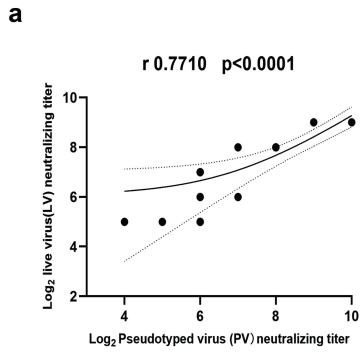
Characterization of type 2 diabetes-related immune response heterogeneity to COVID-19 vaccines via single-cell landscape analyses

Weiqi Wang[1,3#], Wenwen He[1,2#], Shen Wang[1#], Bo Liang[1], Na Feng[1], Yongkun Zhao[1], Tiecheng Wang[1], Xiaotuan Zhang[2], Shiqi Yuan[2], Jian Wang[2], Shanshan Deng[2], Jingsong Guo[2], Songtao Yang[1], Gary Wong[4*], Bin Liu[2*], Feihu Yan[1*], Xianzhu Xia[1,3]

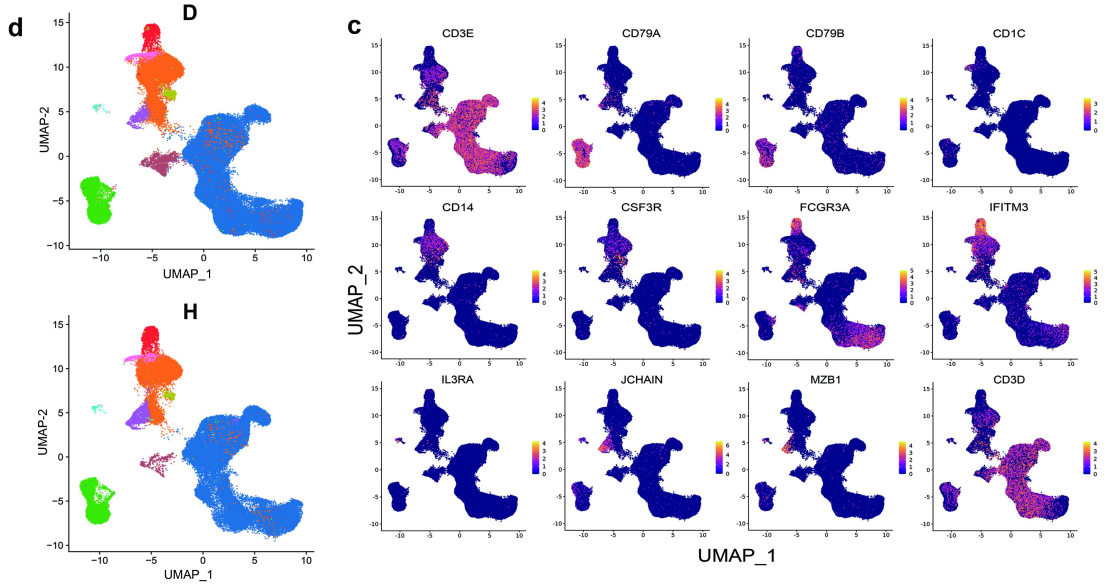
Supplementary Materials

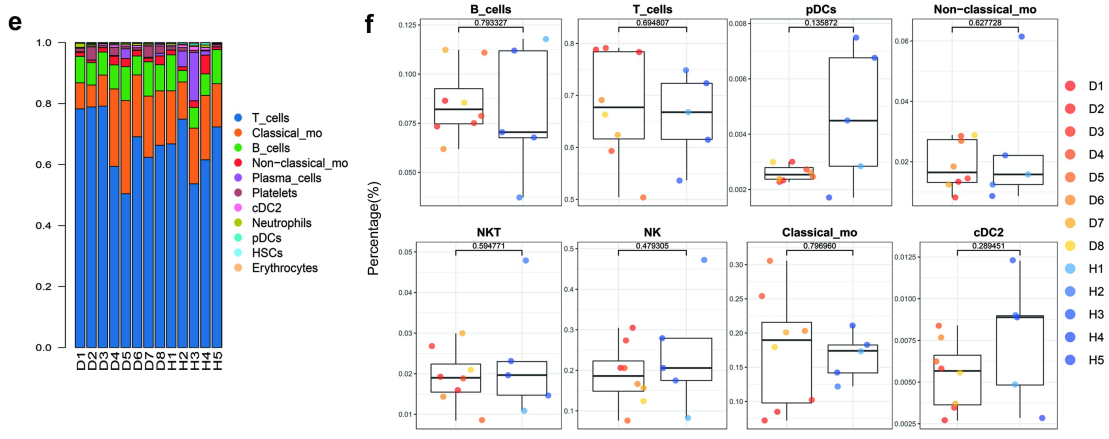
Supplementary Figures



