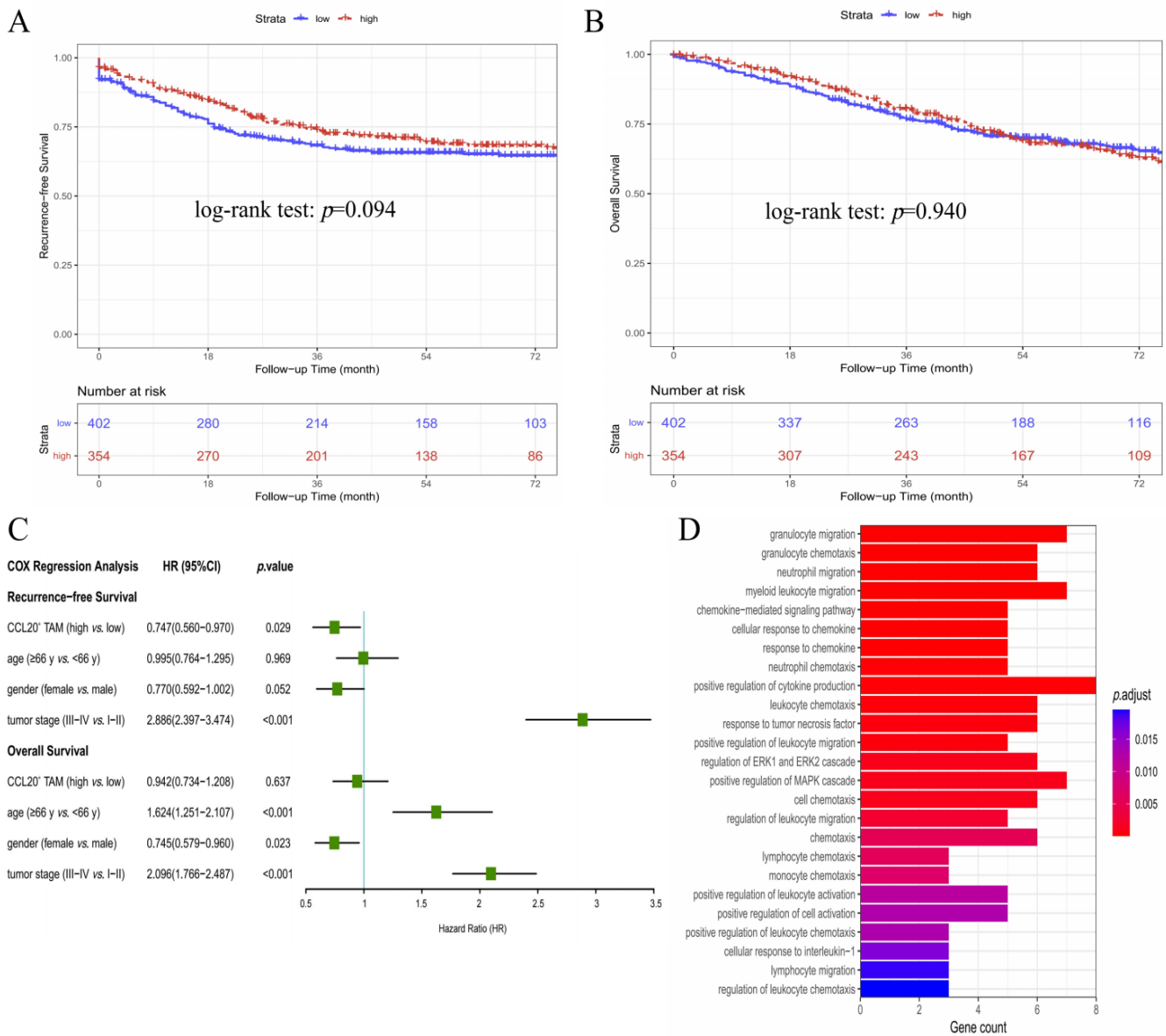
