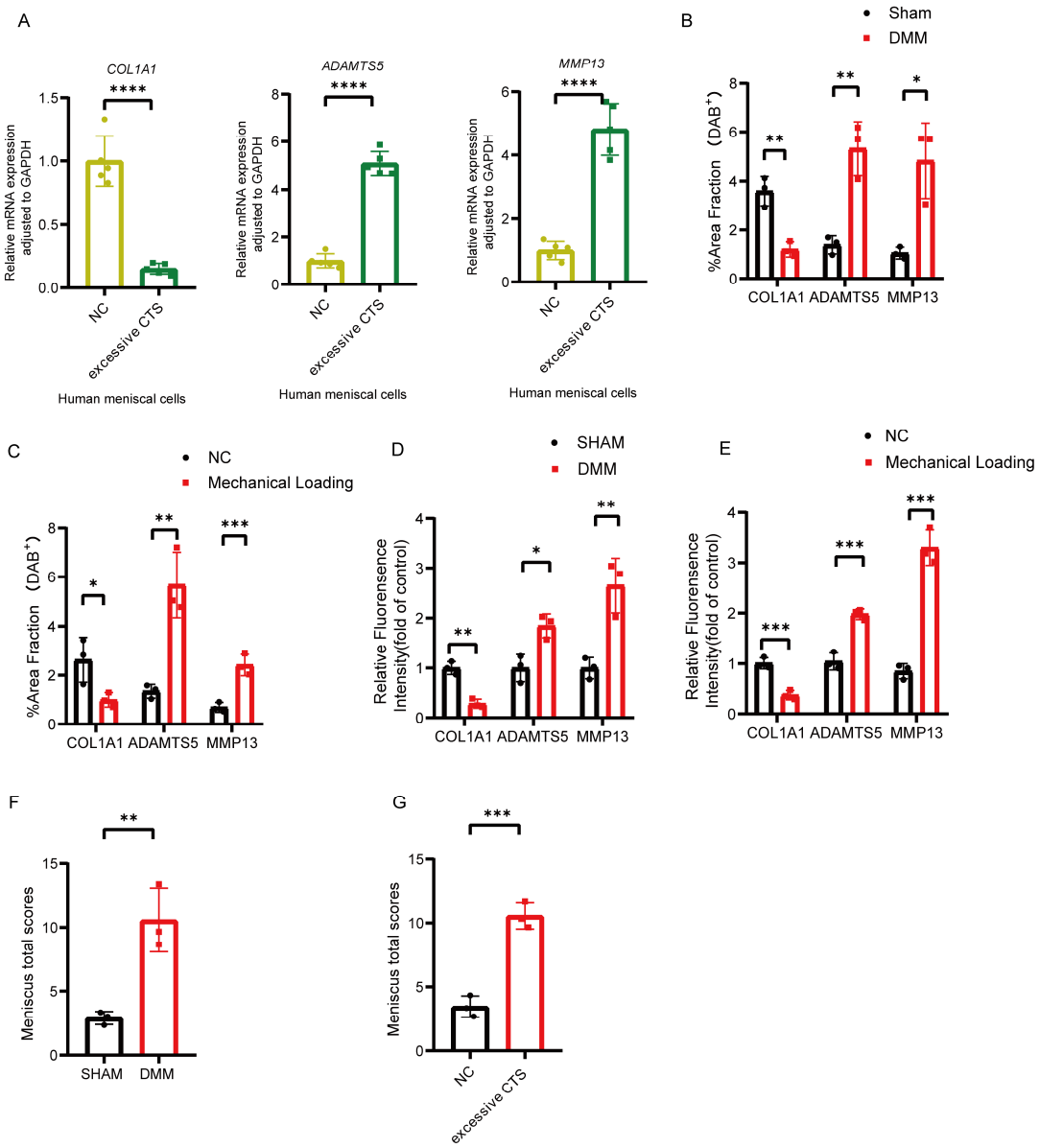
Supplementary Figure 1

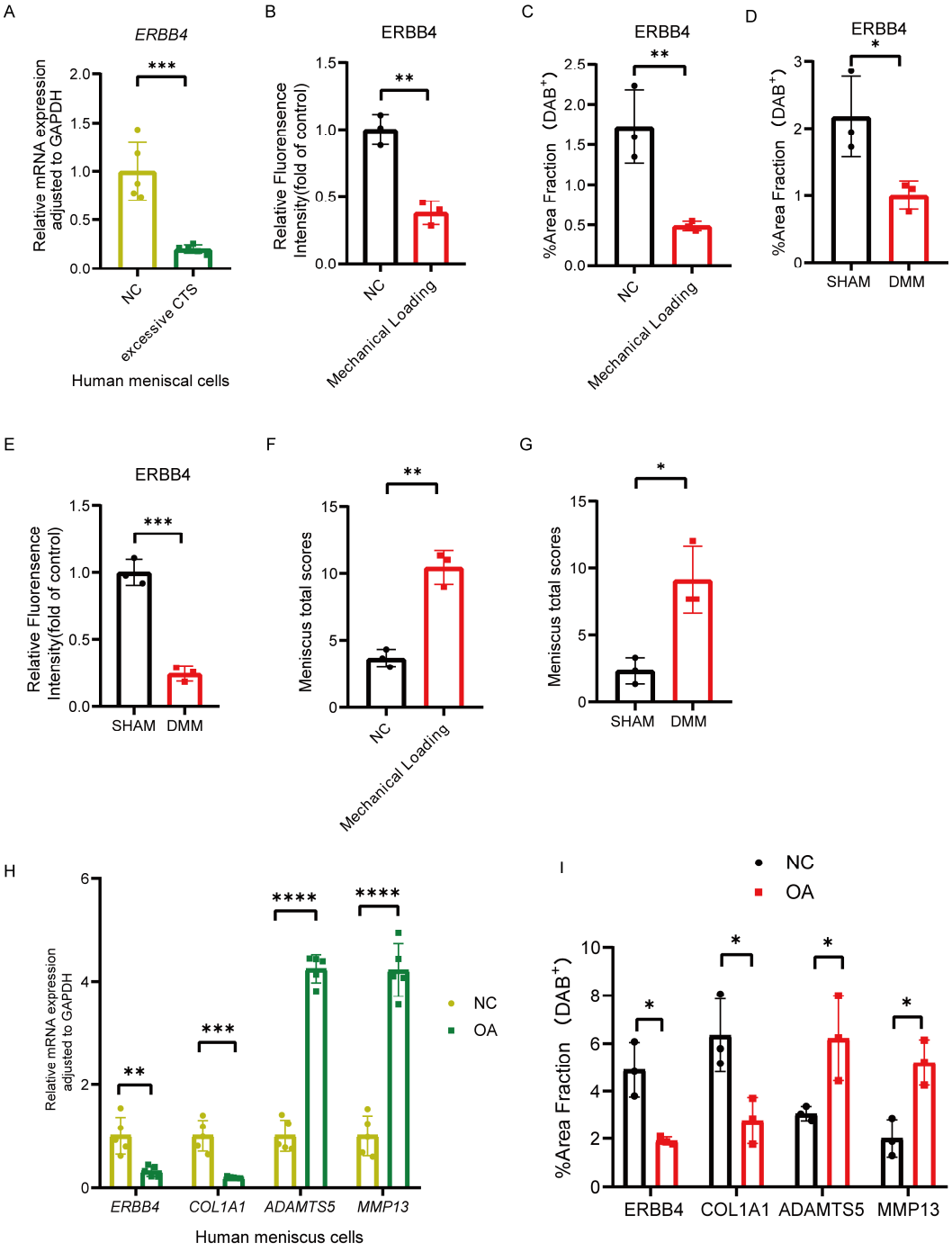


Supplementary Figure 1. Validation and quantification of the meniscal catabolic phenotype induced by excessive mechanical loading.

(A) RT-qPCR analysis of the mRNA expression levels of the anabolic marker *COL1A1* and the catabolic markers *ADAMTS5* and *MMP13* in human meniscal cells subjected to excessive CTS or control conditions. $n = 5$ per group; (B, C) Quantification of immunohistochemical staining, expressed as the percentage of DAB-positive area for COL1A1, ADAMTS5, and MMP13 in the indicated groups. $n = 3$ per group; (D, E) Quantification of the relative