Supplementary Material

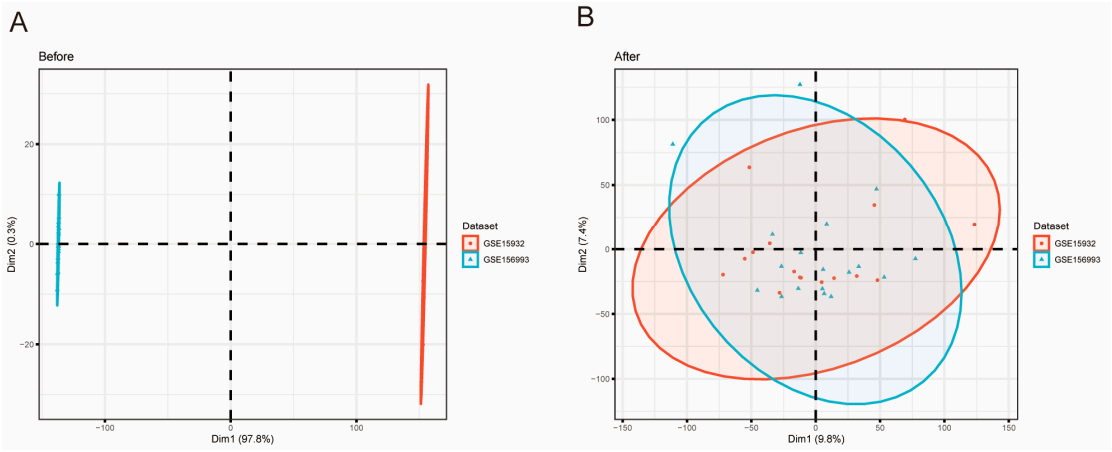


Figure S1 Batch-effect correction improves integration of PBMC cohorts. (A) PCA of GSE15932 and GSE156993 samples before batch correction, showing dataset-driven separation. (B) PCA after normalization and batch-effect correction, showing improved cross-cohort mixing.

