

## **Supplementary Tables and Figures**

### **Intra-articular administration of I $\kappa$ B $\alpha$ kinase inhibitor suppresses mouse knee osteoarthritis via downregulation of the NF- $\kappa$ B/HIF-2 $\alpha$ axis**

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		Vehicle	50 nM	500 nM	5 $\mu$ M	50 $\mu$ M	500 $\mu$ M
Body weight (g)	0 w	24.7	23.5	24.4	23.6	25.4	24.6
	8 w	27.8	28	27.4	26.7	27.8	27.8
Rate of weight gain	(%)	12.6	19.1	12.3	13.1	9.4	13.0
<i>P</i> vs Vehicle			0.40	1.00	0.80	0.82	1.00

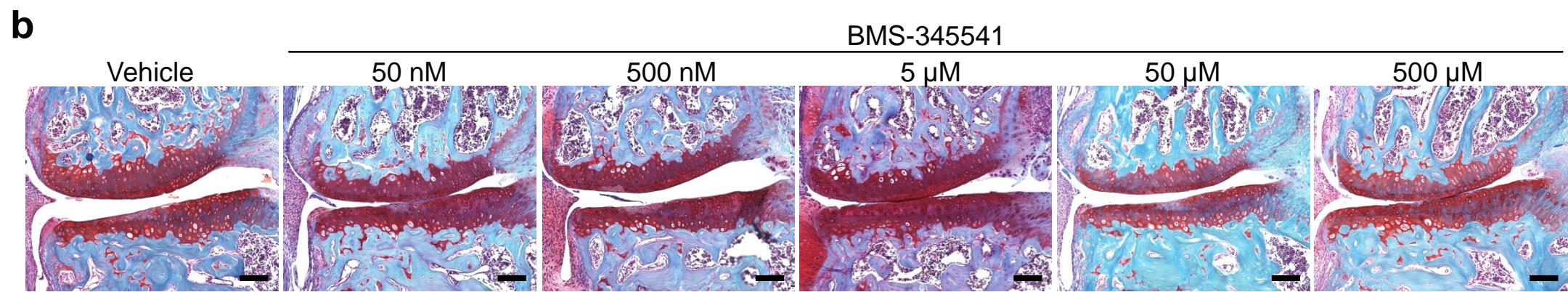
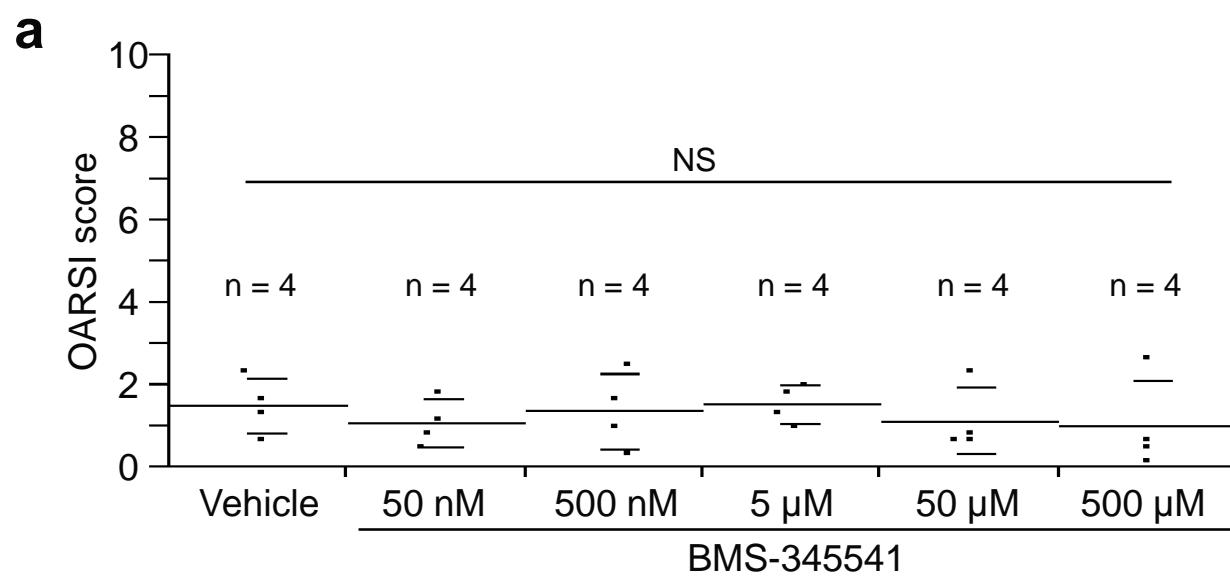
**Supplementary Table S1** Body weights of mice after 8 weeks of BMS-345541 treatment. Data as expressed as means. *P* values were determined by the Kruskal-Wallis & Dunn's post hoc test for unequal variance.

