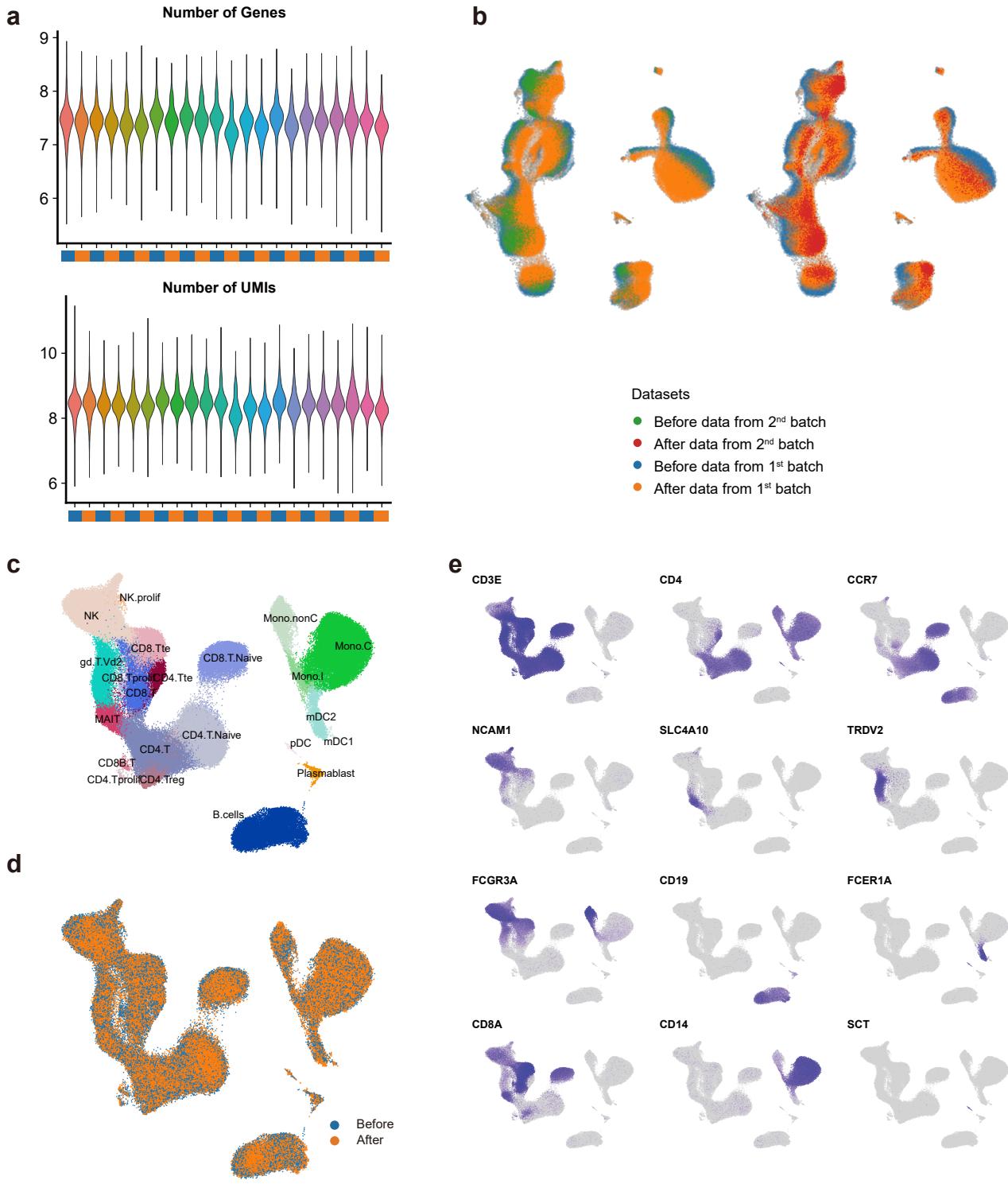