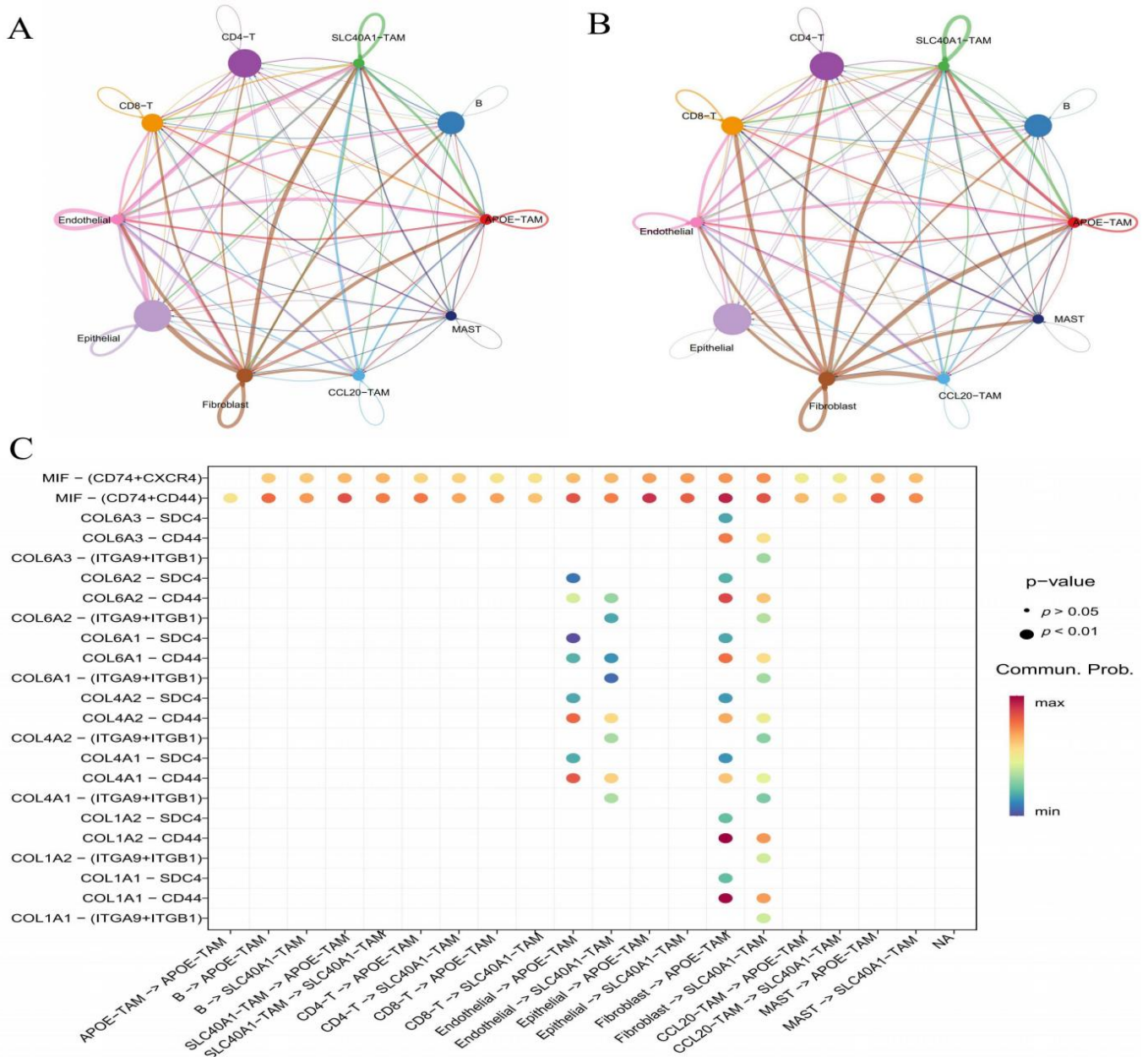


