Supplementary Information

Figure S1.

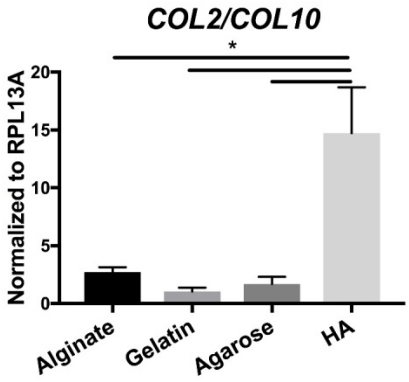

Figure S1. Ratio of *COL2/COL10* expression in MSCs undergoing chondrogenesis within in 4 different chondrosupportive scaffolds after 21 days chondrogenesis. Values are presented as mean ± SD (N = 4; *, $p < 0.05$).

Figure S2.

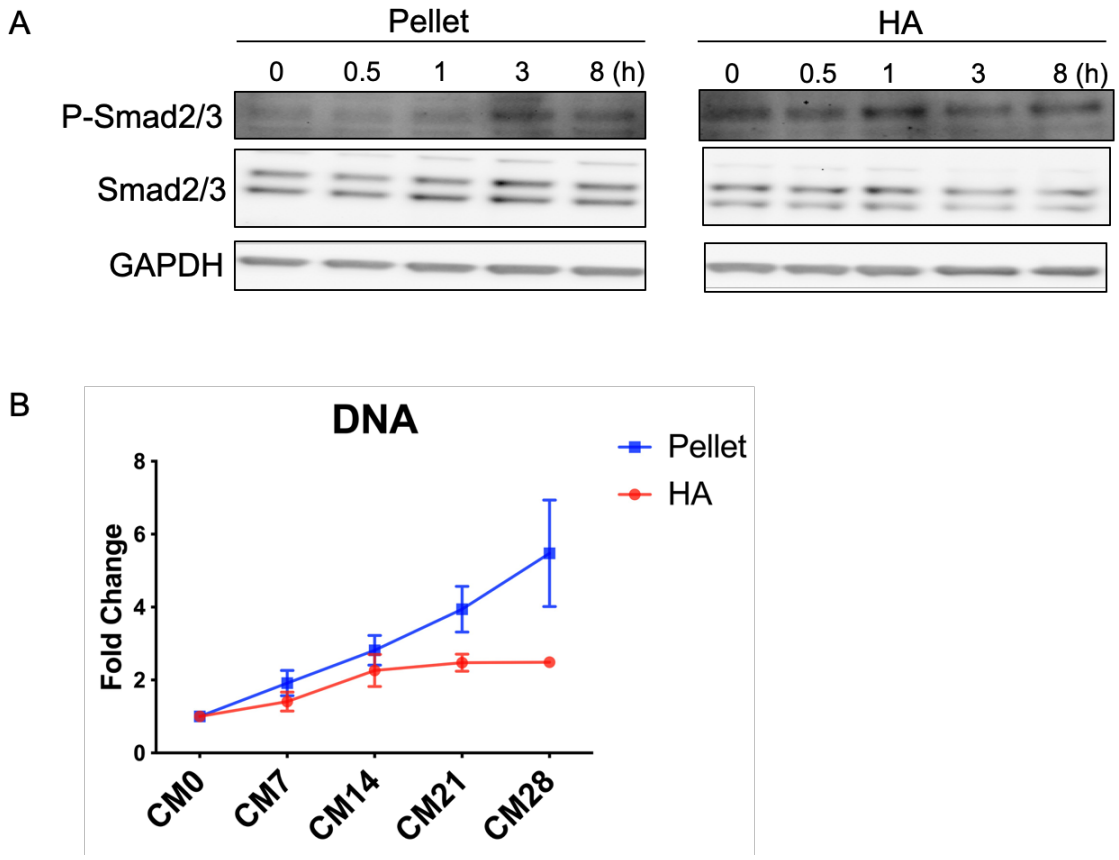
A
Pellet
HA
0
0.5
1
3
8 (h)
P-Smad2/3
Smad2/3
GAPDH
B
DNA
Pellet
HA
Fold Change
0
2
4
6
8
CM0
CM7
CM14
CM21
CM28

Figure S2. **(A)** Western blot analysis of MSC-formed pellet and MSC-laden HA constructs in chondrogenesis medium. Activation of Smad2/3 (phosphorylated-Smad2/3, P-Smad2/3) appeared earlier in HA culture than pellet culture. **(B)** Cell proliferation in Pellet or HA culture in 28 days. Cells in pellet had higher proliferation capacity than those in HA.

