Supplementary Information

IgG4 expressing plasma cells and altered B cell receptor light chain usage in chronic obstructive pulmonary disease

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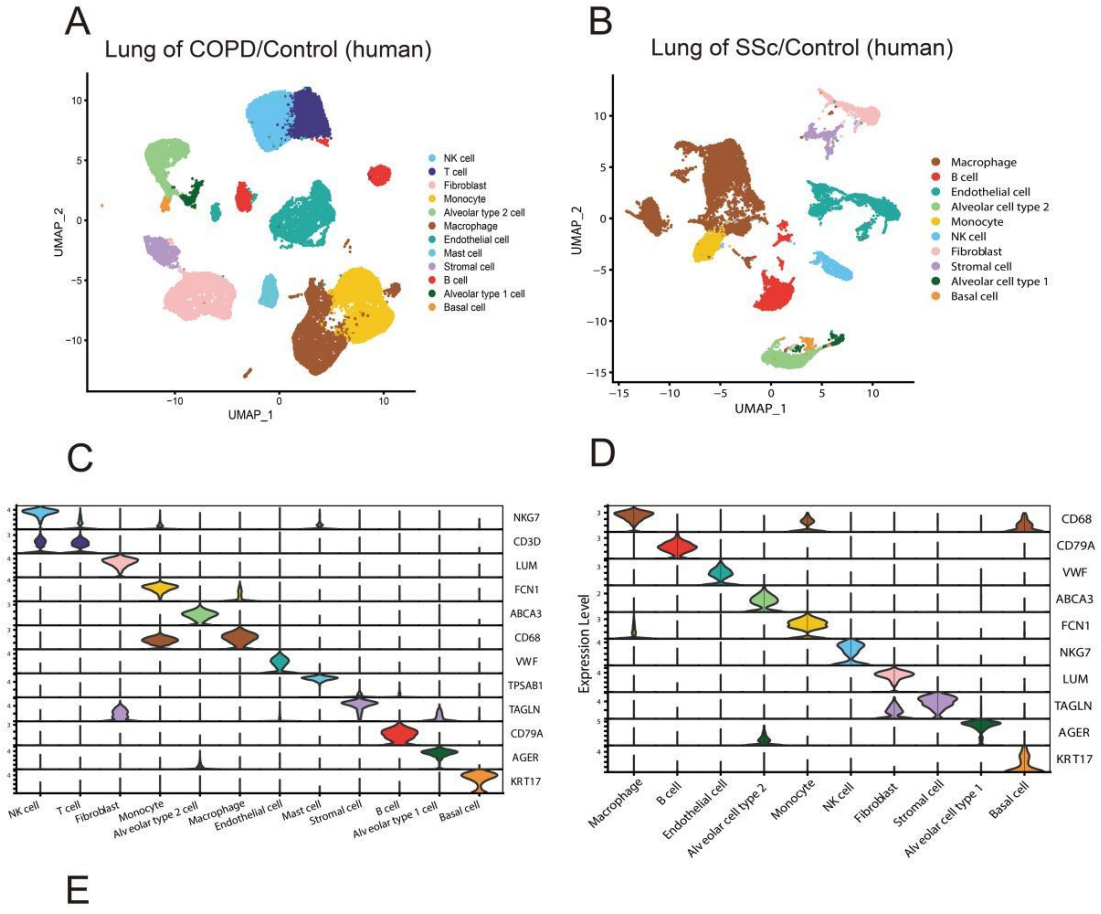
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Supplementary Figures and legends

Supplementary Figure 1



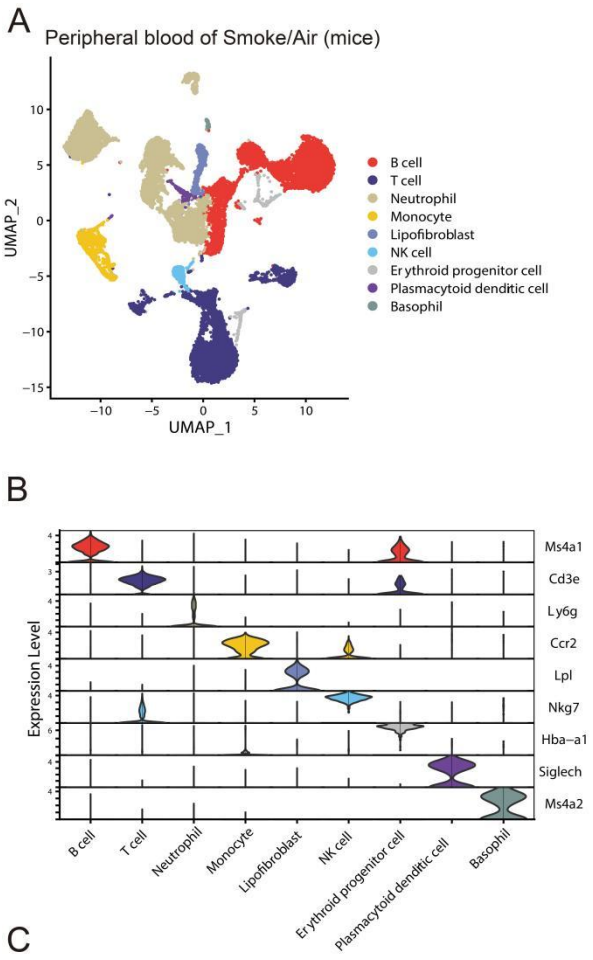
E

cluster Name	Cell number				% of total			
	Control	COPD	Control	SSc	Control	COPD	Control	SSc
B cell	483	1324	66	1452	3.52%	6.72%	0.88%	19.71%
Macrophage	2541	1346	1997	4052	18.50%	6.83%	26.66%	55.01%
Monocyte	2381	2743	874	30	17.34%	13.93%	11.67%	0.41%
NK cell	1734	4416	526	221	12.62%	22.42%	7.02%	3.00%
T cell	1541	2621	0	0	11.22%	13.31%	0.00%	0.00%
Endothelial cell	1843	2331	1517	981	13.42%	11.84%	20.25%	13.32%
Fibroblast	1354	2643	842	213	9.86%	13.42%	11.24%	2.89%
Stromal cell	295	934	340	242	2.15%	4.74%	4.54%	3.29%
Basal cell	142	58	38	103	1.03%	0.29%	0.51%	1.40%
Alveolar cell type 1	44	447	286	1	0.32%	2.27%	3.82%	0.01%
Alveolar cell type 2	1377	832	1006	71	10.03%	4.22%	13.43%	0.96%
total	13735	19695	7492	7366				

Supplementary Figure 1. Single-cell transcriptomic landscape of lung tissues from patients with COPD and systemic sclerosis (SSc). (A–B) Integrated Uniform Manifold Approximation and Projection (UMAP) visualization of lung cells derived from patients with COPD (n = 33,430 cells) and systemic sclerosis (SSc) (n = 14,858

cells). Cell populations were annotated according to canonical marker-gene expression profiles. **(C–D)** Violin plots showing representative marker-gene expression across identified cell clusters in COPD (C) and SSc (D) lung tissues. **(E)** Summary table showing the absolute numbers and relative proportions of cells within each annotated cluster in COPD and SSc lung samples.