fluorescence intensities of COL1A1, ADAMTS5, and MMP13 in the indicated groups. $n = 3$ per group; (F) Total meniscal histopathological scores in the SHAM and destabilization of the medial meniscus (DMM) groups; (G) Total meniscal scores in the negative control (NC) and excessive CTS groups. Data are presented as mean ± SD. Statistical analysis was performed using a two-tailed unpaired

Student’s t test. *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001. ns: not significant.

Supplementary Figure 2

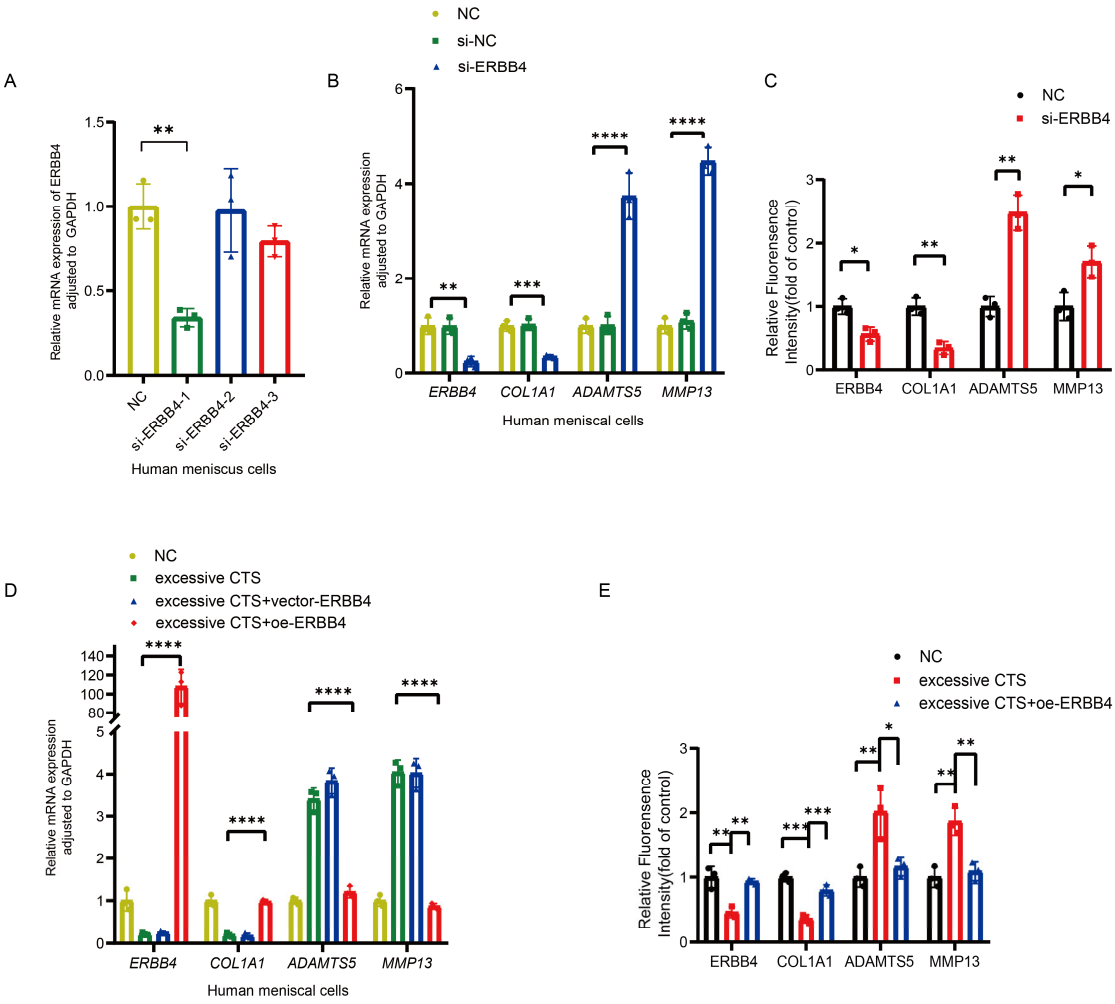


Supplementary Figure 2. Validation of ERBB4 downregulation in mechanically stressed and OA-associated meniscal samples.