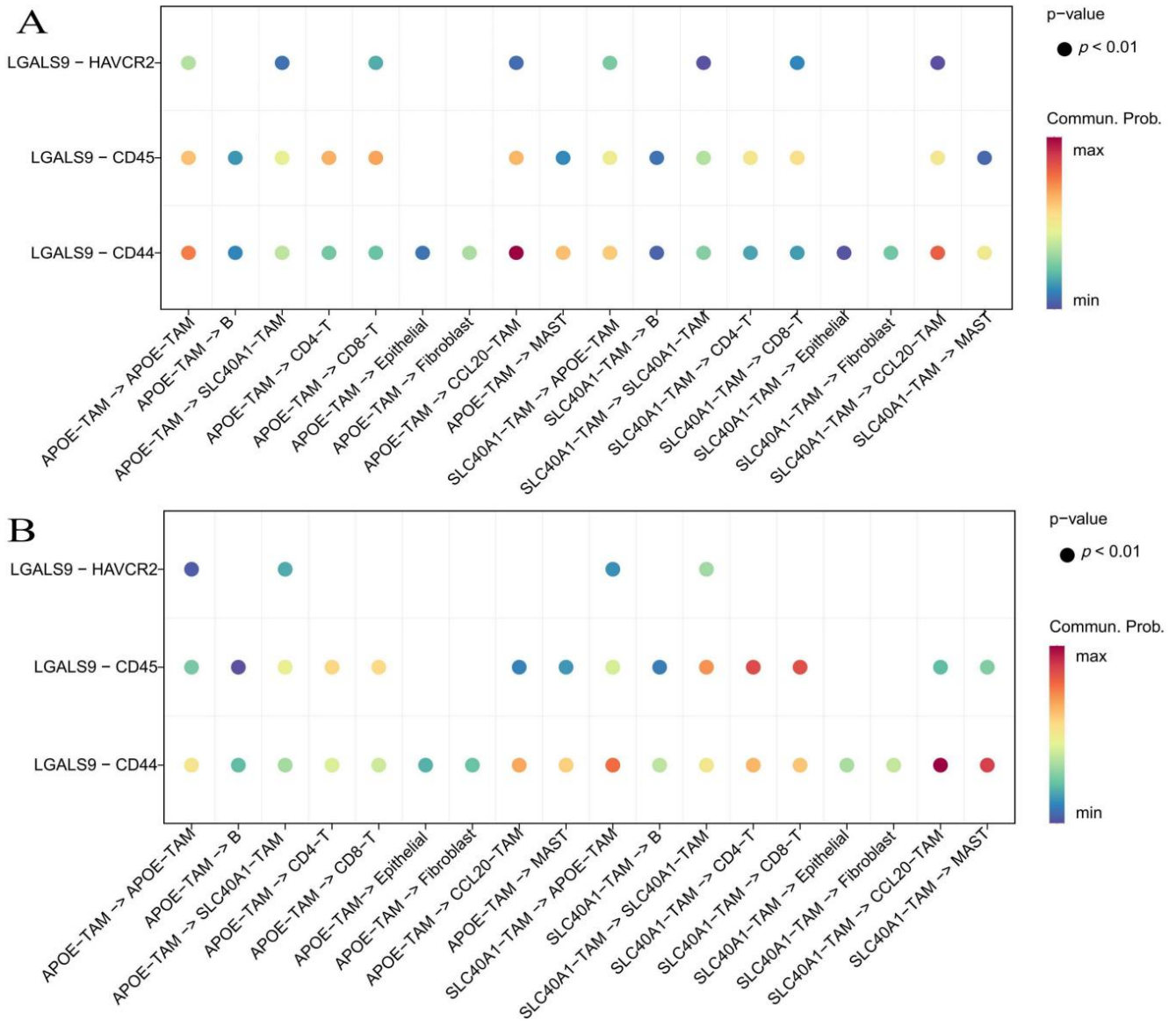
Supplementary Figure S1. The integrated single-cell atlas of primary CRC tumors and adjacent normal tissues in the validation cohort. (A) The t-SNE plot of 202390 cells. (B) Dot plot showing the marker gene expression of seven major cell types. (C) Balloon plot showing the distribution of seven major cell types between primary CRC tumors and adjacent normal tissues. (D) The t-SNE plot of 20997 myeloid cells. (E) Dot plot showing the expression of the marker genes of nine myeloid cell subsets. (F) Balloon plot showing the distribution of nine myeloid cell subsets between primary tumors and adjacent normal tissues.