Supplementary Figure 2



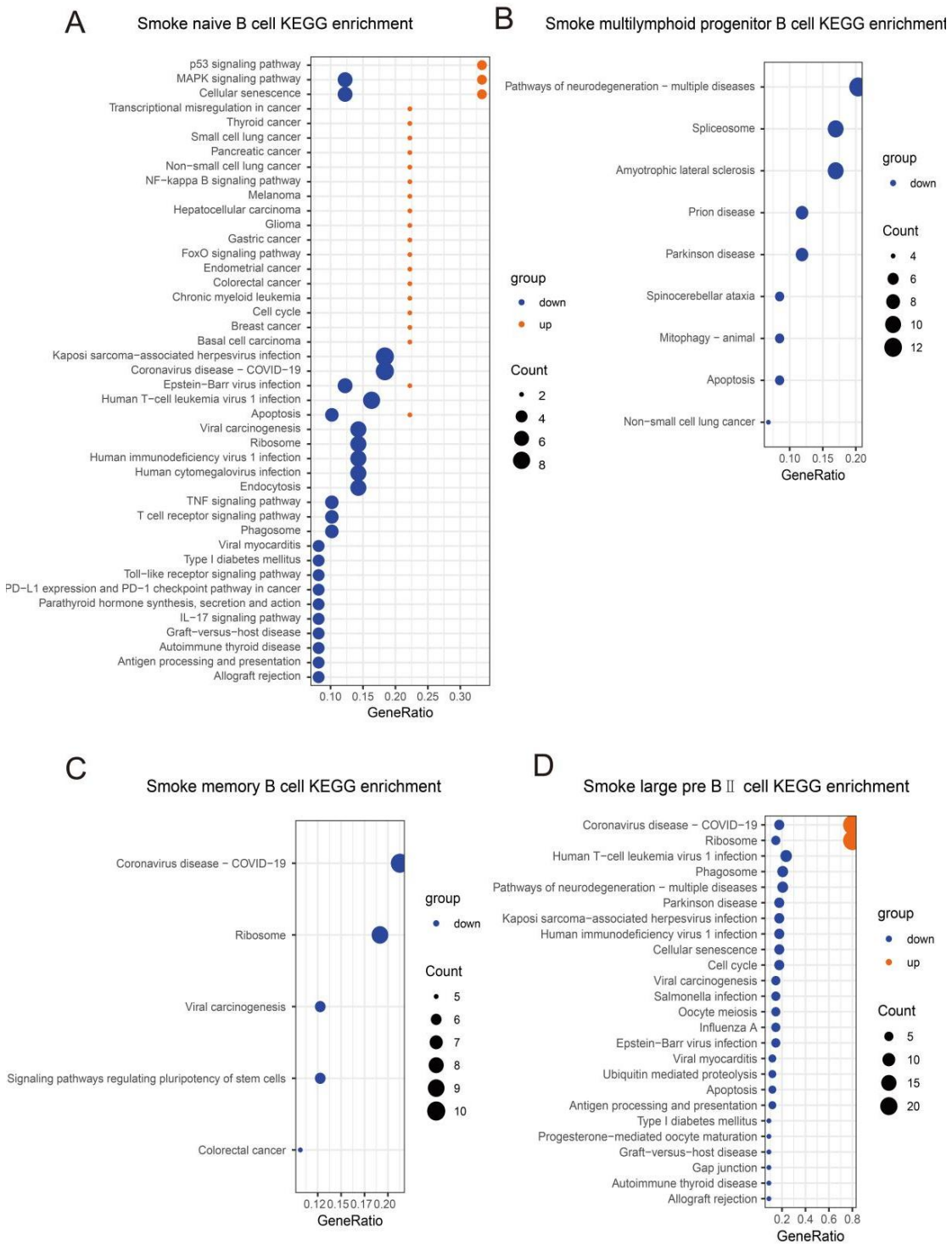
C

cluster Name	Cell number		% of total	
	Air	Smoke	Air	Smoke
B cell	4400	3228	32.43%	29.32%
Neutrophil	4235	3161	31.22%	28.71%
Monocyte	752	620	5.54%	5.63%
Plasmacytoid dendritic cell	136	113	1.00%	1.03%
T cell	3236	3240	23.85%	29.43%
Basophil	68	40	0.50%	0.36%
Plasmacytoid dendritic cell	136	113	1.00%	1.03%
Erythroid progeniter cell	204	145	1.50%	1.32%
Lipofibroblast	400	349	2.95%	3.17%
total	13567	11009		

Supplementary Figure 2. Single-cell transcriptomic landscape of peripheral blood from cigarette smoke-exposed mice. (A) Uniform Manifold Approximation and Projection (UMAP) visualization of 24,576 peripheral blood cells derived from cigarette smoke-exposed mice, coloured according to annotated cell subsets. (B)

Violin plots showing representative marker-gene expression across identified cell clusters. **(C)** Summary table showing the absolute numbers and relative proportions of cells within each annotated cluster.

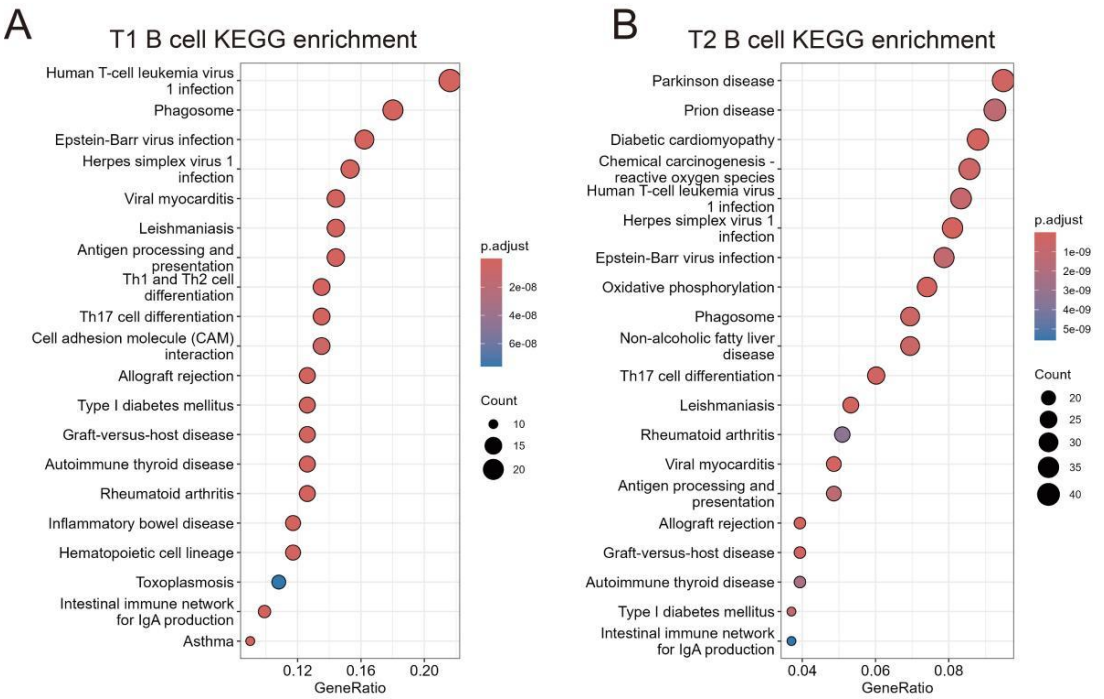
Supplementary Figure 3



Supplementary Figure 3. KEGG pathway enrichment analysis of B-cell subsets in the peripheral blood and bone marrow of cigarette smoke-exposed mice. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses

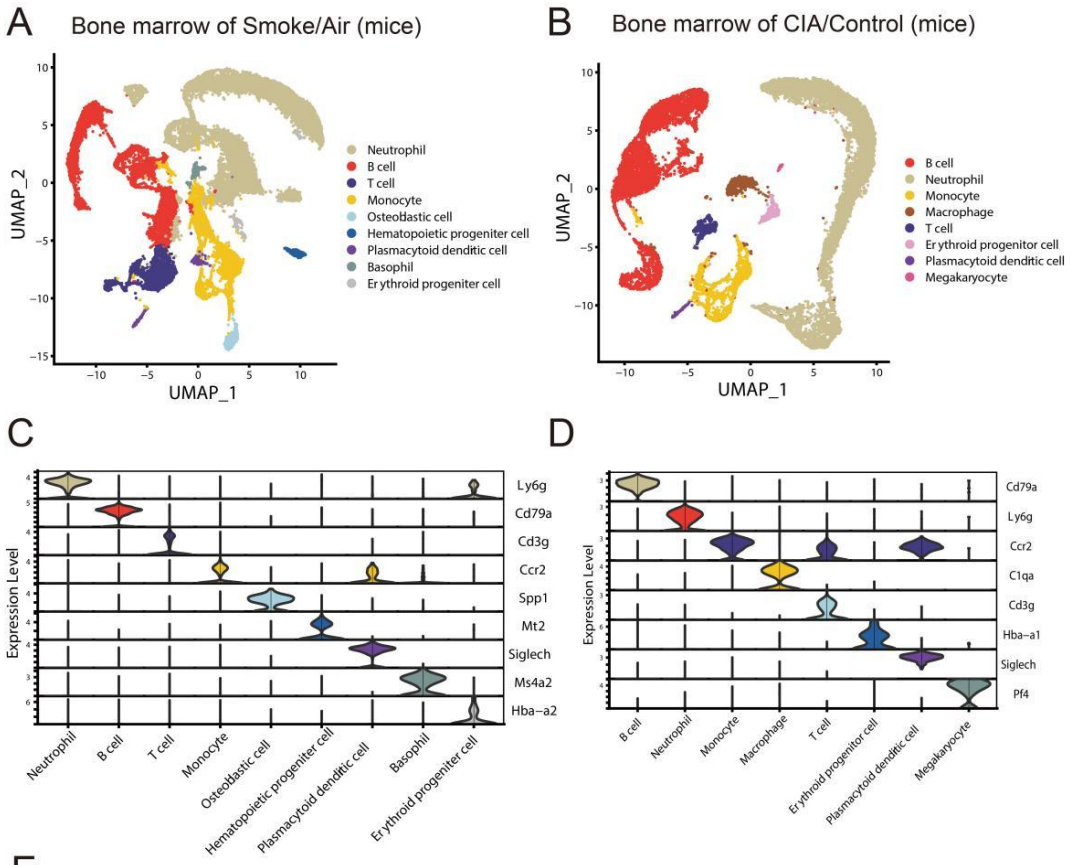
were performed using enrichKEGG for upregulated (red) and downregulated (blue) differentially expressed genes (DEGs) in naïve B cells (A), multi-lymphoid progenitor cells (B) and memory B cells (C) from peripheral blood, as well as large pre-B II cells (D) from bone marrow. Circle size represents the number of genes enriched within each pathway.