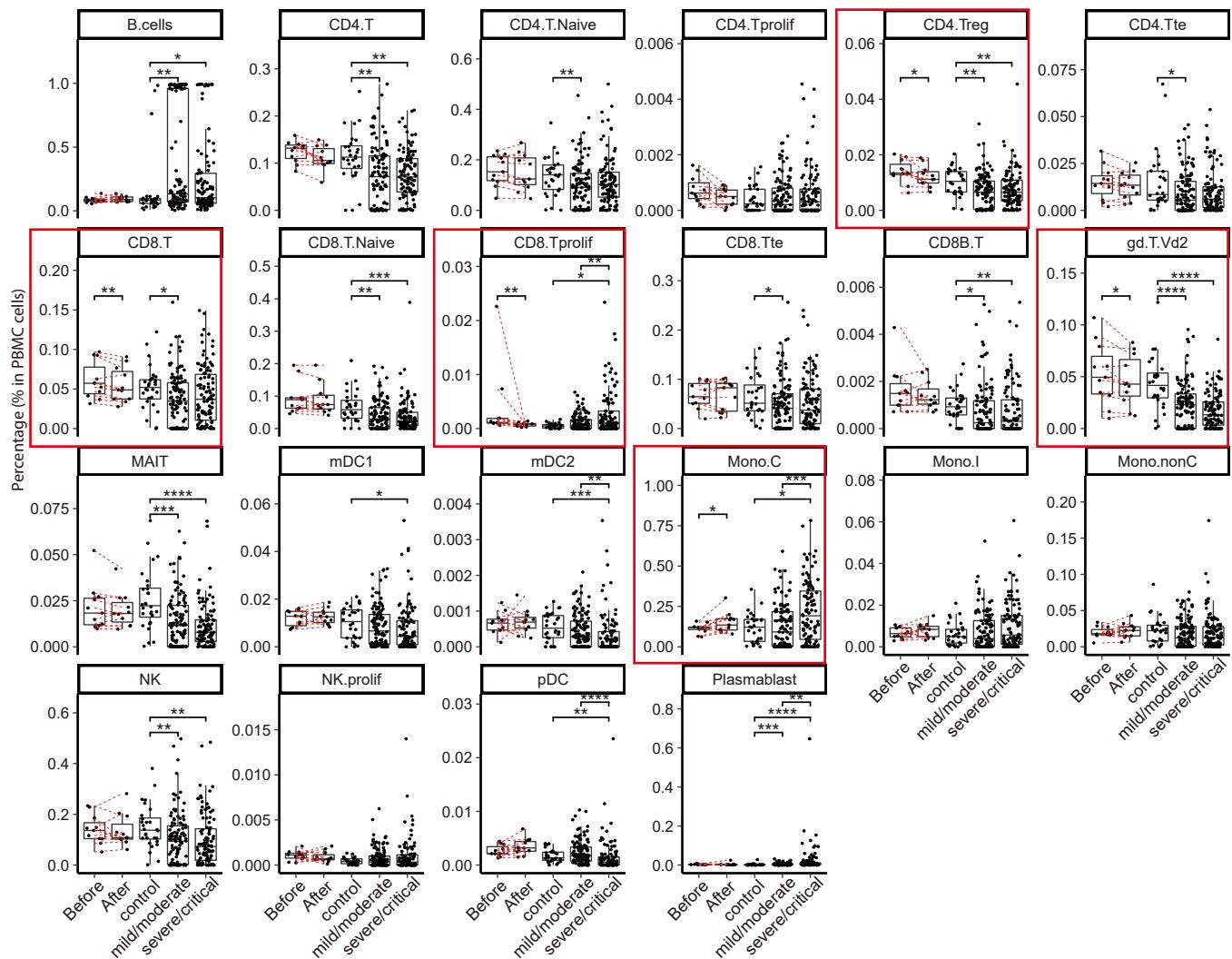