b

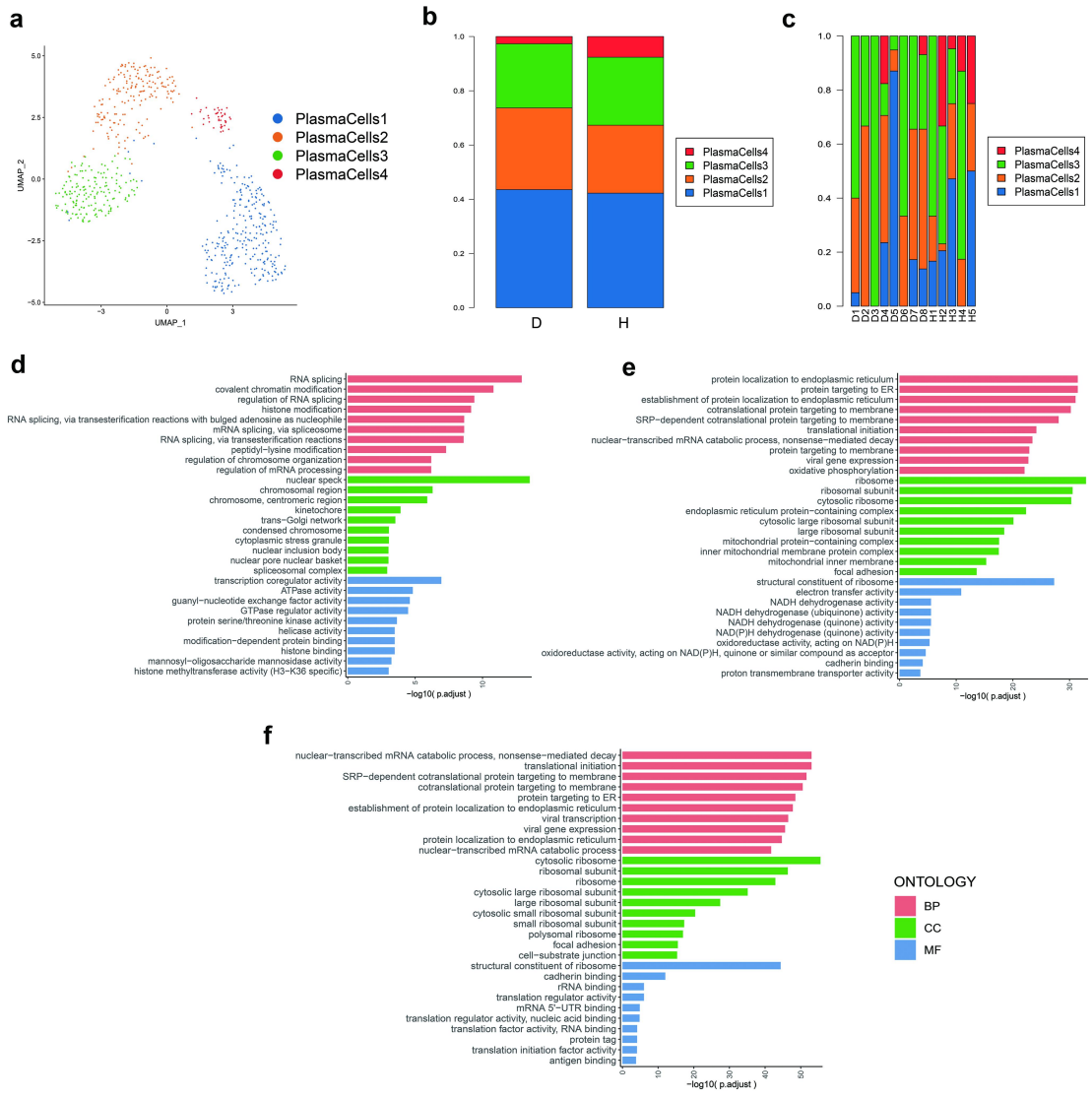
Donor	Sex	Age (Years)	Duration of diabetes (Years)	Diabetes subtype	Fasting blood glucose level(mmol/L)	HbA1c (%)	Comorbidities
D1	M	47	4	T2DM	>7.0	>9	None
D2	M	54	9	T2DM	6-7	7-8	None
D3	M	42	2	T2DM	6-7	7-8	None
D4	M	57	2	T2DM	6-7	7-8	None
D5	F	51	2	T2DM	6-7	7-8	None
D6	F	53	5	T2DM	6-7	7-8	None
D7	F	52	20	T2DM	6-7	6-7	None
D8	F	52	3	T2DM	6-7	6-7	None
H1	M	53	None	None	3.9-6.1	4-6	None
H2	M	53	None	None	3.9-6.1	4-6	None
H3	M	52	None	None	3.9-6.1	4-6	None
H4	F	44	None	None	3.9-6.1	4-6	None
H5	F	47	None	None	3.9-6.1	4-6	None