Supplementary Figure 4



Supplementary Figure 4. KEGG pathway enrichment analysis of B-cell subsets in the peripheral blood of COPD patients. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were performed using enrichKEGG for upregulated (red) and downregulated (blue) differentially expressed genes (DEGs) in transitional 1 (T1) B cells (A), and T2 B cells (B).

Supplementary Figure 5



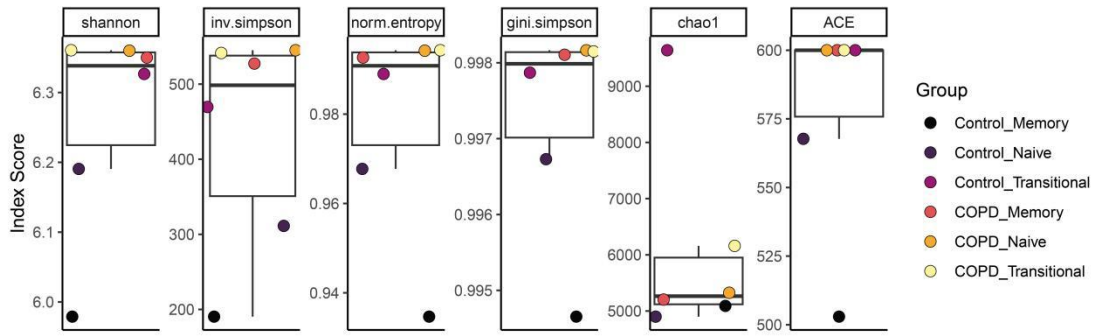
E

cluster Name	Cell number				% of total			
	Air	Smoke	Control	CIA	Air	Smoke	Control	CIA
B cell	3707	2816	2863	1830	23.02%	25.47%	38.72%	24.74%
Neutrophil	6563	5781	3181	4038	40.76%	52.29%	43.02%	54.60%
Macrophage	0	0	222	388	0.00%	0.00%	3.00%	5.25%
Monocyte	2220	1347	648	719	13.79%	12.18%	8.76%	9.72%
Plasmacytoid dendritic cell	287	229	110	87	1.78%	2.07%	1.49%	1.18%
T cell	2289	395	224	193	14.22%	3.57%	3.03%	2.61%
Basophil	139	140	0	0	0.86%	1.27%	0.00%	0.00%
Osteoblastic cell	307	283	0	0	1.91%	2.56%	0.00%	0.00%
Hematopoietic progeniter cell	476	5	0	0	2.96%	0.05%	0.00%	0.00%
Erythroid progeniter cell	112	60	124	126	0.70%	0.54%	1.68%	1.70%
Megakaryocyte	0	0	23	15	0.00%	0.00%	0.31%	0.20%
total	16100	11056	7395	7396				

Supplementary Figure 5. Single-cell transcriptomic landscape of bone marrow cells from cigarette smoke-exposed and collagen-induced arthritis (CIA) mice. **(A–B)** Uniform Manifold Approximation and Projection (UMAP) visualization of bone marrow cells derived from cigarette smoke-exposed (n = 27,156) and CIA (n = 14,791) mice, coloured according to annotated cell subsets. **(C–D)** Violin plots showing representative marker-gene expression across identified cell clusters in

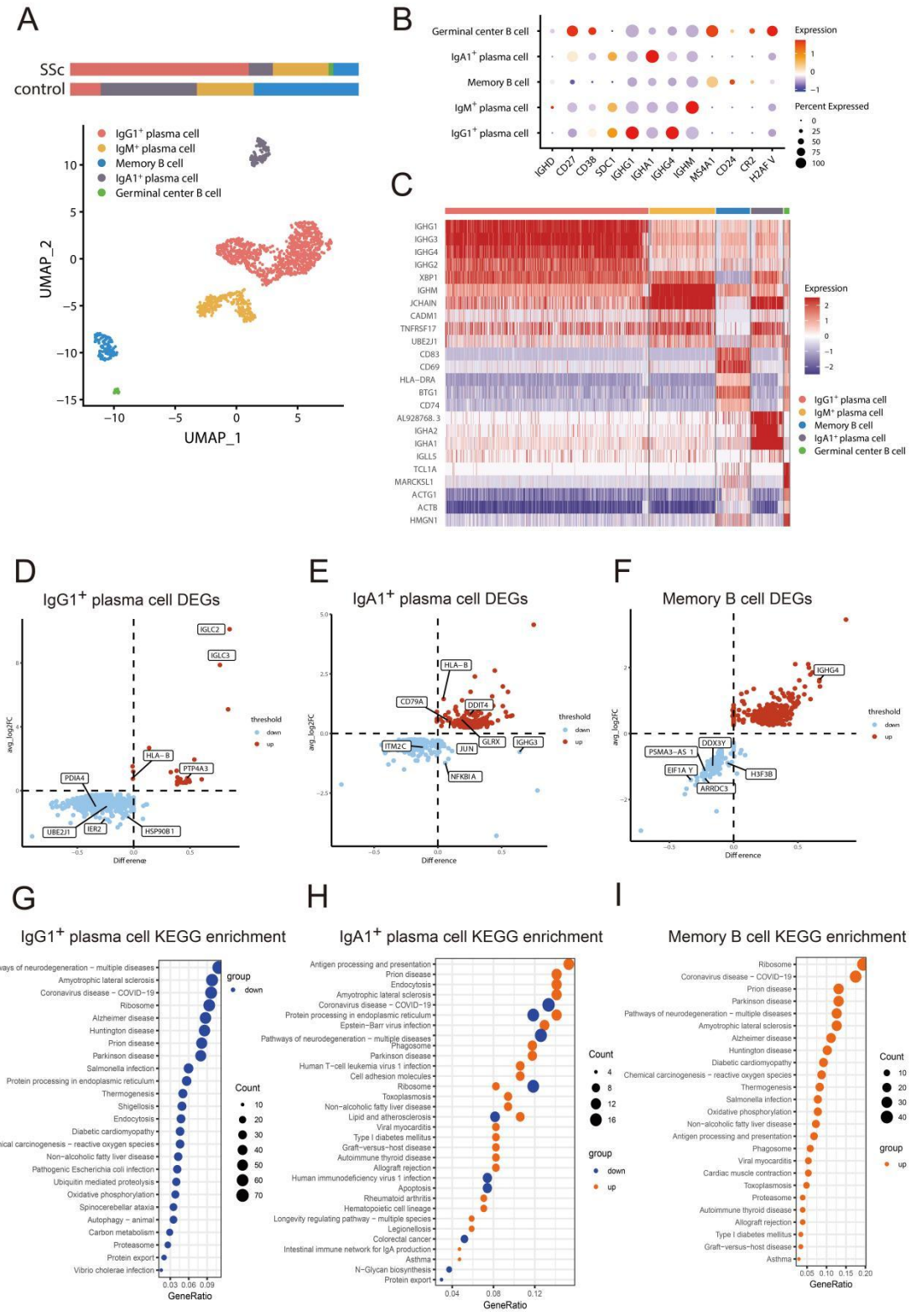
cigarette smoke-exposed (C) and CIA (D) mice. **(E)** Summary table showing the absolute numbers and relative proportions of cells within each annotated cluster.