(A) RT-qPCR analysis of *ERBB4* mRNA expression in human meniscal cells exposed to excessive CTS or control conditions. $n = 5$ per group; (B, C) Quantification of ERBB4 fluorescence intensity and immunohistochemical staining intensity in the control and mechanical loading groups. $n = 3$ per group; (D, E) Quantification of ERBB4 fluorescence intensity and immunohistochemical staining intensity in the sham and DMM groups. $n = 3$ per group; (F) Total meniscal scores in the NC and mechanical

loading groups; (G) Total meniscal scores in the SHAM and DMM groups; (H) RT-qPCR analysis of *ERBB4*, *COL1A1*, *ADAMTS5*, and *MMP13* mRNA expression in human meniscal cells derived from the normal control (NC) and osteoarthritis (OA) groups. $n = 3$ per group; (I) Quantification of immunohistochemical staining, expressed as the percentage of DAB-positive area for ERBB4, COL1A1, ADAMTS5, and MMP13 in the indicated groups. $n = 3$ per group. Data are presented as mean ± SD. Statistical analysis was performed using a two-tailed unpaired Student's t test. *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001. ns: not significant.

Supplementary Figure 3

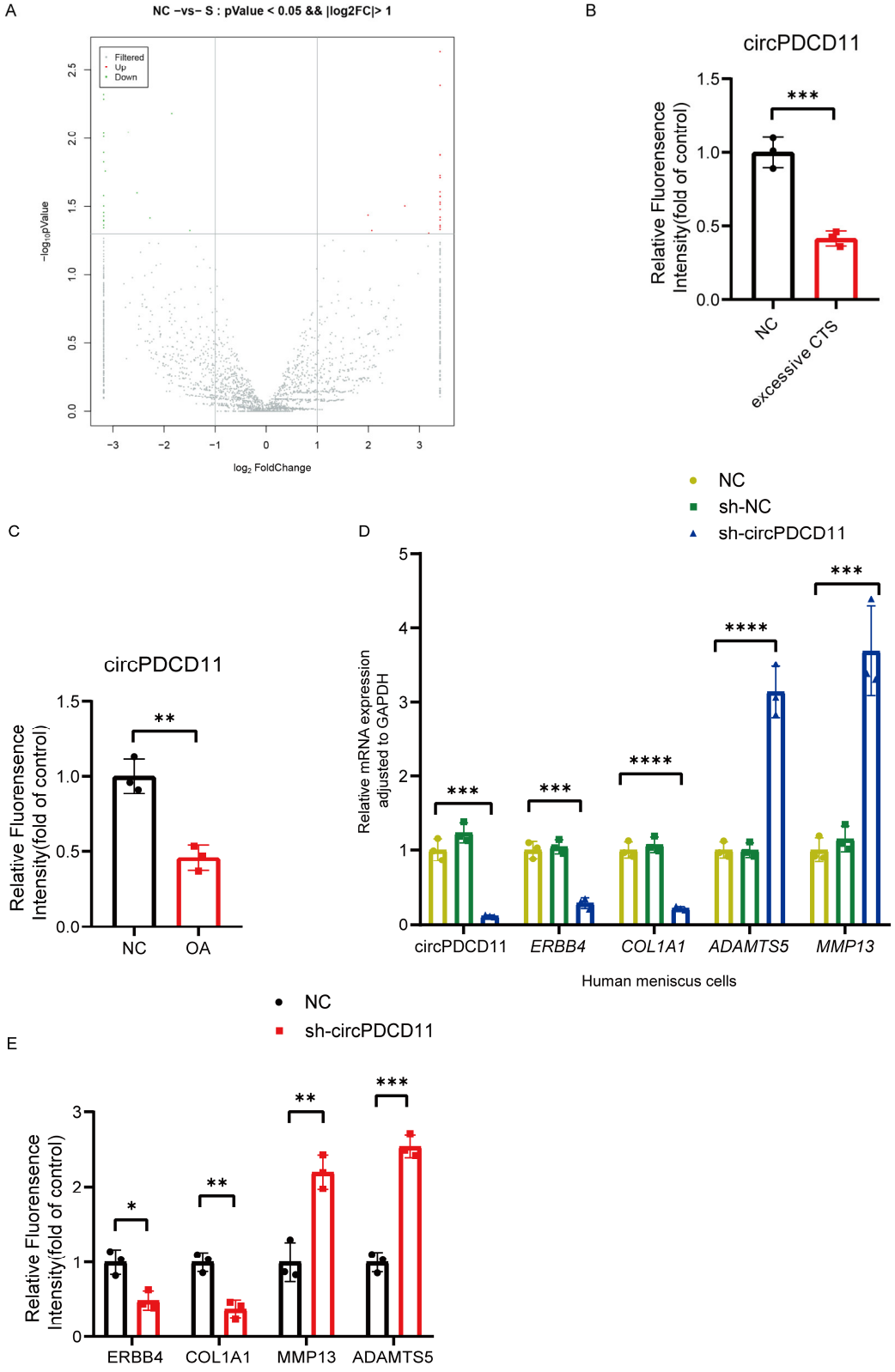


Supplementary Figure 3. Validation of ERBB4 loss- and gain-of-function experiments.

(A) RT-qPCR validation of *ERBB4* siRNA knockdown efficiency. Statistical analysis was performed using one-way ANOVA; (B) RT-qPCR analysis of *ERBB4, COL1A1, ADAMTS5,* and *MMP13* mRNA expression in human meniscal cells transfected with *ERBB4*-targeting siRNA (si-*ERBB4*) or the corresponding negative control (si-NC). Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple-comparison test; (C) Quantitative analysis of ERBB4, COL1A1, MMP13, and ADAMTS5 fluorescence intensities in control and *ERBB4*-silenced meniscal cells. Statistical analysis was performed using a two-tailed unpaired Student's t test; (D) RT-qPCR analysis of *ERBB4, COL1A1, ADAMTS5,* and *MMP13* expression in human meniscal cells subjected to excessive CTS following transfection with an ERBB4-overexpression construct or the corresponding empty vector. Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple-comparison test; (E) Quantitative analysis of ERBB4, COL1A1, MMP13, and ADAMTS5 fluorescence intensities in meniscal cells exposed to excessive CTS, with or without *ERBB4* overexpression. Statistical analysis was performed using one-way ANOVA followed by

Tukey's multiple-comparison test. All data are presented as mean ± SD. $n = 3$ independent experiments per group. *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001. ns: not significant.