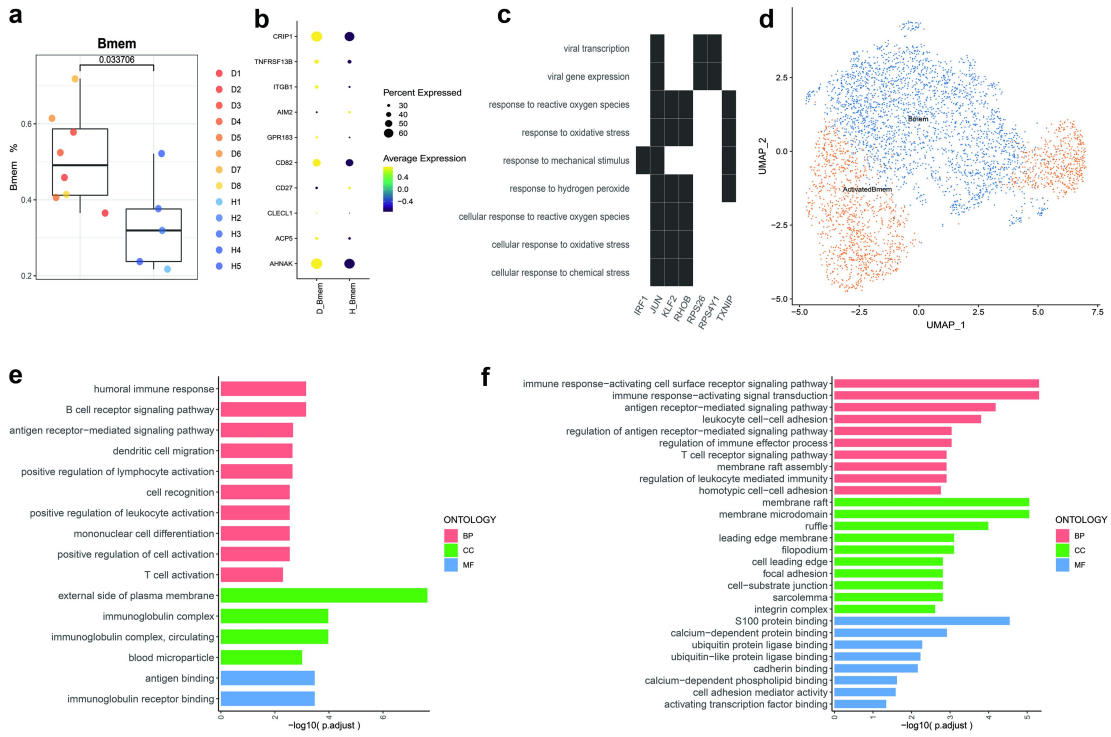


Extended Data Fig. 1, related to Fig. 2. a) Linear correlation between live virus neutralization and SARS-CoV-2 spike pseudotyped virus neutralization for 13 sera from individuals vaccinated with inactivated-virus vaccines. Linear regression line bound by the 95% confidence interval (CI). b) Demographics and sample

