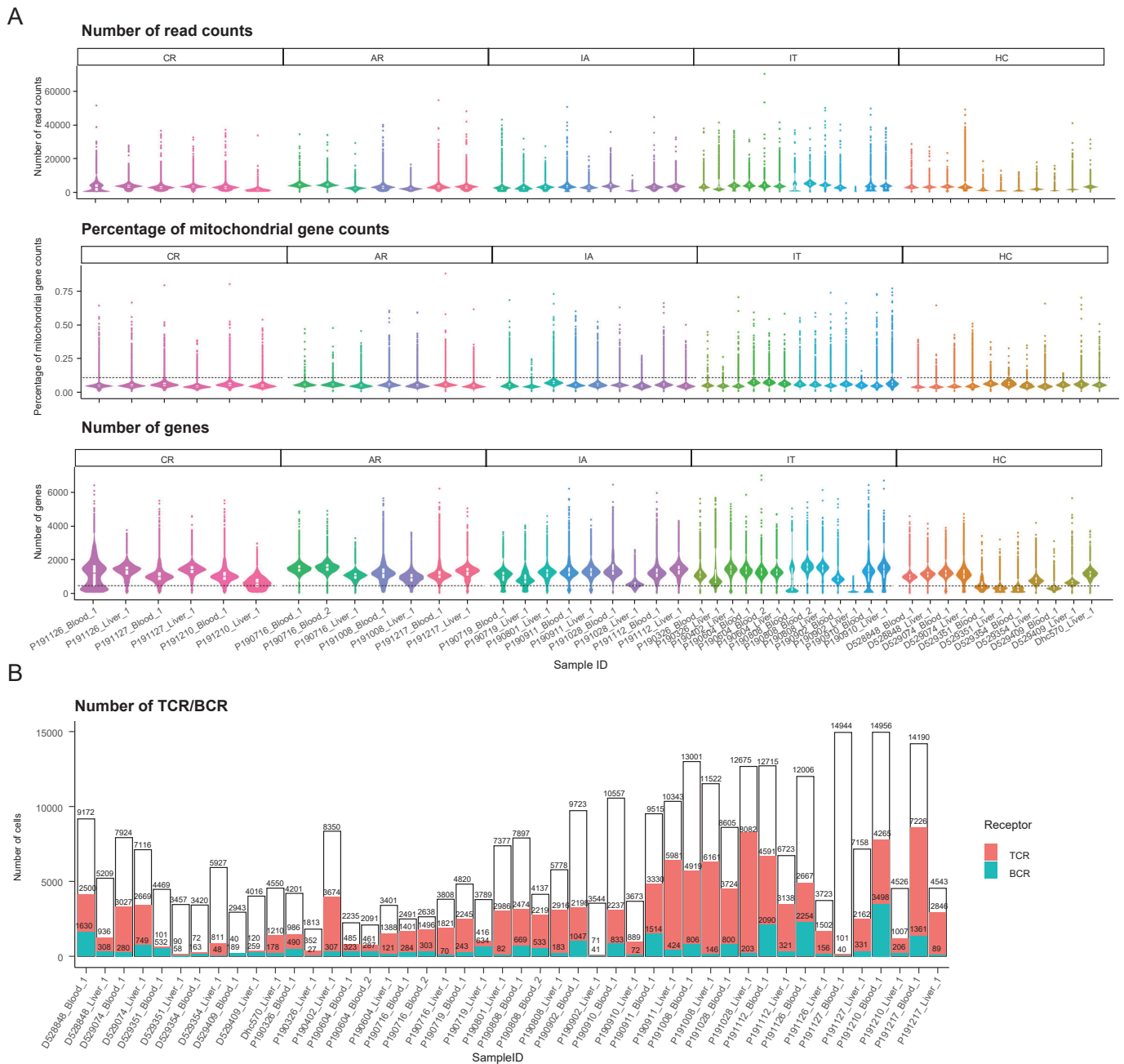


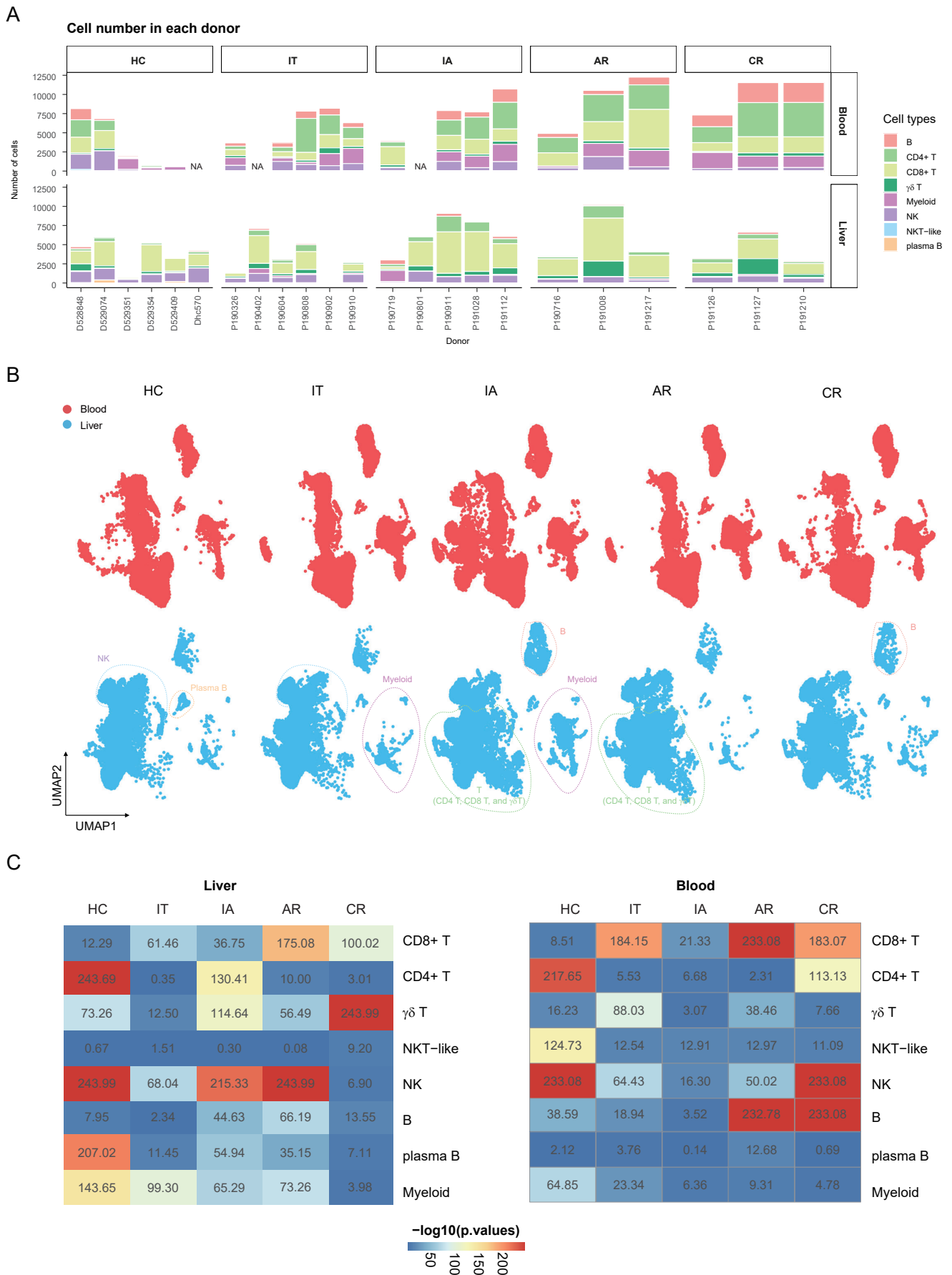
Supplemental figure 1 Information for sample preparation.

(A) Representative images of flow cytometry sorting for viable CD45⁺ cells from liver tissues. (B) Longitudinal changes of serum HBsAg, serum ALT, and serum HBV DNA levels for AR patients. (C) Timeline showing information for diagnosis and management of CR patients enrolled in this study.