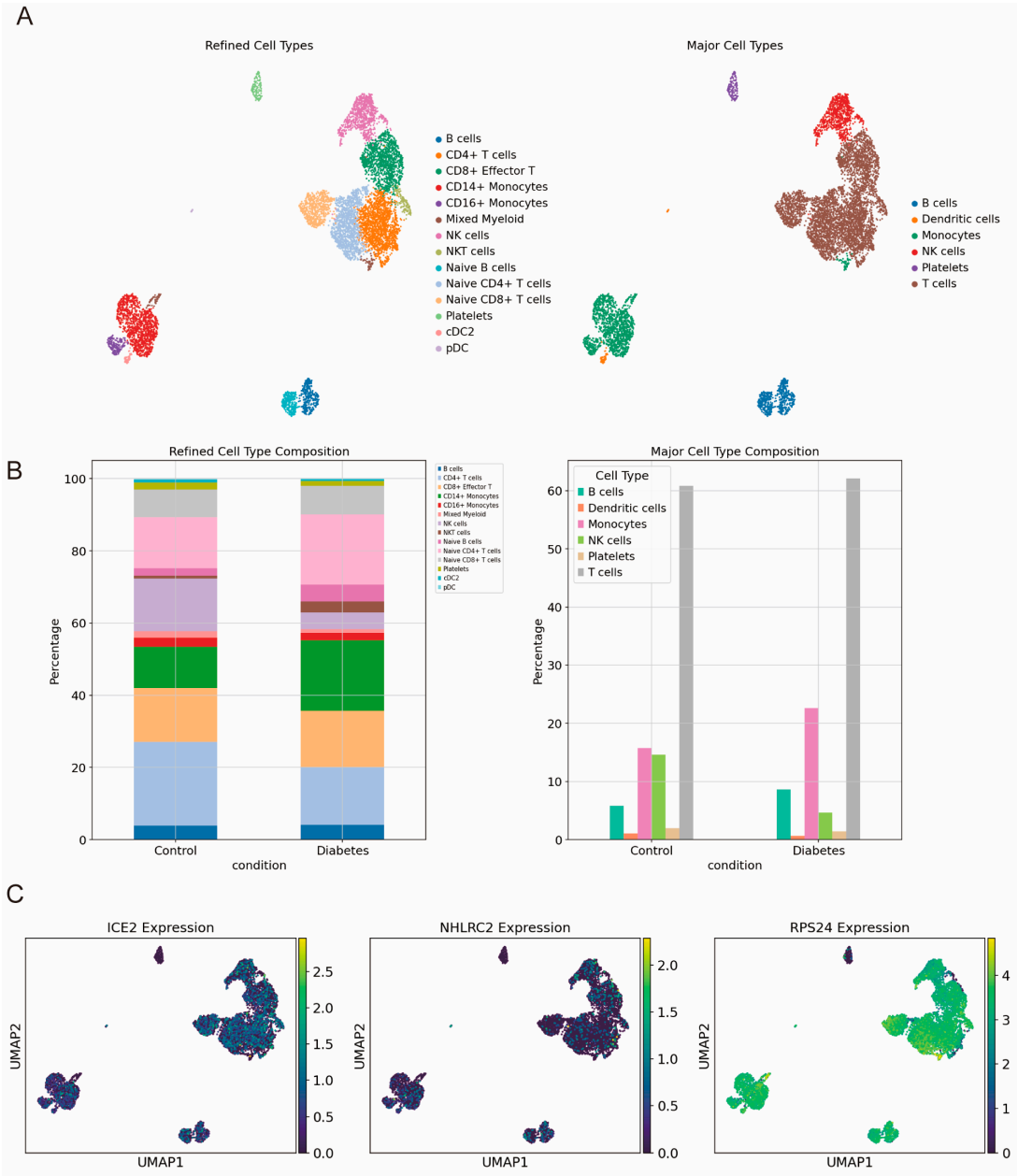


Figure S2 Single-cell PBMC landscape in Control and T2DM. (A) UMAP of integrated PBMCs colored by refined (left) and major (right) cell types. (B) Relative cell-type proportions in Control and T2DM at refined (left) and major (right) levels. (C) Feature plots showing the expression of ICE2, NHLRC2, and RPS24.

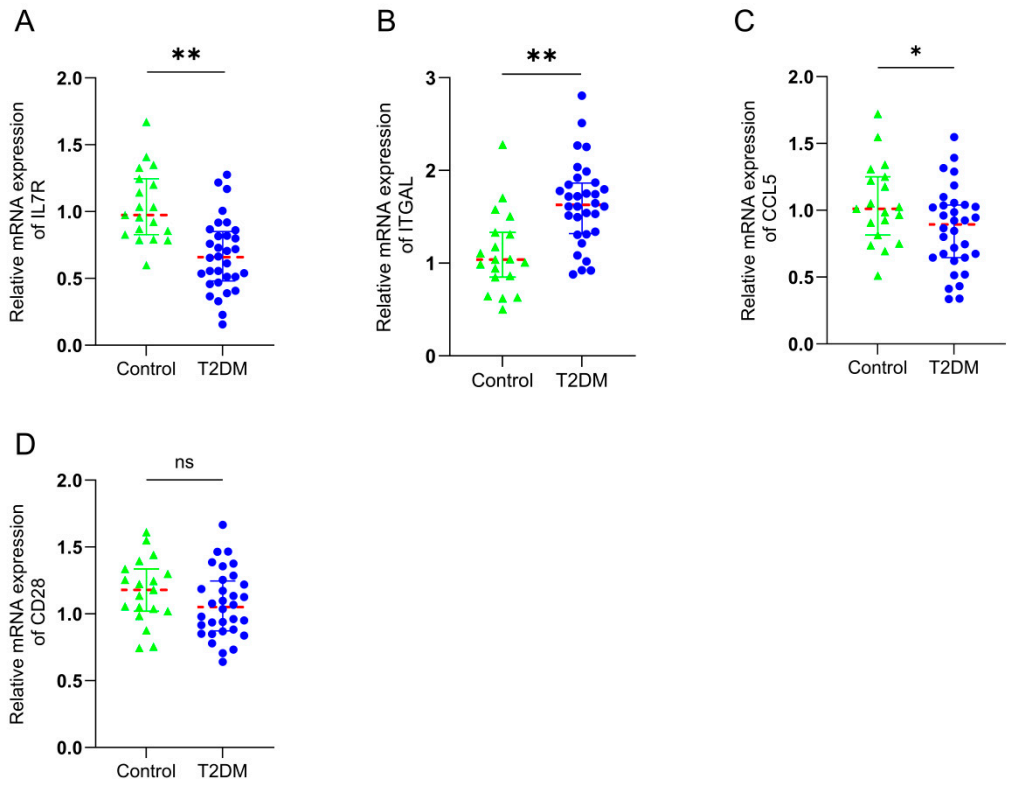


Figure S3 Immune-related candidate genes in Control and T2DM. (A-D) RT-qPCR analysis of the mRNA expression levels of the four immune-related candidate genes IL7R (A), ITGAL (B), CCL5 (C)and CD28 (D) in control and T2DM samples. Statistical significance was determined using an unpaired Student's t-test. *$p < 0.05$, **$p < 0.01$.

