Additional file

Table S1. Data sources

Disease	Data Sources	ID	Platfrom	Samples used	Tissue	Experiment Type
KOA	ArrayExpress	E-MTAB-12184		6 cases vs. 6 controls	articular cartilage	RNA-Seq
COVID-19	GEO	GSE180226	GPL6480	19 cases vs. 3 controls	Lung	Array
URTIs	GEO	GSE197143	GPL24676	6 cases vs. 3 controls	Lung	RNA-Seq
URTIs	GEO	GSE206606	GPL18573	3 cases vs. 3controls	Lung	RNA-Seq
KOA	GEO	GSE220243	GPL18573	6 cases vs. 6 controls	articular cartilage	scRNA-Seq

Table S2. Sensitivity analysis

Exposure	Outcome	Analysis Type	Method	Q	P-value
COVID-19	KOA	sensitivity analysis	MR Egger	20.87	0.467
COVID-19	KOA	sensitivity analysis	IVW	20.93	0.525

IVW: Inverse variance weighted

Table S3. Multiplicity test

Exposure	Outcome	Analysis Type	Egger_intercept	P-value
COVID-19	KOA	Multiplicity test	-0.002 (95%CI: -0.018-0.014)	0.811

Table S4. Mendelian randomization results for additional validation

| Exposure ID	Exposure	Sample sizes	OutcomeID	Outcome	Sample sizes	Method	Nsnp	Beta	p-value
ebi-a-GCST011071	COVID-19	1588783	ebi-a-GCST005812	Osteoarthritis of the hip or knee	32970	Inverse variance weighted	28	0.161	0.044
ebi-a-GCST011073	COVID-19	1683768	ukb-a-563	Gonarthrosis [arthrosis of knee]	337199	Inverse variance weighted	22	0.004	0.007
ebi-a-GCST011073	COVID-19	1683768	ukb-d-KNEE_ARTHROSIS	Gonarthrosis [arthrosis of knee]	361194	Inverse variance weighted	22	0.004	0.01
ebi-a-GCST011073	COVID-19	1683768	ebi-a-GCST007092	Osteoarthritis of the hip or knee	417596	Inverse variance weighted	23	0.061	0.039
ebi-a-GCST011074	COVID-19	1348701	ukb-a-563	Gonarthrosis [arthrosis of knee]	337199	Inverse variance weighted	16	0.003	0.041
ebi-a-GCST011080	COVID-19	16645	ukb-a-563	Gonarthrosis [arthrosis of knee]	337199	Inverse variance weighted	12	0.001	0.03
ebi-a-GCST011085	COVID-19	10365	ebi-a-GCST007090	Knee osteoarthritis	403124	Inverse variance weighted	11	0.033	0.025
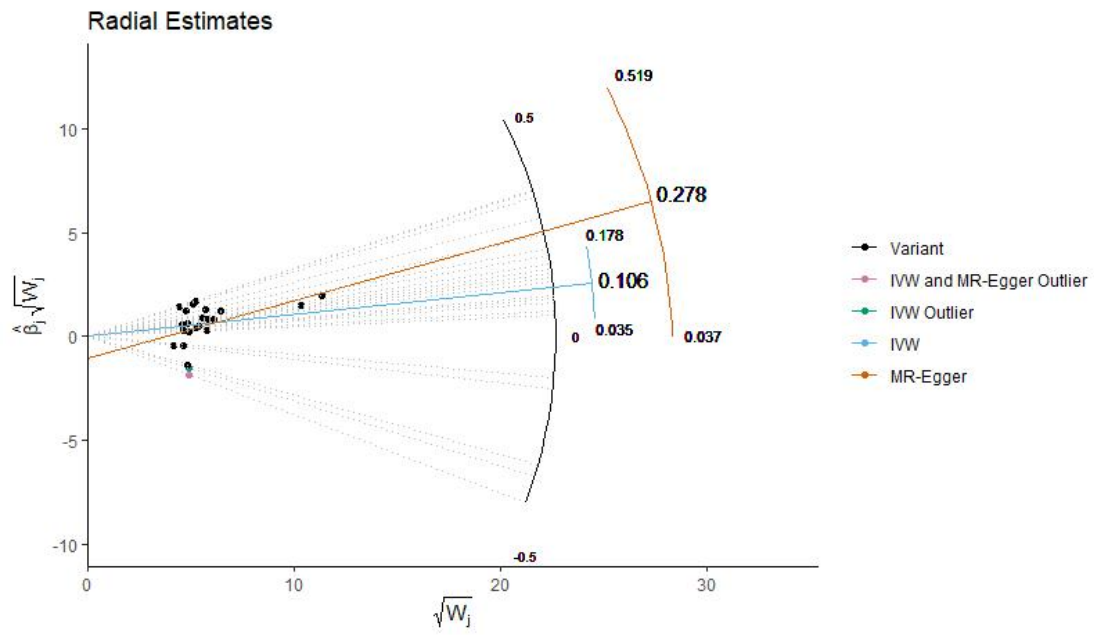
Figure S1. Radial-MR method tests outliers of SNPs. The SNPs "rs140434804" and "rs7786241"
were identified as outliers and excluded from the subsequent MR analysis. R package RadialMR
(https://github.com/WSpiller/RadialMR/) was used for the analysis.

