10.1021/acs.jpcc.1c02048
- [4] Lan, J., Ge, J., Yu, J. et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. *Nature* 581, 215–220 (2020). <https://doi.org/10.1038/s41586-020-2180-5>
- [5] “Tools to Study SARS-CoV-2-Host Interactions”, accessed Apr 6. 2023,
<https://www.caymanchem.com/news/tools-to-study-sars-cov-2-host-interactions>

Backup

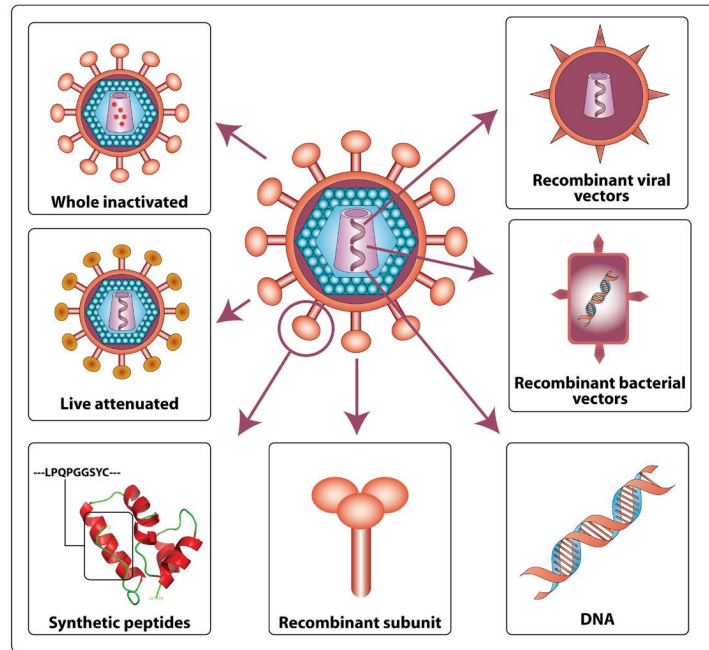


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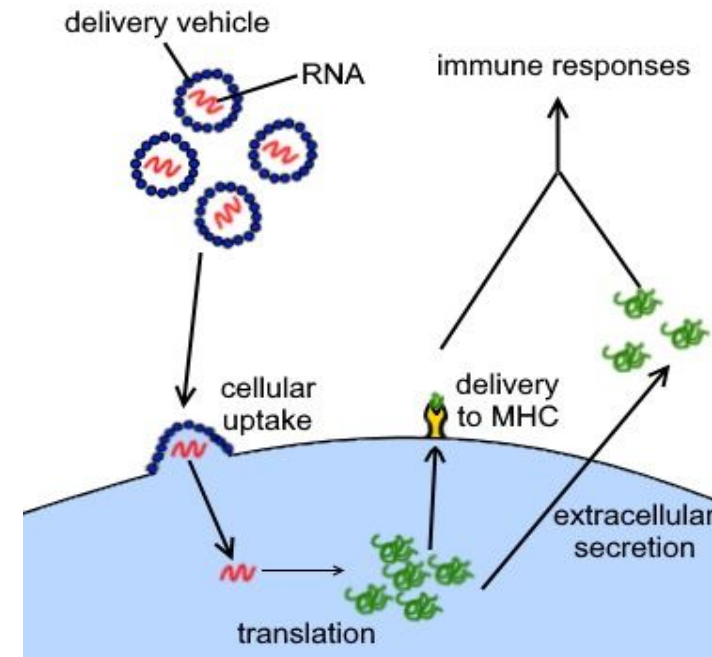
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Introduction

Peptide Based Vaccines



- Based on sequence of amino acid; synthetic
- Easily be modified and target emerging strains
- Greater stability; only focused on relevant parts of the protein
- No cold chain storage



- Based on messenger RNA taken from the virus.
- Loose efficacy within a few months post immunization
- Reproduce quickly

Materials and Methods

Materials and Methods

START YOUR SEARCH HERE

Epitope ?

☒ Any
☐ Linear peptide
☐ Discontinuous
☐ Non-peptidic

Ex: SIINFEKL

Assay ?