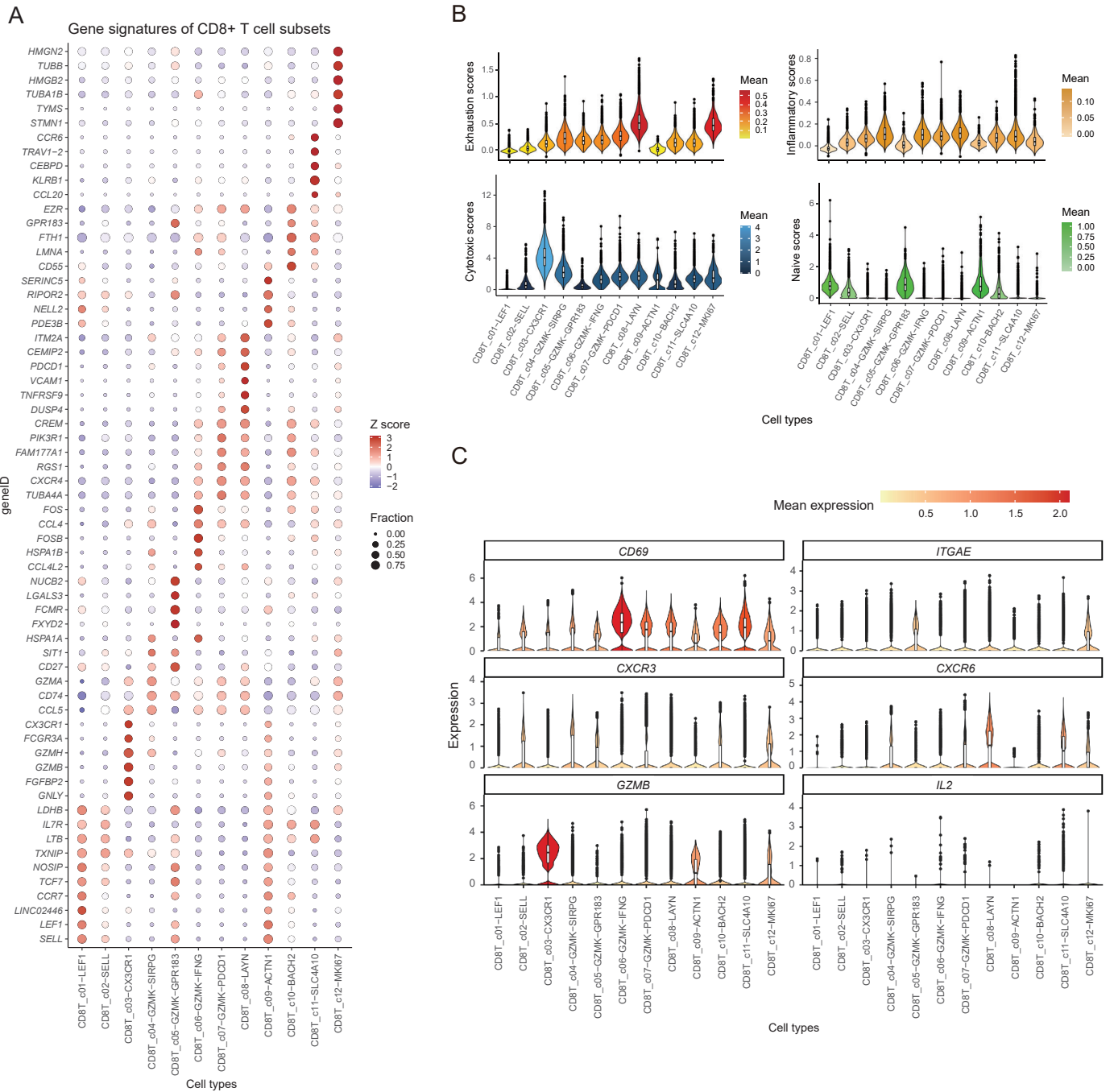
Supplemental figure 2 Basic information of the scRNA-seq data.

(A) Number of read counts (upper), percentage of mitochondrial gene counts (middle), and number of genes (lower) detected in each sample. (B) Bar graph showing the TCR/BCR counts detected in each sample.



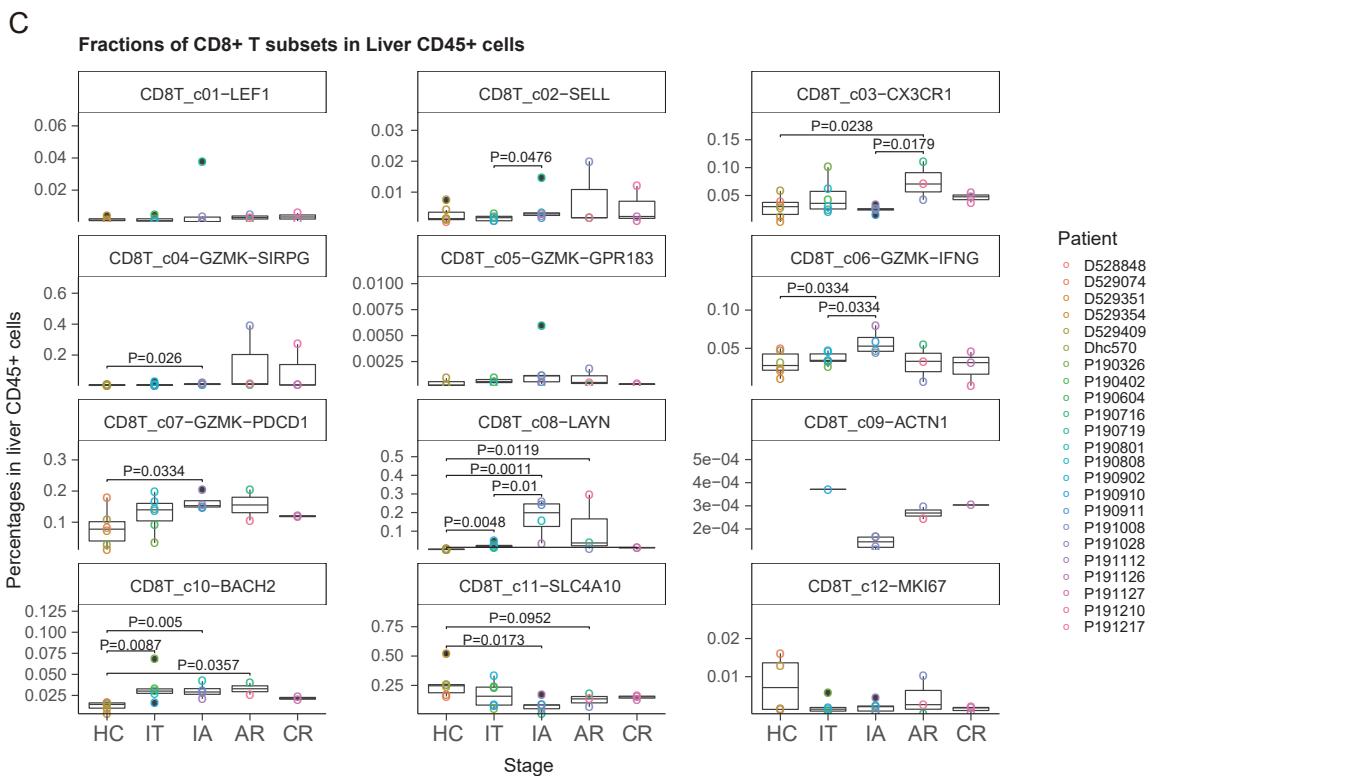
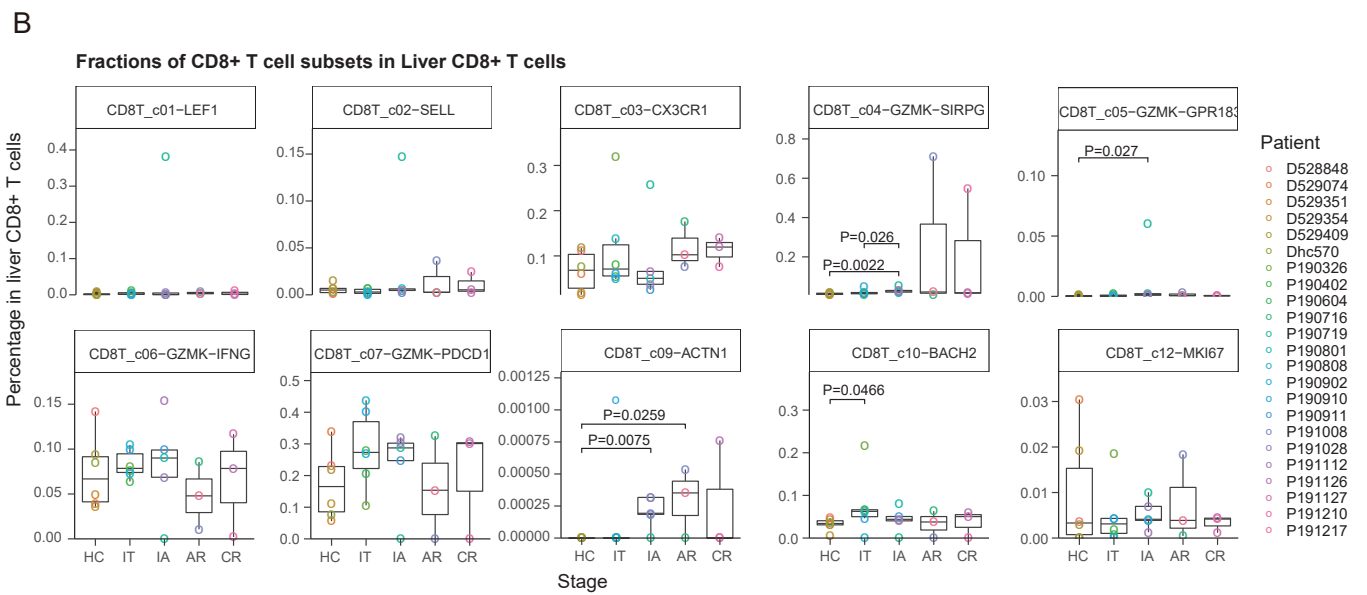
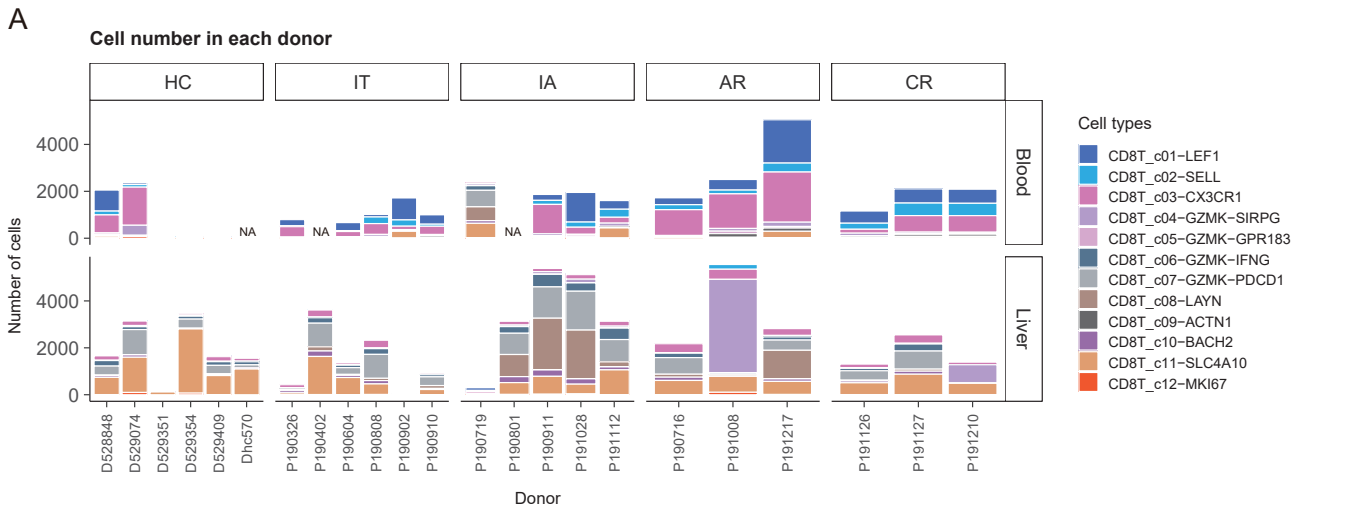
Supplemental figure 3 Major cell types in the blood and liver.