Table S1. The information of GEO datasets in this study

GSE series	Platform	Samples size	Tissue	Species
GSE156993	GPL570	T2DM(n=12),Control(n=6)	PBMC	Homo sapiens
GSE15932	GPL570	T2DM(n=8),Control(n=8)	PBMC	Homo sapiens
GSE189005	GPL23126	T2DM(n=18),Control(n=9)	whole blood cells	Homo sapiens
GSE185011	GPL24676	T2DM(n=5),Control(n=5)	PBMC	Homo sapiens
GSE81608	GPL16791	1,492 pancreatic cells from non-diabetic and T2DM organ donors.	pancreatic islets(Single-cell RNA sequencing)	Homo sapiens
GSE280401	GPL16791	T2DM(n=2),Control(n=2)	PBMCs(Single-cell RNA sequencing)	Homo sapiens

Table S2. Participant baseline characteristics

Participant	Control	T2DM	*P*
n	19	32	
Age(yr)	52.8±8.0	55.8±9.4	ns
Gender(M/F)	9/10	16/16	ns
FPG(mmol/L)	5.2±0.4	9.2±2.3	< 0.001

Table S3. Primer sequences for target genes

Genes	Forward（5′→3′）	Reverse（5′→3′）
β-actin	AAGTTCACAATGTGGCCGAG	AGTGGGGTGGCTTTTAGGATG
ICE2	GCGGACCATGAGCTGAGTAA	CCATCTTGGAGCTCATCTTCCT
NHLRC2	ACCTCCCATCAGGATCAAAGC	TCCAGCTGCTATCTGTCCTTG
RPS24	AGCAACGAAAGGAACGCAAGG	CTCCAGCTCACTTCTTTTTGCC
IL7R	AATGGATCGCAGCACTCACTG	ACGAGGGCCCCACATATTTC
ITGAL	CAGTCACCCTGAGAGGTTCC	CTGGTCACACGTTCGAGACA
CCL5	TCATTGCTACTGCCCTCTGC	TCGGGTGACAAAGACGACTG
CD28	GAACCCTAGCCCATCGTCAG	GCTTCACCAAAATCTTGTTTCC TGT

Table S4. Cohort-specific assessment of the expression patterns of ICE2, NHLRC2, and RPS24 in T2DM

Cohort	Gene	T2DM (n)	Control (n)	log2FC (95% CI)	P value	FDR
GSE15932	ICE2	8	8	−0.654 (−0.901, −0.407)	3.483×10^{-6}	1.045×10^{-5}
GSE15932	NHLRC2	8	8	0.298 (0.051, 0.545)	0.0193	0.0290
GSE15932	RPS24	8	8	−0.148 (−0.395, 0.099)	0.2340	0.2340
GSE156993	ICE2	12	6	−0.024 (−0.207, 0.159)	0.7897	0.7897
GSE156993	NHLRC2	12	6	−0.123 (−0.341, 0.096)	0.2585	0.3878
GSE156993	RPS24	12	6	−0.156 (−0.298, −0.015)	0.0319	0.0958
GSE185011	ICE2	5	5	0.163 (−0.398, 0.725)	0.5537	0.5537
GSE185011	NHLRC2	5	5	0.219 (−0.330, 0.769)	0.4186	0.5537
GSE185011	RPS24	5	5	0.459 (−0.269, 1.187)	0.2056	0.5537

Abbreviations: log2FC, $\log_2$ fold change (T2DM versus controls); CI, confidence interval; FDR, false discovery rate. Positive log2FC indicates higher expression in T2DM, and negative log2FC indicates lower expression. FDR values were calculated using the prespecified Benjamini–Hochberg correction applied to the three prespecified genes within each cohort (m = 3). Cohort roles: GSE15932 and GSE156993 both contribute to the discovery cohort and therefore assess between-cohort consistency only, not independent validation; GSE185011 is an independent cross-platform PBMC cohort (n = 5 per group). No cross-platform pooling of effect sizes was performed.