Supplementary Figure 4

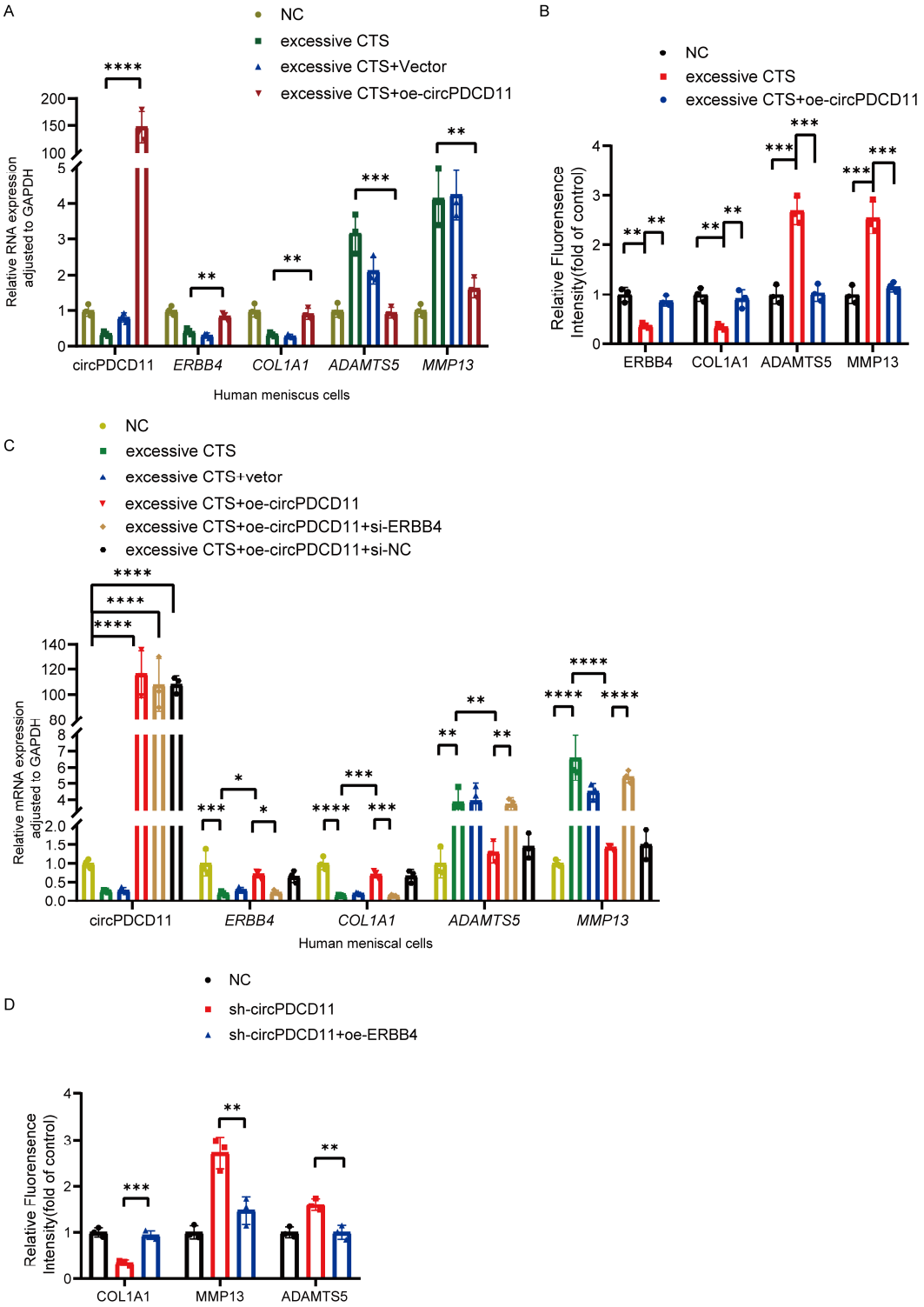


Supplementary Figure 4. Validation of circPDCD11 expression and knockdown phenotypes.

(A) Volcano plot showing differentially expressed circRNAs in human meniscal cells

subjected to excessive CTS compared with normal control (NC) cells; (B, C) Quantification of the relative circPDCD11 fluorescence intensity in the indicated groups. Statistical analysis was performed using a two-tailed unpaired Student's t test; (D) RT-qPCR analysis of circPDCD11, *ERBB4, COL1A1, ADAMTS5,* and *MMP13* expression in human meniscal cells following circPDCD11 knockdown. Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple-comparison test; (E) Quantification of the relative fluorescence intensities of ERBB4, COL1A1, MMP13, and ADAMTS5 in the indicated groups. Statistical analysis was performed using a one-tailed unpaired Student's t test. Data are presented as mean ± SD. $n = 3$ independent experiments per group. *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001. ns: not significant.

