



**Figure S3. CD4 T cell responses are induced by AS03-adjuvanted RBD-nanoparticle vaccination. (A and B)** The frequency of Spike protein-specific CD4 T cell responses in peripheral blood mononuclear cells (PBMCs) were measured against ancestral (left panel) and

Omicron (right panel) strains in the RBD-Wu/RBD-Wu/RBD-Wu vaccinated group (**A**) and the RBD-Wu/RBD-Wu/RBD- $\beta$  (blue) and HexaPro/HexaPro/RBD- $\beta$  (red) vaccinated groups (**B**). CD4 T cells secreting interleukin (IL)-2, interferon (IFN)- $\gamma$ , or tumor necrosis factor (TNF) are plotted as Th1-type responses and IL-4-producing CD4 T cells are shown as Th2-type responses. (**C**) The ratio of the frequency of Th1 (cells expressing IL-2, IFN- $\gamma$ , or TNF plotted in the left panels of A and B) to Th2 (cells expressing IL-4 plotted in the right panels of A and B) CD4 T cell response elicited against the variants is indicated on the X-axis. Data are presented as box plots in which the boxes show median and 25<sup>th</sup> to 75<sup>th</sup> percentiles and the whiskers show the range. (**D**) The frequency of Spike protein-specific CD8 T cell responses expressing IFN- $\gamma$  and TNF against ancestral (left panel), Omicron (middle panel), and Beta (right panel) strains were measured in PBMC samples from in the RBD-Wu/RBD-Wu/RBD-Wu group (**A**) in the RBD-Wu/RBD-Wu/RBD-Wu (top panels) and the RBD-Wu/RBD-Wu/RBD- $\beta$  (blue) and HexaPro/HexaPro/RBD- $\beta$  (red) groups (bottom panels).