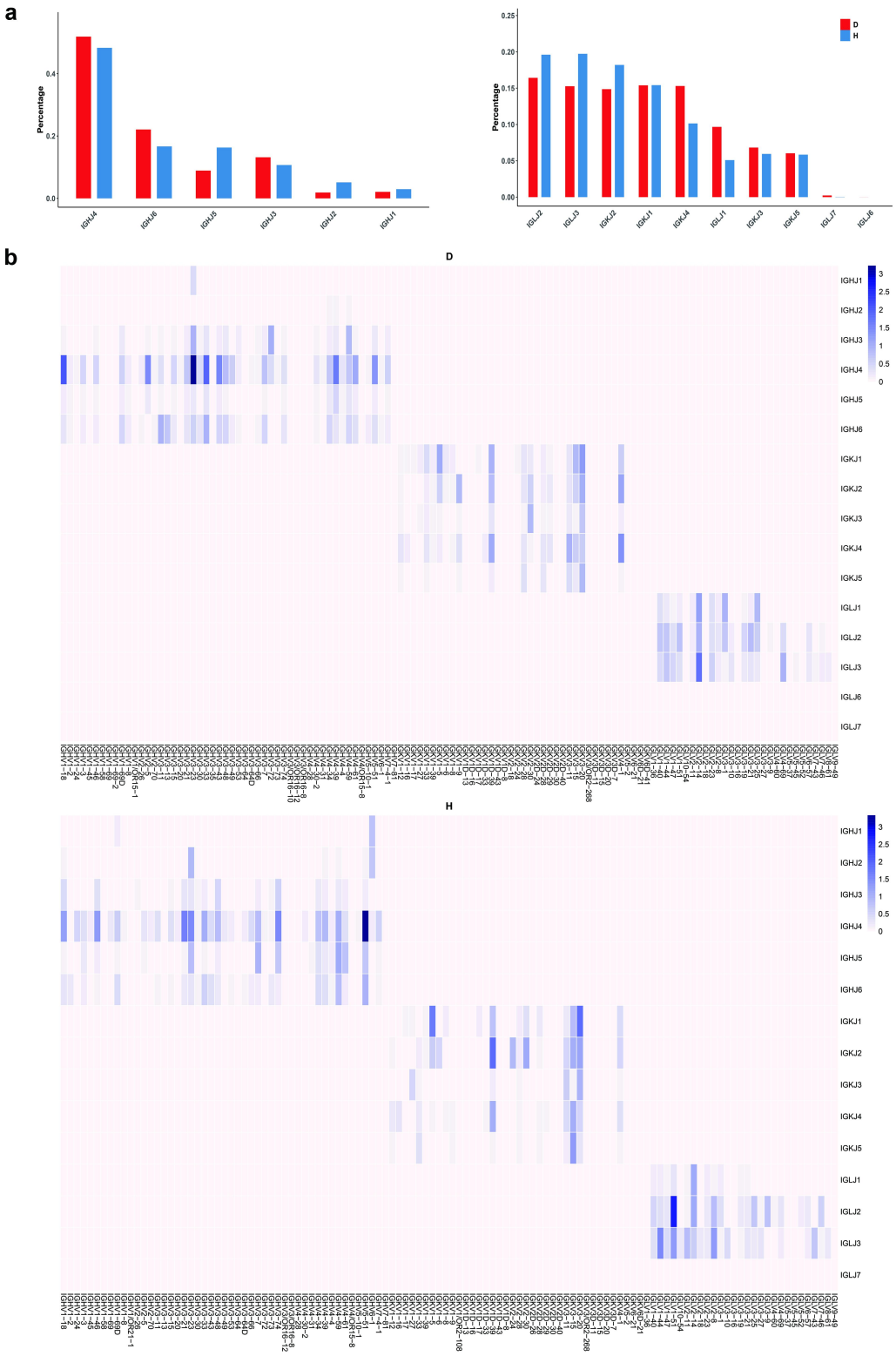
characteristics of 13 volunteers who received COVID-19 vaccines. c) UMAP plot of each detected cell type stratified by H and D. d) Typical cell markers were used to label eight subsets based on cell identity as represented in the UMAP. All datasets were colored according to expression levels, and the legend was labeled based on the log scale. e) Bar plot showing the cell composition at the single sample level. f) Proportions of each cell cluster in single samples colored by proband. The x-axes correspond to the eight T2D volunteers (red) and five healthy volunteers (blue).