Supplementary Figure 5

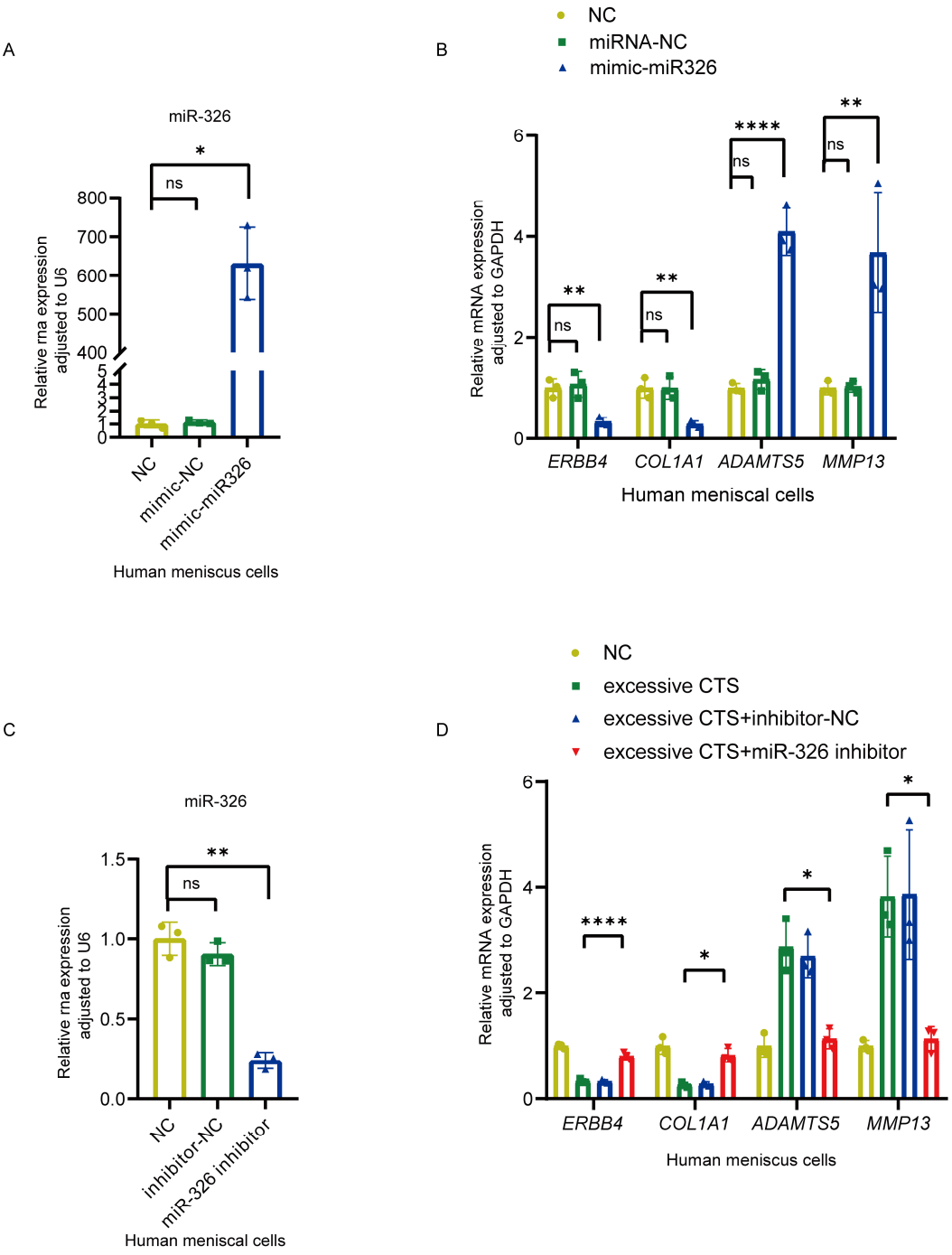


Supplementary Figure 5. Validation of circPDCD11 overexpression and ERBB4 rescue experiments.

(A) RT–qPCR analysis of circPDCD11, *ERBB4, COL1A1, ADAMTS5*, and *MMP13* expression in human meniscal cells subjected to excessive CTS following circPDCD11 overexpression or transfection with the corresponding empty vector; (B) Quantitative

analysis of ERBB4, COL1A1, MMP13, and ADAMTS5 fluorescence intensities in human meniscal cells exposed to excessive CTS, with or without circPDCD11 overexpression; (C) RT-qPCR analysis of circPDCD11, *ERBB4*, *COL1A1*, *ADAMTS5*, and *MMP13* expression in human meniscal cells subjected to excessive CTS following circPDCD11 overexpression, with or without concomitant ERBB4 knockdown; (D) Quantification of the relative fluorescence intensities of COL1A1, MMP13, and ADAMTS5 in the indicated groups. Data are presented as mean ± SD. $n = 3$ independent experiments per group. Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple-comparison test. *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001. ns: not significant.

Supplementary Figure 6

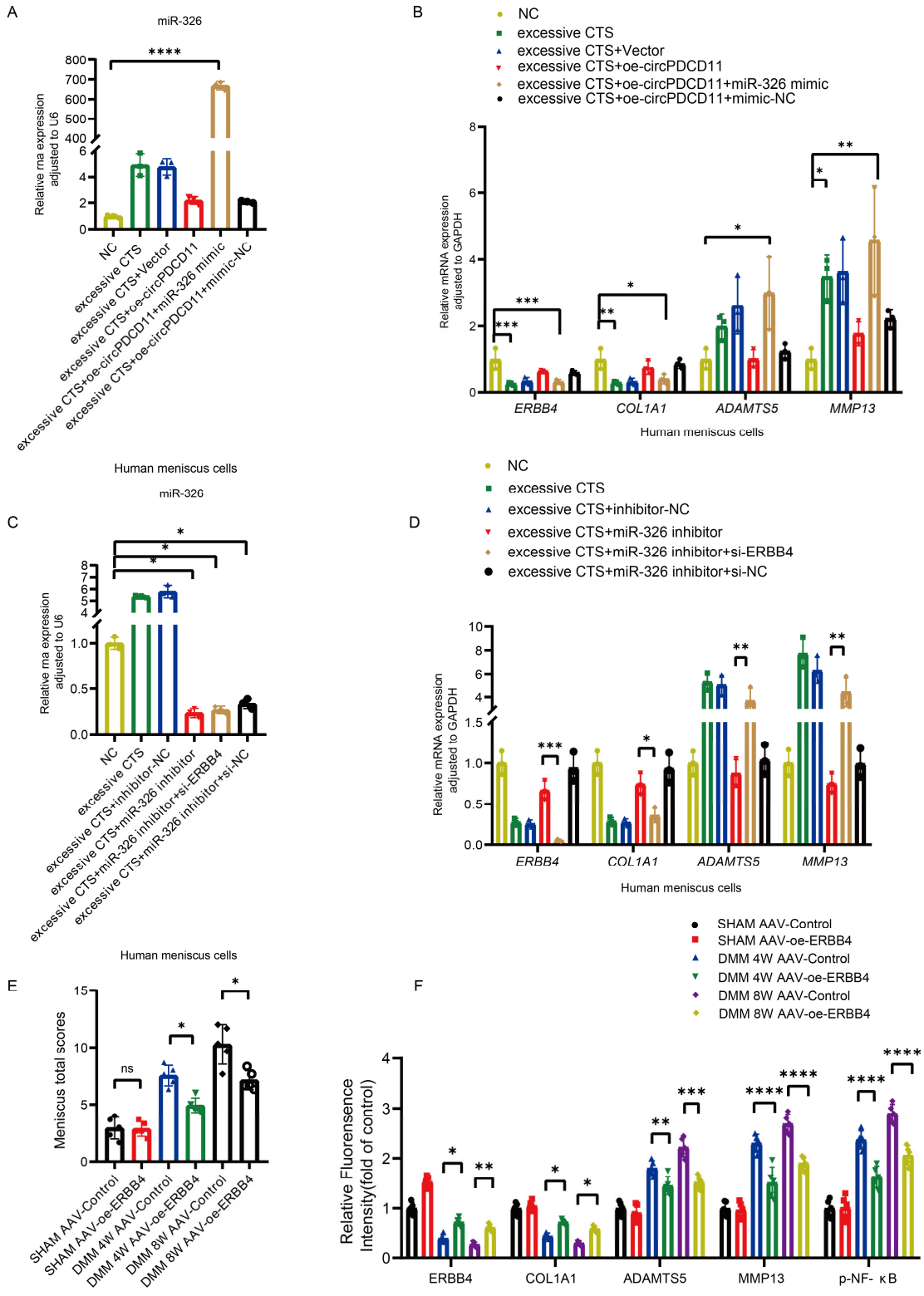


Supplementary Figure 6. Validation of miR-326 gain- and loss-of-function experiments.