**Supplementary Fig. S1**



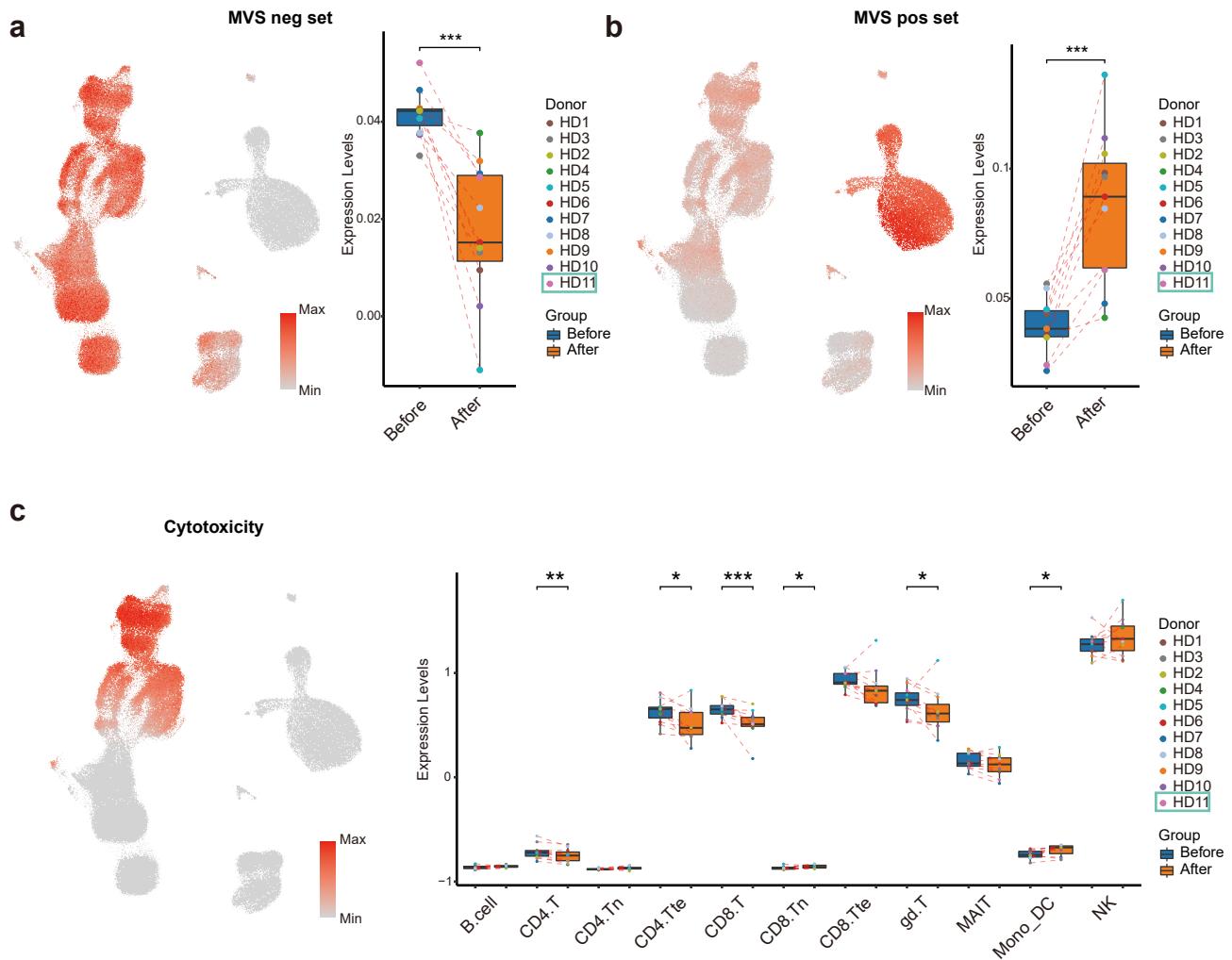
**Supplementary Fig. S1 a** QC analysis of scRNA-seq data. Numbers of genes, numbers of mRNA molecules (counts) in each sample. **b** UMAP distribution of samples from the 2<sup>nd</sup> batch of sequencing overlaid on top of data from the 1<sup>st</sup> batch showing consistent changes before and after vaccination. **c, d, e** UMAP representation of all cells after batch effect correction eliminated changes before and after vaccination (**d**), but clearly demonstrated cell-type specific expression of marker genes (**e**).