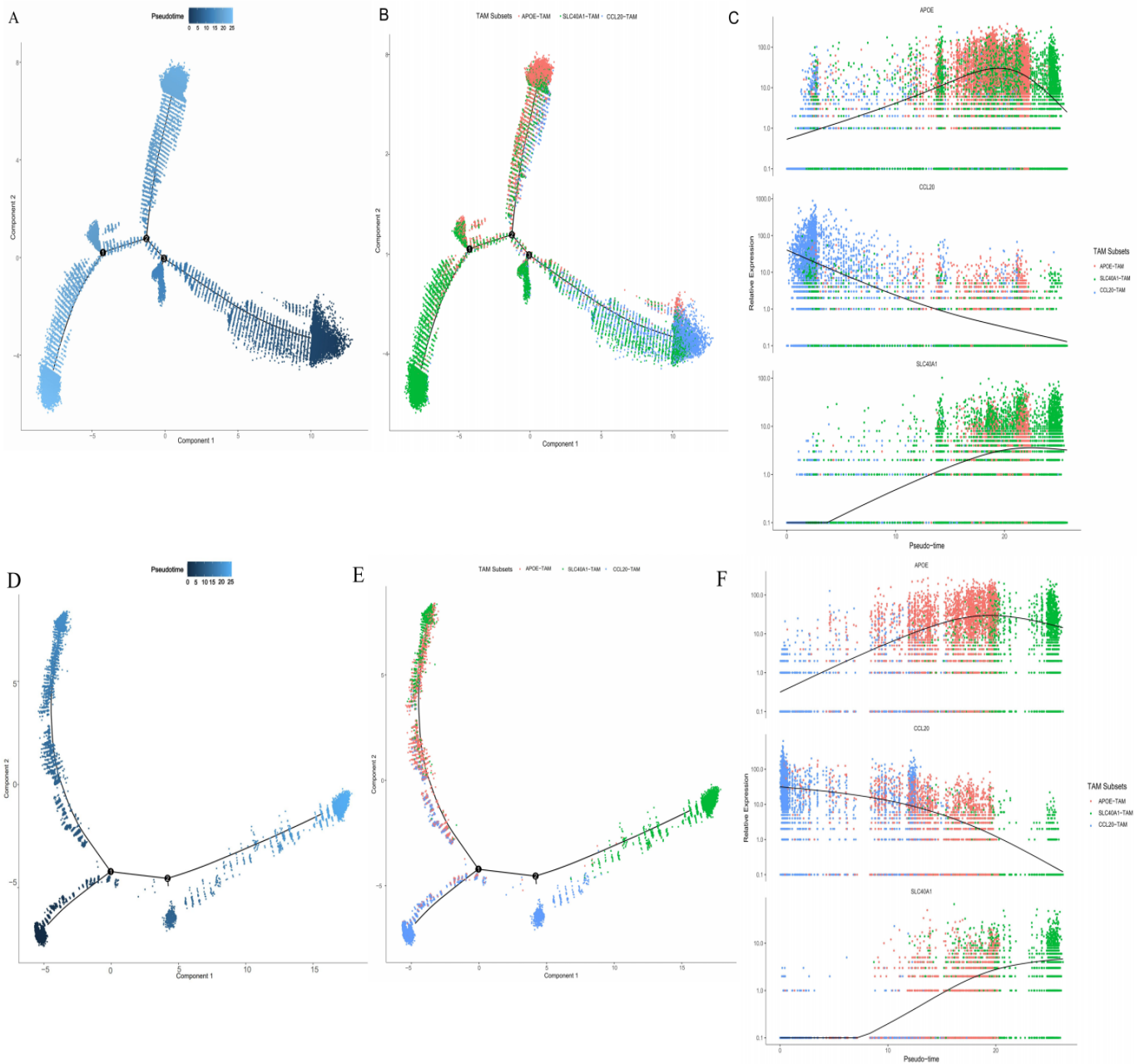
Supplementary Figure S2. Survival analysis and functional analysis of CCL20⁺ TAMs. (A) The Kaplan–Meier curve of recurrence-free survival for CCL20⁺ TAMs. (B) The Kaplan–Meier curve of overall survival for CCL20⁺ TAMs. (C) The COX regression analysis of recurrence-free and overall survival for CCL20⁺ TAMs. (D) GO analysis of CCL20⁺ TAMs.