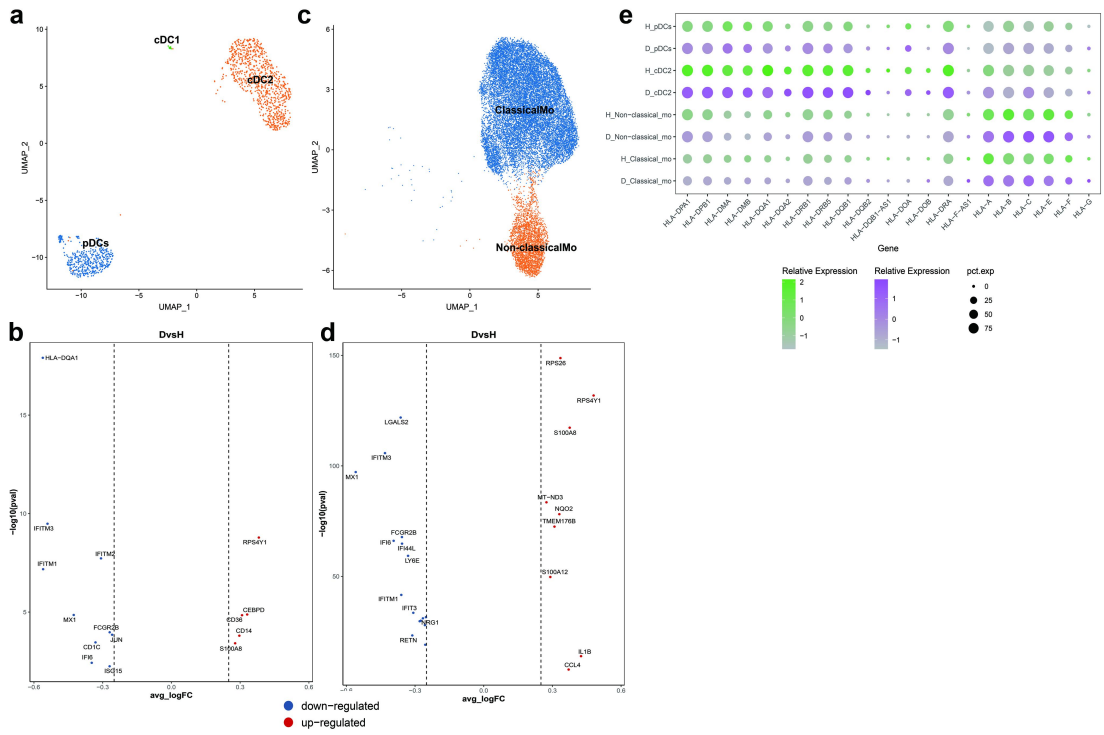
Extended Data Fig. 2. related to Fig. 2. a) UMAP of all embedded B cells colored based on unsupervised clustering. Three clusters with 12,422 single cells were detected. b) Proportions of plasma cell clusters 1–4 in D and H. c) Proportions of plasma cell clusters 1–4 in individual samples colored by proband. d–f) GO enrichment analysis of plasma cell clusters 1–3. Each row represents one of the top 10 enriched pathways. Bar plot showing the -log10 (P value) of the enriched pathways.



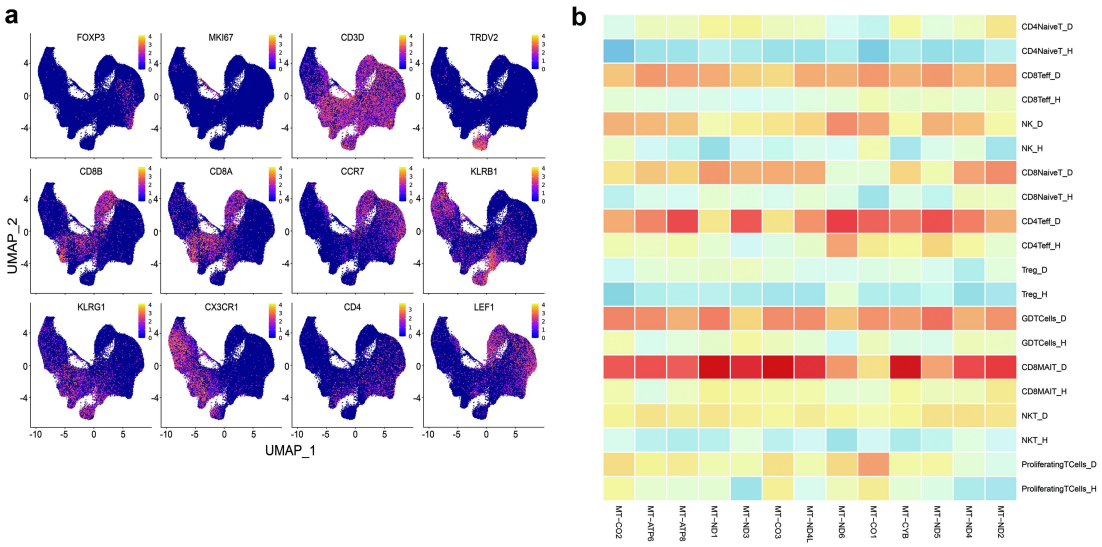
Extended Data Fig. 3. Oxidative stress-driven memory B cell dysfunction in COVID-19-vaccinated patients with T2D. a) Boxplot showing the proportions of memory B cells in D (red) and H (blue). b) Dot plot of DEGs of memory B cells in D and H. Expression levels were color-coded, and the percentage of cells expressing the respective gene was indicated based on size. c) GO enrichment analysis of memory B cells showing genes that are positively correlated with significantly enriched pathways. Each row represents one enriched pathway, and each column represents a gene. d) UMAP of all embedded memory B cells colored based on unsupervised clustering. e, f) GO enrichment analysis of active memory B cell (e) and memory B cell (f) pathways. Each row represents one of the enriched pathways. Bar plot showing the -log10 (P value) of the enriched pathways.