**Supplementary Fig. S2**



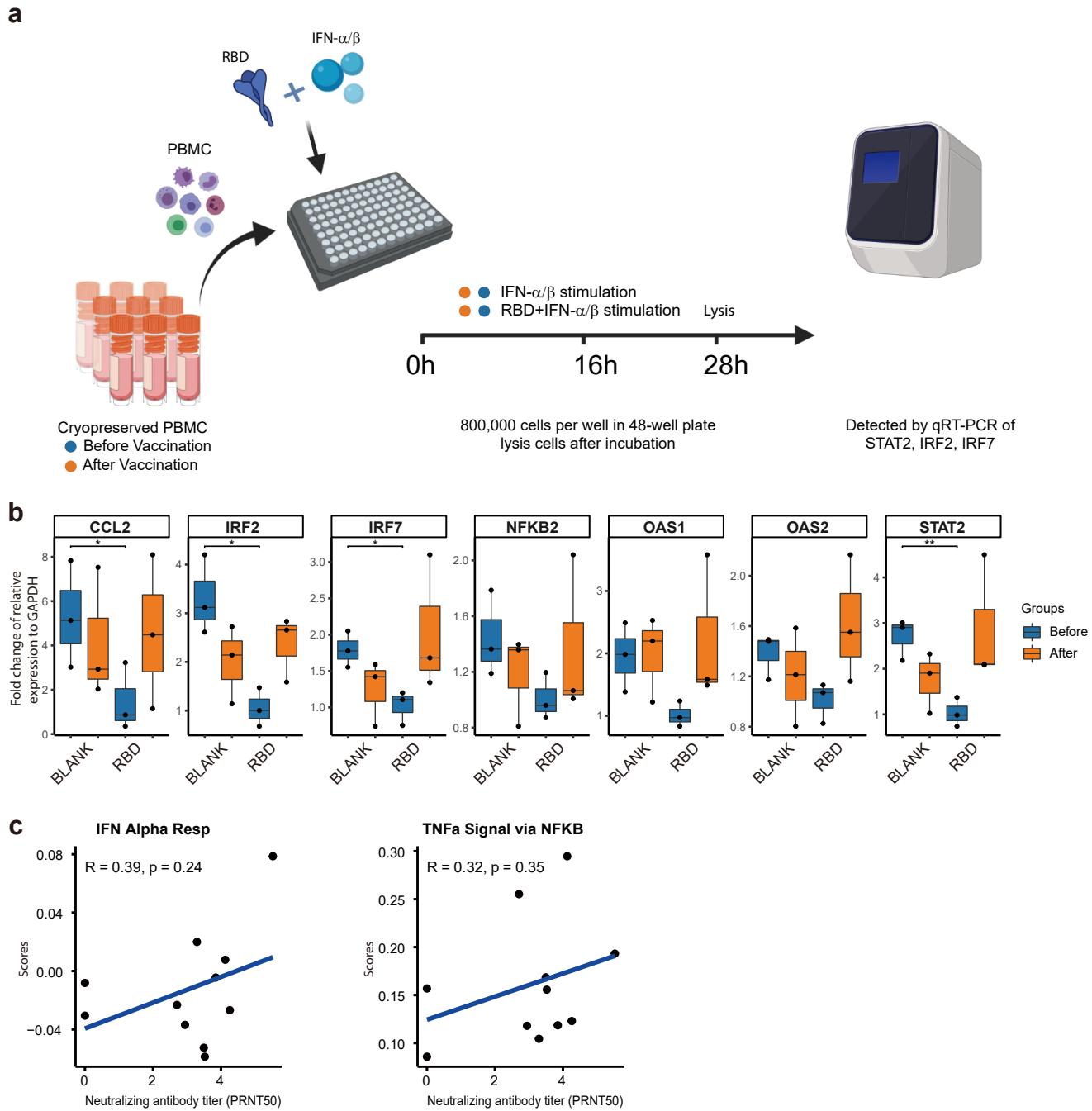
**Supplementary Fig. S2** Cell type specific content changes before and after vaccination, in relate to changes in mild and severe COVID-19 patients and healthy individuals.

**Supplementary Fig. S3**



**Supplementary Fig. S3 a** Averaged expression of genes negatively contributing to MVS scores on UMAP plot and box plots demonstrating down-regulation of this gene set after vaccination. **b** Averaged expression of genes positively contributing to MVS scores on UMAP plot and box plots demonstrating up-regulation of this gene set after vaccination. **c** Average expression of cytotoxicity signature genes on UMAP plot and box plots depicting expression changes of this gene set amongst 11 major immune cell types before and after vaccination.