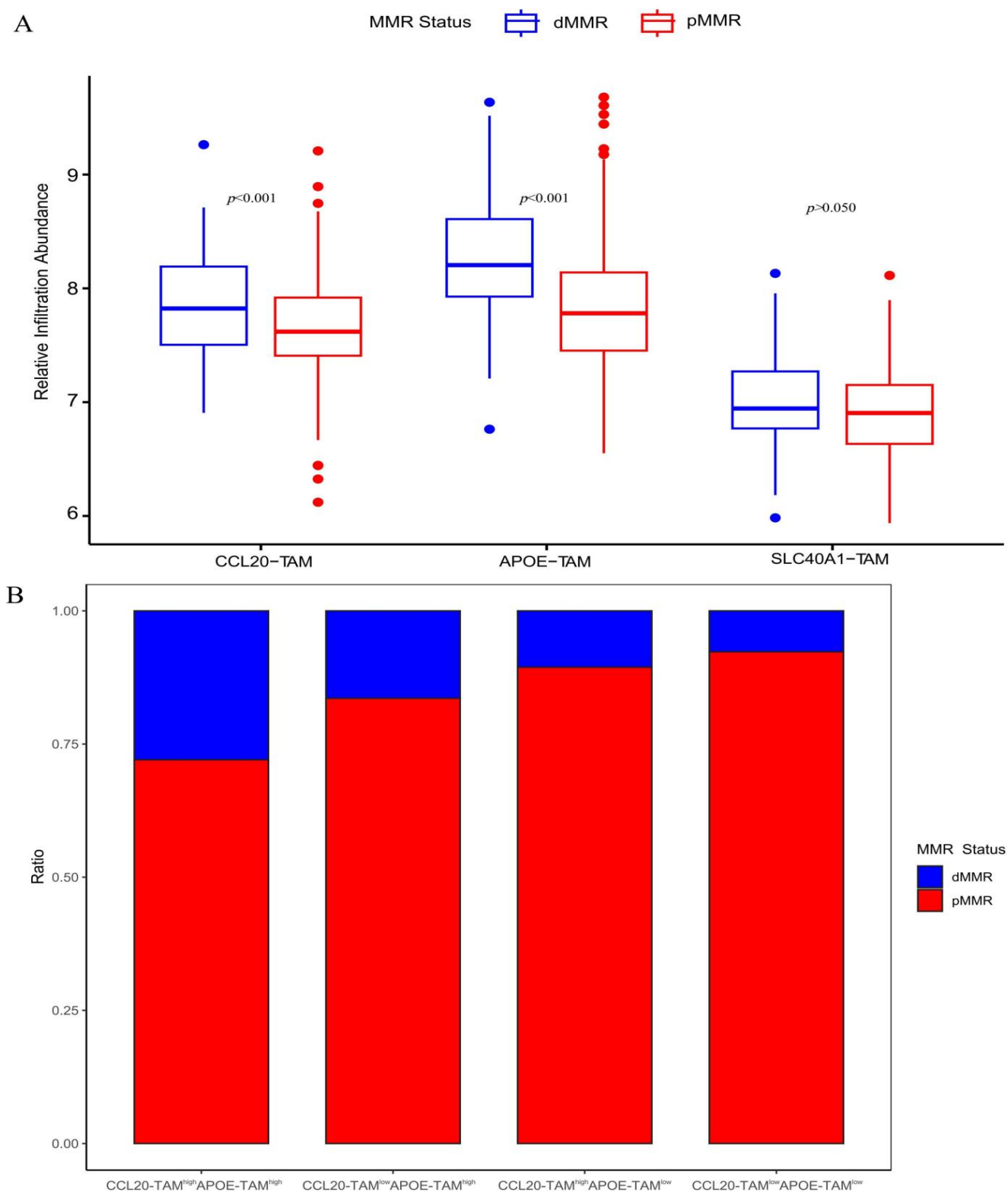


Supplementary Figure S3. Cell communication analysis between different TAM subsets and other cell types in the validation cohort. (A) Number of interactions between different cell types. (B) Strength of interactions between different cell types. (C) Dot plot of cell communications between other cell types and TAM subtypes.