☒ T Cell
☐ B Cell
☒ MHC Ligand

Outcome: ☒ Positive ☒ Negative

Epitope Source ?

Organism

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MHC Restriction ?

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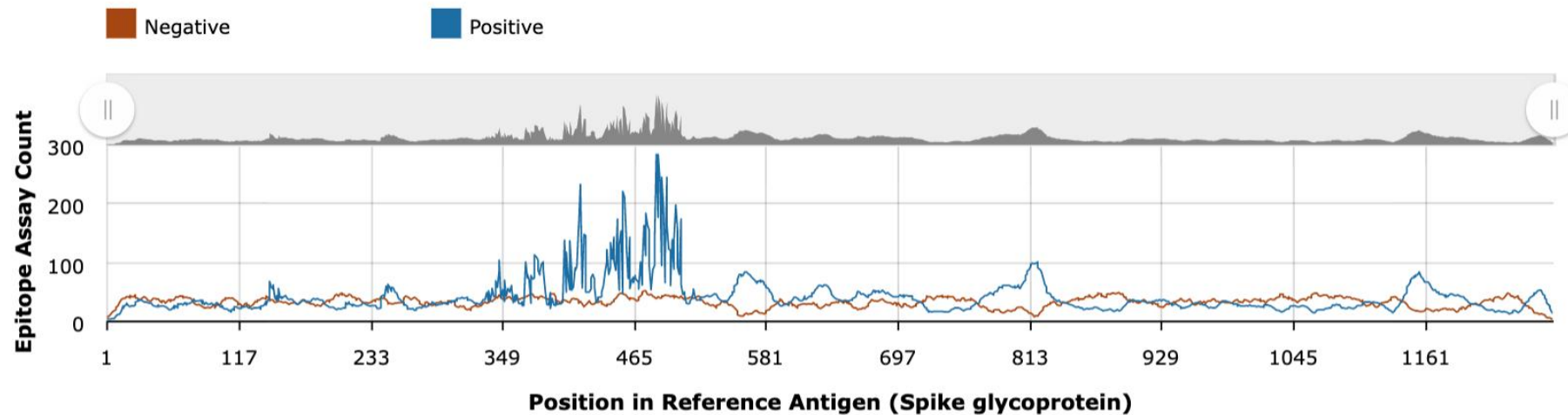
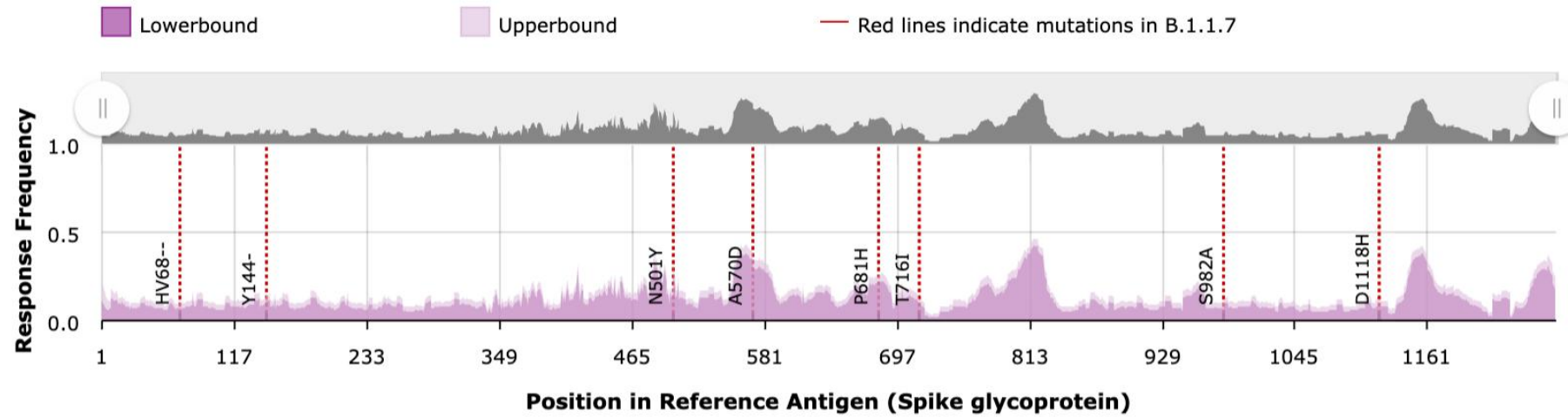
Host ?