(A) Bar graph showing the number for major cell types detected in each donor. NA, sample not available. (B) The UMAP plots of cell clusters from blood or liver in each group. (C) Heatmap showing the p values for tissue prevalence of major cell clusters estimated by Ro/e score in figure 1E. Fisher's exact test.



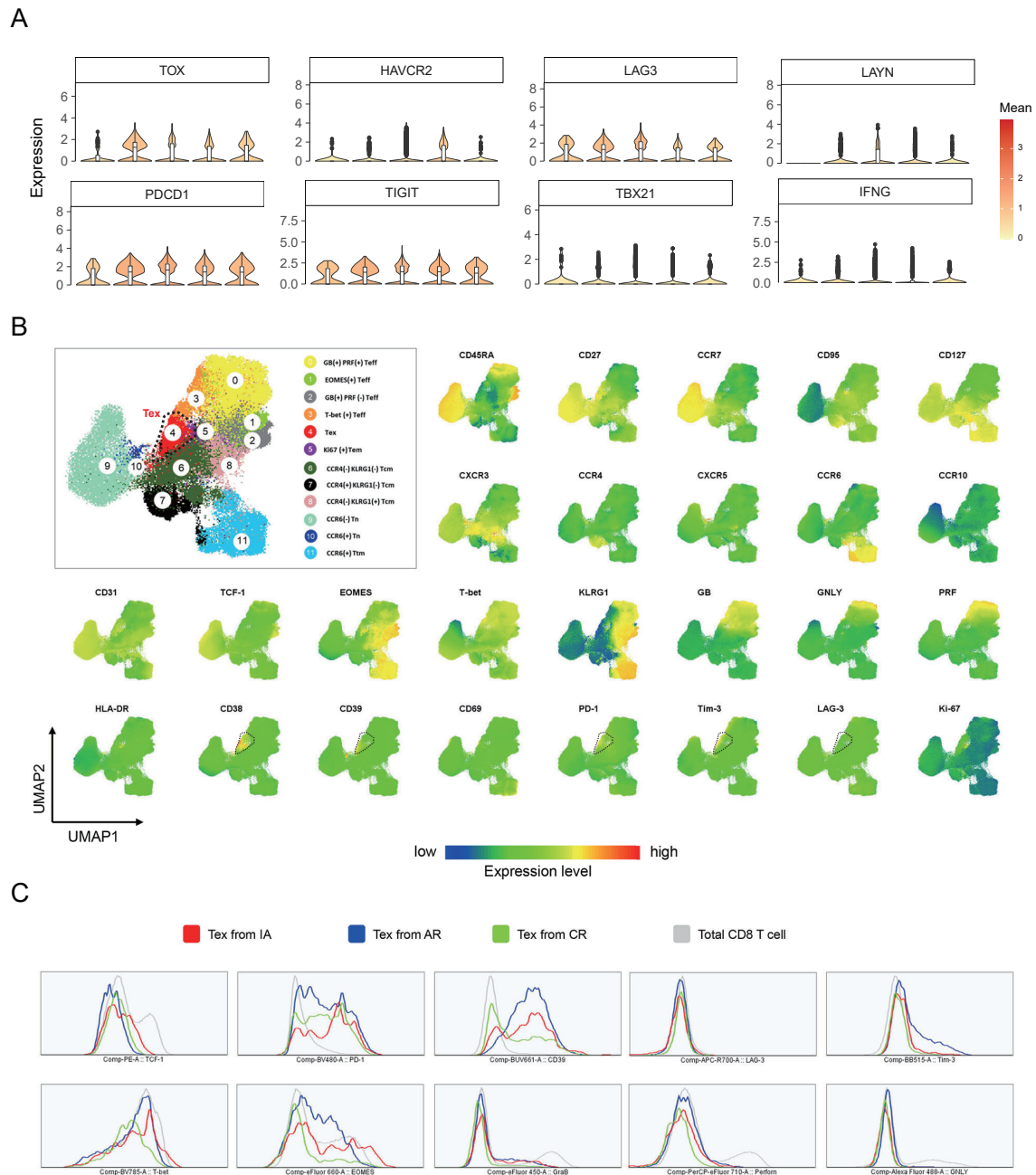
Supplemental figure 4 Gene and functional signatures of CD8+ T cell subsets.

(A) Bubble heatmap showing the gene signatures of CD8+ T cell subsets. (B) Violin plot showing the indicated functional scores of CD8+ T cell subsets. (C) Violin plot showing expression of selected genes in CD8+ T cell subsets.