Grade	Osteoarthritic damage
0	Normal
0.5	Loss of Safranin-O without structural changes
1	Small fibrillations without loss of cartilage
2	Vertical clefts down to the layer immediately below the superficial layer and some loss of surface lamina
3	Vertical clefts/erosion to the calcified cartilage extending to <25% of the articular surface
4	Vertical clefts/erosion to the calcified cartilage extending to 25-50% of the articular surface
5	Vertical clefts/erosion to the calcified cartilage extending to 50-75% of the articular surface
6	Vertical clefts/erosion to the calcified cartilage extending >75% of the articular surface

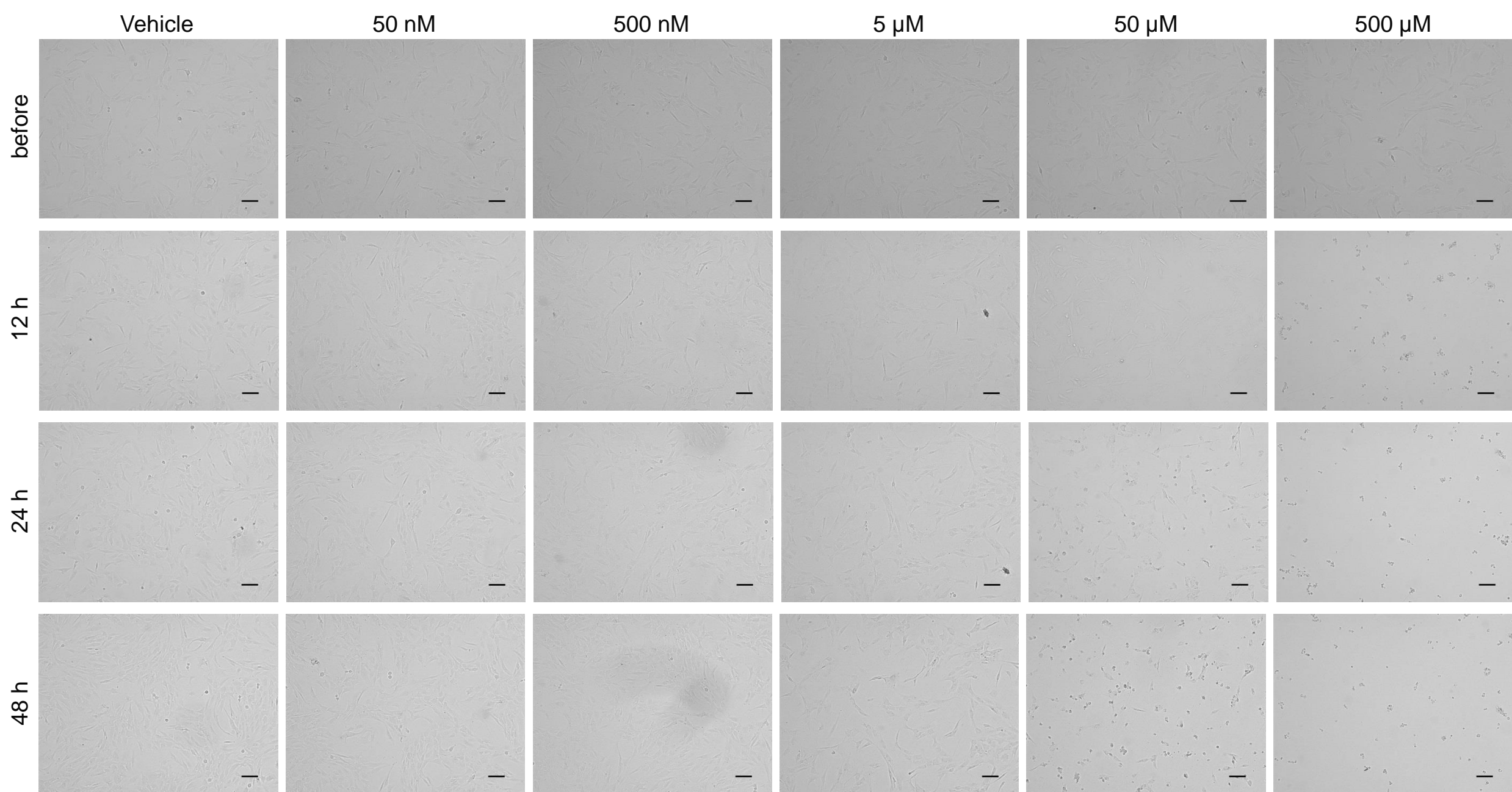
**Supplementary Table S2** The OARSI scoring system.