Supplementary Figure S4. Dot plot of cell communication between TAM subtypes and other cell types in the training (A) and validation (B) cohorts.





Supplementary Figure S6. The relationship of TAM subsets and MMR status in the microarray dataset. (A) The infiltration abundance of three TAM subsets between dMMR and pMMR status. (B) The proportion of dMMR status among four groups.

Supplementary Table S1. Sources of the scRNA-seq and bulk RNA-seq datasets in the discovery and validation cohorts.

Study Cohort	Dataset	Platform	Original	Number of Primary Tumor	Number of Normal Tissue
Training Cohort	GSE178341	10x Genomics	USA	129	52
	GSE200997	10x Genomics	USA	16	7
	GSE231559	10x Genomics	USA	6	3
Validation Cohort	GSE132257	10x Genomics	South Korea	5	5
	GSE132465	10x Genomics	South Korea	23	10
	GSE144735	10x Genomics	South Korea	6	6
	GSE221575	10x Genomics	China	2	2
	GSE245552	10x Genomics	China	16	4
Microarray Cohort	GSE39582	GPL570	France	556	–
	GSE17538	GPL570	USA	200	–

Supplementary Table S2. Canonical markers for determining seven major types and eight myeloid cell subsets in the training and validation cohorts.

Cell Types	Canonical Markers
Seven Major Types	
T/NK cells	CD3D, CD3E, CD3G, GZMB
B cells	MS4A1, CD79A, FCRL5
mast cells	CPA3, TPSAB1, TPSB2, KIT
myeloid cells	MS4A6A, LYZ, CD68, CD14
endothelial cells	VWF, PECAM1, ENG
epithelial cells	EPCAM, CDH1, KRT8
fibroblasts	COL1A2, COL1A1, COL3A1, DCN
Eight Myeloid Cell Subsets	
monocyte	S100A8, S100A9, S100A12
neutrophils	G0S2, FCGR3B, CSF3R
CCL20 ⁺ TAMs	CCL20, IL1B, EREG
APOE ⁺ TAMs	APOE, FABP5, SPP1, APOC1
SLC40A1 ⁺ TAMs	SLC40A1, SEPP1, C1QC, C1QB
CD1C ⁺ dendritic cells	FCER1A, CD1C, CD1E, CLEC10A
LAMP3 ⁺ dendritic cells	LAMP3, BIRC3, FSCN1, CCR7
LILRA4 ⁺ dendritic cells	JCHAIN, LILRA4, CLEC4C, MZB1

Supplementary Table S3. all co-upregulated genes of CCL20⁺ TAMs, APOE⁺ TAMs, and SLC40A1⁺ TAMs in the training and validation cohorts .

