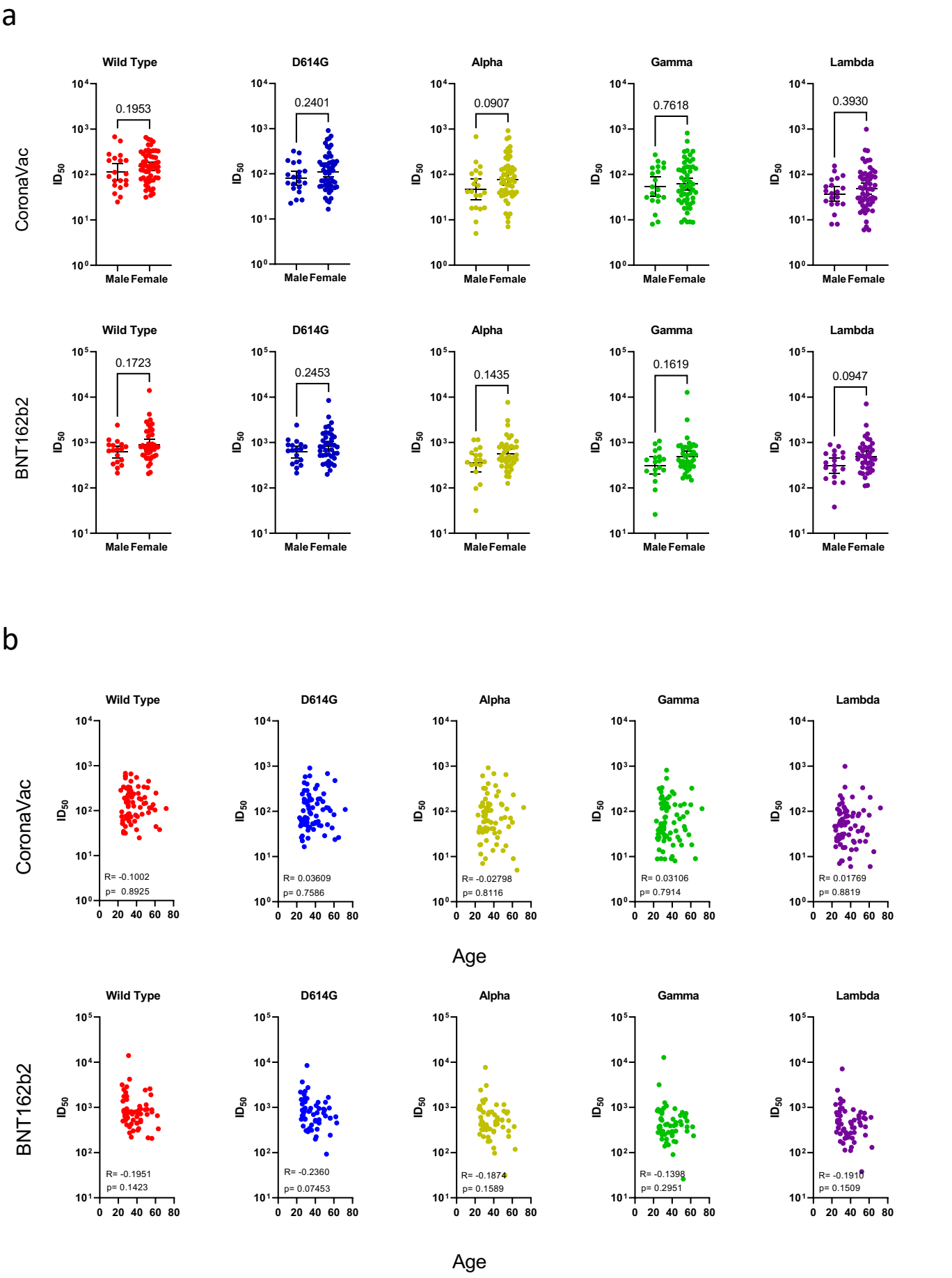