Supplementary Figure 6



Supplementary Figure 6. Increased BCR diversity and repertoire richness in COPD B cells. Compared with healthy controls, B cells from patients with COPD exhibited significantly increased BCR diversity, including higher Shannon entropy, inverse Simpson index and Gini–Simpson index values, together with increased repertoire richness estimates, including Chao1 and ACE scores.

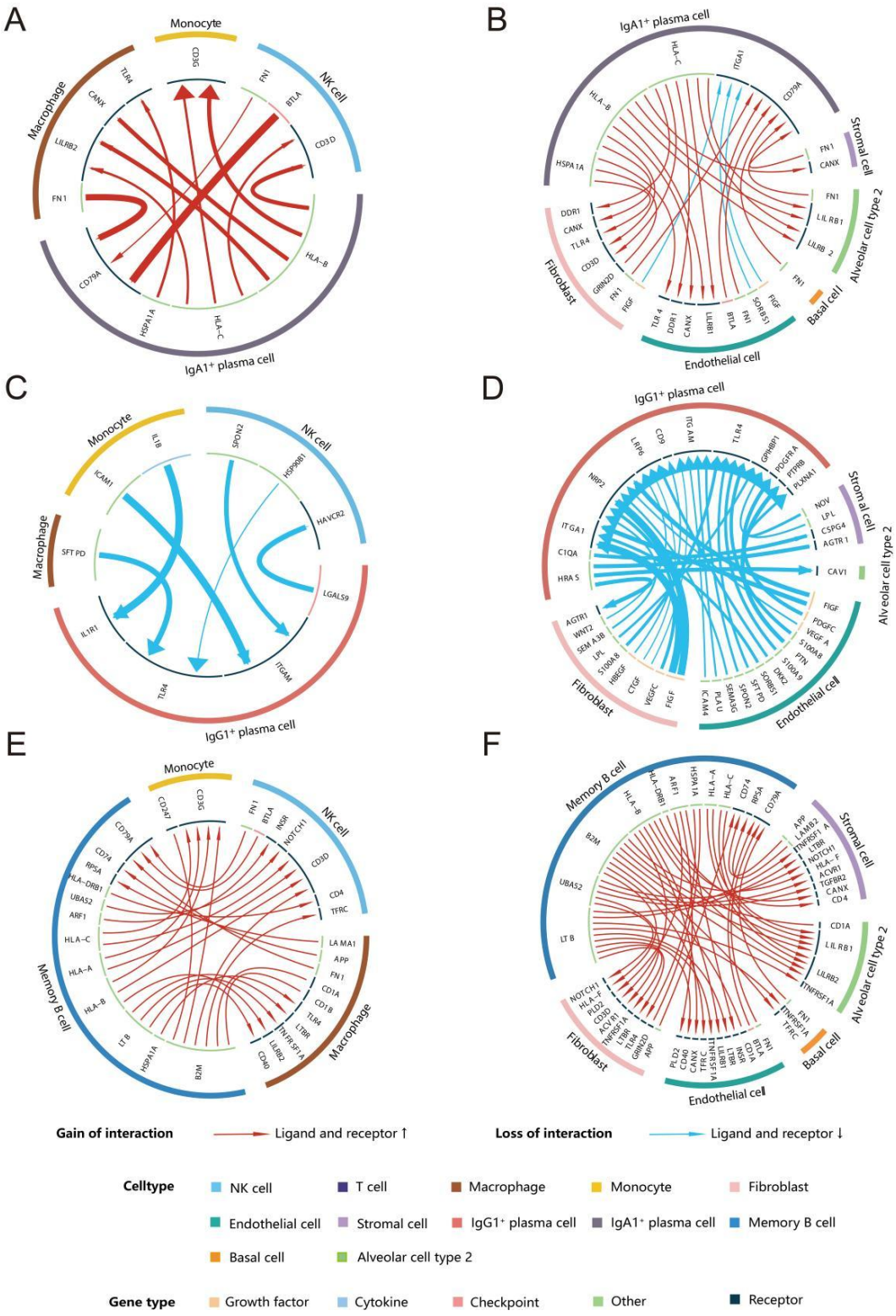
Supplementary Figure 7



Supplementary Figure 7. Characteristics of B-cell subclusters in the lungs of patients with systemic sclerosis (SSc). (A) Uniform Manifold Approximation and

Projection (UMAP) visualization of B cells derived from the lungs of patients with systemic sclerosis (SSc) and healthy controls (total n = 1,518 cells), coloured according to annotated B-cell subsets, with relative proportions of each subset indicated. **(B)** Dot plot showing representative marker-gene expression across B-cell subsets. **(C)** Heatmap displaying transcriptional features of individual B-cell subsets. **(D–F)** Volcano plots showing differentially expressed genes (DEGs) in $IgG1^+$ plasma cells (D), $IgA1^+$ plasma cells (E), and memory B cells. (F). Upregulated and downregulated genes are shown in red and blue, respectively. **(G–I)** Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses of upregulated and downregulated pathways in $IgG1^+$ plasma cells (G), $IgA1^+$ plasma cells (H), and memory B cells (I). Upregulated and downregulated pathways are shown in red and blue, respectively. Black circle size represents the number of genes enriched within each pathway.

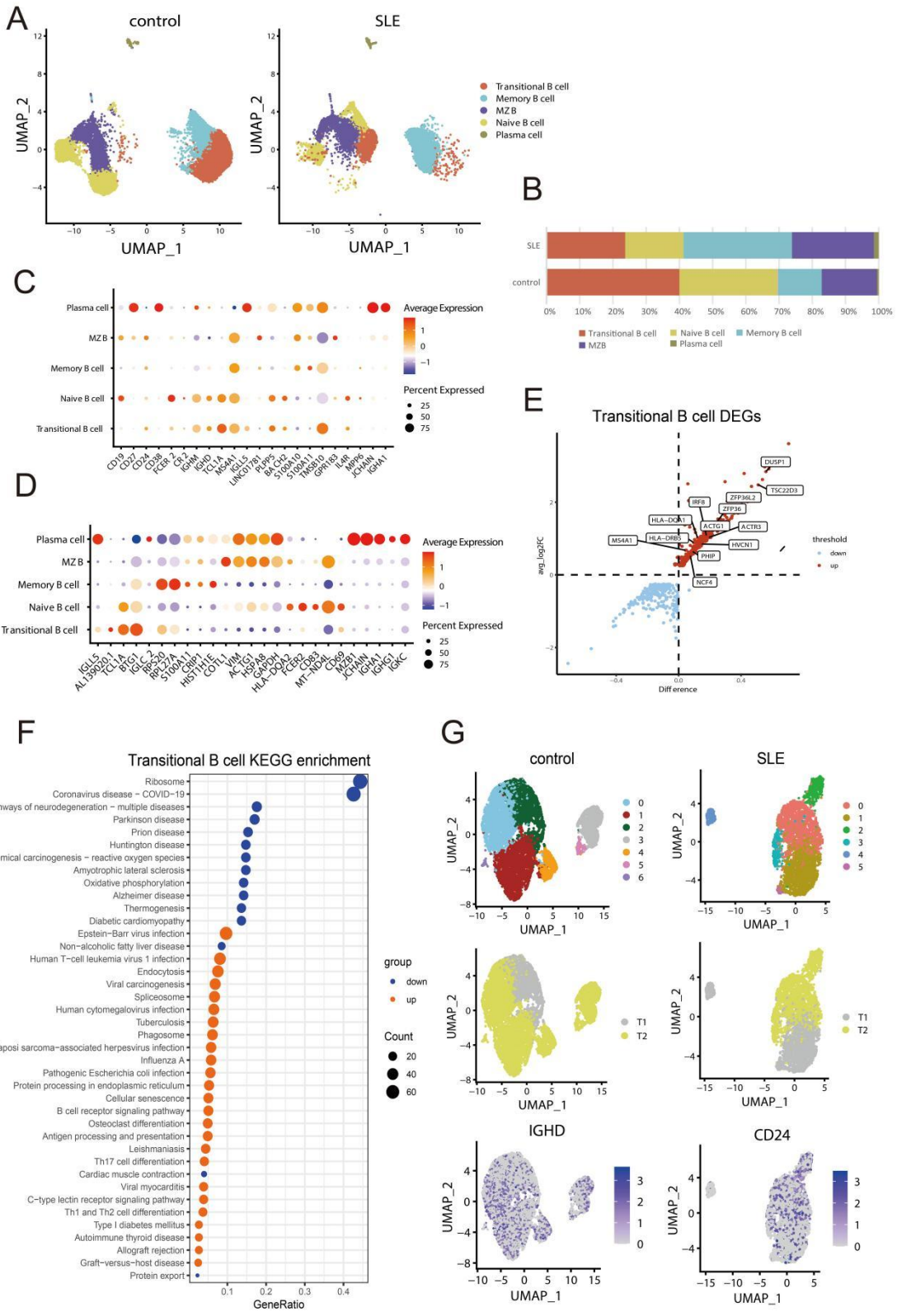
Supplementary Figure 8



Supplementary Figure 8. Cell–cell communication analysis of B-cell subsets in the lungs of patients with systemic sclerosis (SSc). Cell–cell communication

analyses were performed to investigate predicted interactions between $IgA1^+$ plasma cells (A–B), $IgG1^+$ plasma cells (C–D), and memory B cells (E–F) with surrounding immune and non-immune cell populations in the lungs of patients with systemic sclerosis (SSc).