Table S5. Mendelian randomization results for COVID19 and KOA risk factors

| Exposure	Exposure ID	Outcome	OutcomeID	Methods	Nsnp	Beta	p-value	P_FDR
COVID-19	ebi-a-GCST011073	Body mass index (BMI)	ukb-b-19953	Inverse variance weighted	23	0.0333	0.001	0.006
COVID-19	ebi-a-GCST011073	Osteoporosis	finn-b-M13_OSTEOPOROSIS	Inverse variance weighted	21	-0.1256	0.285	0.4275
COVID-19	ebi-a-GCST011073	Pain in joint	ukb-b-13019	Inverse variance weighted	5	0.0006	0.457	0.457
COVID-19	ebi-a-GCST011073	muscle or soft tissue injuries	ukb-b-7603	Inverse variance weighted	12	0.0008	0.401	0.457
COVID-19	ebi-a-GCST011073	Type 1 diabetes	finn-b-E4_DM1	Inverse variance weighted	21	0.133	0.169	0.338
COVID-19	ebi-a-GCST011073	Type 2 diabetes	finn-b-E4_DM2	Inverse variance weighted	21	0.1018	0.162	0.338
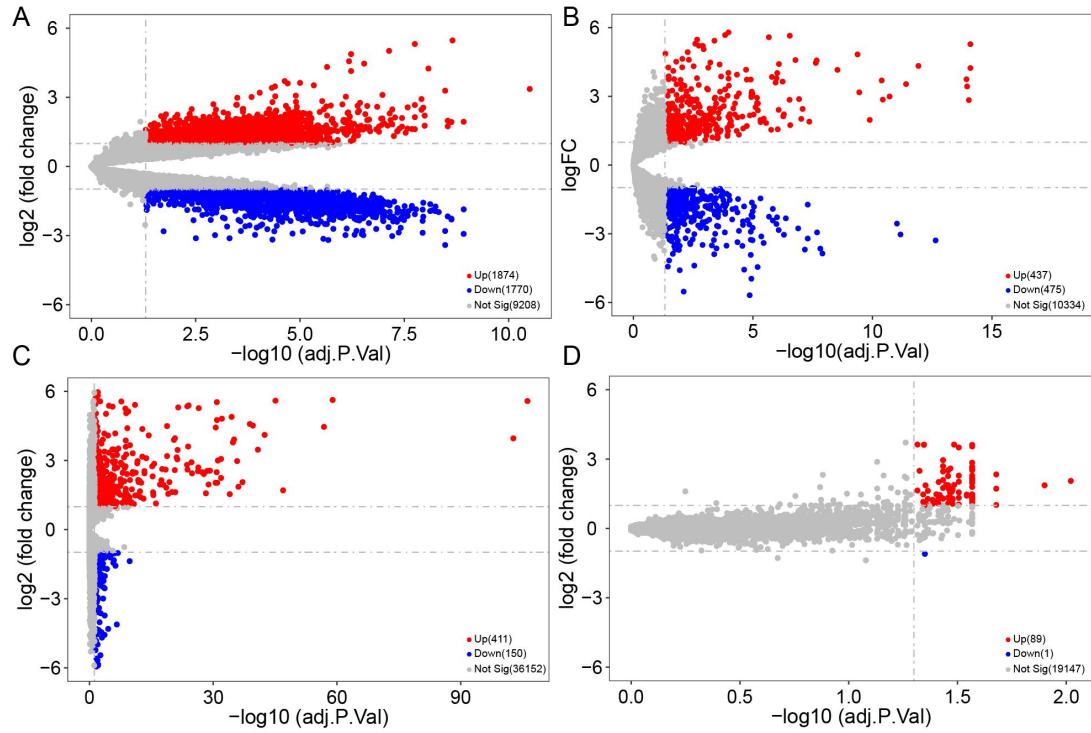