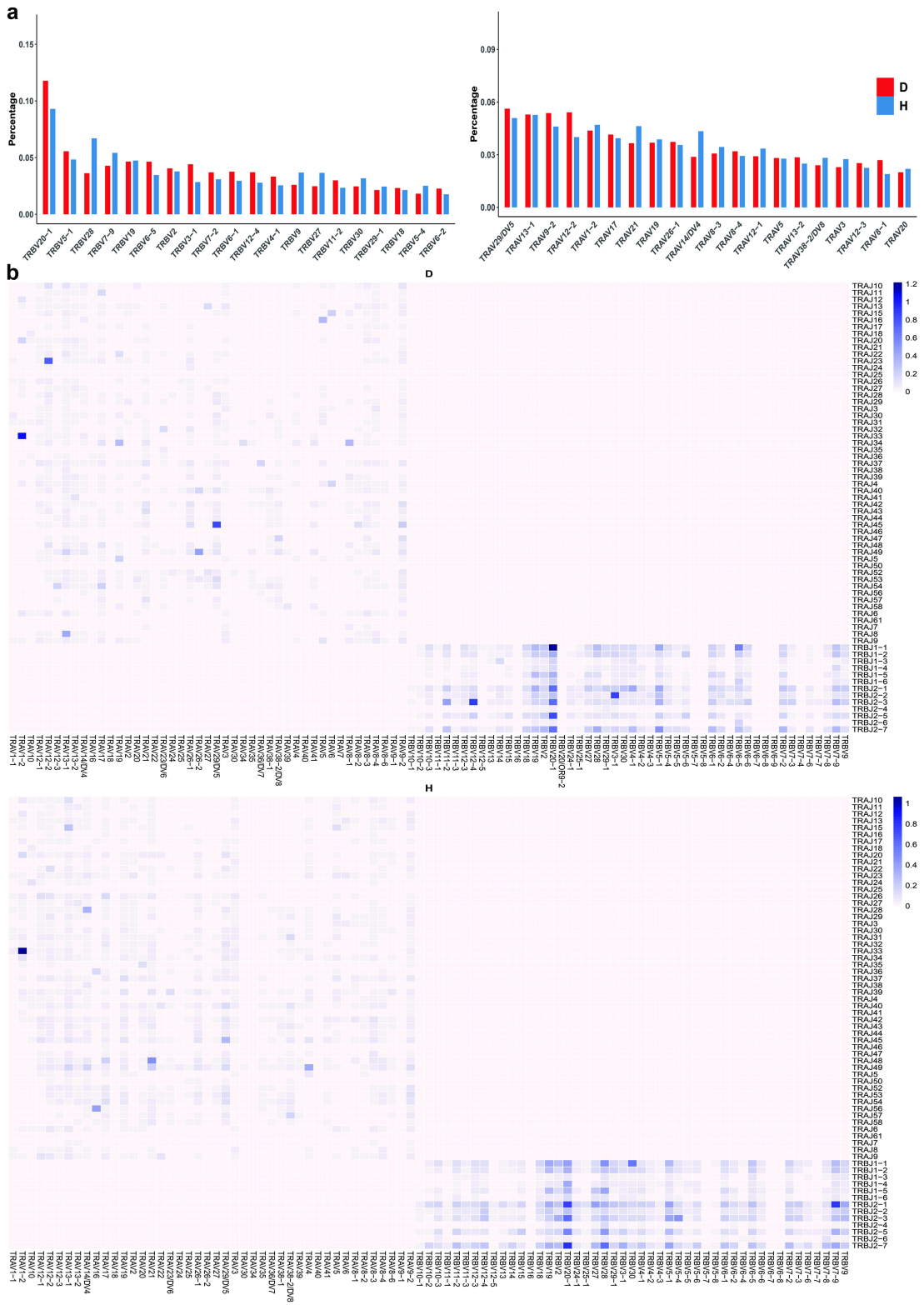
Extended Data Fig. 4, related to Fig. 3. a) Bar plot showing the usage of the IGHJ (left) and IGKJ/IGLJ (right) genes in D (red) and H (blue). b) Heatmaps showing IGH/K/L rearrangement differences in D and H. Colors indicate the usage percentages of specific V-J gene pairs.