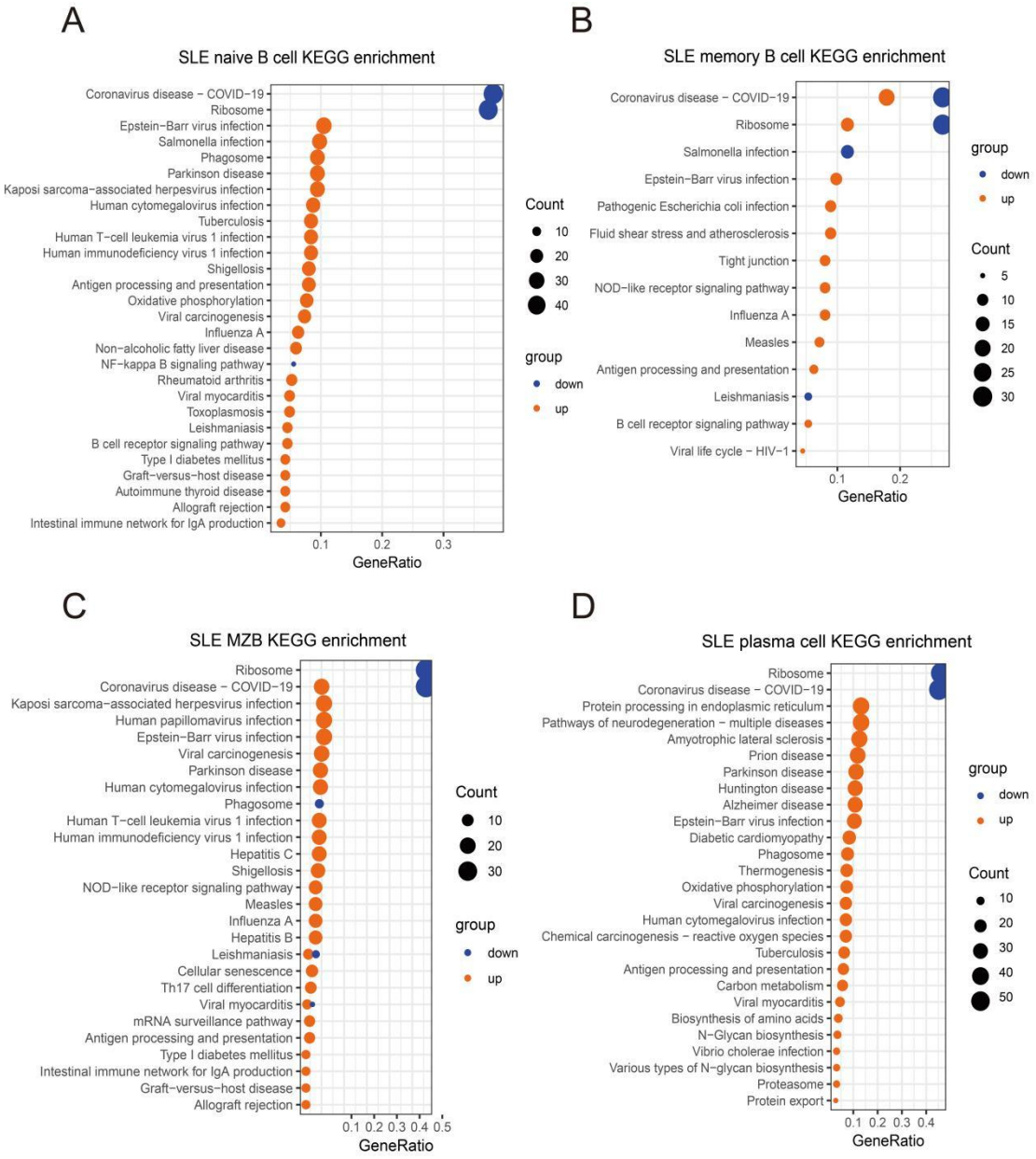
Supplementary Figure 9



Supplementary Figure 9. Characteristics of B-cell subclusters in the peripheral blood of patients with systemic lupus erythematosus (SLE). (A–B) Uniform

Manifold Approximation and Projection (UMAP) visualization (A) and relative proportions (B) of B-cell subclusters identified from the peripheral blood of patients with systemic lupus erythematosus (SLE), coloured according to annotated subsets. **(C–D)** Dot plots showing the expression of representative functional marker genes (C) and the top five marker genes (D) across plasma cells, marginal zone B cells (MZBs), activated naïve B cells, naïve B cells, and transitional B cells. **(E)** Volcano plot showing differentially expressed genes (DEGs) in transitional B cells. Upregulated and downregulated genes are shown in red and blue, respectively. Shared DEGs between COPD and SLE are highlighted. **(F)** Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis of upregulated and downregulated pathways in transitional B cells. Upregulated and downregulated pathways are shown in red and blue, respectively. Black circle size represents the number of genes enriched within each pathway. **(G)** Uniform Manifold Approximation and Projection (UMAP) visualization of transitional B cells from patients with SLE and healthy controls, coloured according to automatically classified clusters and developmental subsets. Expression patterns of classification markers, including IGHD and CD24, are shown for both SLE and control groups.