Figure S2. Identification of differential expressed genes. **A** Volcano map of DEGs in COVID-19; blue indicates downregulated DEGs and red upregulated DEGs. **B** Volcano map of DEGs in KOA; blue indicates downregulated DEGs and red upregulated DEGs. **C- D** Volcano map of DEGs in URTI; blue indicates downregulated DEGs and red upregulated DEGs
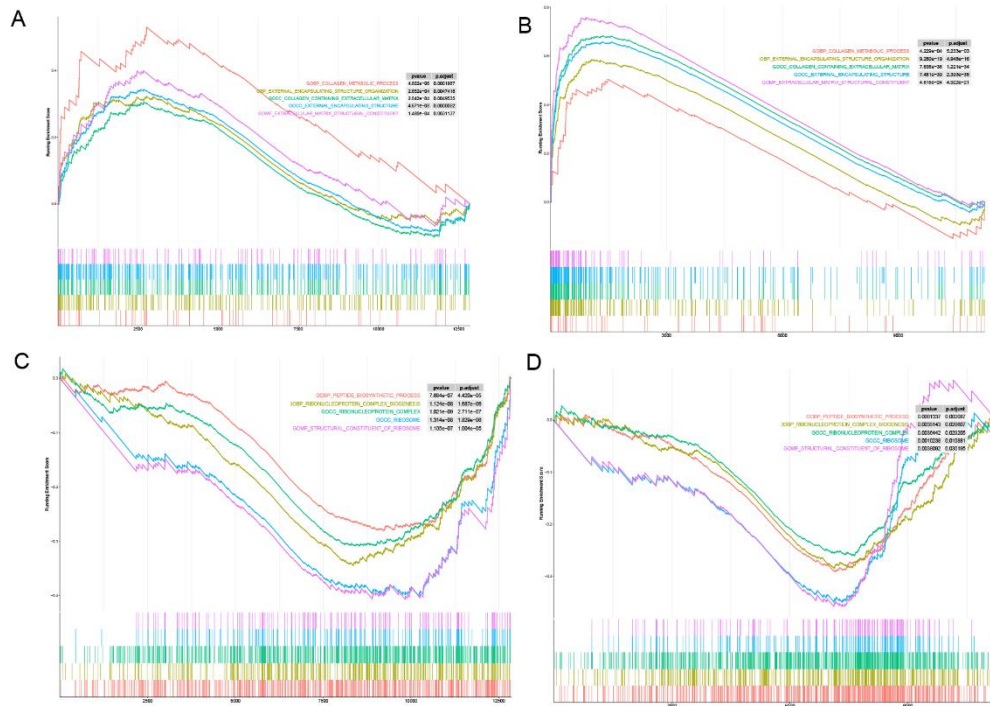
Figure S3. Gene set enrichment analysis. **A-B** Five common positive enrichment pathways of COVID-19 and KOA (collagen metabolic process; external encapsulating structure organization; collagen containing extracellular matrix; external encapsulating structure; extracellular matrix structural constituent). **C-D** Five common negative enrichment pathways of COVID-19 and KOA (peptide biosynthetic process; ribonucleoprotein complex biogenesis; ribonucleoprotein complex; ribosome structural constituent of ribosome)
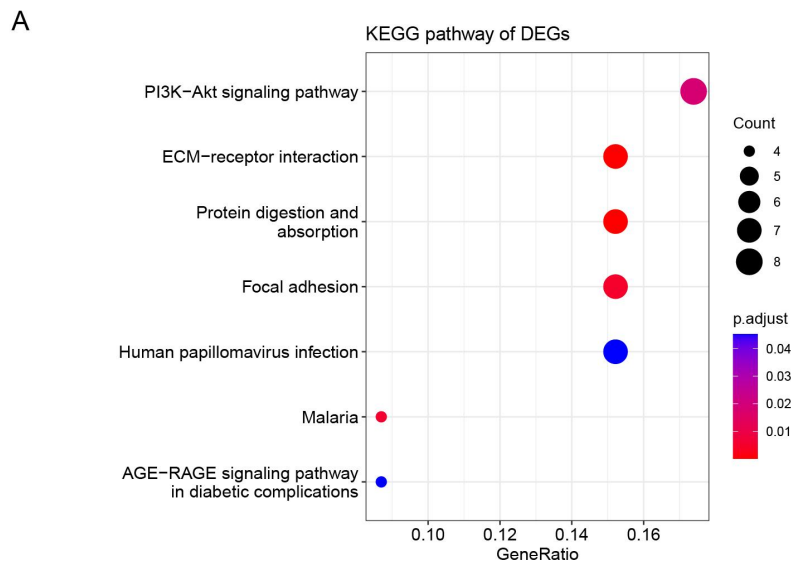