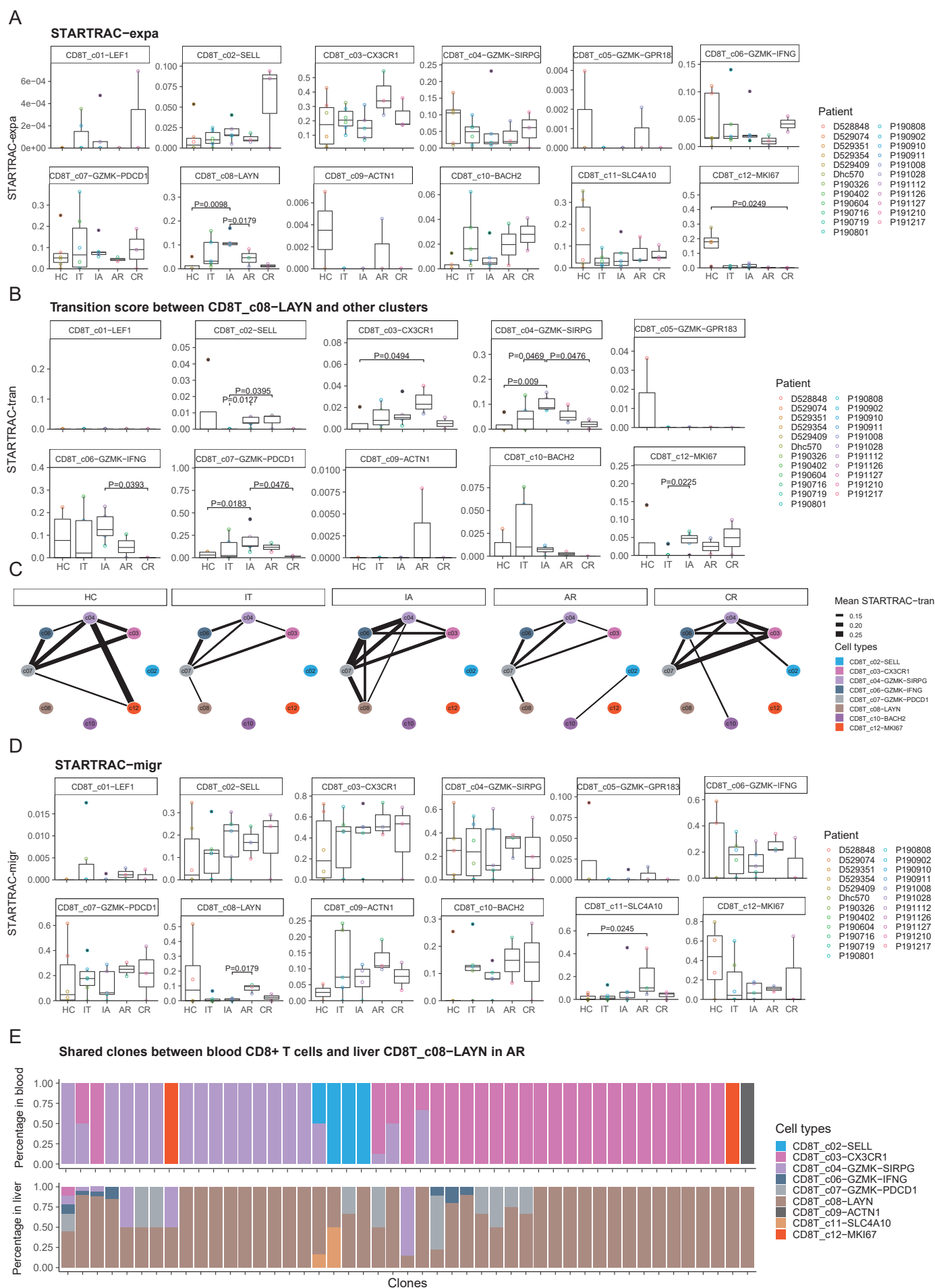
Supplemental figure 5 Changes of intrahepatic CD8+ T cell subsets among stages.

(A) Bar graph showing the number for CD8+ T cell subsets detected in each donor. NA, sample not available. (B) Box plots showing the proportions of indicated cell subsets in liver CD8+ T cells across stages. One-sided unpaired Wilcoxon test. (C) Box plots showing the proportions of CD8+ T cell subsets in liver CD45+ cells across stages. One-sided unpaired Wilcoxon test.



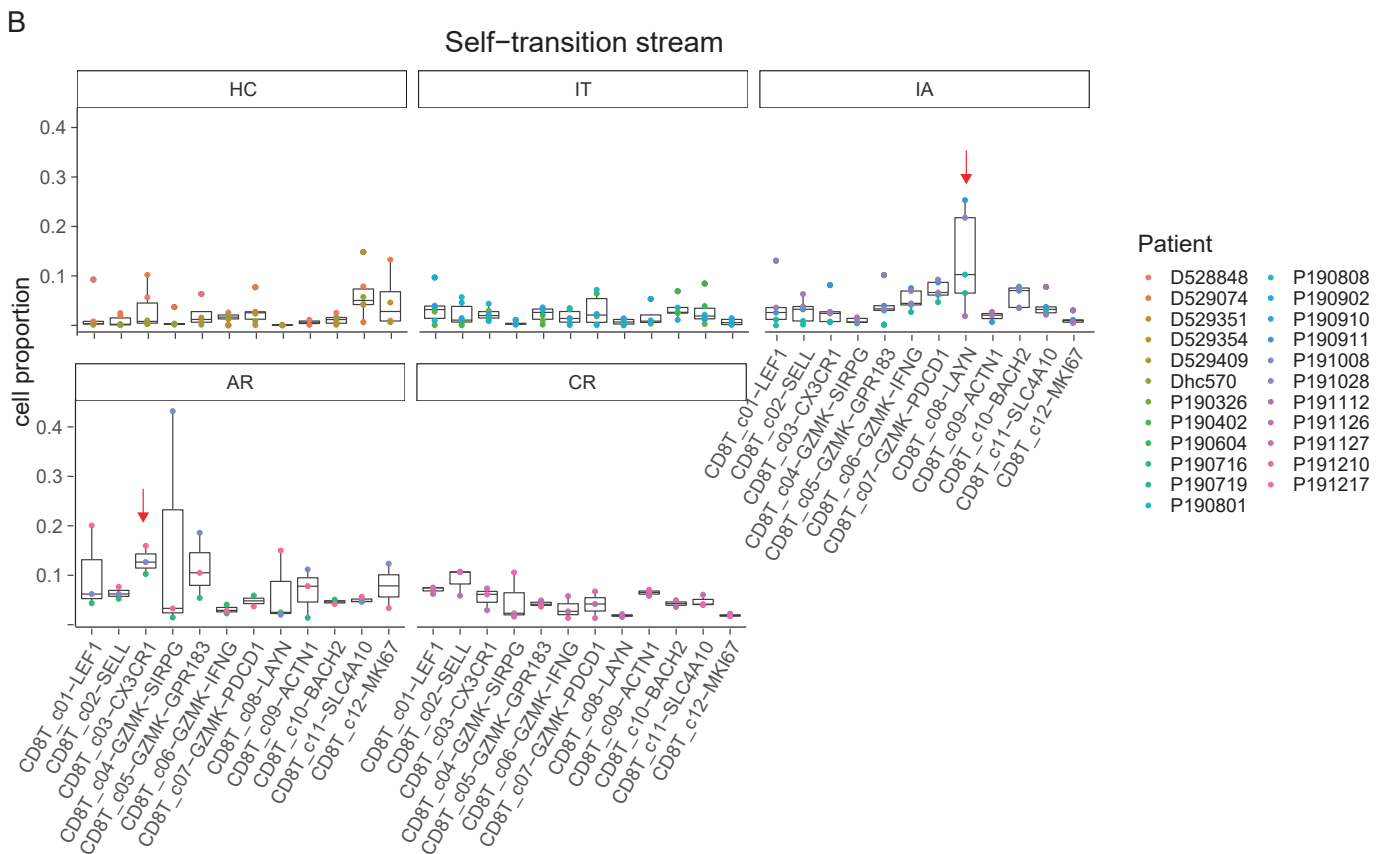
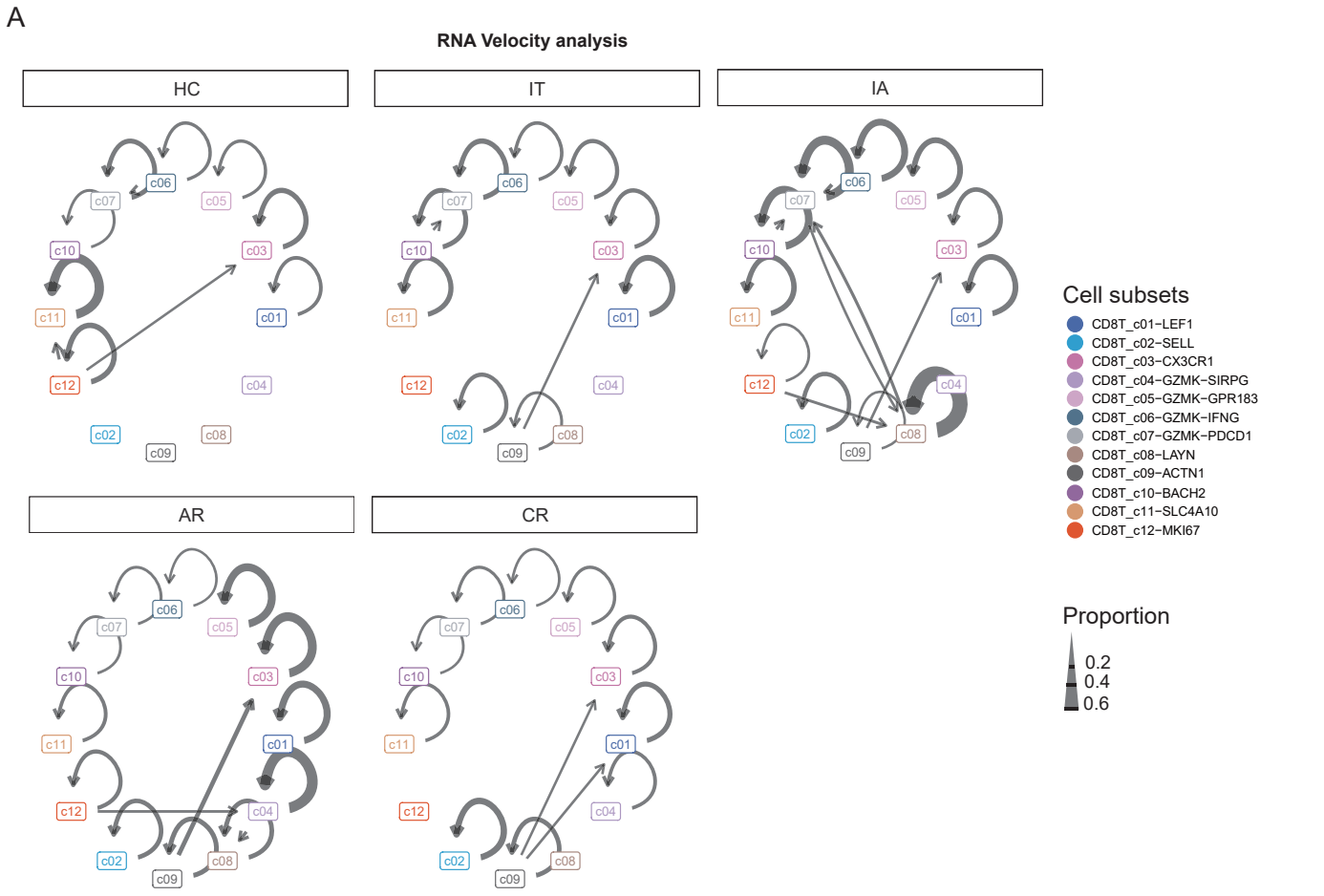
Supplemental figure 6 Phenotypes of exhausted CD8+ T cells in AR patients.