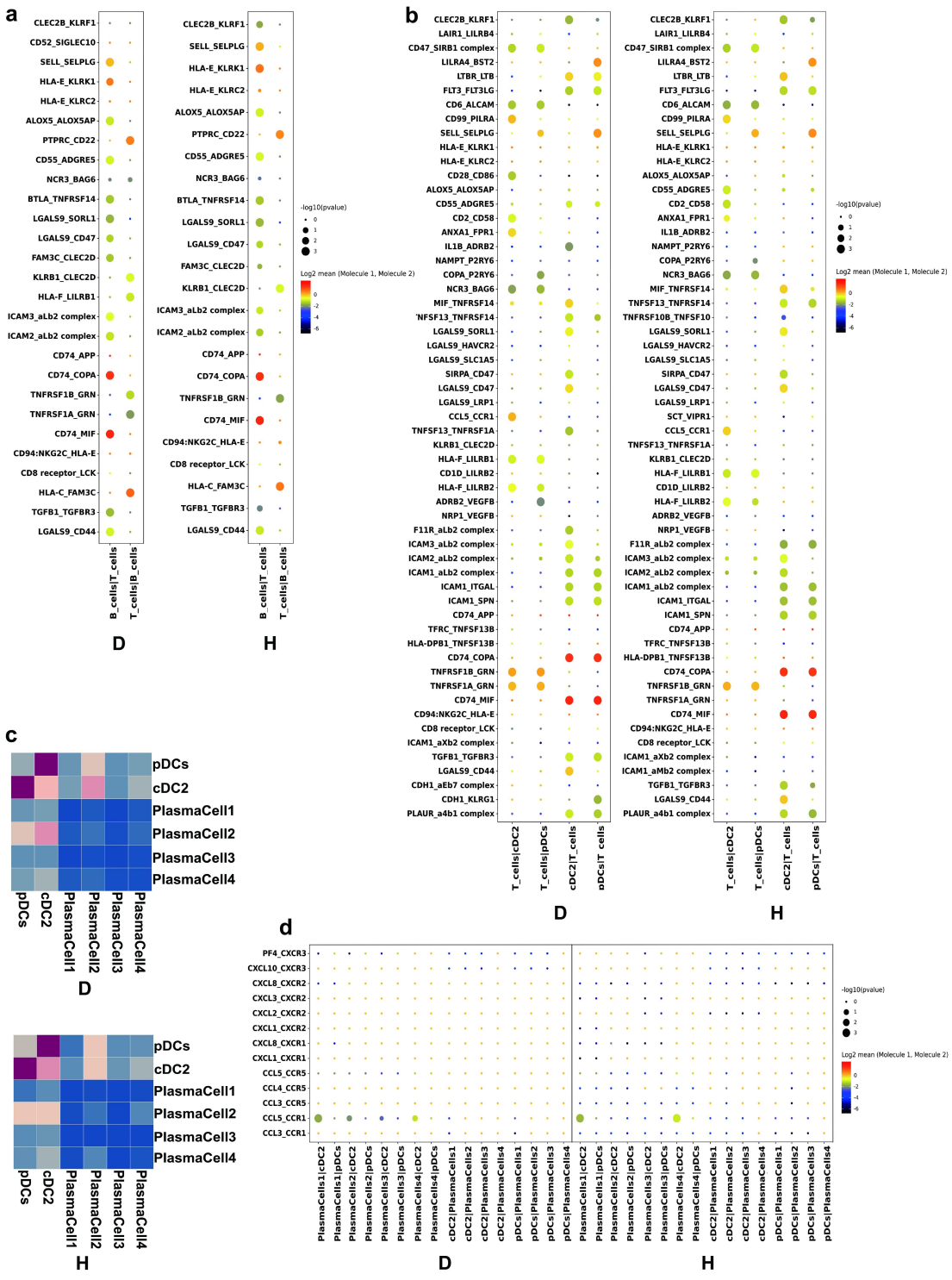
Extended Data Fig. 5, related to Fig. 4. a,c) UMAP of embedded DCs and monocytes colored by unsupervised clustering. b,d) Volcano plot of the DEGs in D vs. H cDC2 and monocytes. e) Dot plot of the HLA genes and enrichment analysis of APCs. Score levels were color-coded, and the percentage of cells expressing the pathway was indicated by size.