Figure S4. KEGG enrichment analysis of 91 DEGs
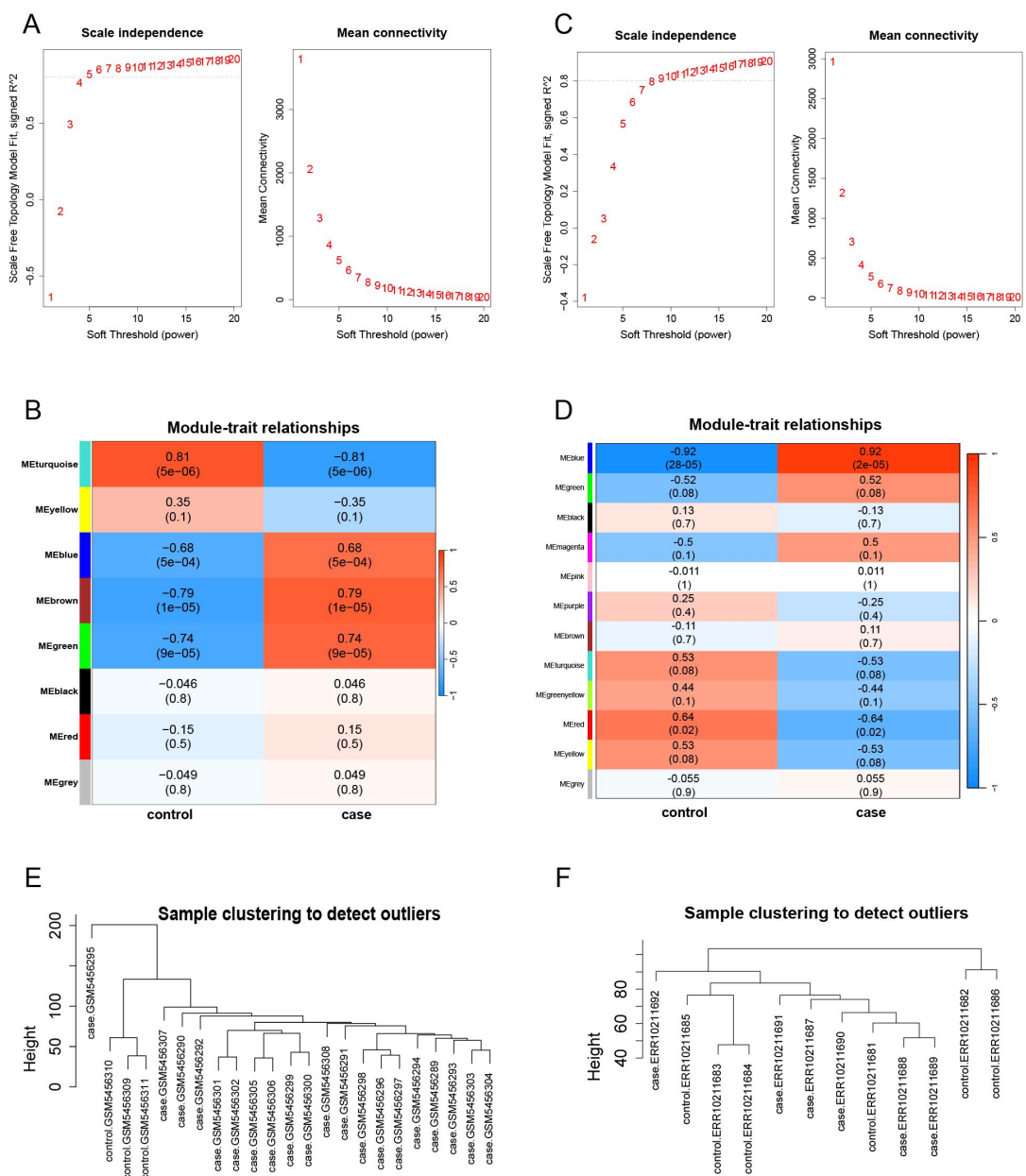
Figure S5. WGCNA. **A, C** Scaleless index and average connectivity of individual soft thresholds for COVID-19 and KOA, **A** for COVID-19 and **C** for KOA. **B, D** Heatmap of the correlation between module characteristic genes and COVID-19 and KOA, **B** for COVID-19 and **D** for KOA; blue indicates a negative correlation, while red a positive correlation. **E, F** Cluster tree of COVID-19 and KOA samples, **E** for COVID-19 and **F** for KOA. One sample (case.GSM5456295) was eliminated as an outlier from the COVID-19 samples.
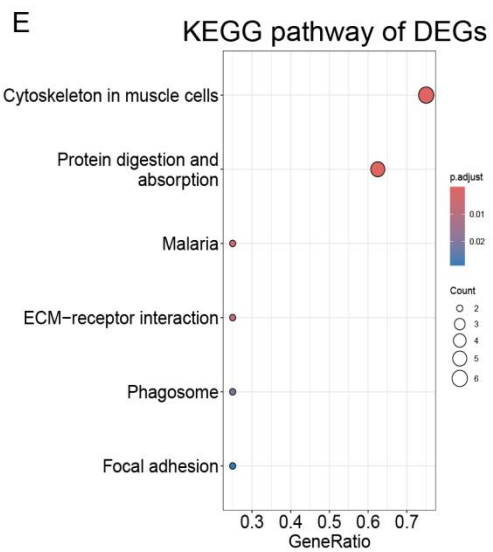
A