(A) Violin plot showing expression of selected genes in Tex cells in each group. (B) UMAP with FlowSOM overlay showing total CD3+CD8+ T cells of three combined blood samples (including one IA, one AR and one CR). Fifty thousand cells were subsetted from each sample. The UMAP plots of each marker were shown. (C) Histogram graph showing the expression levels of indicated markers in Tex cells among IA, AR and CR.



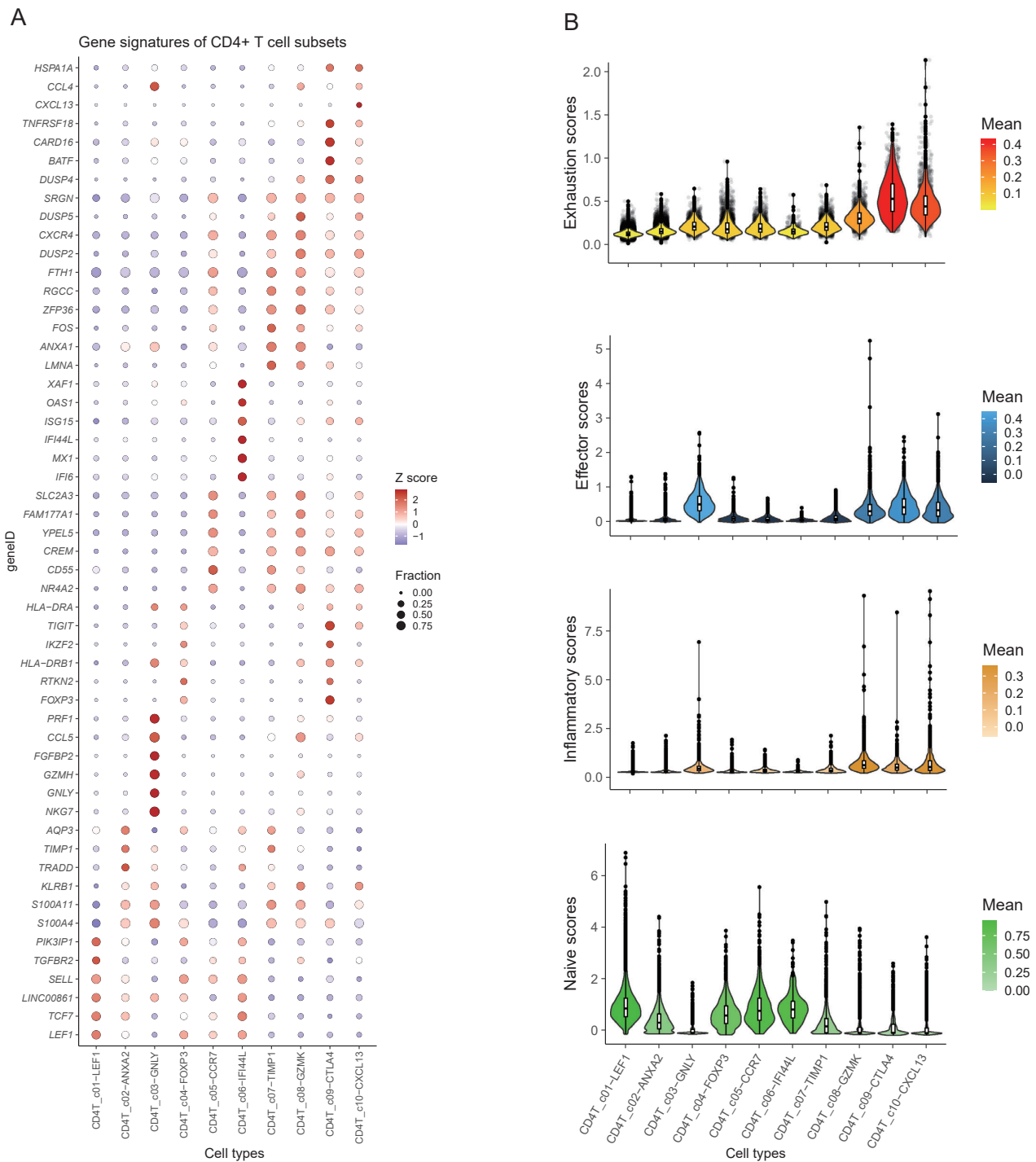
Supplemental figure 7 Dynamics of CD8+ T cells revealed by STARTRAC analysis.

(A) Box plots showing the expansion scores (STARTRAC-expa) of CD8+ T cell subsets across stages. One-sided unpaired Wilcoxon test. (B) Box plots showing the transition scores (STARTRAC-tran) between Tex subsets and other clusters across stages. One-sided unpaired Wilcoxon test. (C) Diagram of transitions among CD8+ T cell subsets in each stage. (D) Box plots showing the migratory scores (STARTRAC-migr) of CD8+ T cell subsets across stages. One-sided unpaired Wilcoxon test. (E) Bar graph showing shared clones between blood CD8+ T cells and liver CD8T_c08-LAYN in AR. Each column represents a unique TCR clonotype.



