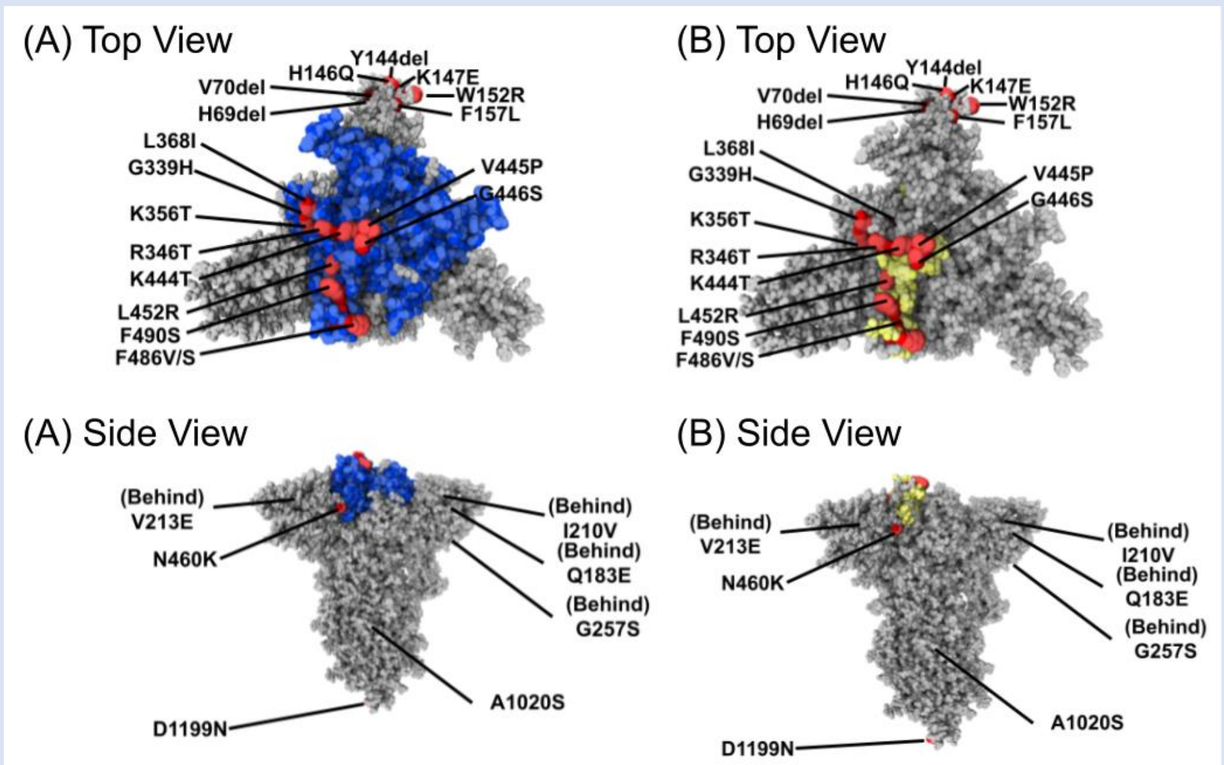
A Mechanistic Basis for the Analysis of SARS-CoV-2 Omicron Variant Severity

New COVID-19 variants are caused by structural changes in the antibody-RBD complex of the SARS-CoV-2 protein. Thus, identifying regions in this complex where mutations are less prone is crucial in identifying areas of the protein that are less likely to evade antibodies, which can set a blueprint for future vaccine creation.

Dataset

- Data obtained from **GISAID** of 8,377 patients worldwide that had COVID-19 Omicron variant
  - Used data of **Spike protein mutations and patient severity**



(A) Receptor Binding Domain in blue, mutations in red. (B) Antibody Binding Domain in yellow, mutations in red.

