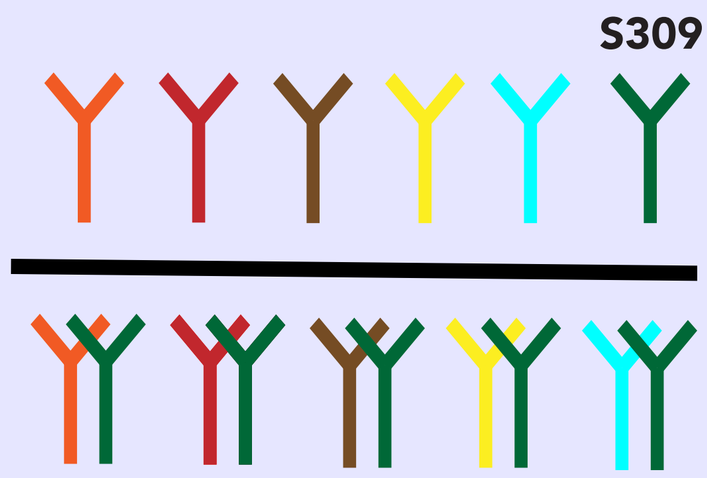
Investigating Synergistic Interactions Among SARS-CoV-2 Neutralizing Antibodies

Objective: Understand when and why antibody combinations exhibit synergy

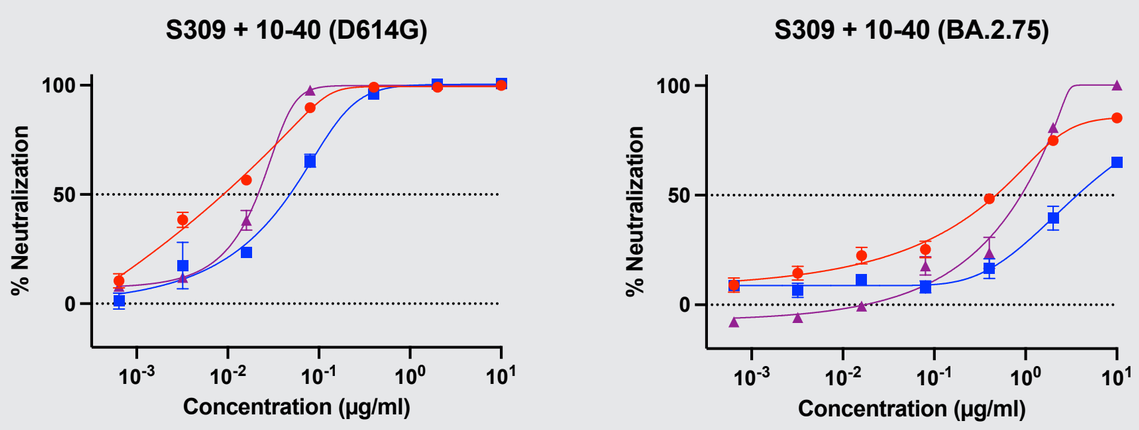
Methods

- There are four classes of SARS-CoV-2 antibodies based on binding behavior and location on the receptor binding domain (RBD).
- This study tested S309 (a Class 3 antibody) as well as five other antibodies alone and in combination with S309.
- PyMOL protein modeling was used to visualize binding to the SARS-CoV-2 RBD, and antibodies that did not exhibit overlap with S309 were selected.
- Antibodies were tested against the D614G variant, an original SARS-CoV-2 variant, and the BA.2.75 variant, a variant that first emerged in 2022.