Supplemental figure 8 Dynamics of CD8+ T cells revealed by RNA velocity analysis.

(A) Diagram showing the self-expansion and transitions of CD8+ T cell subsets in each stage. (B) Box plots showing the levels of self-transition for each CD8+ T cell subset across stages.



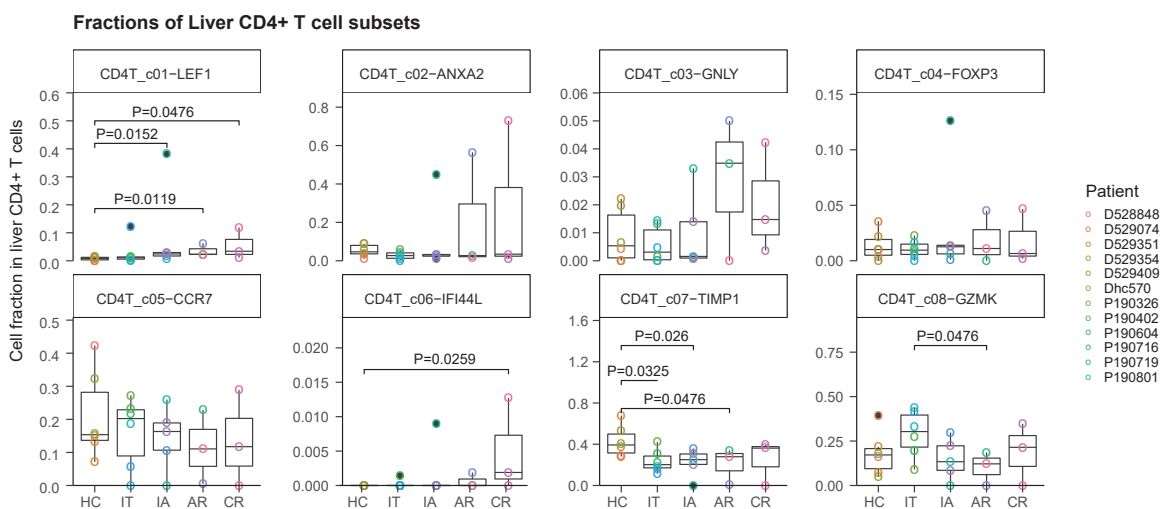
Supplemental figure 9 Gene and functional signatures of CD4+ T cell subsets.

(A) Bubble heatmap showing the gene signatures of CD4+ T cell subsets. (B) Violin plot showing the indicated functional scores of CD4+ T cell subsets.