B **Biological Process of DEGs**

C **Cell Component of DEGs**

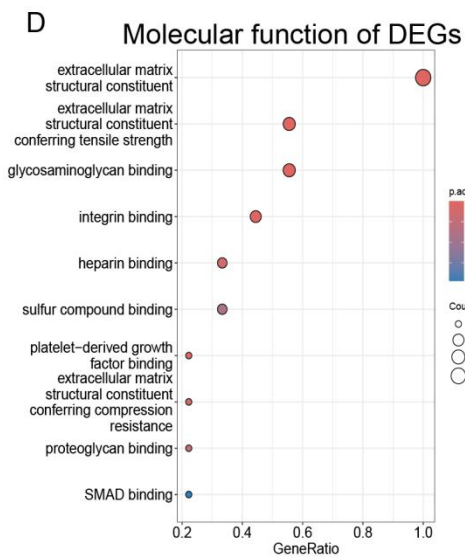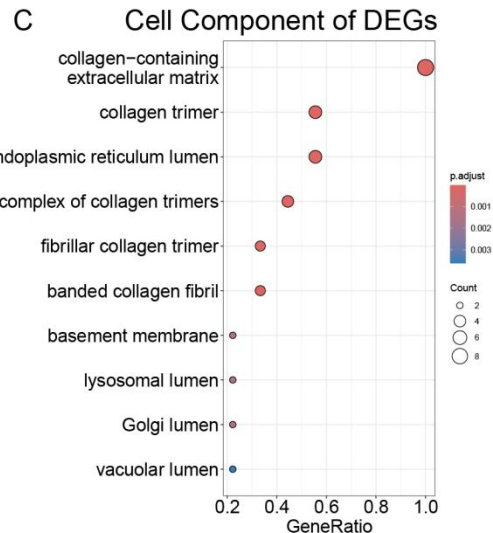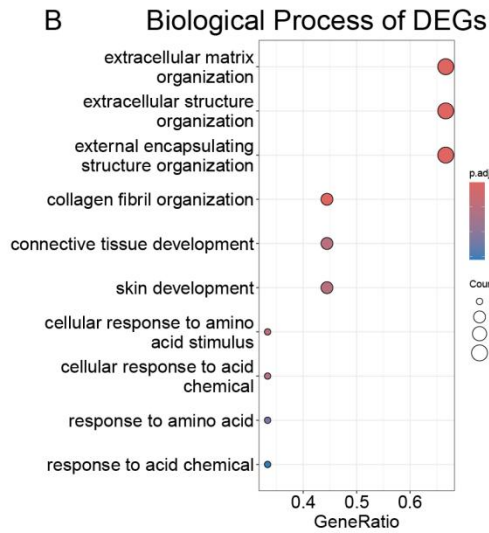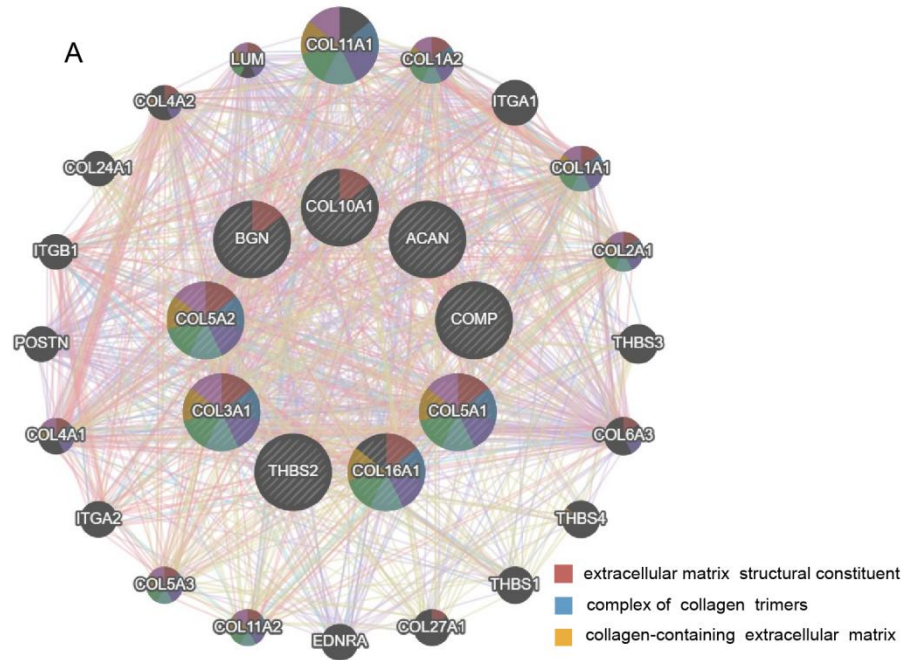D **Molecular function of DEGs**