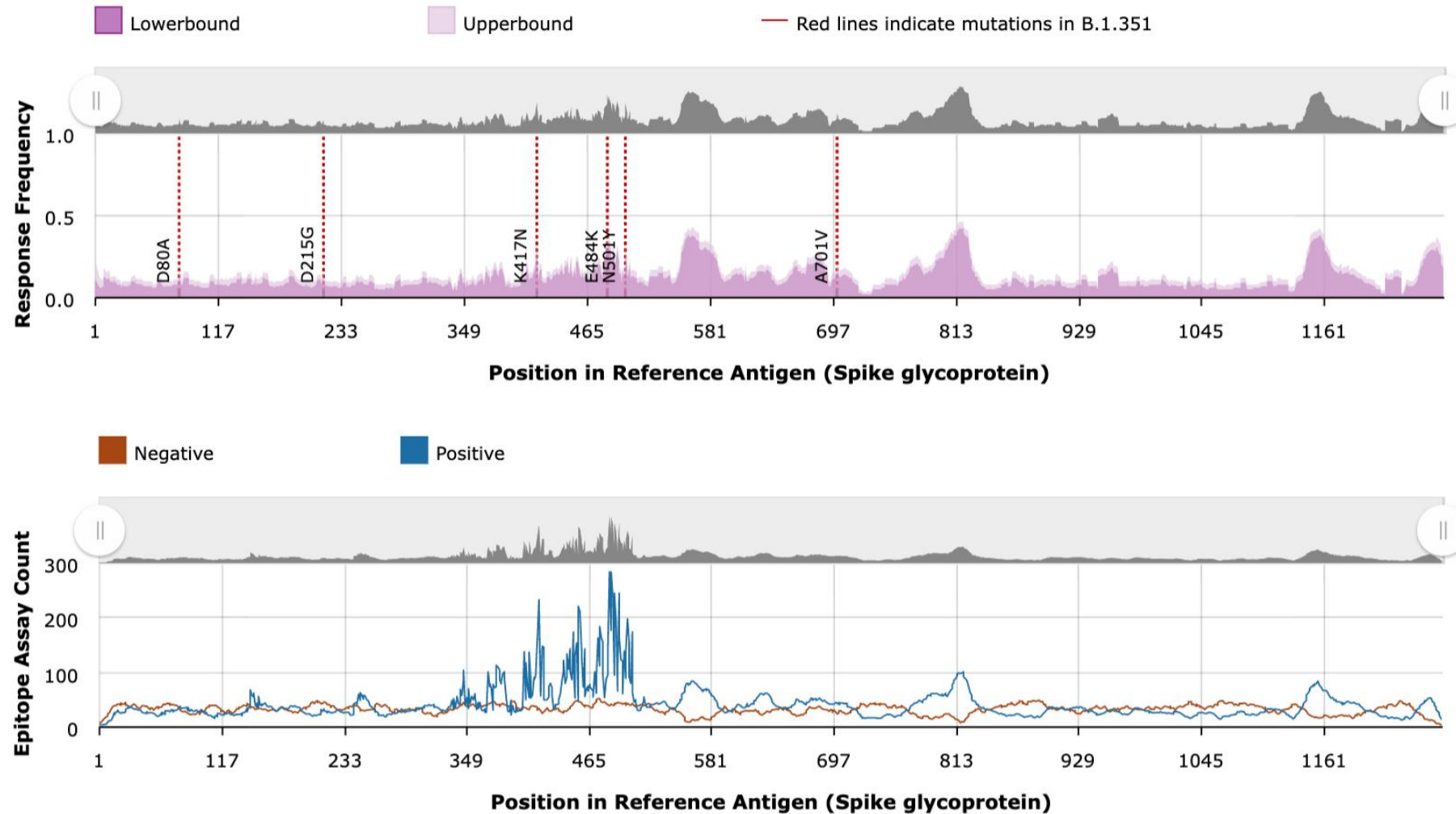
☐ Any
☒ Human
☐ Mouse
☐ Non-human primate