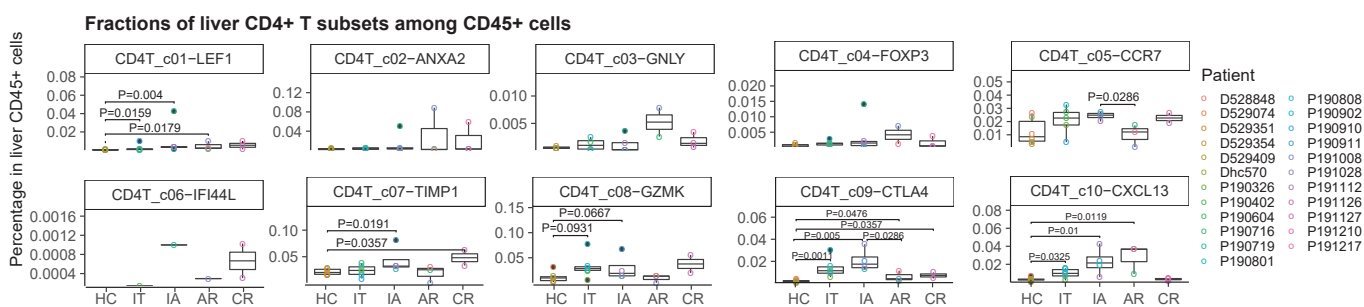
A



B

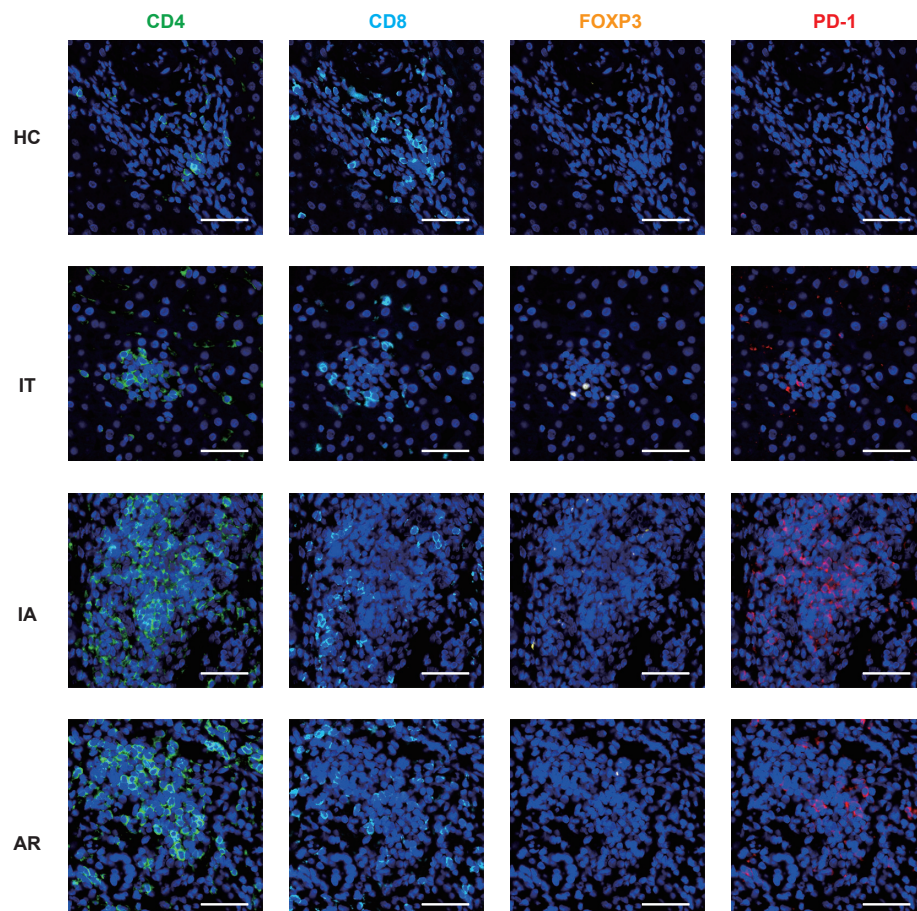


C

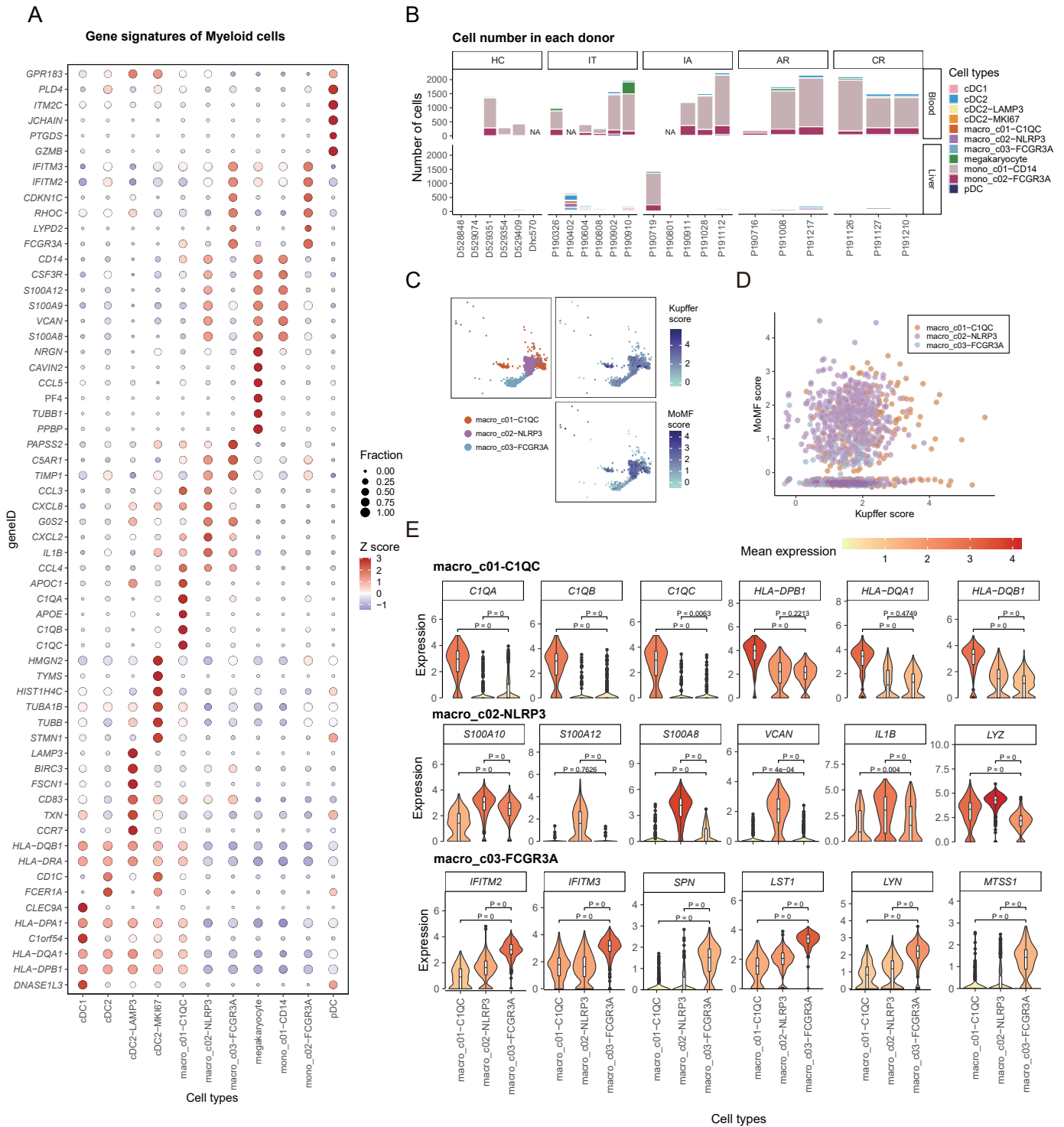


Supplemental figure 10 Changes of intrahepatic CD4+ T cell subsets among stages.

(A) Bar graph showing the number for CD4+ T cell subsets detected in each donor. NA, sample not available. (B) Box plots showing the proportions of indicated cell subsets in liver CD4+ T cells across stages. One-sided unpaired Wilcoxon test. (C) Box plots showing the proportions of CD4+ T cell subsets in liver CD45+ cells across stages. One-sided unpaired Wilcoxon test.



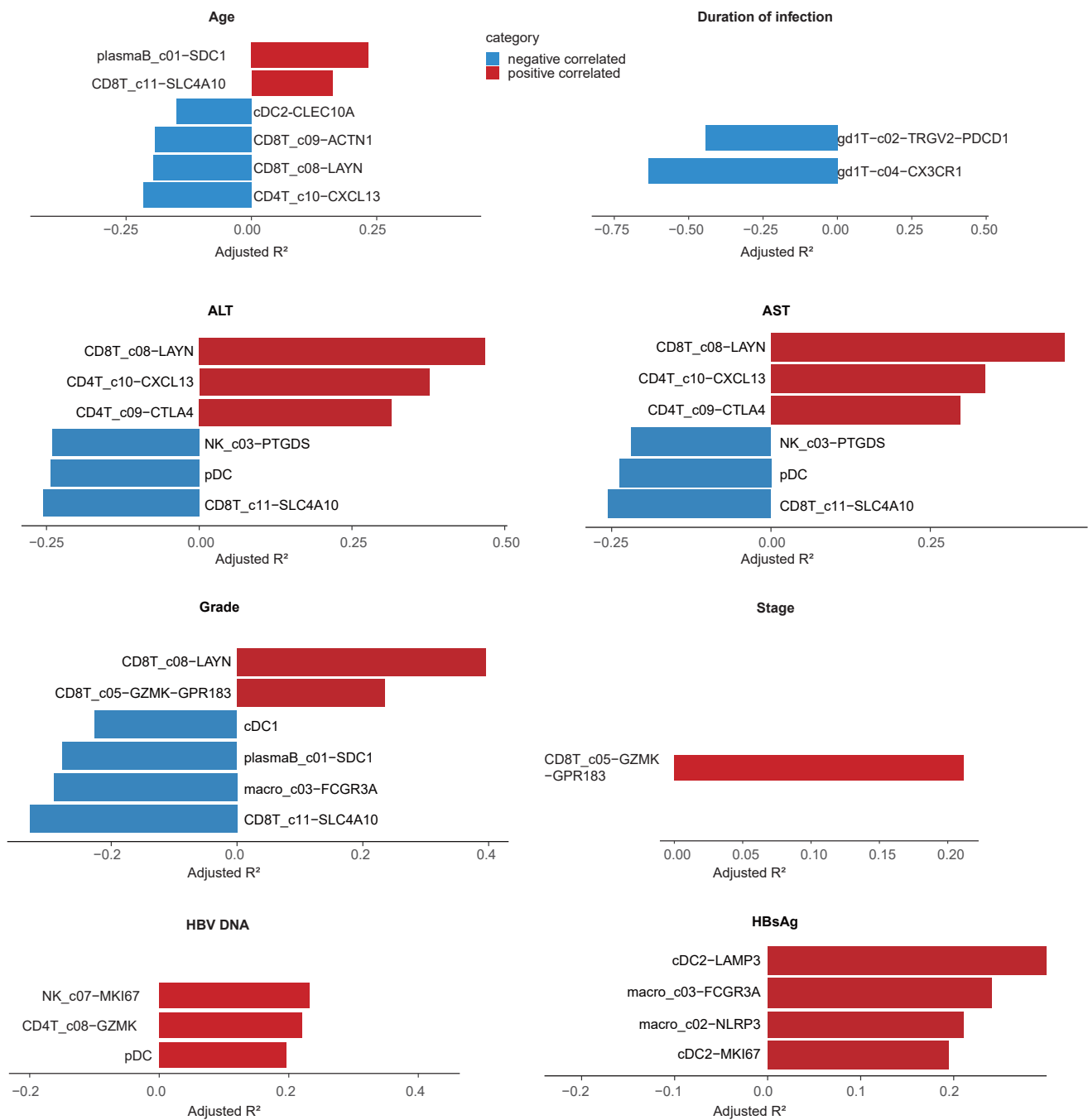
Supplemental figure 11 Multicolor IHC staining of Treg and Tex cells in the liver across HC, IT, IA and AR groups. Single-marker staining in representative visual fields as shown in figure 4B. Scale bar, 50 μ m.



Supplemental figure 12 Gene and functional signatures of Myeloid cell subsets.