E **KEGG pathway of DEGs**

Figure S6. **A** GeneMANIA diagram shows the coexpression interactions between the nine identified shared core genes and their neighbouring genes. Colour codes indicate functions shared by genes. **B-E** GO and KEGG enrichment analyses of the nine core genes
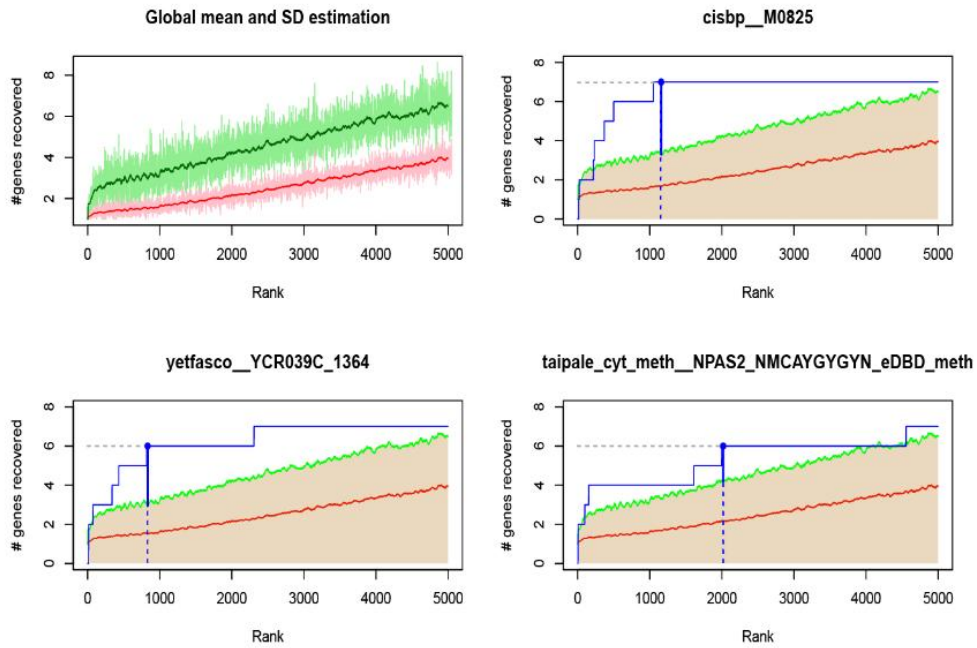

Figure S7. Three motifs exhibiting the highest AUC values. The recovery curve of each motif was averaged and represented by the red line, while the mean plus standard deviation was depicted by the green line. The recovery curve of the current motif is illustrated by the blue line. The maximum enrichment level was determined as the point of maximum distance between the current motif and the green curve (mean + standard deviation)
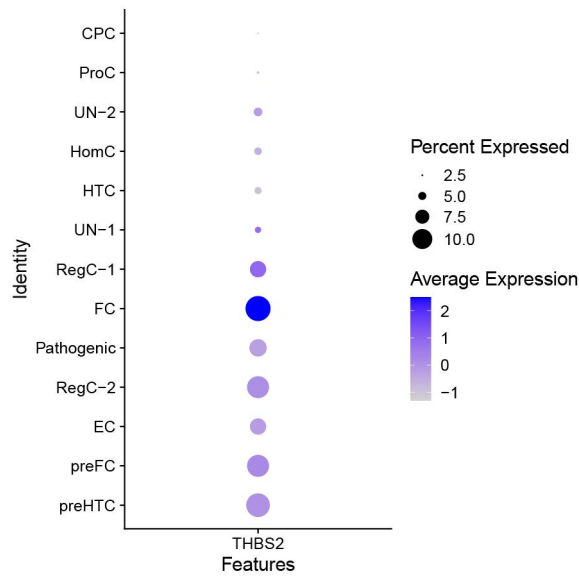
Figure S8. Bubble plot depicting the expression of THBS2 in different cellular subtypes of cartilage tissue

Table S6. The intersection of 91 genes between WGCNA module genes and common DEGs

91 genes list				
SRPX2	DNAJC22	DAPK2	THBS3	MAOA
ANGPTL2	BCL2	ALDH6A1	IQSEC1	RABGGTB
COL3A1	LYNX1	CCNG2	NPAS3	CITED2
COL5A2	CRLF1	NUP153	SLC22A17	RAB11FIP1
SMOC1	GFRA2	ZSCAN18	SSC5D	ENO2
CILP2	SHISA4	GLUL	DIO2	GPX3
BGN	FOXA3	SETD6	CKAP4	WSB1
COMP	AHDC1	RELA	ARPC5	EFCAB2
COL5A1	BAALC	ECHS1	SERPINH1	PRDM16
SLC35B4	THBS1	UFM1	SPON2	RBP4
COL10A1	LMF1	STXBP1	RPL24	CDC37L1
NPTN	ENHO	FKBP15	MXI1	COL1A1
MXRA8	GPX8	ASL	ZC3H7A	LTBP3
COL6A1	GALNT10	SDC4	UBA2	ATOH8
SMO	SOX8	PTPN1	CCNI	GPM6B
COL16A1	NDRG1	DCXR	FBXO21	ECI2
ACAN	NSA2	ASCC1	CDK2AP2	UAP1
THBS2	LETMD1	ZBTB16	CCNB1IP1	BTG2
METTL16				