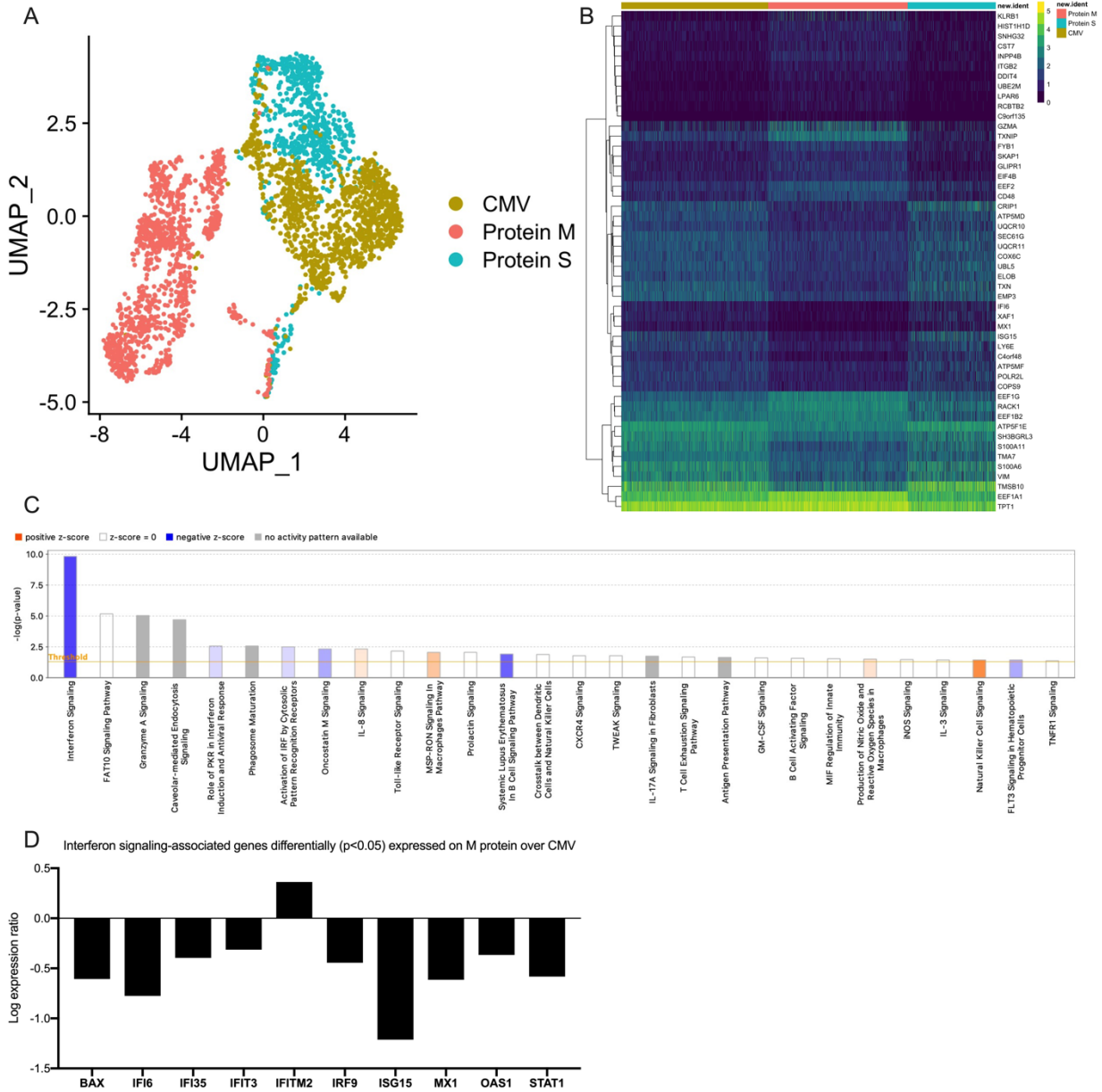
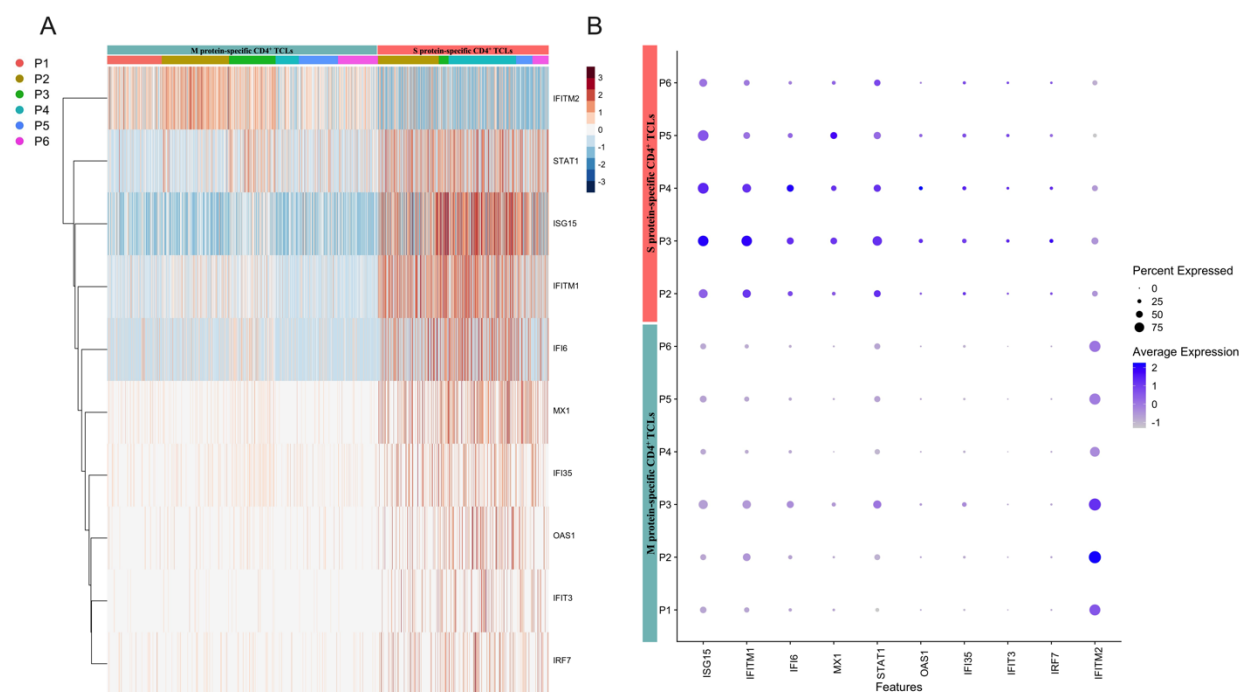