Figure S3.

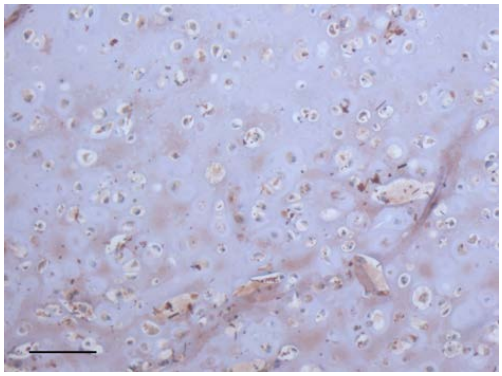

Figure S3. Collagen type X immunohistochemistry of samples from CM21 in HA group, indicating moderate deposition of collagen type X. Bar = 100 μm.

Figure S4.

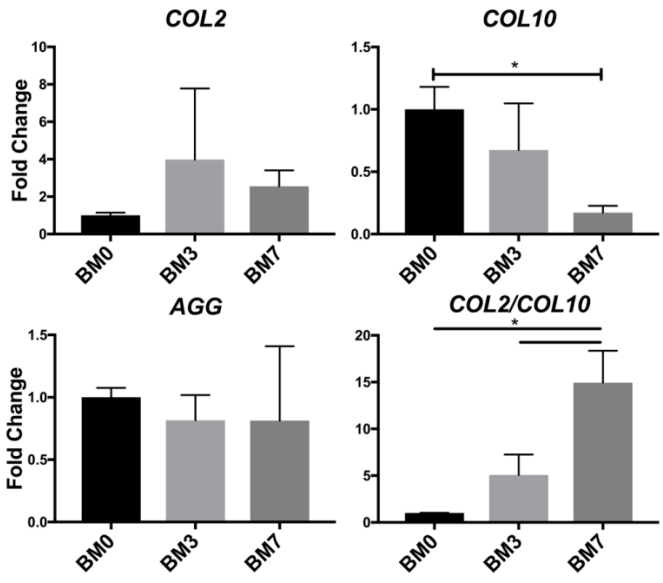

Figure S4. MSC-laden HA constructs cultured in chondrogenic medium for 21 days, and then subjected to additional culture in BM for 0 (BM0), 3 (BM3) and 7 (BM7) days. Gene expression of *COL2, COL10, AGG and COL2/COL10* were analyzed. N=4; *, $p < 0.05$.

Figure S5.