(A) RT-qPCR detection of miR-326 mimic transfection efficiency; (B) RT-qPCR detection of *COL1A1*, *ADAMTS5*, and *MMP13* levels in meniscal cells after miR-326 overexpression; (C) RT-qPCR detection of miR-326 inhibitor transfection efficiency; (D) RT-qPCR analysis of *ERBB4*, *COL1A1*, *ADAMTS5*, and *MMP13* expression in human meniscal cells treated with miR-326 inhibitor under excessive CTS stimulation.

All data are presented as mean ± SD. Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple-comparison test. $n = 3$ independent experiments per group. *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001. ns: not significant.

Supplementary Figure 7

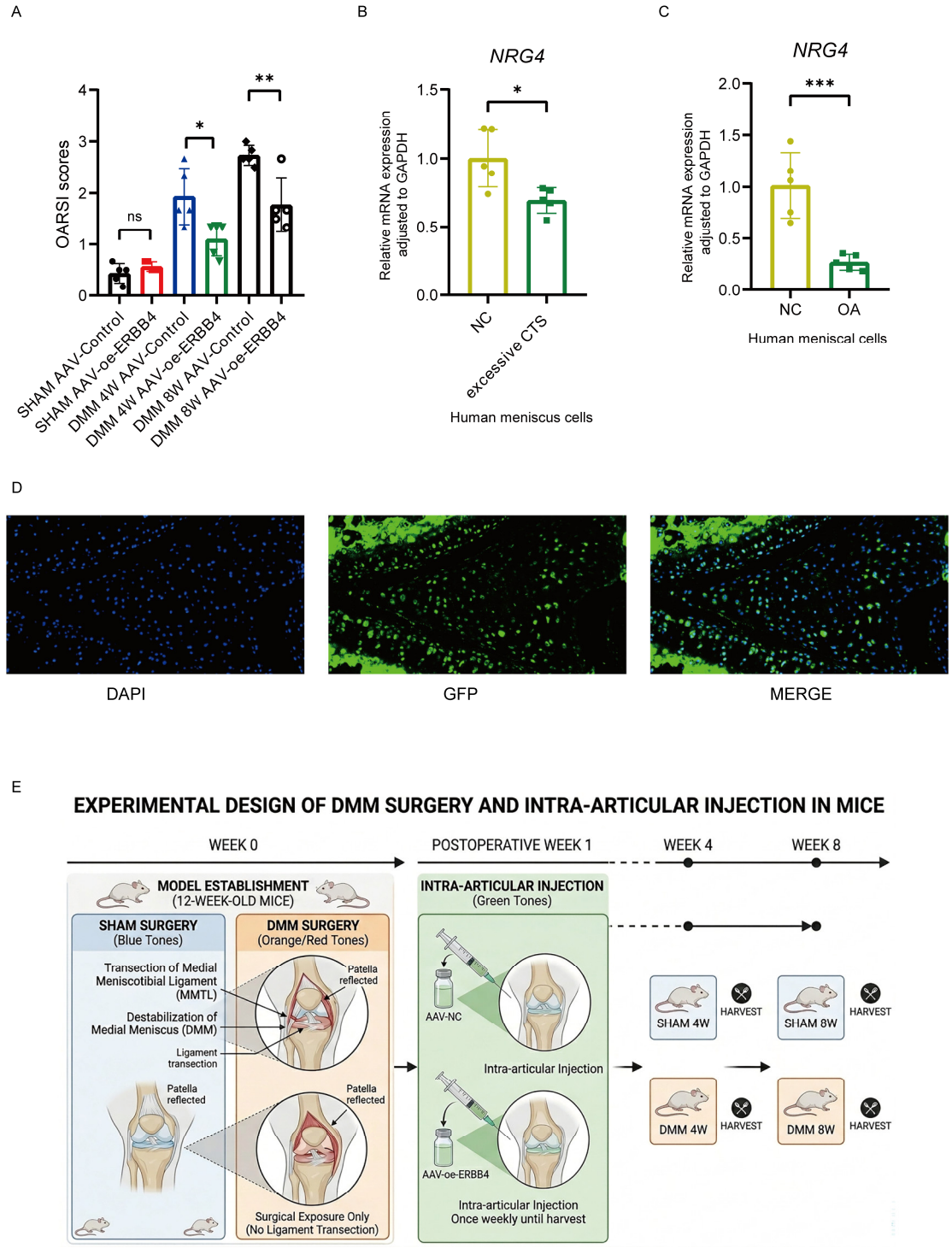


Supplementary Figure 7. Validation of circPDCD11/miR-326/*ERBB4* rescue experiments.

(A) RT-qPCR validation of miR-326 mimic transfection efficiency in the control and indicated experimental groups. $n = 3$ per group; (B) RT-qPCR analysis of *ERBB4*,

COL1A1, *ADAMTS5*, and *MMP13* expression in human meniscal cells subjected to excessive CTS after circPDCD11 overexpression with or without miR-326 mimic transfection. $n = 3$ per group; (C) RT-qPCR validation of miR-326 inhibitor transfection efficiency in the control and indicated experimental groups. $n = 3$ per group; (D) RT-qPCR analysis of *ERBB4*, *COL1A1*, *ADAMTS5*, and *MMP13* expression in human meniscal cells treated with miR-326 inhibitor with or without ERBB4 knockdown under excessive CTS stimulation. $n = 3$ per group; (E) Meniscal histological scores in SHAM and DMM mice receiving AAV-Control or AAV-oe-ERBB4 treatment at the indicated time points; (F) Quantification of the relative fluorescence intensities of ERBB4, COL1A1, ADAMTS5, MMP13, and p-NF-κB. $n = 5$ per group. All data are presented as mean ± SD. Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple-comparison test. $n = 3$ independent experiments per group. *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001. ns: not significant.