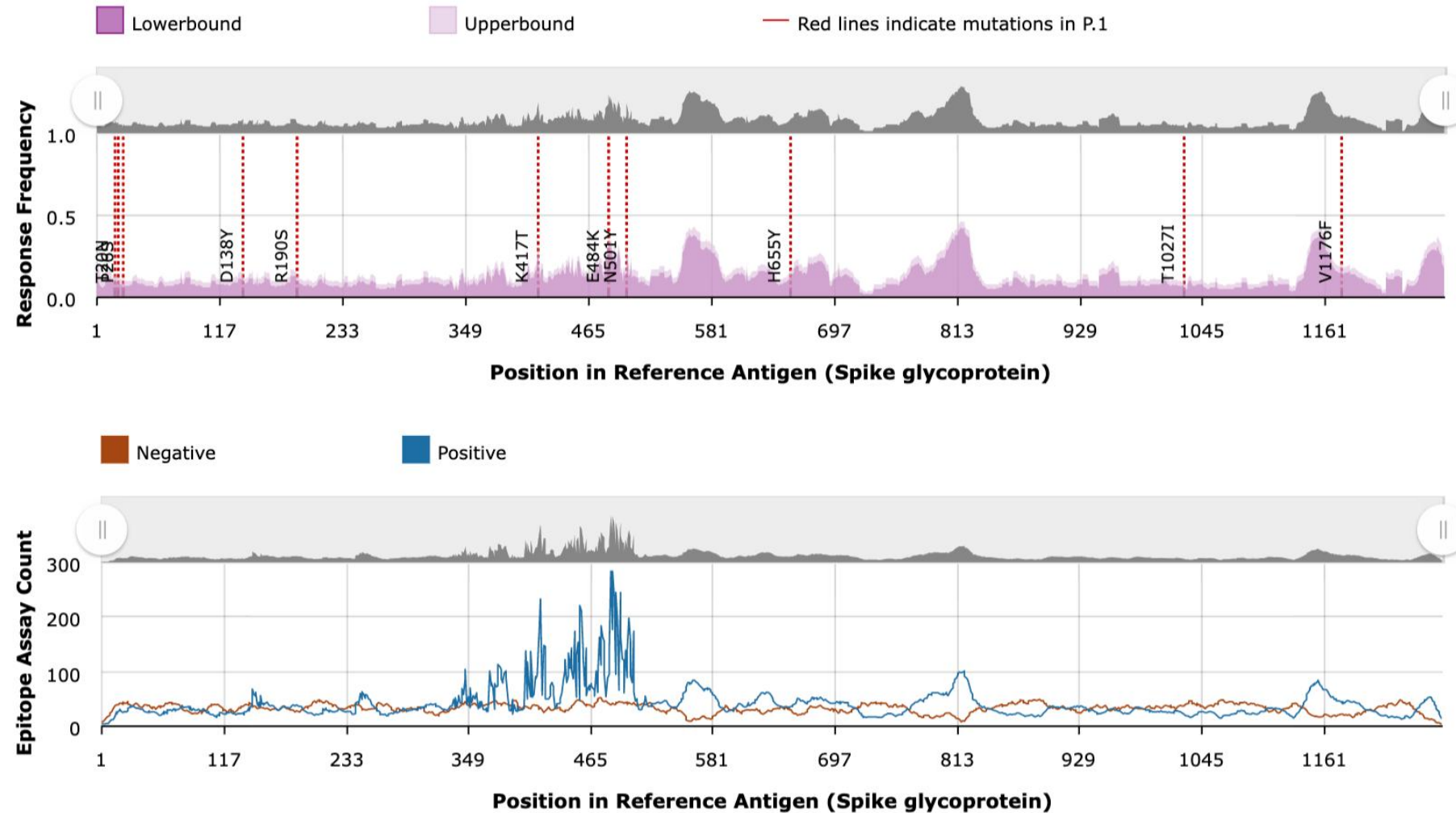
Disease ?

