Review 1: "Robust SARS-CoV-2-specific T-cell immunity is maintained at 6 months following primary infection"

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RR: COVID-19 Evidence Scale rating by reviewer:

- **Reliable.** The main study claims are generally justified by its methods and data. The results and conclusions are likely to be similar to the hypothetical ideal study. There are some minor caveats or limitations, but they would/do not change the major claims of the study. The study provides sufficient strength of evidence on its own that its main claims should be considered actionable, with some room for future revision.

Review:

This manuscript characterizes SARS-CoV-2 specific T cells 6 months after primary infection in a cohort of 100 individuals. To accomplish this the authors, use standard IFN-γ ELISPOT and intracellular cytokine stain flow cytometric assays. T cell responses to both the prime antibody target (the Spike protein) and also to Nucleocapsid and Membrane are studied, as well as responses to a range of accessory proteins. Further, T cell responses detected at 6 months are analyzed with respect to SARS-CoV-2 antibody profiles generated from serum samples obtained in the preceding months.

The study is of high interest as there is a fear that immunity to SARS-CoV-2 would wane very quickly; a fear that was raised by a few studies from endemic seasonal coronaviruses. This paper adds to the growing body of literature that highlights that both rigorous antibody responses and T cell responses are mounted following infection and that memory responses persist. The finding that memory T cells are readily detectable at 6 months following infection clearly emphasizes the establishment of substantial immune memory.

The finding that individuals with asymptomatic primary infection have fewer memory T cells at 6 months is of great interest and warrants further studies as to the impact of such lower levels of immune memory.

The study is however not equipped to extrapolate the T cell immunity data to any conclusions regarding relative protection from re-infection and the authors cannot infer any in vivo functionality from the detected responses.
I have some problems deciphering the data and the conclusions based on the correlations in Figure 5B+5C. On the x-axis the IFN-g ELISPOT data is depicted and on the y-axis different antibody specificities are denoted. It is well established (and the authors show the ICS data in Figure 4) that CD8 T cells primarily produce IFN-g while CD4 T cells produce primarily IL-2 (albeit some IFN-g). Further CD4 responses are necessary for B cell maturation and differentiation and these CD4 responses are obtained in the ICS assay. Therefore, I think the plots using the ELISpot data have limited value as is.

Minor comments

· The RBD antibody detection scheme is not described or referenced

· Figure 3 could include a Figure depicting the compiled T cell data. I.e. highlighting the high proportion of individuals with positive T cell responses in the two assays

· Were the donors verified SARS-CoV-2 positive by PCR?

· How was the cut-off for positivity determined in ICS? And are all ICS values background subtracted from the non-peptide incubated control?