Supplementary Figure 8

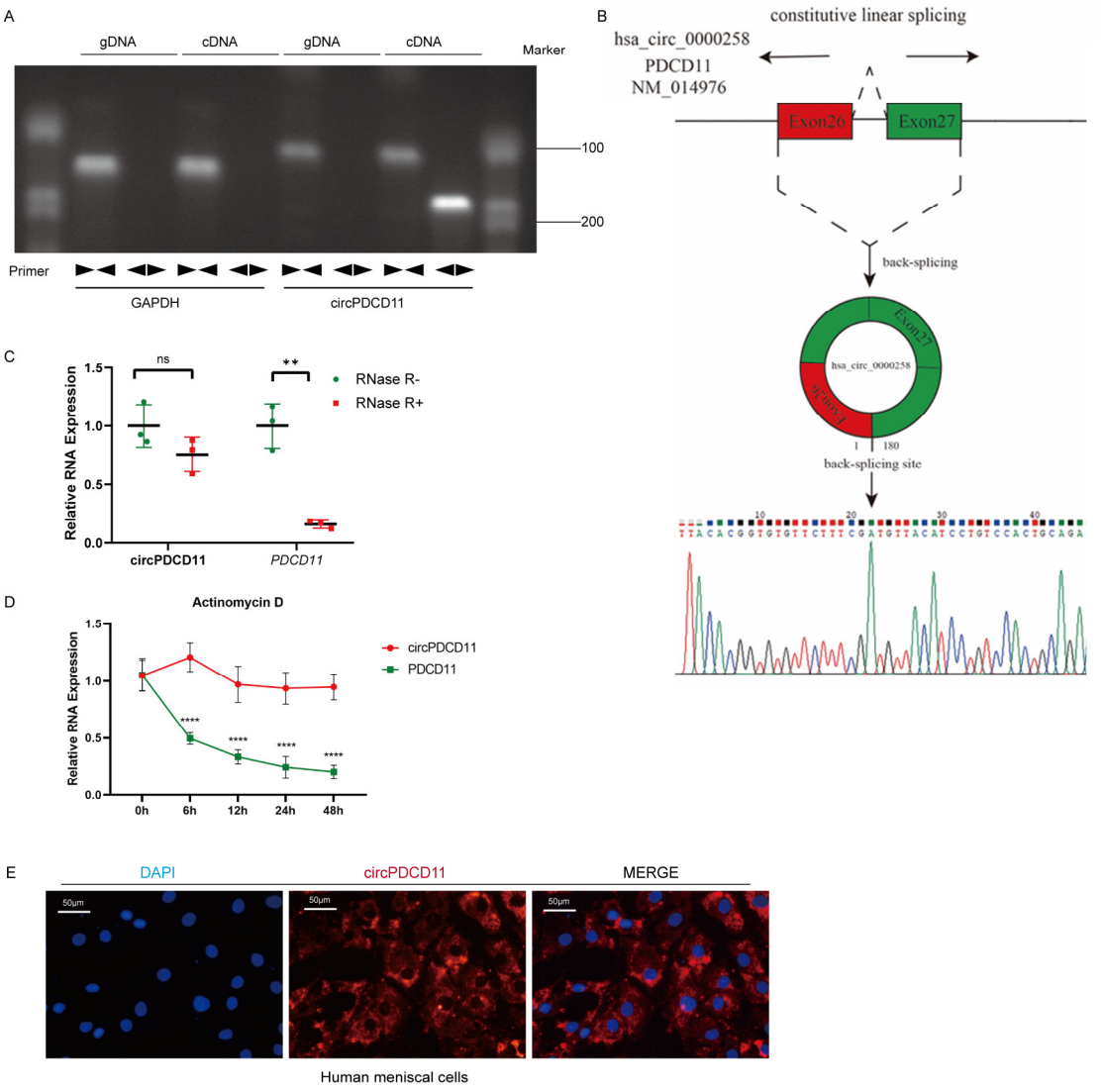


Supplementary Figure 8. Exploratory NRG4 expression and validation of intra-articular AAV delivery.

(A) Cartilage OARSI scores in SHAM and DMM mice receiving AAV-Control or AAV-oe-ERBB4 treatment at the indicated time points. $n = 5$ per group. Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple-comparison test; (B) RT-qPCR analysis of NRG4 expression in human meniscal cells subjected to excessive mechanical stress and control conditions. $n = 5$ per group. Statistical analysis

was performed using a two-tailed unpaired Student's t test; (C) RT-qPCR analysis of NRG4 expression in human meniscal cells derived from the OA and NC groups. $n = 5$ per group. Statistical analysis was performed using a two-tailed unpaired Student's t test; (D) Fluorescence microscopy for frozen sections confirmed that AAV-oe-ERBB4 carrying GFP fragment could be taken up by meniscal cells after articular injection in mice; (E) Schematic diagram illustrating the procedure of in vivo experiment. All data are presented as mean ± SD. Statistical analysis was performed using a two-tailed unpaired Student's t test. *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001. ns: not significant.