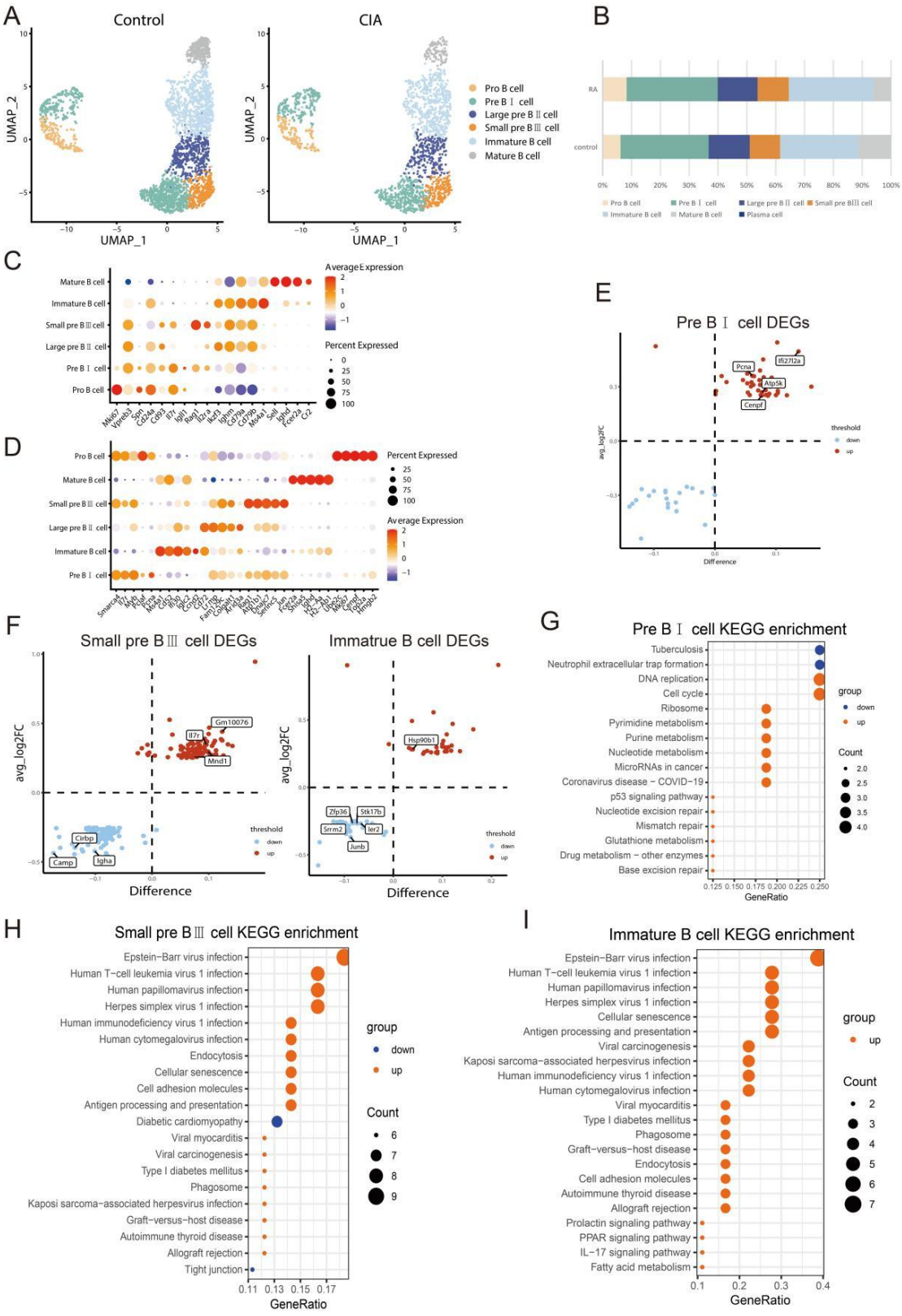
Supplementary Figure 10



Supplementary Figure 10. KEGG pathway enrichment analysis of peripheral blood B-cell subsets in patients with systemic lupus erythematosus (SLE). (A–D) Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses of upregulated and downregulated pathways among differentially expressed genes (DEGs) in naïve B cells (A), memory B cells (B), marginal zone B cells (C), and plasma cells (D) derived from the peripheral blood of patients with systemic lupus

erythematosus (SLE). Upregulated and downregulated pathways are shown in red and blue, respectively. Black circle size represents the number of genes enriched within each pathway.

Supplementary Figure 11



Supplementary Figure 11. Characteristics of B-cell subclusters in the bone marrow of CIA mice. (A–B) Uniform Manifold Approximation and Projection

(UMAP) visualization (A) and relative proportions (B) of B-cell subclusters identified from the bone marrow of CIA mice, coloured according to annotated subsets. **(C–D)** Dot plots showing the expression of representative functional marker genes (C) and the top five marker genes (D) across pro-B cells, pre-B I cells, large pre-B II cells, small pre-B III cells, immature B cells, and mature B cells. **(E–G)** Volcano plots showing differentially expressed genes (DEGs) in pre-B I cells (E), small pre-B III cells (F) and immature B cells (G). Upregulated and downregulated genes are shown in red and blue, respectively. Shared DEGs between cigarette smoke-exposed and CIA mice are highlighted. **(H–J)** Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses of upregulated and downregulated pathways in pre-B I cells (H), small pre-B III cells (I) and immature B cells (J). Upregulated and downregulated pathways are shown in red and blue, respectively. Black circle size represents the number of genes enriched within each pathway.

Supplementary Tables

Supplementary Table 1. Information concerning scRNA-seq data from GEO.

Datasets	Organism	Sample source	Platforms	Information concerning models or patients
GSE196638	Homo sapiens (Control, n=3; COPD/ Emphysema, n=3)	Lung cells from the distal fragments	GPL24676 Illumina NovaSeq 6000 (Homo sapiens)	The normal lung species were obtained from brain-dead donors that were rejected for lung transplantation, while COPD/emphysema lung specimens were taken from the patients undergoing lung transplantation for COPD with radiographic evidence of severe emphysema [1].
GSE205078	Mus musculus (Air, n=4; Smoke, n=4)*	$CD45^+$ whole blood and $CD45^+$ bone marrow cells	GPL24247 Illumina NovaSeq 6000 (Mus musculus)	Mice were exposed to normal air or cigarette smoke through custom-designed and purpose-built nose-only exposure system. The smoke of up to twelve 3R4F reference cigarettes was administered twice per day, 5 days a week for 12 weeks [2].
GSE132771	Homo sapiens (Normal, n=3; SSc, n=2)	Lung cells	GPL24676 Illumina NovaSeq 6000 (Homo sapiens)	Fibrotic lung tissues were obtained at the time of lung transplantation from patients with a diagnosis of scleroderma, while normal lung tissues were obtained from lungs rejected for

				transplantation by the Northern California Transplant Donor Network [3].
GSE193867	Homo sapiens (Healthy, n=3; SLE, n=3)	$CD19^+$ peripheral blood mononuclear cells	GPL16791 Illumina HiSeq 2500 (Homo sapiens)	SLE patients samples were obtained with detection of some auto-antibodies, such as ANA, dsDNA, Sm, RNP, C1Q and La [4].
GSE221704	Mus musculus (Control, n=3; CIA, n=3; treated CIA, n=3)*	Mononuclear cells from bone marrow of femur	GPL24247 Illumina NovaSeq 6000 (Mus musculus)	The collagen-induced arthritis (CIA) model was established by injecting chicken type II collagen subcutaneously into the mouse tail of female DBA/1J mice at the 6th week of age [5].

*Cells from all the animals within each group were pooled for scRNA-seq for each tissue compartment.

Supplementary Table 2. Primers used for qPCR

	Forward primer	Reverse primer
Igk	TCCATCTTCCCACCATCCAG	GATGTCTTGTGAGTGGCCTC
λ5	TGTGAAGTTCTCCTCCTGCTG	ACCACCAAAGTACCTGGGTAG
λ5 promoter	GGGTTAAGACAGGCAGCTGTGAG	CAAACCCCAGGCTGTCTCTAGTT
VpreB promoter	TGCCAAGCTGGCCATGTGAACAC	GATGTTCCTCTACCATATGTGAG
IL-7R	GGGGCTCTTTTACGAGTGAAATGC	TGTGAGTCTGAGGTAGATGGCCTGC
β-actin	AAGACCTCTATGCCAACAC	TAGGAGCCAGAGCAGTAAT

Supplementary Table 3. Cellular communication between B cell subsets and other cells in the lung of COPD patients.

