

The target. We have produced new high-affinity mouse monoclonal antibodies to the spike ectodomain of the novel coronavirus (**Figure 1**, denoted SARS-CoV2, pdb 6vxx, NCBI reference sequence YP_009724390.1). We identified 17 promising peptide sequences, mostly in the S1 domain, developed virus-like particle immunogens displaying those peptides, and immunized with these constructs and various versions of the intact recombinant domain proteins. The most interesting involve sequences important to viral entry and to distinguishing this pathogen from previous human coronaviruses.

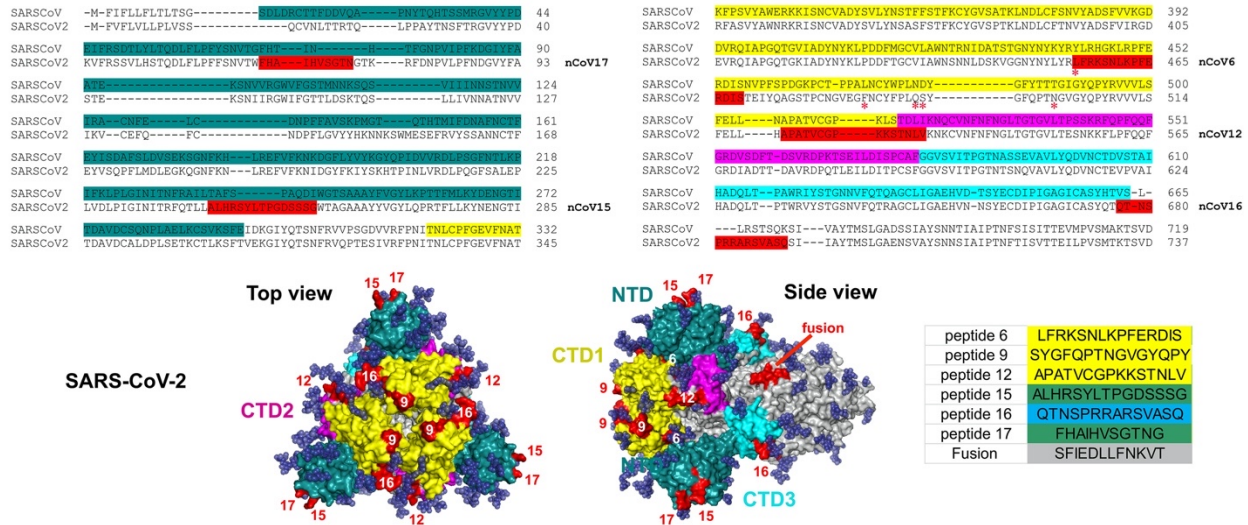


Figure 1. Sequences (*top*) of the spike protein S1 subunit from SARS-CoV and SARS-CoV2. Color coding matches the colors of the domains in the cryo-EM structure (*bottom*). In red are highlighted the positions of the seven initial peptides chosen for VLP display and immunization. The positions and approximate size of attached glycans are shown in dark blue (and do not appear in the cryo-EM structure), by homology with coronavirus HCoV-NL63.²⁷ CTD# = C-terminal domains 1-3; NTD = N-terminal domain. Asterisks in the sequence mark five key residues for RBD binding to ACE2.

Antibodies. The table below shows our current top six mAbs in terms of binding strength, from a panel of 40 showing dissociation constants below 5 nM. These will be isotyped shortly, but we believe them to be IgG₁ or IgG_{2a/b}. These first six show sub-nanomolar binding avidities on a biolayer interferometry assay against recombinant ectodomain protein. In the coming weeks, we hope to identify the peptides contained within the binding epitopes. If that information becomes available before we select samples for cryoEM analysis, we will prioritize the binding sites thought to be of greatest therapeutic relevance. We will have no difficulty providing sufficient quantities of these antibodies and the ectodomain target, all produced at the CDC.

mAb ID	k_{on} (M ⁻¹ s ⁻¹)	k_{off} (s ⁻¹)	K_d (M)	mAb ID	k_{on} (M ⁻¹ s ⁻¹)	k_{off} (s ⁻¹)	K_d (M)
3H6	3.1×10^5	$<1 \times 10^{-7}$	$<1 \times 10^{-11}$	3A7	3.0×10^5	$<1 \times 10^{-7}$	$<1 \times 10^{-11}$
2G4	2.9×10^5	4.3×10^{-5}	$1.5 \pm 0.2 \times 10^{-10}$	3F2	5.5×10^5	1.1×10^{-4}	$2.0 \pm 0.1 \times 10^{-10}$
5A1	5.5×10^5	1.4×10^{-4}	$2.5 \pm 0.1 \times 10^{-10}$	3G2	3.6×10^5	1.0×10^{-4}	$2.8 \pm 0.2 \times 10^{-10}$