**Supplemental figure 1. SARS-CoV-2 S and M proteins-specific CD4<sup>+</sup> T cells reactivity and specificity.**  $2 \times 10^5$  S-reactive T cells (A) and  $2 \times 10^5$  M-reactive T cells (B) from the 6 donors were incubated with  $2 \times 10^5$  autologous irradiated PBMCs and stimulated separately in the absence (media) or in the presence of MP-S ( $1 \mu\text{g/mL}$ ) and MP-M ( $1 \mu\text{g/mL}$ ) and CMV MP ( $1 \mu\text{g/mL}$ ) for 48 hours at  $37^\circ\text{C}$  and 5%  $\text{CO}_2$ . IFN- $\gamma$  and TNF- $\alpha$  levels were measured in the culture supernatant by Luminex platform. All differences by Wilcoxon matched-pairs test with  $P < 0.05$  are indicated in the graph.



**Supplemental figure 2.** Single-cell transcriptional profiling of SARS-CoV-2 S, M and CMV-specific CD4<sup>+</sup> T cells (A). Heatmap showing expression of the most significantly 50 enriched transcripts in M protein-specific CD4<sup>+</sup> T cell lines over S protein- and CMV-specific CD4<sup>+</sup> T cell lines (B). Canonical signaling pathways (IPA, QIAGEN) of immunological relevance affected in M protein-specific TCLs over CMV-specific TLCs indicating a marked suppression of interferon signaling pathway (C), with the associated gene expression levels and directions presented individually (D).



**Supplemental figure 3.** Heatmap (A) and the feature dot plot graph (B) showing the average expression and the percent expression of the interferon signaling pathway genes in the respective S-protein-specific CD4<sup>+</sup> T cell lines and M-protein-specific CD4<sup>+</sup> T cell lines by a donor-specific manner (colored from P1-P6).