	Classification	T cells	NK cells	Monocyte-macrophages	Fibroblast	Endothelial	Stromal cells	Basal cells	Alveolar cells
IgA1+ plasma cells	GFs	TGFB1-ACVRL1/CAV1/CD109/TGFBR2/CXCR4↑	TGFB1-CAV1/CXCR4/TGFBR2/TGFBR3↑ FGF2/COL14A1/HBEGF/HAS2-CD44↑	TGFB1-TGFBR3/ITGB8/CD109/SDC2/ITGAV↑ FGF2/HBEGF/-CD44↑	TGFB1-CXCR4/ITGB8↑ FGF1/FGF2/HGF/HBEGF-CD44↑	TGFB1-CXCR4/TGFBR1/ITGAV/ACVRL1↑ FGF2-SDC1↓	TGFB1-CXCR4/ENG/SDC2/TGFBR2↑	TGFB1-ITGB6↑ HBEGF-CD44↑	TGFB1-CXCR4/ITGB8/CD44/ACVRL1/ENG/ITGAV↑ HBEGF-CD44↑
	CKs	IL1B-IL1R1↑ IL6-IL6R↑	IL1B-IL1R1↑ IL6-IL6R↑	IL1B/IL1A/IL1RN-IL1R1↑	IL1RN/IL1B-IL1R1↑ IL6-IL6R↑	IL1RN-IL1R1↑ IL6-IL6R↑	IL1B-IL1R1↑ IL6-IL6R↑	IL1B-IL1R1↑ IL6-IL6R↑	IL1B/IL1RN-IL1R1/IL1RAP↑ IL6-IL6R↑
	Chemokines	CCL20-CCR6↑ CCL7-CCR2↓ CCL13-CCR2/5↓	CCL7/13-CCR1/2↓	XCL2-XCR1↑ CCL20-CCR6/CXCR3↑ CCL13-CCR5↓ CCL13-CCR1/2↓	CCL2-ACKR4↑ CCL20-CXCR3↑ CCL13-CCR2↓	CCL2/3/5-CCR4↑ CCL20-CCR6↑	CCL2-CCR10↑ CCL5-SDC4↑	CCL5-SDC4↑	CCL5-GPR75↑
	Checkpoints	ICOSLG-ICOS↑	ICOSLG-ICOS↑ CD40LG-TRAF3↑	ICOSLG-ICOS↑ CD40LG-TRAF3↑	ICOSLG-ICOS↑ CD40LG-TRAF3↑	ICOSLG-ICOS↑	ICOSLG-ICOS↑		ICOSLG-ICOS↑
	Receptors	CD70-CD27↓ SELPLG-SELL↓ SPP1-S1PR1/ITGB1↓		PTGS2-PTGDR2↑ HLA-A/HLA-B-KIR2DL3↑ WNT4-FZD2↓		HLA-A-KIR3DL2↑			HLA-A-KIR3DL2↑ WNT5A-FZD2 ↓
	Others	PTGS2-CAV1↑ SERPING1-SELE↑ GPC3-CD81↑	PTGS2-CAV1↑ SERPING1-SELE↑ FN1-C5AR1/CD79A↑	SERPING1-SELE↑ FN1-COL13A1↑ BTLA-CD79A↑ SEMA6D-TYROBP↑ HDC-HRH2↑ COL18A1-	HDC-HRH1↑ THBS1-ITGB3/SDC4/ITGA6/ITGA4/SDC1↑	FN1-MAG↑ C3-CD19↑ HDC-HRH1↑ THBS1-TNFRSF11B/ITGB3↑	FN1-CD79A↑ HGF/HBEGF/-CD44↑ HDC-HRH2↑ PTGS2-ALOX5↑ THBS1-ITGA4/L	HDC-HRH1↑ THBS1-ITGA6/ITGB1/SDC4/CD47↑ FBLN1-ITGB1↑	HDC-HRH1/2↑ SELPLG-SELE↑ THBS1-ITGA4↑

				GPC1↑ CALM1/2-MYLK↑ HGF-SDC1↓ SPP1-ITGA9↓			RP1↑ RARRES2-CMKLR1↑		
IgG1+ plasma cells	GFs		FGF2/HBEGF/COL14A1/HAS2-CD44↑	HBEGF/FGF2/COL14A1-CD44↑	FGF1/2/HGF/HBEGF-CD44↑		HGF/HBEGF-CD44↑	HBEGF-CD44↑	HBEGF-CD44↑
	CKs	IL1B-IL1R1↑ IL6-IL6R↑	IL1B-IL1R1↑ IL6-IL6R↑	IL1B-IL1R1/IL1R2/IL1RAP↑ IL6-IL6R↑	IL1B-IL1R1/IL1RAP↑ IL6-IL6R↑	IL1B-ADRB2/IL1RAP/IL1R1↑ IL6-IL6R↑	IL1B-IL1R1↑ IL6-IL6R↑	IL1B-IL1R1↑ IL6-IL6R↑	IL1B-IL1R/IL1RAP/ADRB2↑ ICAM1-IL2RA↑ IL6-IL6R↑
	Chemokines			CCL2/3/4-CCR5↑ CXCL2-XCR1↑	CCL2-ACKR4↑	CCL2/3-CCR4↑	CCL2-CCR10↑		
	Checkpoints		CD40LG-TRAF3↑	CD40LG-TRAF3↑	CD40LG-TRAF3↑				
	Receptors			HLA-B-KIR2DL3↑					
	Others	SERPING1-SELE↑ FN1-C5AR1↑ COL14A1-CD44↑ COL6A2-ITGA1↑	SERPING1-SELP↑ CALM1/2-MYLK↑ VWF-SELP↑	SERPING1-SELE↑ CALM1-MYLK/IL2RA↑ FN1/BTLA-COL13A1/SDC2/CD79A↑ SCGB1A1-LMBR1L↑	CALM1/2/3-MYLK↑ THBS1-ITGB3/SDC4↑ DCN-ERBB4↑	THBS1-TNFRSF11B/ITGB3↑ CALM2-MYLK↑ FN1-MAG↑ ICAM1-IL2RA↑ VWF-TNFRSF11B↑	SERPING1-SELE↑ CALM1/2/3-MYLK↑ FN1-CD79A↑ THBS1-ITGA4↑	CALM2-MYLK↑ COL6A2/THBS1-ITGA6/ITGB1↑ ITGA6/ITGB6↑-ITGB1↑	CALM1/2-MYLK↑ COL6A2-ITGA2↑ FN1-ITGA2↑ APOE-LRP8↑
Memory B cells	GFs	TGFB1/CYR61/ICAM1-CAV1/CXCR4↑	TGFB1/PTGS2/CYR61-CAV1↑ TGFB1/CXCL12-CXCR4↑ FGF2/HBEGF/COL14A1/HAS2-CD44↑	FGF2/HBEGF/-CD44↑	TGFB1/ICAM1-CAV1/CXCR4↑ FGF1/FGF2/HGF/HBEGF-CD44↑	TGFB1-CAV1/CXCR4↑	TGFB1/ICAM1-CAV1↑ TGFB1/CXCL12-CXCR4↑ HGF/HBEGF/-CD44↑	HBEGF-CD44↑	HBEGF-CD44↑ TGFB1-CAV1↑ HBEGF-CD44↑ TGFB1-CXCR4↑
	CKs	IL1B-	IL1B-	IL1B-		IL1B-	IL1B-	IL1B-	

	IL1R1↑ IL10-IL10RA↑ TNFRSF14/CD247-BTLA↓	IL1R1↑ TNFRSF14-BTLA↓	IL1R1/IL1R2↑		ADRB2↑	IL1R1↑ ICAM1-IL2RA↑	IL1R1↑	IL1B-IL1R1/IL1RAP↑
Chemokines	CCL21-CCR7↑ CXCL12-CXCR4↑ CCL18-C14orf1↓	CCL19/CCL21-CCR7↑ CCL18-C14orf1↓	CCL19/CCL21-CCR7/CXCR3↑ CCL3L3/CCL2/CCL4-CCR5↑	CCL2/CCL21-ACKR4/CCR7/-CXCR3↑ CCL5-CXCR3↑	CCL19/CCL21-ACKR2/CCR7↑ CCL2/5-CCR4↑	CCL21-CCR7↑ CCL2-CCR10↑ CCL5-SDC4↑	CCL21-CCR7↑ CCL5-SDC4↑	CCL19/21-CCR7↑ CCL5-GPR75↑ CCL18-C14orf1↓
Receptors	CD70-CD27↓		HLA/B2M-A-KIR2DL3↑	CD70-CD27↑ NCR3LG1-NCR3↑	HLA-A-KIR3DL2↑ NCR3LG1-NCR3↑			CD70-CD27↑ NCR3LG1-NCR3↑ BTLA-TNFRSF14↓ TNFRSF14-BTLA ↓
Others	CCL5-SDC4↑ ANXA1-FPR2↑ COL1A2-ITGA1↑ ICAM1-IL2RA↑ BMP8B-ACVR1↓	FN1-CD79A↑ COL1A2-CD93↑	BTLA-CD79A↑ FN1-SDC2/ITGA8/COL13A1↑ ICAM1-IL2RA↑ COL1A2-ITGA2↑ BMP8B-ACVR1/2A/2B/BMPR2↓	TGM2/COL1A2-ITGB3/SDC4/ITGA9↑ BMP8B-ACVR2B↓	FN1-MAG↑ COL1A2-CD44↑ BMP8B-ACVR1/ACVR2A/BMPR1A↓	TGM2-ITGA4↑ CALM1-SCTR↑	ICAM1-CAV1↑ TGM2-ITGB1↑ TGM2-SDC4↑ COL1A2-ITGB1↑ ICAM1-IL2RA↑ FN1-ITGB6↑	BMP8B-ACVR2A↓ BMP8B-BMPR1A ↓ HLA-A-KIR3DL2↑ COL1A2-ITGA2↑ ICAM1-IL2RA↑ COL1A2-CD93↑

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Supplementary Table 4. The common DEGs between COPD and other autoimmune diseases in bone marrow, peripheral blood and lung.