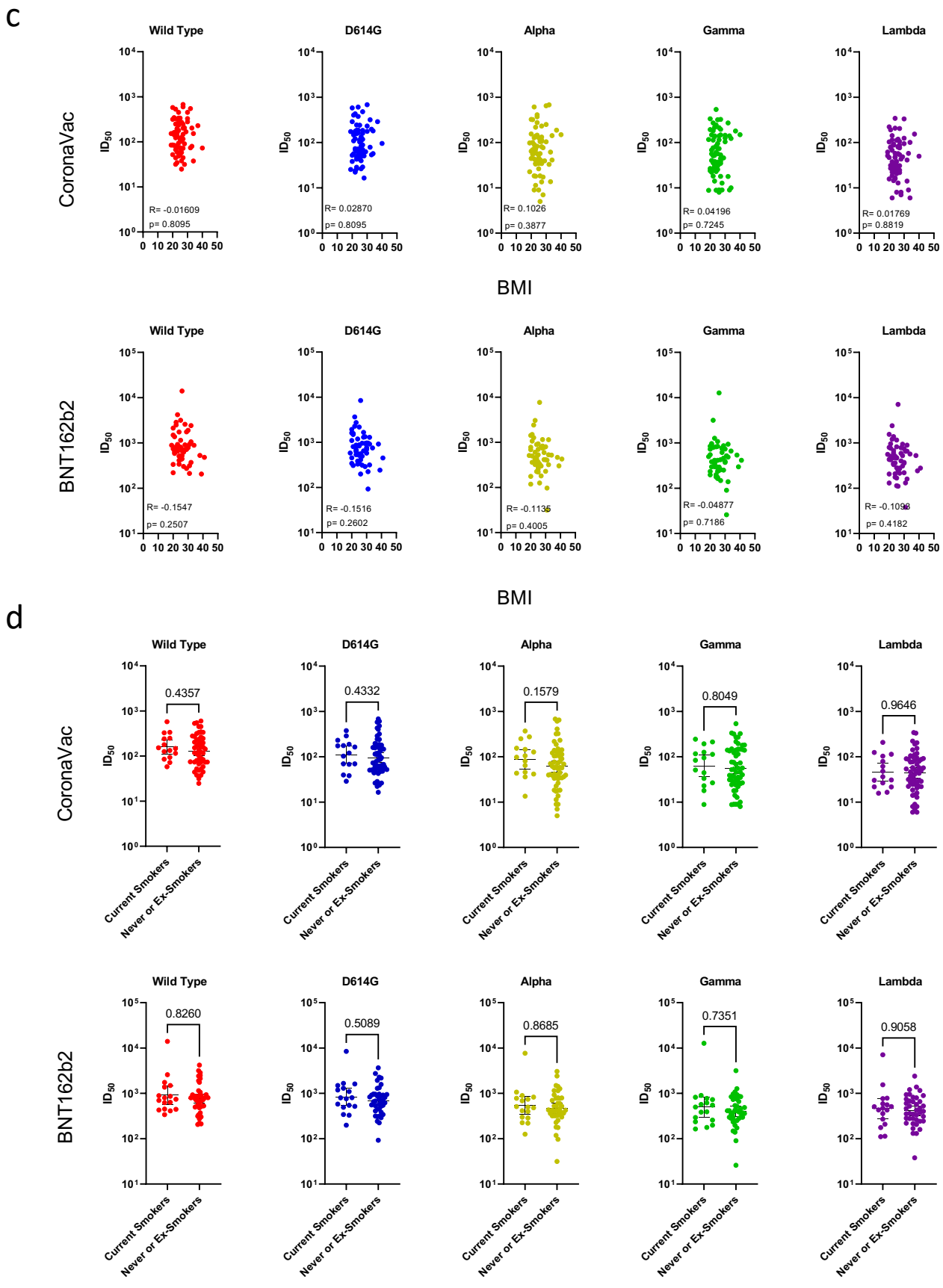