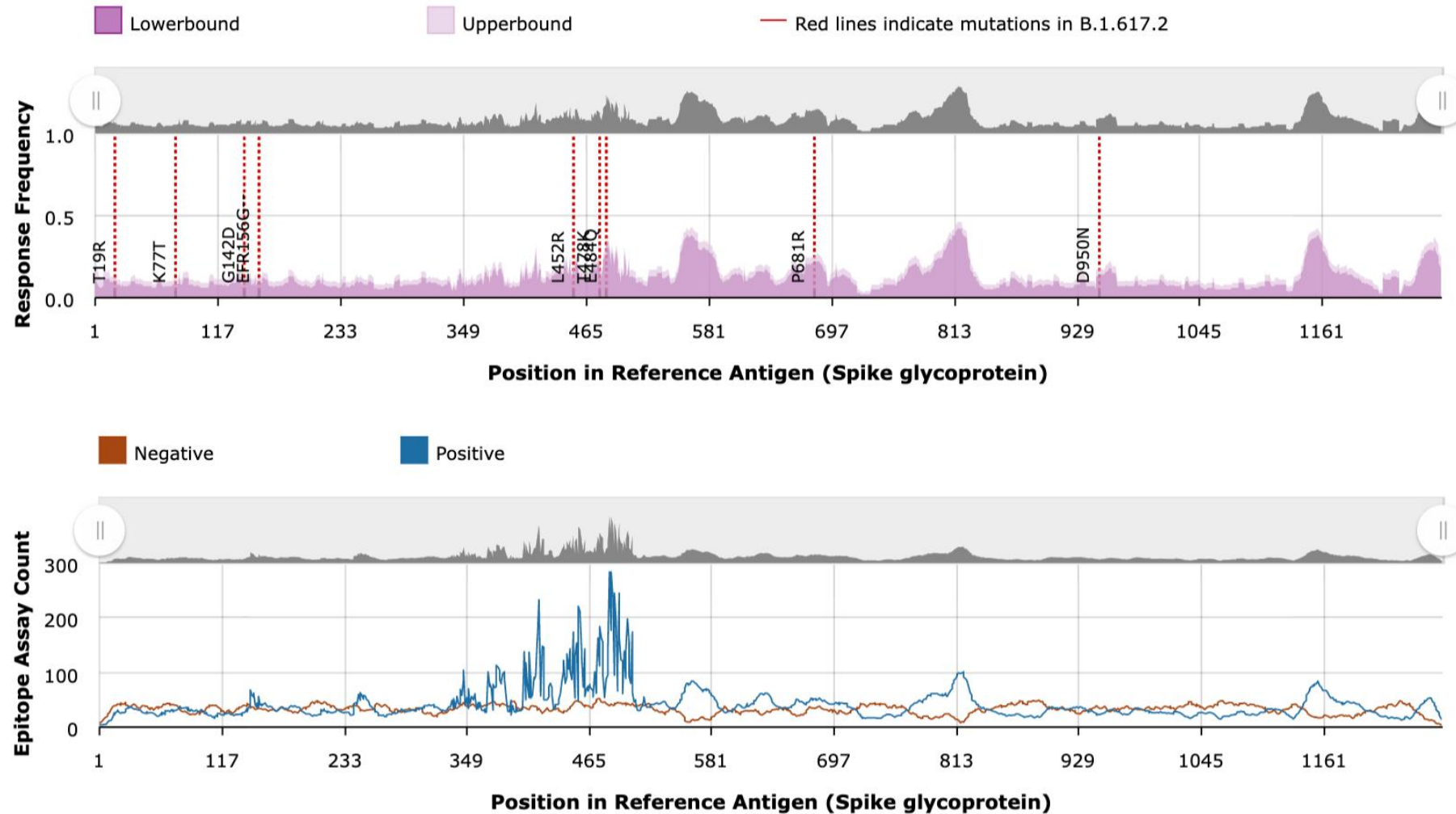
☒ Any
☐ Infectious
☐ Allergic
☐ Autoimmune

Overview of The Immune Epitope Database









Mutations in B.1.1.529 (Omicron)