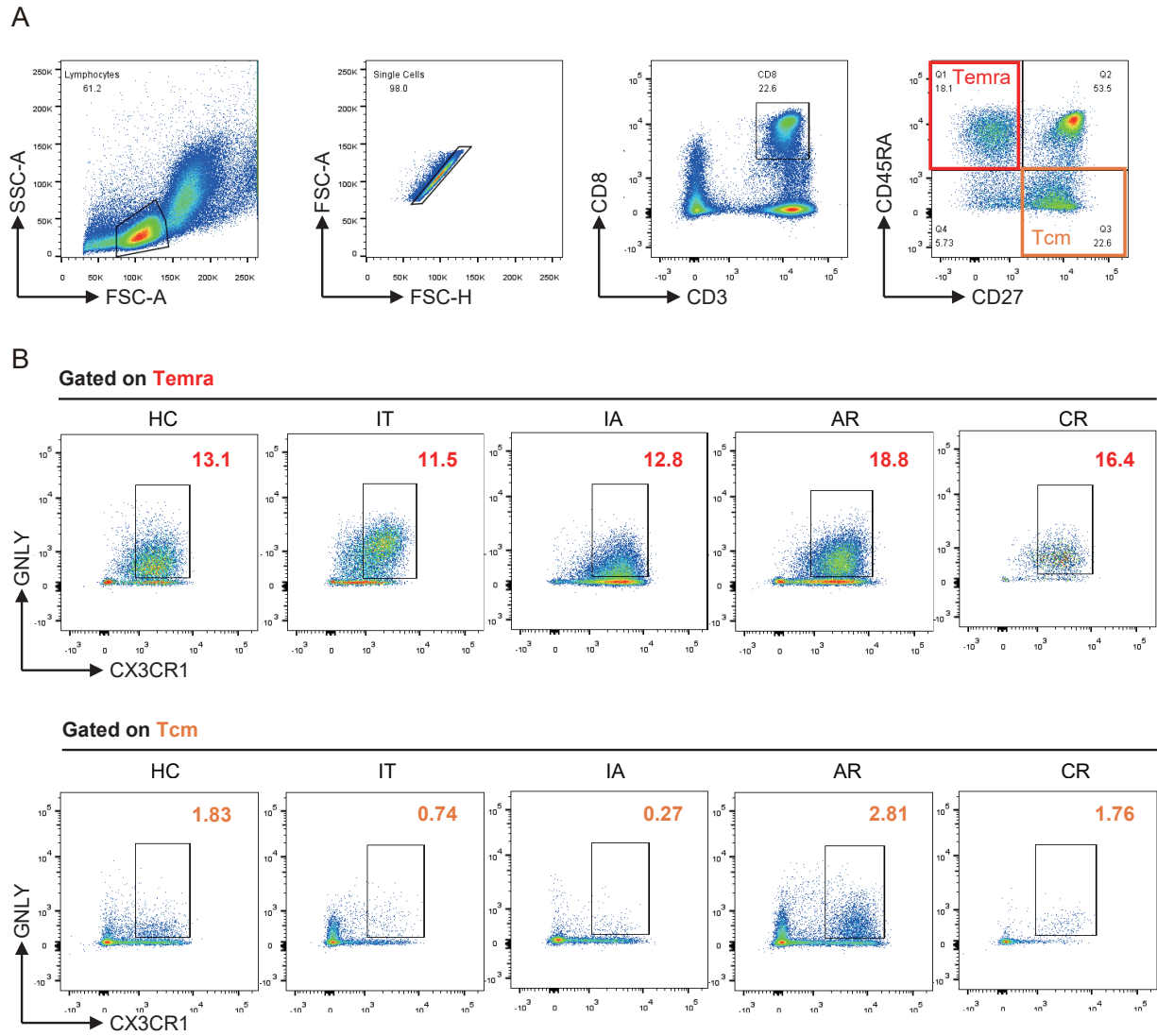
(A) Bubble heatmap showing the gene signatures of Myeloid cell subsets. (B) Bar graph showing the number for Myeloid cell subsets detected in each donor. NA, sample not available. (C) The UMAP plots of macrophage subsets showing distributions of Kupffer score and MoMF score. (D) Dot plots of macrophages defined by Kupffer score and MoMF score. (E) Violin plot showing the expression of indicated genes in macrophage subsets. One-sided unpaired Wilcoxon test.

Associations of liver immune subsets with clinical parameters



Supplemental figure 13 Associations of liver immune subsets with clinical parameters.

Horizontal bar plots showing the correlations of liver immune subsets with indicated clinical parameters.



Supplemental figure 14 Flow cytometric validation of CX3CR1+ CD8+ T cells.

(A) Gating strategies for Temra and Tcm. (B) Representative flow cytometry plots showing gating strategy and individual frequencies of GNLY+CX3CR1+ cells among CD8+ T cells in each stage.

The characteristics of T cells and myeloid cells across different phases of HBV-infected patients

Cell clusters	Representative genes	Functional properties	Tissue preference	Stage enrichment (liver)					
				HC	IT	IA	AR	CR	
CD8+ T	CD8T_c01-LEF1	<i>LEF1, CCR7</i>	Tn	blood	-	-	-	-	-
	CD8T_c02-SELL	<i>SELL</i>	Tcm	blood	-	-	-	-	-
	CD8T_c03-CX3CR1	<i>GZMB, GNLY, CX3CR1, FCGR3A, ADGRG1, PRSS23</i>	Temra	blood	-	-	-	+	-
	CD8T_c04-GZMK-SIRPG	<i>GZMK, SIRPG</i>	Tem	liver	-	-	+	-	-
	CD8T_c05-GZMK-GPR183	<i>TCF7, HAVCR2, GZMK</i>	Tem	blood	-	-	-	-	-
	CD8T_c06-GZMK-IFNG	<i>GZMK, IFNG</i>	Tem	liver	+	+	+	+	+
	CD8T_c07-GZMK-PDCD1	<i>GZMK, PDCD1</i>	Tem	liver	+	++	++	++	+
	CD8T_c08-LAYN	<i>PDCD1, TIGIT, LAYN, TOX, TNFRSF9, CTLA4, HAVCR2</i>	Tex	liver	-	+	+++	++	-
	CD8T_c09-ACTN1	<i>LEF1, SERINC5, MAL, NELL2, ACTN1, TXK, STX16</i>	Tcm	blood	-	-	-	-	-
	CD8T_c10-BACH2	<i>BACH2</i>	Tcm	liver	+	++	++	++	+
CD8T_c11-SLC4A10	<i>SLC4A10</i>	MAIT	liver	+++	++	+	++	++	
CD8T_c12-MKI67	<i>MKI67, PCNA</i>	proliferating T	blood and liver	+	+	+	+	+	
CD4+ T	CD4T_c01-LEF1	<i>LEF1, SELL, TCF7</i>	Tn	blood	+	+	+	+	+
	CD4T_c02-ANXA2	<i>S100A4, ANXA2, KLRB1</i>	Tcm	blood	-	-	-	Tcm	-
	CD4T_c03-GNLY	<i>GNLY, GZMH, CCL5, PRF1, GZMB, CX3CR1, CCL4, TBX21</i>	Temra	blood	-	-	-	+	-
	CD4T_c04-FOXP3	<i>FOXP3, TIGIT, IL2RA, SELL</i>	Treg	blood	-	-	-	-	-
	CD4T_c05-CCR7	<i>CCR7, NR4A2, CREM, CD55, SLC2A3</i>	Tcm	liver	+	+	+	+	+
	CD4T_c06-IFI44L	<i>IFI44L, OAS1, IFIT3, IFIT1</i>	interferon-induced Tn	blood	-	-	-	-	-
	CD4T_c07-TIMP1	<i>TIMP1, FOS, CCR6, TIPARP</i>	Tcm	liver	+	+	+	+	+
	CD4T_c08-GZMK	<i>CXCR4, CCL5, GZMA, GZMK, DUSP5, RGS1, FOSL2</i>	Tem	liver	+	++	+	+	+
	CD4T_c09-CTLA4	<i>CTLA4, FOXP3, TNFRSF18, BATF, PDCD1, CXCR6, TIGIT, MAF, TOX, TOX2</i>	Treg	liver	+	++	+++	+	+
CD4T_c10-CXCL13	<i>CXCL13, HSPA1A, DUSP4, TIGIT, ICOS</i>	Th-1 like	liver	-	+	++	+++	-	
Myeloid	cDC1	<i>CLEC9A, DNASE1L3, C1orf54</i>	cDC1	liver	+	++	+	+	+
	cDC2-CLEC10A	<i>CLEC10A, CD1C, FCER1A</i>	cDC2	liver	+	++	+	+	+
	cDC2-LAMP3	<i>LAMP3, FSCN1, CD83, TXN, CCR7</i>	acitved cDC2	liver	-	+	-	-	-
	cDC2-MKI67	<i>MKI67</i>	proliferating cDC2	liver	-	+	-	-	-
	macro_c01-C1QC	<i>C1QA, C1QB, C1QC, APOE, CD83</i>	mature macrophage	liver	+	++	+	+	+
	macro_c02-NLRP3	<i>IL1B, CXCL2, CXCL8</i>	proinflammatory macrophage	liver	+	+	+	+	+
	macro_c03-FCGR3A	<i>FCGR3A, C5AR1, TIMP1</i>	regulatory macrophage	liver	+	++	+	+	+
	megakaryocyte	<i>PPBP, TUBB1, PF4</i>	megakaryocyte	blood	-	-	-	-	-
	mono_c01-CD14	<i>S100A8, VCAN, CD14</i>	CD14+ monocyte	blood	-	-	-	-	-
	mono_c02-FCGR3A	<i>FCGR3A, IFITM2, IFITM3</i>	CD16+ monocyte	blood	-	-	-	-	-
pDC	<i>GPR183, GZMB, PLD4, PTGDS</i>	pDC	liver	+	++	+	+	++	

Supplemental figure 15 Summary of findings from scRNA-seq data in this study.

The characteristics of T cells and myeloid cells across different phases of HBV-infected patients.