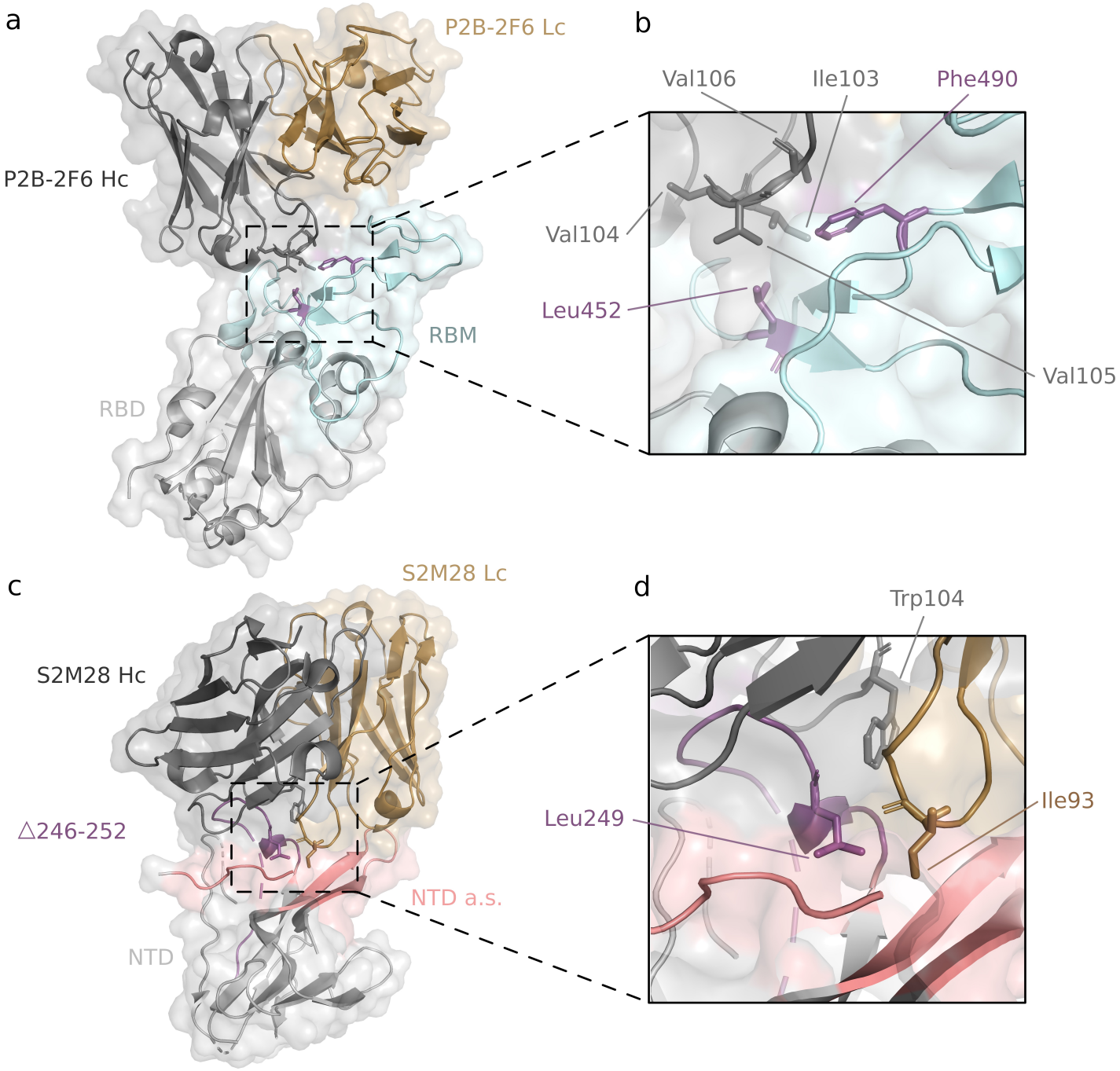