Results

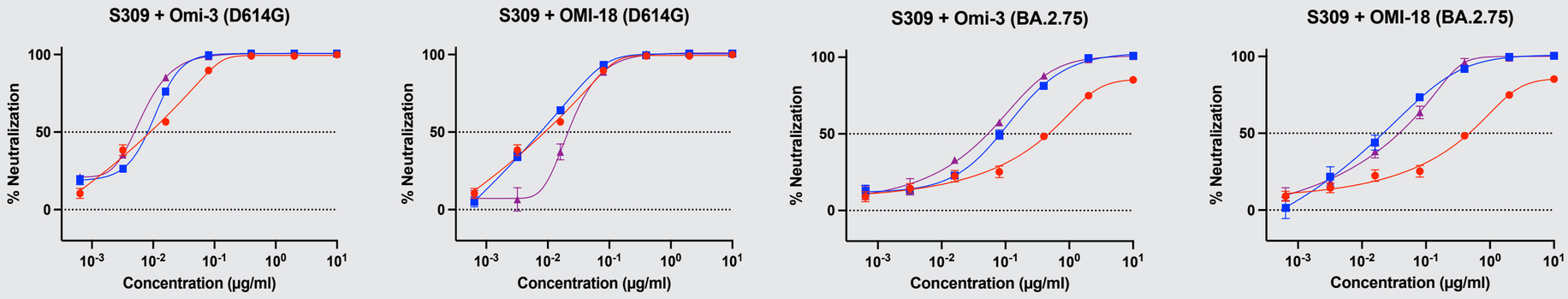
Class 4 + S309



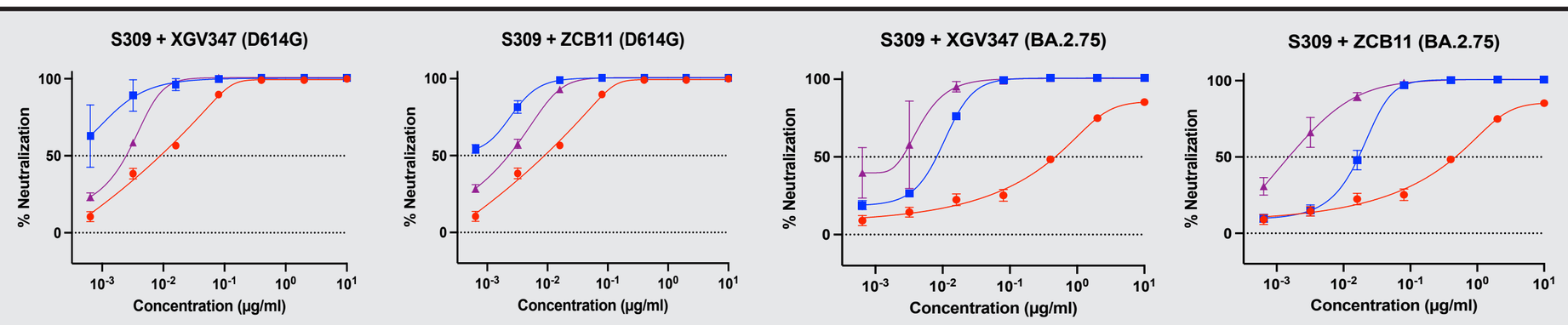
Key

- S309
- Other Antibody
- 1:1 Combination

Class 1 + S309



Class 2 + S309

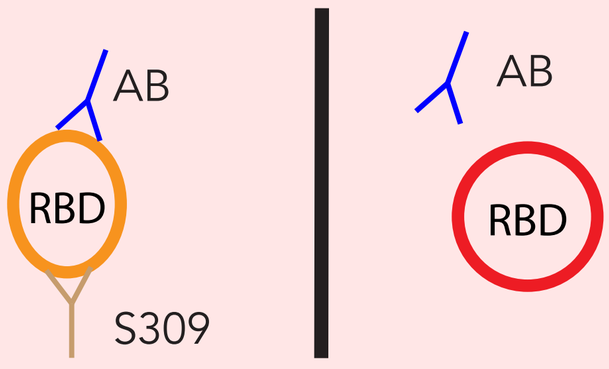


Discussion

Synergy was only observed when **Class 2** antibodies in combination with S309 were tested against the **BA.2.75** variant.

Variant

- The BA.2.75 variant undergoes a conformational change upon S309 binding (Cao et al., 2022).
- This change could make it easier for the antibody in combination with S309 to bind to the RBD.



Class

- Class 1: Binds to "**up**" RBDs
- Class 2: Binds to "**up**" and "**down**" RBDs
- Class 4: Binds to "**up**" RBDs
- S309 (Class 3): Binds to "**down**" RBDs

(Barnes et al., 2020; Pinto et al., 2020)

- Therefore, only Class 2 antibodies can bind to the same RBD conformation as S309 and benefit from synergistic interactions.

****All images displayed were created by Jacob Gross****