Gene Symbol		sequence
<i>MMP13</i>	F	TCCTACAAATCTCGCGGGAAT
	R	GCATTTCTCGGAGCCTCTCA
<i>ADAMTS5</i>	F	TATGACAAGTGC GGAGTATG
	R	TTCAGGCTAAATAGGCAGT
<i>COL2A1</i>	F	GGTGGCTTCCATTCAGCTA
	R	TACCGGTATGTTTCGTGCAG
<i>GAPDH</i>	F	GAAGGTGAAGGTCGGAGTCA
	R	GAAGATGGTGATGGGATTTC

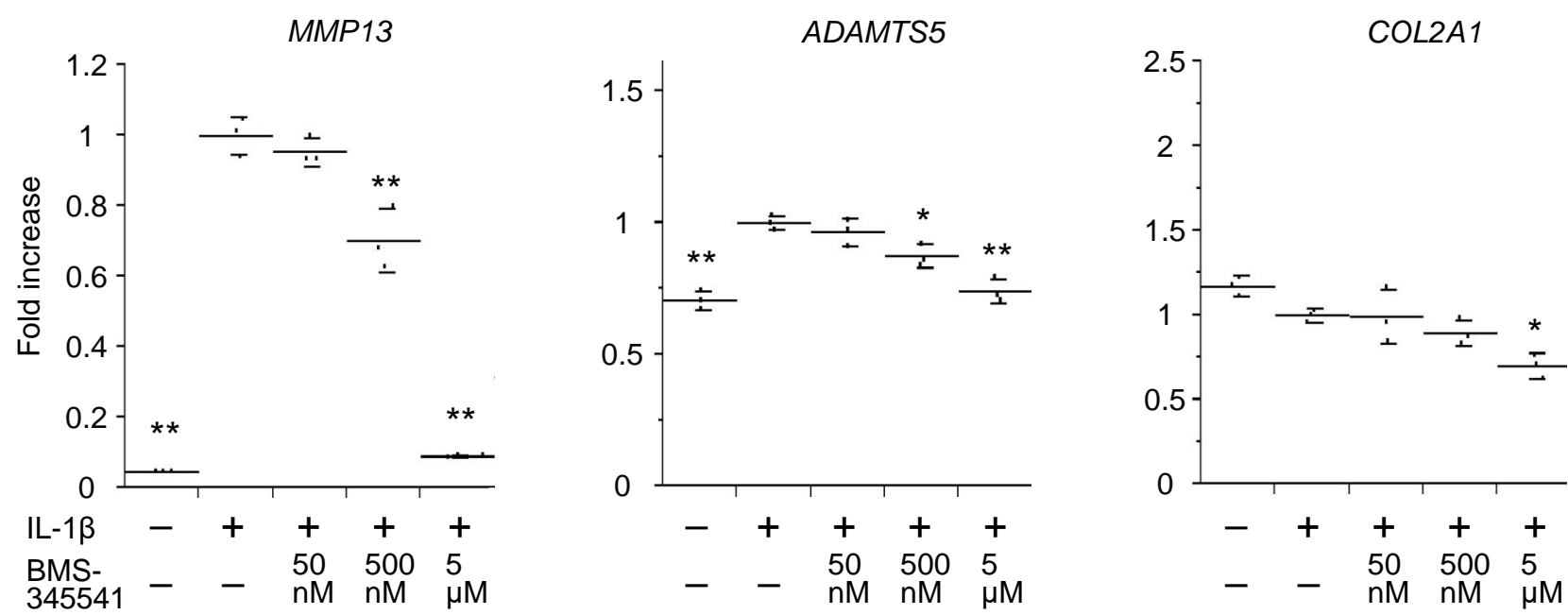
**Supplementary Table S3** Primers used for qRT-PCR.