Sample sources	subclusters	common DEGs between COPD and autoimmune diseases	
		Up	Down
lung	$IgG1^+$ plasma cell	IGLC2, IGLC3, PTP4A3, HLA-B, RP11-138A9.2	IER2,SUB1,PPIB,HSP90B1,UBE2J1,TMED9,TPD52,TNFRSF17,COX5B,RPS26,RSRP1,PPIA,SRP14,EGR1,PDIA4,TAF7,MYDGF,SEC61G,COPE,SPCS1,UBXN4,QPCT,PRDX1,UQCR10,EDF1,SON,SPCS2,MTCO1,C11orf31,GOLGB1,RPS4Y1,BMI1,DUSP6,EAF2,SEC62,PSAP,SMARCB1,LRRC16A,ATP5H,HSH2D,C14orf2,TMEM208,USO1,ZNHIT1,TMED2,NDUFB3,TMEM134,C19orf60,C1QB,CD2BP2,MTND4,MPHOSPH8,ANAPC5,ACIN1,TRAPPC2L,MRPL57,AKAP17A,NDUFA4,KLF4,IL2RG,KATNBL1,MZB1,SMC1A,CCDC167,IK,PFDN6,VPS36,DOCK8,ANXA6,B9D1,GOLGA8B,CD27,SDF4,SESN1,BTN3A2,ILF3-AS1,EDEM3,ATP5E
	$IgA1^+$ plasma cell	HLA-B, RPL17, HLA-DPA1, DDIT4, IGKV3-20, GLRX, RPS10, CD79A, RPL41, H2AFZ, HLA-A, CHST2, BASP1, PRDM1	NFKBIA, RPS26, IGHG3, JUN, ITM2C, BRD2, ARGLU1, AMPD1, BCL2, RPN2, PAIP2B, HNRNPA2B1
	Memory B cell	IGHG4, RPL17, RPL36A, RPS10, RP11-138A9.1, PTGES3, RPS21, HLA-DPB1, HLA-DQA1, RPL41	RPS4Y1, EIF1AY,ARRDC3, N4BP2L2, LINC00969, PSMA3-AS1, ASH1L, AES, DDX3Y, H3F3B, PNISR, SFTPB, ATF7IP2, LRRK2, LRRC16A, SLPI
Peripheral blood	Transitional B cell	Zfp36l2,Tsc22d3,Ms4a1,Dusp1,Zfp36,Actr3,Ncf4,Actg1,Irf8,Napsa,Phip,Rgs19,Hvcn1,H2-Aa,H2-Eb1	Rpl37,Rps29,Rps27,Rpl38,Rpl35,Rps28,Rpl27,Rpl29,Uba52
	Resting naive B cell	Dusp1,Gadd45b	Gdi2,Pnrc1,Arf6,Id3,Rpl27,mt-Nd4l,Rpl29
	Memory B cell	Tsc22d3,March1,Irf8,Ms4a1,Bdp1,Pou2f2,Chordc1	Rps28,H3f3b,Jchain
	Plasma cell	Arf1,Gapdh,Ergic2,Wipi1,Bloc1s2,Trabd,Spn,Uqcr10	None
Bone marrow	Pro B cells	None	Tmsb10, Cirbp
	Pre B I cells	Ifi27l2a, Pcna, Atp5k, Cenpf	None
	Large pre B II cells	Mnd1, Gm10076	Cirbp, Pafah1b3, Igha
	Small pre B III cells	Il7r、Mnd1、Gm10076	Cirbp、Camp、Igha
	Immature B cells	Hsp90b1	Zfp36,Ier2,Stk17b,Srrm2,Junb
	Mature B cells	Ptpn22、Ddit4、Zfp36l2、Pou2af1、Ccnd3、Kmt2e、Scd1、Tnfrsf13c、Mybbp1a、Dnaja1	Nup210,B4galnt1,Clec2i,Tomm6,Zfp36l1

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Supplementary Table 5. Cell communication between B subclusters with other cells in SSc patients.

B subclusters	Classification	NK cell	Mono-macropage	Fibroblast	Endothelials	Stromal cells
IgA1+ plasma cells	Receptors	HLA-B/C-CD3D↑	HSPA1A-TLR4↑ HLA-B/C-CD3G/LILRB2↑	HSPA1A-TLR4↑ HLA-B/C-CD3D↑	HSPA1A-TLR4↑ HLA-B/C-LILRB1↑	
	Others	BTLA/FN1-CD79A↑	FN1-CD79A↑ HLA-B-CANX↑	FN1-CD79A↑ HLA-B-CANX↑ HLA-C-DDR1↑ FIGF-ITGA1↓ HSPA1A-GRIN2D↑	BTLA/FN1-CD79A↑ HLA-C-DDR1↑ HLA-B-CANX↑ FIGF/SORBS1-ITGA1↓	FN1-CD79A↑ HLA-B-CANX↑
IgG1+ plasma cells	GFs			VEGFC-NRP2↓	VEGFA-NRP2↓ PDGFC-PDGFRA↓	
	CKs		IL1B-IL1R1↓			
	Receptors	HSP90B1-TLR4↓ LGALS9-HAVCR2↓	SFTPD-TLR4↓ ICAM1-ITGAM↓	WNT2-LRP6↓ S100A8-TLR4↓	DKK2-LRP6↓ S100A8/S100A9/SFTPD-TLR4↓ ICAM4-ITGAM↓	
	Others	SPON2-ITGAM↓		CTGF-LRP6/ITGAM↓ FIGF-ITGA1↓ HBEGF-CD9↓ LPL-GPIHBP1↓ HRAS-AGTR1↓ FIGF/SEMA3B-NRP2↓	FIGF/SEMA3G-NRP2↓ FIGF-ITGA1↓ PTN-PTPRB↓ SORBS1-ITGA1↓ SPON2/PLAU-ITGAM↓	HRAS-AGTR1↓ C1QA-CSPG4↓ LPL-GPIHBP1↓ NOV-PLXNA1↓
Memory B cell	CKs		LTB-LTBR/TNFRSF1A/CD40↑	LTB-LTBR/TNFRSF1A↑	LTB-LTBR/TNFRSF1A/CD40↑	LTB-LTBR/TNFRSF1A↑
	Receptors	HLA-A/B/C/B2M-CD3D↑ HLA-	HSPA1A-TLR4↑ HLA-A/B/C-CD3G/LILRB2↑ B2M-CD3G/CD1A/B/247	HSPA1A-TLR4↑ HLA-B-CD3D↑ B2M-HLA-F↑	B2M-CD1A↑ HLA-B-LILRB1↑	B2M-HLA-F↑ HLA-DRB1-CD4↑

	Others	DRB1-CD4↑ ARF1-INSR↑ UBA52-NOTCH1↑ FN1/BTLA-CD79A↑ B2M-TFRC↑	↑ FN1-CD79A↑ APP-CD74↑ LAMA1-RPSA↑	HSPA1A-GRIN2D↑ ARF1-PLD2↑ UBA52-NOTCH1↑ APP-CD74↑ UBA52-ACVR1↑	ARF1-INSR↑ FN1/BTLA-CD79A↑ ARF1-PLD2↑ HLA-B-CANX↑ B2M-TFRC↑	UBA52-ACVR1/NOTCH1/TGFBR2↑ APP-CD74↑ HLA-B-CANX↑ LAMB2-RPSA↑
	Receptors	HLA-B/C-CD3D↑ C1QA-CD93↓	HSPA1A-TLR4↑ HLA-B/C-CD3G/LILRB2↑	EFNB2-EPHB6↓ WNT2-FZD7↓ C1QA-CD93↓	EFNB1-EPHA4↓ HLA-B/C-LILRB1↑	C1QA-CD93↓
IgM^+ plasma cell	Others	FN1/BTLA-CD79A↑ VIM-CD44↑ OSM-LIFR↓ SFTPA2-CD93↓	HLA-B-CANX↑ VIM-CD44↑ FN1-CD79A↑	HSPA1A-GRIN2D↑ SEMA3B-NRP2↓ ADM-RAMP2/CALCRL↓ SLIT2-ROBO4↓ SFTPA2-CD93↓ LPL-GPIHBP1↓ HBEGF-PRLR↓	OSM-LIFR↓ FN1/BTLA-CD79A↑ HLA-C-DDR1↑ VIM-CD44↑ SFTPA2-CD93↓ EFNA5-EPHA4↓ PTN-PTPRB↓	VIM-CD44↑ FN1-CD79A↑ HLA-B-CANX↑ C1QA-CSPG4↓ SFTPA2-CD93↓ LPL-GPIHBP1↓

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