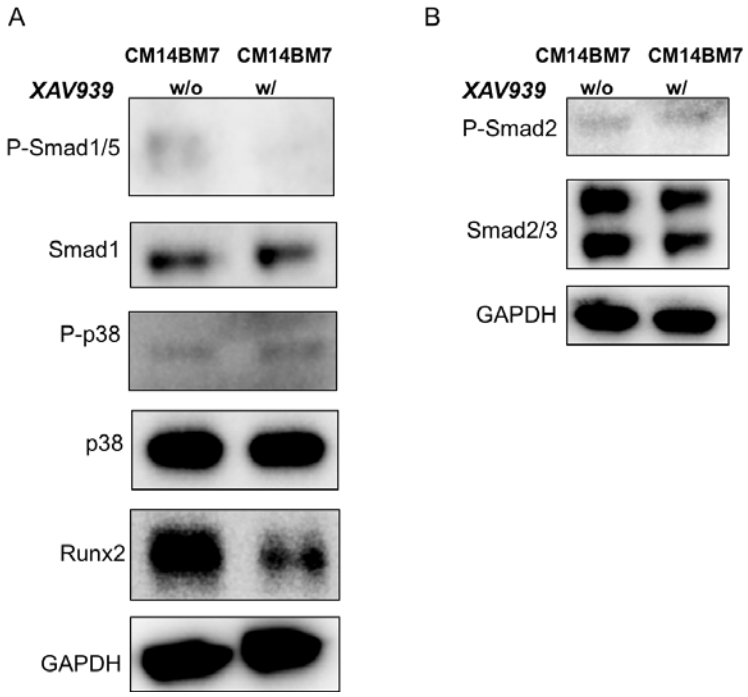

Figure S5. Analysis of signaling pathway perturbation by XAV939. **(A)** Western blot of P-p38, p38, P-Smad1/5, Smad1, and Runx2 in DMSO or XAV-treated CM14BM7 HA

groups, showing that XAV939 treatment (from days 10-21) significantly decreased P-Smad1/5 and Runx2 levels. **(B)** Western blot of P-Smad2, Smad2/3 in DMSO or XAV-treated CM14BM7 HA groups, showing that XAV939 treatment did not affect P-Smad2 level.

Figure S6.

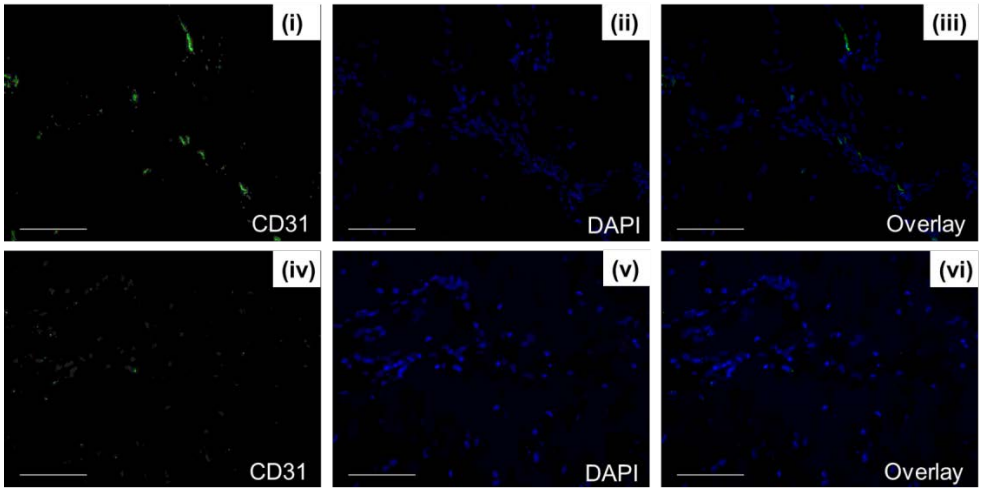

Figure S6. Assessment of vascularization in implanted MSC HA constructs. Immunohistochemistry of CD31, a marker for endothelial cells showed that XAV-treated

CM14BM7 HA implanted constructs (iv,v,vi) showed significantly less vascularization, indicated by fewer CD31 positive endothelial cells, compared to the control, CM21 HA constructs (i,ii,iii). Bar = 50 μm.

Gene	**Forward Primer (5'-3')**	**Reverse Primer (5'-3')**
RPL13a	CATAGGAAGCTGGGAGCAAG	GCCCTCCAATCAGTCTTCTG
18S rRNA	GTAACCCGTTGAACCCCATT	CCATCCAATCGGTAGTAGCG
COL2	GGATGGCTGCACGAAACATACCGG	CAAGAAGCAGACCGGCCCTATG
AGG	AGTCACACCTGAGCAGCATC	AGTTCTCAAATTGCATGGGGTGTC
COL10	CCCTCTTGTTAGTGCCAACC	AGATTCCAGTCCTTGGGTCA
MMP-13	ATGCAGTCTTTCTTCGGCTTAG	ATGCCATCGTGAAGTCTGGT
ALP	ATCTTTGGTCTGGCCCCCATG	AGTCCACCATGGAGACATTCTCTC

COL1	ATGATTGTCTTTCCCCATTCATTT	GGGCTCTAATGATGTTGAACTTGT

1068

1069

1070

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