Figure S1

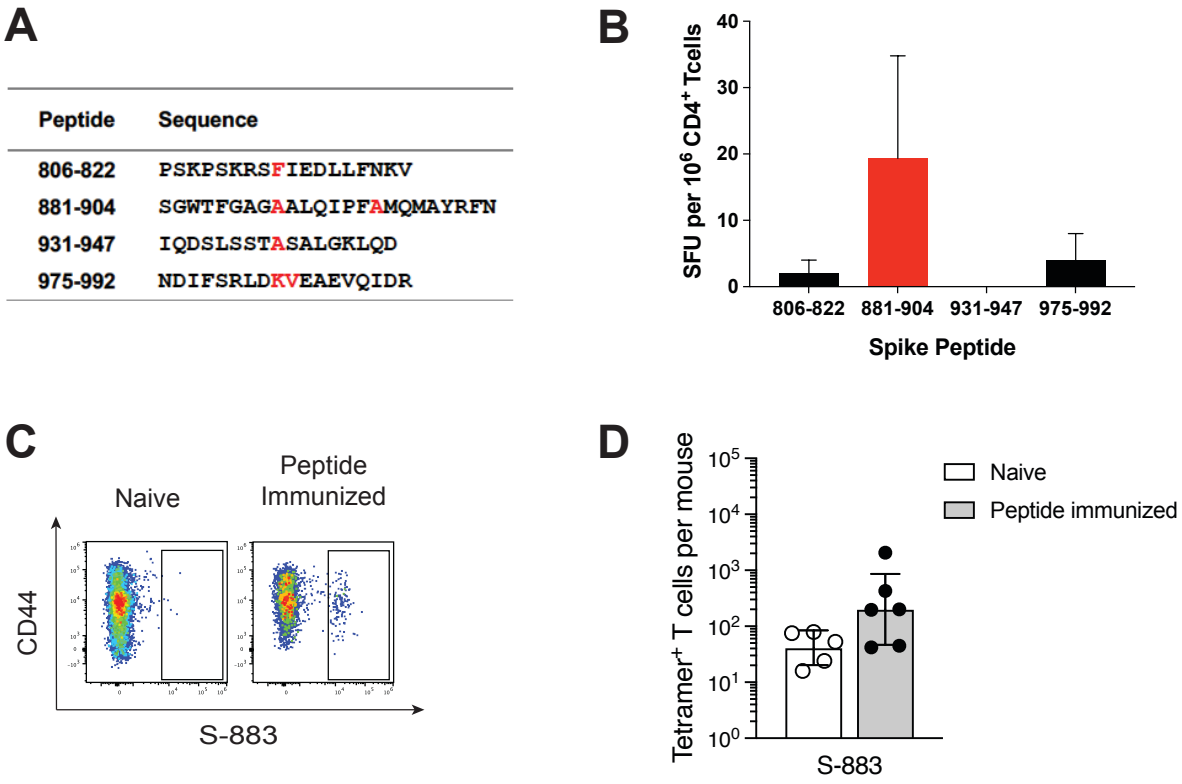

Figure S1. Identification of lost epitopes in Hexapro spike
A) Peptides were generated covering the regions of spike that were affected by proline substitutions in the Hexapro construct. Native residues that were replaced by prolines are indicated in red. **B)** C57BL/6 mice were immunized s.c. with a mix of the 4 peptides plus CFA as adjuvant and 9-10 days later, $CD4^+$ T cells were tested for reactivity to each individual peptide by IFNγ ELISpot assay. Mean values ± SEM are shown for n=2-6 mice processed across multiple independent experiments. **C)** Representative flow cytometry plots of $CD4^+$ gated events illustrating S-883 tetramer staining of epitope-specific T cells from naïve and S-883 peptide-immunized mice. **D)** Quantification of S-883-specific $CD4^+$ T cells from naïve and peptide-immunized mice. Mean values ± SEM are shown for n=5-6 mice per epitope across multiple independent experiments.

Figure S2

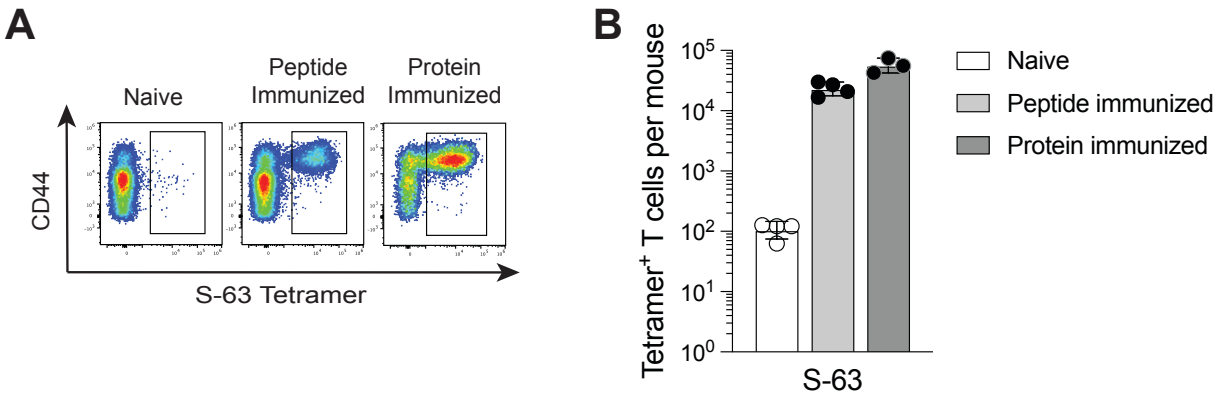

Figure S2. Tetramer analysis of CD4⁺ T cells specific for the S-63 epitope present in the ancestral strain of SARS-CoV-2, but not BA.1
A) Representative flow cytometry plots of CD4⁺ gated events illustrating S-63 tetramer staining of epitope-specific T cells from naïve, S-63 peptide-immunized, or Wuhan D614G spike protein-immunized mice. **B)** Quantification of S-63-specific CD4⁺ T cells from naïve, peptide-immunized, and protein-immunized mice. Mean values ± SEM are shown for n=3-4 mice per epitope across multiple independent experiments.