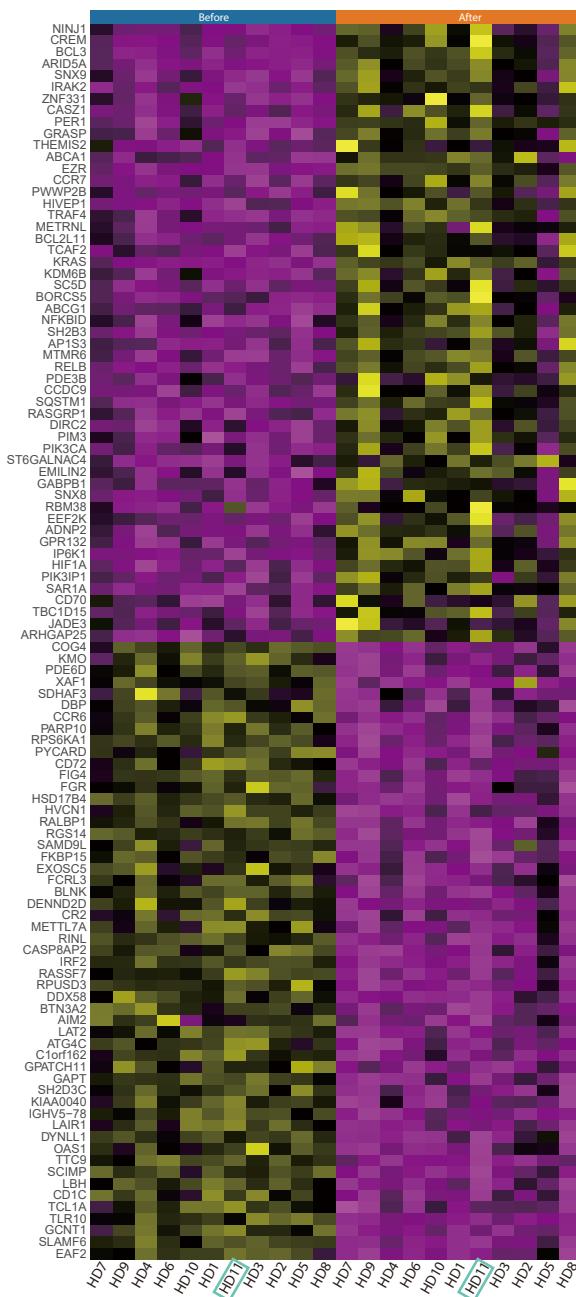
**Supplementary Fig. S4**



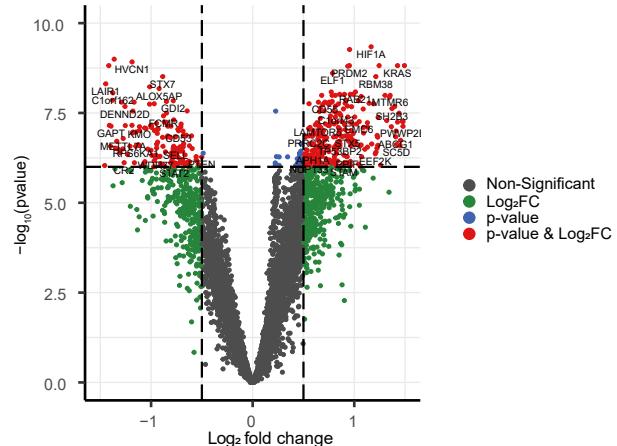
**Supplementary Fig. S4 a** Schematic overview of experiment. **b** Expression of 7 genes related to type I IFN responses in cultured PBMCs from healthy volunteers before and 28 days after vaccination, with or without RBD pretreatment. (\* $p < 0.05$ , \*\* $p < 0.01$ ,  $n = 3$ ) **c** Pearson's Correlation Coefficient between neutralizing antibody titers and inflammatory responses measured by averaged gene expression of genes associated with TNF $\alpha$  Signaling via NF- $\kappa$ B and with Interferon- $\alpha$  (type I interferon) responses.

## Supplementary Fig. S5

a



b



mitochondrial electron transport, NADH to ubiquinone

positive regulation of B cell differentiation, nucleotide-excision repair, preincision complex stabilization, regulation of B cell differentiation

establishment of protein localization to chromosome

negative regulation of protein localization to membrane

positive regulation of gamma-delta T cell activation

negative regulation of protein localization to plasma membrane

negative regulation of immunoglobulin production

positive regulation of gamma-delta T cell differentiation

ribonucleoprotein complex assembly

cytoplasmic translation

regulation of mRNA processing

regulation of mRNA stability

regulation of mRNA splicing, via spliceosome

RNA export from nucleus

ribosomal large subunit biogenesis

ribosome assembly

ribosomal small subunit biogenesis

regulation of protein deubiquitination



**Supplementary Fig. S5 a** Differentially expressed genes before and after vaccination in B cells based on scRNA-seq data after pseudo-bulk aggregation. **b** Volcano plot of B-cell specific differentially expressed genes (DEGs) before and after vaccination. **c** Gene Ontology analysis of B-cell specific DEGs.