Study Procedure

(1)

Mutation M	Severe	Nonsevere
# of Patients with M		
# of Patients without M		

(2) $$RMSD = \sqrt{\frac{\sum_{i=0}^{N}[m_i * (X_i - Y_i)^2]}{M}}$$

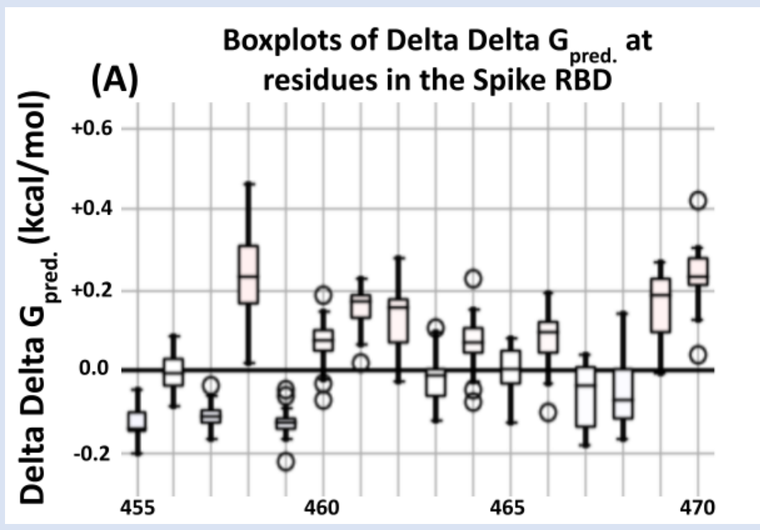
(3) $\Delta\Delta G = \Delta G_{Wild\ Type} - \Delta G_{Mutant}$, where $\Delta G_{folding} = \Delta H - T\Delta S$

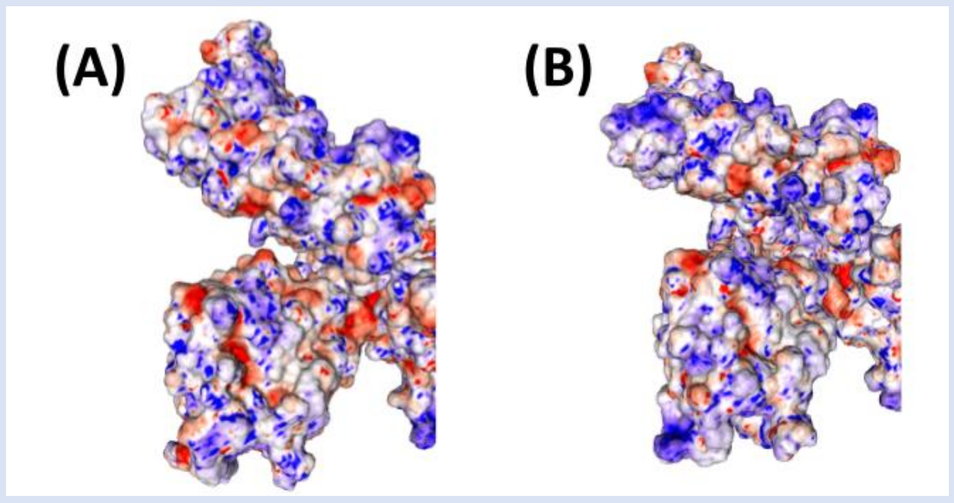
(4) $$Z = \frac{W_{DDG}}{W_{DDG}+W_{SE}} Z_{DDG} + \frac{W_{SE}}{W_{DDG}+W_{SE}} Z_{SE}$$

(1, 2) Eliminate mutations that do not have clinical significance, (3) determine chemical implications of protein mutations, (4) rank destabilizing mutations

Results & Applicability

- Comparison of ΔΔG values in the **Receptor Binding Domain**
  - **Mutated RBD has DDG values consistently above 0** in comparison to the wild type → **isolated mutations** have **destabilizing** implications





- Mutated RBD (A) shows red (**electronegativity**) in greater proportion
- Mutations decrease electrostatic potential, which means that the vaccine **binding is looser**

1. Results prove that this set of mutations induces **structural implications** on SARS-CoV-2 virus
   a. These mutations can be targets of **reduced vaccine evasion**
2. For any virus which we have patient and genomic data, we can apply this strategy to create more **targeted vaccines**

All graphics generated by researcher unless cited otherwise.