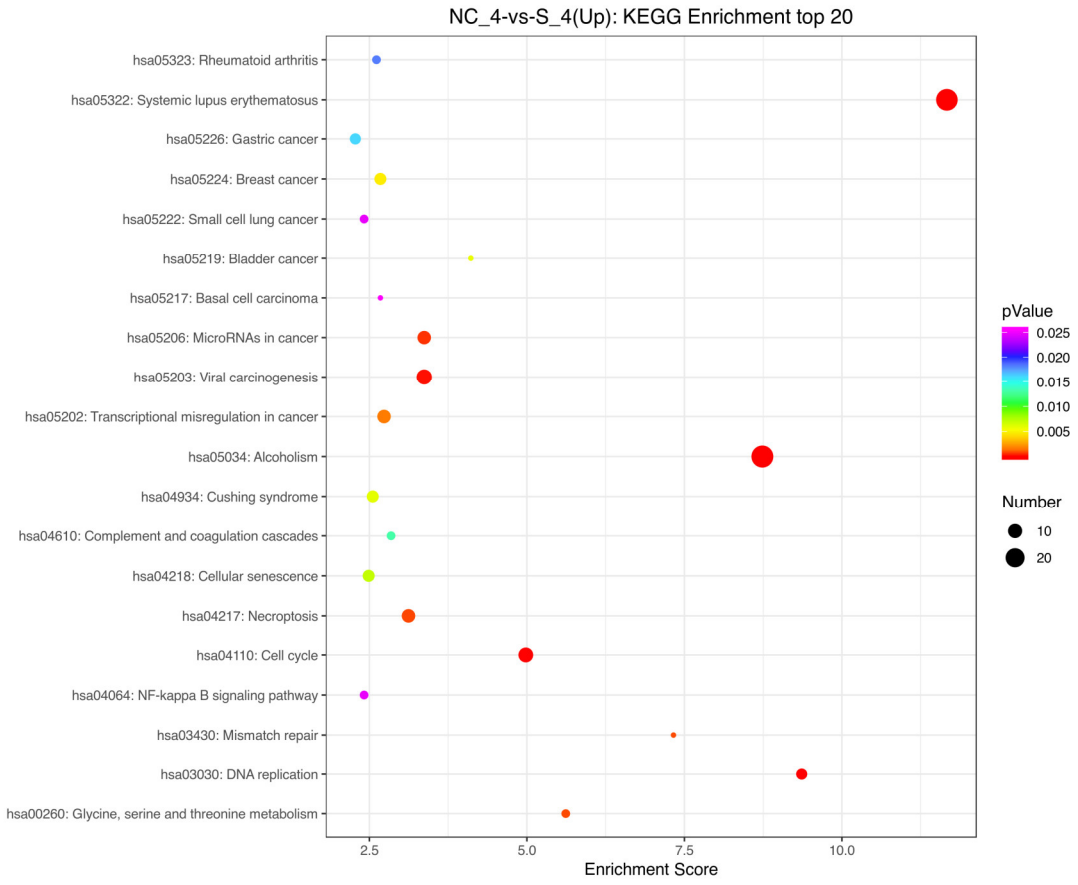
Supplementary Figure 9



Supplementary Figure 9. Experimental validation of the circular structure and stability of circPDCD11.

(A) Divergent and convergent primers for amplifying circPDCD11 in cDNA and gDNA; (B) Sanger sequencing indicating the head-to-tail splicing site of circPDCD11; (C) RT-qPCR detection of circPDCD11 and linear mRNA (PDCD11) expression levels in human primary meniscal cells stimulated with RNase. Statistical analysis was performed using a two-tailed unpaired Student's t test; (D) RT-qPCR detection of circPDCD11 and linear mRNA (PDCD11) expression levels in human primary meniscal cells stimulated with actinomycin D. Statistical analysis was performed using two-way ANOVA followed by Tukey's multiple-comparison test; (E) FISH localization of circPDCD11 expression in human primary meniscal cells; All data are presented as mean ± SD. *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001. ns: not significant.

Supplementary Figure 10



Supplementary Figure 10. KEGG enrichment analysis.

Supplementary Table 1. Primary Antibody Information

Antibodies for Western Blots	Article number and manufacturer	Working concentration
ERBB4	# YT1613, Immunoway	1：1000
CollagenI	#72026, CST	1：1000
ADAMTS5	# GB150099-100, Servicebio	1：1000
MMP13	#69926, CST	1：1000
NF-κB	#80979-1-RR, ProteinTech	1：5000
p-NF-κB	#82335-1-RR, ProteinTech	1：2000
GAPDH	# GB15004-100, Servicebio	1：5000
Antibodies for IF	Article number and manufacturer	Working concentration
ERBB4	# YT1613, Immunoway	1：200
CollagenI	#67288-1-Ig, ProteinTech	1：2500
ADAMTS5	# GB150099-100, Servicebio	1：500
MMP13	#18165-1-AP, ProteinTech	1：50
NF-κB	#80979-1-RR, ProteinTech	1：125
p-NF-κB	#82335-1-RR, ProteinTech	1：100
Antibodies for IHC		
ERBB4	# YT1613, Immunoway	1：100
CollagenI	#67288-1-Ig, ProteinTech	1：400
ADAMTS5	# GB150099-100, Servicebio	1：500
MMP13	#18165-1-AP, ProteinTech	1：50

Supplementary Table 2. Primer Information

Gene	Primiers
GAPDH-F	CGCTCTCTGCTCCTCCTGTTC
GAPDH-R	ATCCGTTGACTCCGACCTTCAC
ERBB4-F	GCAGATGCTACGGACCTTACG
ERBB4-R	GACACTGAGTAACACATGCTCC
COL1A1-F	GAGGGCCAAGACGAAGACATC
COL1A1-R	CAGATCACGTCATCGCACAAC
ADAMTS5-F	GGGCACTGGCTACTATGTGG
ADAMTS5-R	CGTCACAGCCAGTTCTCACA
MMP13-F	CCAGACTTCACGATGGCATTG
MMP13-R	GGCATCTCCTCCATAATTTGGC
NRG4-F	TGTGGCATTGGCGGTCCTAGTA
NRG4-R	ACTGCTCGTCTCTACCAGGTTG
hsa_circPDCD11-F	ACACGGTGTGTTCTTTCGATGT
hsa_circPDCD11-R	ACCCTACATAGCCCCTCAGAAG
U6-F	CTCGCTTCGGCAGCACA
U6-R	AACGCTTCACGAATTTGCGT
miR-326-F	CGCCTCTGGGCCCTTC
miR-326-R	AGTGCAGGGTCCGAGGTATT
MiR-326 RT primer	GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACCTGGAG
miR-330-5p-F	CGCGGATTCTGTGTCCGG
miR-330-5p-R	AGTGCAGGGTCCGAGGTATT
miR-330-5p RT primer	GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACAGAGAC

Supplementary Table 3. Plasmid Information

hsa-mir-326 mimics	CCUCUGGGCCCUUCCUCCAG
hsa-mir-326 mimics Complementary	CUGGAGGAAGGGCCCAGAGG
hsa-mir-326 inhibitor	CUGGAGGAAGGGCCCAGAGG
hsa-mir-330-5p mimics	CGGAUUCUGUGUCCGGGUCUCU
hsa-mir-330-5p mimics Complementary	AGAGACCCGGACACAGAAUCCG
hsa-mir-330-5p inhibitor	AGAGACCCGGACACAGAAUCCG
s-ERBB4-1	GAGCAAGAATTGACTCGAA
si-ERBB4-2	GGCCTATTGTGGCAGAGAA
si-ERBB4-3	GACCATTGGTGGAAGAGTA
si-hsa_circPDCD11	GTTCTTTCGATGTTACATCCT
hsa_circPDCD11-probe	AGTGGACAGGATGTAACATCGAAAGAACACACCGTGTGG