Supplementary Figure 1

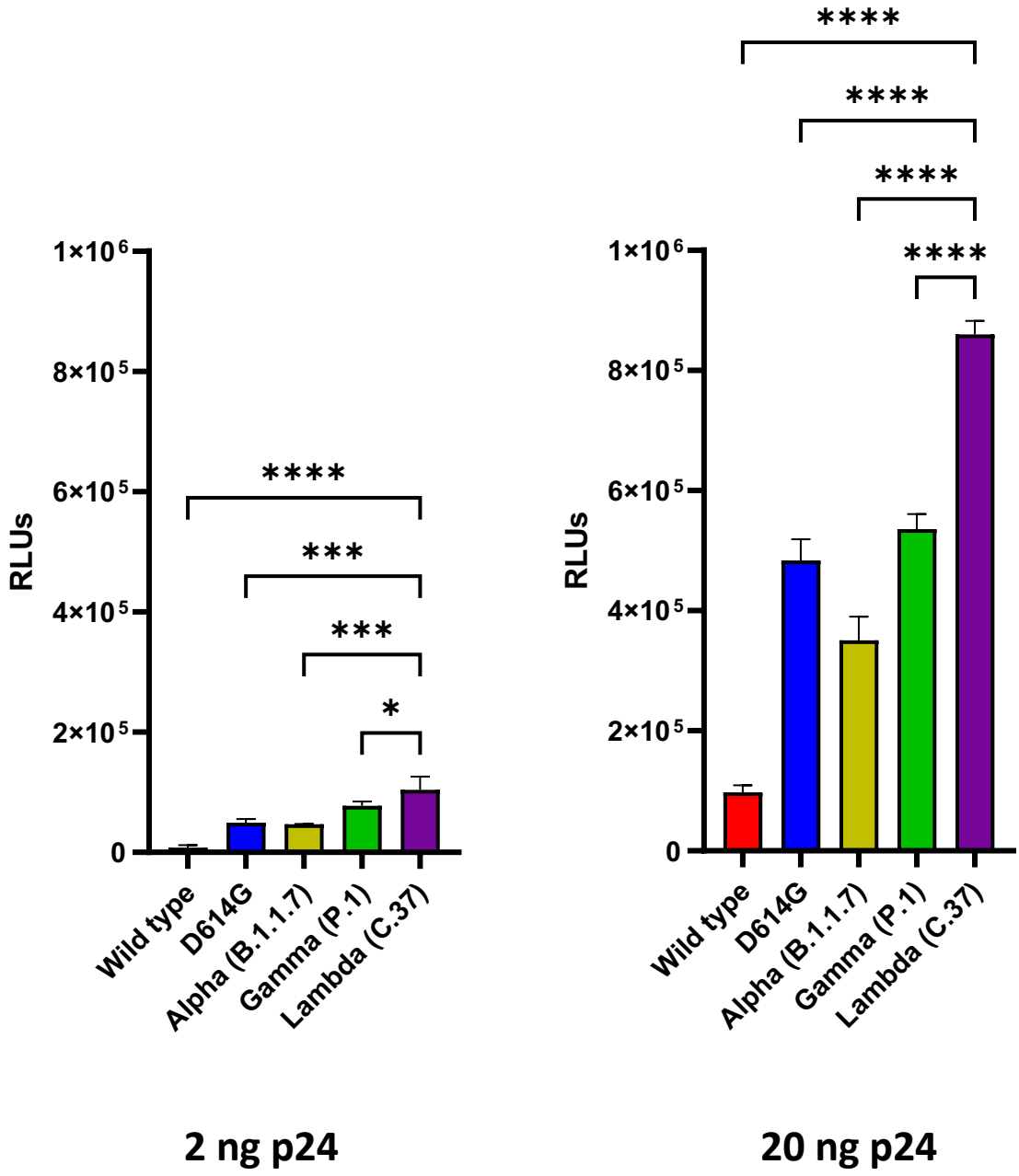


Supplementary Figure 1: Correlation of neutralizing antibody titers against SARS-CoV-2 variants and participants' sex, age, BMI or smoke status.

Stratification neutralizing antibody titres (NAbTs) against SARS-CoV-2 variants by sex (A), Age (B), BMI (C) and smoke status (D). Neither factor significantly affects neutralizing antibody titers.