TAM subsets	Gene Symbol	Discovery Cohort			Validation Cohort			
		log2FC	pct.1	pct.2	log2FC	pct.1	pct.2	
CCL20 ⁺ TAMs	CCL20	4.547	0.476	0.116	3.671	0.680	0.178	
	IL1A	3.429	0.287	0.038	3.178	0.402	0.126	
	INHBA	3.393	0.331	0.078	3.244	0.445	0.092	
	CXCL3	3.280	0.583	0.265	2.640	0.751	0.322	
	CXCL2	2.717	0.631	0.302	2.475	0.858	0.396	
	EREG	2.715	0.563	0.162	2.791	0.744	0.197	
	CD300E	2.237	0.567	0.171	1.841	0.427	0.113	
	CCL3	2.133	0.684	0.432	2.691	0.918	0.452	
	TIMP1	2.097	0.924	0.670	2.902	0.956	0.535	
	THBS1	1.980	0.386	0.194	1.693	0.288	0.112	
	CLEC5A	1.969	0.477	0.217	1.813	0.274	0.109	
	MMP19	1.942	0.387	0.188	1.626	0.274	0.143	
	HSPH1	1.903	0.378	0.346	1.919	0.447	0.335	
	EAF1	1.787	0.278	0.133	1.926	0.251	0.109	
	DNAJB1	1.747	0.422	0.380	1.629	0.535	0.452	
	CD44	1.729	0.937	0.667	1.660	0.937	0.599	
	CCL4	1.719	0.493	0.339	1.881	0.814	0.430	
	OLR1	1.672	0.576	0.292	1.946	0.537	0.212	
	C15orf48	1.659	0.810	0.563	2.365	0.905	0.448	
	APOE ⁺ TAMs	PLIN2	1.633	0.627	0.446	1.804	0.628	0.373
SDC4		1.541	0.273	0.151	2.065	0.254	0.110	
APOC1		2.531	0.835	0.258	3.568	0.796	0.157	
APOE		2.674	0.850	0.241	3.388	0.836	0.168	
NUPR1		2.271	0.515	0.092	3.554	0.487	0.076	
SPP1		2.31	0.779	0.264	2.848	0.581	0.122	
GPNMB		2.54	0.908	0.239	2.558	0.760	0.173	
TREM2		2.488	0.661	0.135	2.573	0.522	0.096	
MMP12		2.285	0.48	0.191	2.363	0.467	0.111	
MSR1		2.281	0.721	0.193	2.212	0.580	0.143	
CD9		2.128	0.854	0.284	2.092	0.728	0.202	
CTSD		2.043	0.992	0.605	1.685	0.951	0.504	
FABP5		1.748	0.834	0.398	1.977	0.723	0.279	
MMP14		1.741	0.687	0.216	1.904	0.584	0.161	
MMP9		1.501	0.529	0.201	1.872	0.574	0.158	
LIPA		1.654	0.852	0.349	1.553	0.625	0.216	
ACP5		1.622	0.851	0.362	1.734	0.393	0.113	
SLC40A1 ⁺ TAMs		SEPP1	3.315	0.375	0.133	3.330	0.293	0.100
		FOLR2	2.222	0.291	0.120	3.991	0.586	0.080
		PDK4	2.141	0.277	0.129	3.937	0.379	0.046
	SLC40A1	2.586	0.517	0.190	3.260	0.743	0.128	
	STMN1	2.770	0.414	0.184	2.533	0.535	0.143	
	GATM	2.236	0.291	0.110	3.065	0.387	0.058	
	C1QC	1.802	0.755	0.375	3.392	0.962	0.259	
	GPR34	1.940	0.445	0.209	3.242	0.595	0.094	
	FUCA1	1.995	0.384	0.229	3.087	0.528	0.111	
	ENPP2	1.543	0.291	0.144	3.058	0.456	0.089	
	CKS1B	2.329	0.253	0.117	2.150	0.265	0.083	
	HIST1H4C	2.240	0.323	0.209	2.130	0.444	0.136	
	C1QB	1.614	0.771	0.386	2.697	0.961	0.272	
	C1QA	1.606	0.792	0.415	2.472	0.968	0.292	
	AXL	1.851	0.388	0.168	2.114	0.487	0.113	
S100B	1.789	0.331	0.145	1.666	0.297	0.079		

Abbreviations: log2FC=log2 fold-change;pct.1=the percentage of cells in the cluster where the gene is detected; pct.2=the percentage of cells on average in all the other clusters where the gene is detected.

Supplementary Table S4. Marker Genes for Three TAM subsets (CCL20⁺ TAMs, APOE⁺ TAMs, and SLC40A1⁺ TAMs).

TAM Subsets	Marker Genes
CCL20 ⁺ TAMs	CCL20, IL1A, INHBA, CXCL3, EREG, CXCL2, TIMP1, CCL3, C15orf48, HSPH1, CLEC5A, EAF1, THBS1, OLR1, SDC4
APOE ⁺ TAMs	APOE, APOC1, NUPR1, SPP1, GPNMB, TREM2, MMP12, MSR1, CD9, CTSD, FABP5, MMP14, MMP9, LIPA, ACP5
SLC40A1 ⁺ TAMs	SLC40A1, SEPP1, FOLR2, PDK4, STMN1, GATM, C1QC, GPR34, FUCA1, ENPP2, CKS1B, C1QB, C1QA, AXL, S100B