Fig. S1. Chondrocyte-specific deletion of Tak1 results in reduced chondrocyte proliferation. (A) BrdU immunohistochemistry of growth plate cartilage sections from one-month-old Col2a1-CreER^{2}; Tak1^{f/f} (Cre^{+}; Tak1^{f/f}) mice and Cre-negative control littermates (Tak1^{f/f}) injected with Tamoxifen at one week of age and with BrdU three hours prior to sacrifice. (B) Primary sternal chondrocytes isolated from Tak1^{f/f} mice were infected with adenovirus encoding GFP (Ad-GFP), Cre recombinase (Ad-Cre), or TAK1 (Ad-TAK1). After 72 hours, cells were labeled with BrdU for 4 hours and subsequently harvested for BrdU incorporation analysis. *P<0.01, one-way ANOVA followed by Newman-Keuls post test.
Fig. S2. Postnatal chondrocyte-specific deletion of Tak1 results in reduced proteoglycan content in the articular cartilage at three months of age. (A) Radiographic analyses of three-month-old Col2a1-CreERT2; Tak1f/f (Cre+; Tak1f/f) mice and Cre-negative control littermates (Tak1f/f) following injection with Tamoxifen at one week of age. (B) 5× images of Alcian blue/hematoxylin/Orange G staining of knee joint sections from three-month-old Col2a1-CreERT2; Tak1f/f (Cre+; Tak1f/f) mice and Cre-negative control littermates (Tak1f/f) injected with Tamoxifen at one week of age. (C) High magnification images (20×) of the articular cartilage (upper panels) or growth plate cartilage (lower panels) from corresponding boxed regions in panel B. (D) SOX9 immunohistochemistry of articular cartilage sections from three-month-old Col2a1-CreERT2; Tak1f/f (Cre+; Tak1f/f) mice and Cre-negative control littermates (Tak1f/f) injected with Tamoxifen at one week of age.

Fig. S3. TAK1 kinase activity positively regulates BMP2-mediated Sox9 gene expression. RCS cells were starved of serum for 12 hours and then treated with vehicle, 5Z-7-oxozeanol (TI-2, 3 μM) alone, BMP2 (100 ng/ml) alone, or TI-2 and BMP2 in combination for either 3 hours (A) or 24 hours (B). Total RNA was harvested from the cultures for quantitative real-time RT-PCR analysis of Sox9 gene expression. *P<0.01, one-way ANOVA followed by Newman-Keuls post test.
Fig. S4. TGF-β1 does not induce Sox9 gene expression in committed chondrocytes. RCS cells (A) or wild type primary sternal chondrocytes (B) were starved of serum for 12 hours and then treated with vehicle, 5Z-7-oxozeanol (TI-2, 3 μM) alone, BMP2 (100 ng/ml) alone, TGF-β1 (5 ng/ml) alone, TI-2 and BMP2 in combination, or TI-2 and TGF-β1 in combination for 3 hours. Total RNA was harvested from the cultures for quantitative real-time RT-PCR analysis of Sox9 gene expression. *P<0.01, one-way ANOVA followed by Newman-Keuls post test. (C) Luciferase reporter assay using lysates from RCS cells transfected with a luciferase reporter construct containing a 1.0 kb fragment of the Sox9 promoter. The cells were serum starved for 12 hours and then treated with either vehicle, 5Z-7-oxozeanol (TI-2, 3 μM) alone, BMP2 (100 ng/ml) alone, TGF-β1 (5 ng/ml) alone, TI-2 and BMP2 in combination, or TI-2 and TGF-β1 in combination for 8 hours. *P<0.05, one-way ANOVA followed by Newman-Keuls test. (D) Primary sternal chondrocytes from Tak1<sup>fl/fl</sup> mice were infected with adenovirus encoding GFP (Ad-GFP) or Cre-recombinase (Ad-Cre). Forty-eight hours later, cells were harvested for quantitative real-time RT-PCR analyses of the indicated genes. *P<0.05, Student’s t-test.
Fig. S5. ATF2 binds to the Sox9 promoter in response to BMP2 signaling. ChIP assay using cell lysates from primary sternal chondrocytes serum starved for 12 hours and then treated with vehicle or BMP2 (100 ng/ml) for 90 minutes. PCR amplification of chromatin from these lysates before (input) or after immunoprecipitation with an anti-ATF2 antibody or non-immune IgG is shown. PCR primers are described in Fig. 6C.
Table S1. Primers used for RT-PCR

| Mouse primers | Tak1                        | 5’-CTGCCAGTGAAGATGATCG-3’  
|               |                            | 5’-CAGGCTCATACAACTTGAC-3’  
|               | Aggrecan I                 | 5’-CCTGCTACTTCATCGACCCC-3’ 
|               |                            | 5’-AGATGCTTGTGACTGAACCT-3’ 
|               | Col2a1                     | 5’-CCACACCAAAATCCTGTTCA-3’ 
|               |                            | 5’-ACTGGTAAGTGGGGCAAGAC-3’ 
|               | Col10a1                    | 5’-CTTTGTGTCCTTTCAATCG-3’  
|               |                            | 5’-GTGAGGTACAGCCTACCAGT-3’ 
|               | Col1a1                     | 5’-TGGTTTGGGAGAGGCTGAGCA-3’ 
|               |                            | 5’-TTGCTGAGATGCTACGCTGGT-3’ 
|               | Col9a1                     | 5’-CGACCGACCAGCACATCAA-3’  
|               |                            | 5’-AGGGGGACCTTAAATGCCT-3’  
|               | Adamts5                    | 5’-CCCAGGATAAAACAGGCAG-3’  
|               |                            | 5’-CGGCAAGGGATTTGAAATGG-3’ 
|               | Mmp13                      | 5’-TTTGGGACACCGGGAAAGA-3’  
|               |                            | 5’-ACTTTGTCGAATCGTGCTT-3’  
|               | Sox9                       | 5’-AGGAAGCTGCGAGACCAGTA-3’ 
|               |                            | 5’-CGTTCTTCACCCGACTTTCT-3’ 
|               | Sox5                       | 5’-ATGGGAGCTGCGAGGAATAAGT-3’ 
|               |                            | 5’-CCACCACTCGTCAGCTAGG-3’  
|               | Sox6                       | 5’-ATGGCAACACAAACCTCACTCT-3’ 
|               |                            | 5’-AGGTAGACGTATTTCCGGAAGGA-3’ 
|               | Id1                        | 5’-TGACAGCAGAGTGATGGAAC-3’  
|               |                            | 5’-GCACTGTAGTCTCGCGTCAGG-3’ 
|               | Pai-1                      | 5’-GGTCATGGAACAAAGAATG-3’  
|               |                            | 5’-GCTGAGACTGAGATGGCTG-3’  
|               | β-actin                    | 5’-AGATGCTGATGACGAAGCAG-3’  
|               |                            | 5’-GGGGAAGTGGTGGTTTGCTA-3’ 
|               | Atf2                       | 5’-CTACGAGGGCGTCAGAGTA-3’  |
5’-GGGGAATCAATGAAAACCAA-3’

Rat primers

Sox9
5’-CGCCATCTTCAAGGCGCT-3’
5’-GTGTAGTCGTACTGTGAG-3’

β-actin
5’-GCTACAGCTTCACCACCACA-3’
5’-ATCGTACTCCTGGCTTCTGA-3’