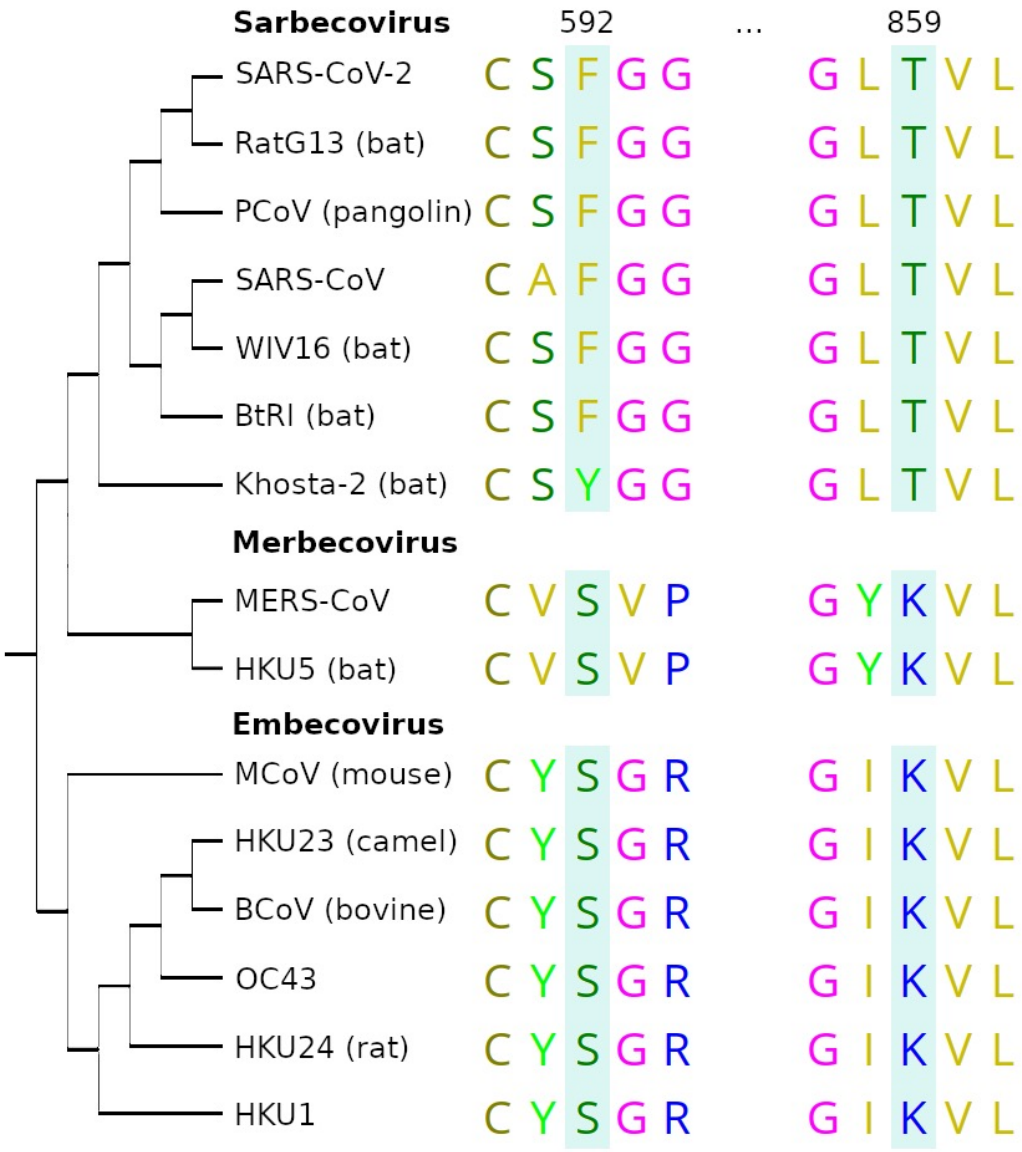


Supplementary Figure 2: Lambda mutations mapping on known antibody recognition epitopes. a) X-ray structure (PDBid:7BWJ) of a complex between wild type RBD from SARS-CoV2 and the monoclonal antibody P2B-2F6, isolated from B-cells from an infected individual. b) Close up on the hydrophobic interactions established by L452 and F490 in the protein-protein interface. Mutations to polar amino acids as L452Q, F490S clearly disrupt the hydrophobic interface. c) Same as a) for antibody S2M28 solved by CryoEM (PDBid:7LY0), which recognizes the highly antigenic segment of the NTD domain. d) The close-up highlights the NTD-antibody interaction L249-I93. The deletion 246-252 would completely abrogate the binding by drastically reducing the binding epitope.



Supplementary Figure 3. Increased infectivity of Lambda pseudoviruses

Levels of infection of pseudotyped viruses carrying Wild type, D614G, Alpha, Gamma or Lambda spikes in HEK293T cells stably expressing ACE2. Cells were seeded in 96-well plates and infected with low (2 ng, left) or high (20 ng, right) concentrations of the indicated pseudotyped viruses for 48 h. Two biological replicates were assessed in three independent experiments.



Supplementary Fig 4. **Multiple sequence alignment of betacovronaviruses around F592 and T859**. The hydrophobic interaction between T859 and F592 is only possible in Sarbecovirus as other subgenera present a putatively correlated mutation at those positions (K and S, respectively).