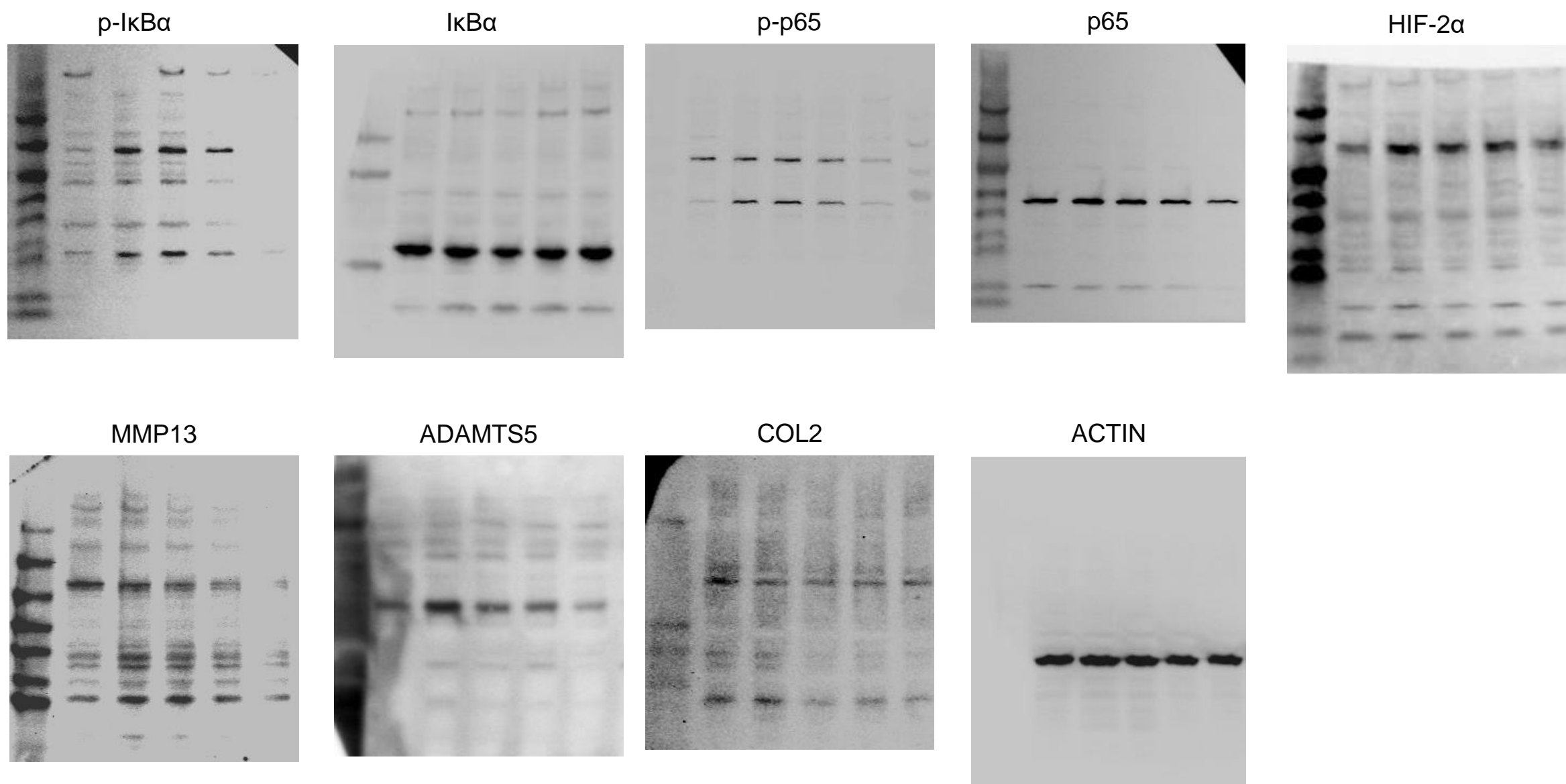
**Supplementary Figure S1 | OA development after 2-week BMS-345541 treatment.** (a) Quantification of OA development using the OARSI score. Symbols represent individual mice; long and short bars show the mean and SD, respectively. NS, not significant. (b) Representative safranin O staining from each experimental group. Scale bar, 100 μm.



**Supplementary Figure S2 | Human articular chondrocytes treated with BMS-345541.** Phase-contrast images of human articular chondrocytes treated with vehicle or 50 nM, 500 nM, 5 μM, 50 μM, 500 μM BMS-345541 for 48 hours. Scale bars, 100 μm.



**Supplementary Figure S3 | Effects of BMS-345541 in cultured human articular chondrocytes.** mRNA levels of *MMP13*, *ADAMTS5*, and *COL2A1* in human primary articular chondrocytes treated with different concentrations of BMS-345541 with or without 10 ng/ml IL-1 $\beta$ . BMS-345541 was added 3 h after IL-1 $\beta$  stimulation, and the cells were cultured for an additional 24 h. The cells obtained from the three individuals showed similar responses, and a representative result is shown. Symbols represent individual points; long and short bars show the mean and SD of three wells per group, respectively. \* $P < 0.05$ , \*\* $P < 0.0001$  vs IL-1 $\beta$ + / BMS-345541- by the Kruskal-Wallis test and Dunn's *post hoc* test for unequal variance.



**Supplementary Figure S4 | Original images of the immunoblots shown in Fig. 5b.**