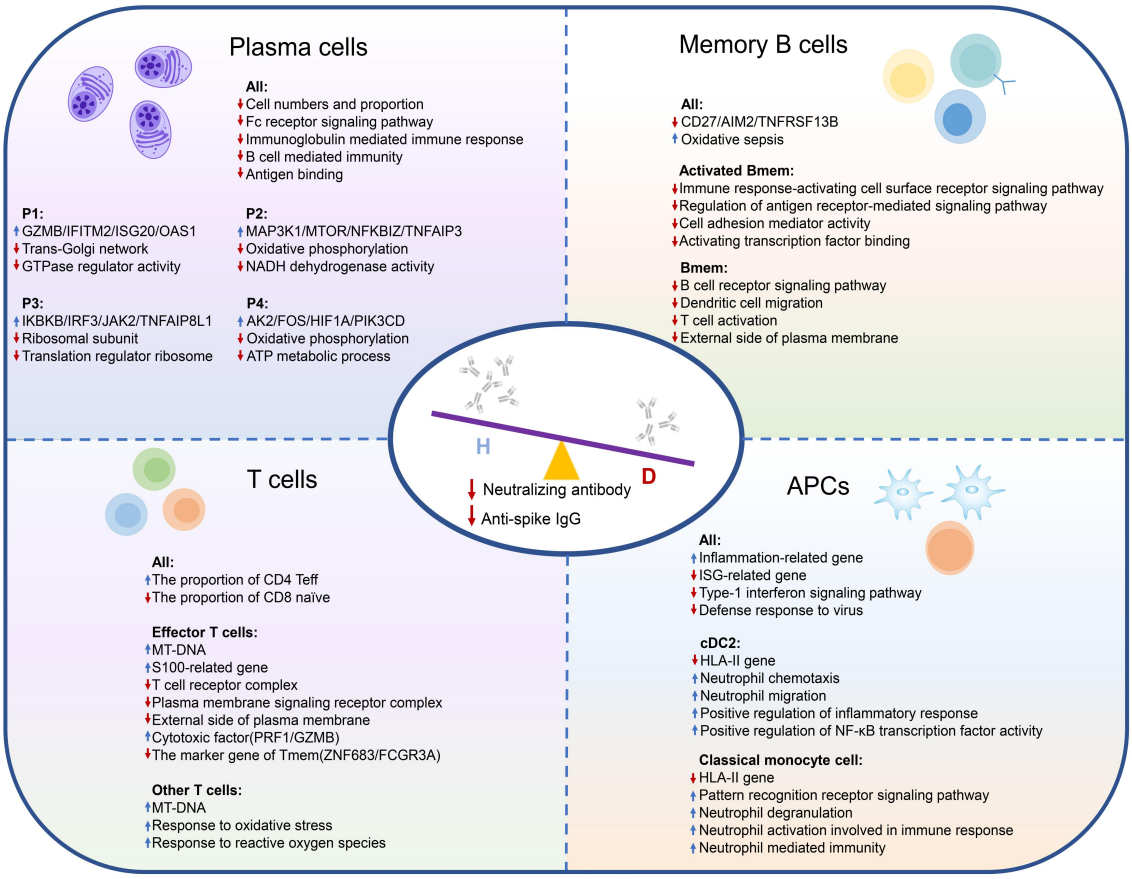
Extended Data Fig. 6, related to Fig. 5. a) Canonical T cell subset markers were used to label clusters by cell identity as represented in the UMAP plot. b) Heatmap showing the differentially expressed mitochondrially-encoded genes in each T cell.



Extended Data Fig. 7, related to Fig. 6. a) Bar plot showing the usage of the TRBV (left) and TRAV (right) genes in D and H. b) TRA/B rearrangement differences in D and H. The colors indicate the usage percentages of specific V-J gene pairs.



Extended Data Fig. 8, related to Fig. 7. a) Predicted chemokine interaction pairs between the T and plasma cells. b) Predicted chemokine interaction pairs between the DCs and T cells. c) Heatmaps showing the number of predicted interactions between DCs and plasma cell clusters based on CellPhoneDB in D and H. d) Predicted chemokine interaction pairs between the DCs and plasma cell clusters 1–4.



Extended Data Fig. 9. Summary of reprogramming in the peripheral immune cell response of individuals with T2D to COVID-19 vaccines. Dramatic changes manifest in the peripheral immune response and can be assessed per cell type following the administration of COVID-19 vaccines in patients with T2D. These diverse alterations may correspond to low levels of neutralizing antibodies.

Supplementary Tables

Table 1. Study participant characteristics and serological assays to identify the presence of antibodies.