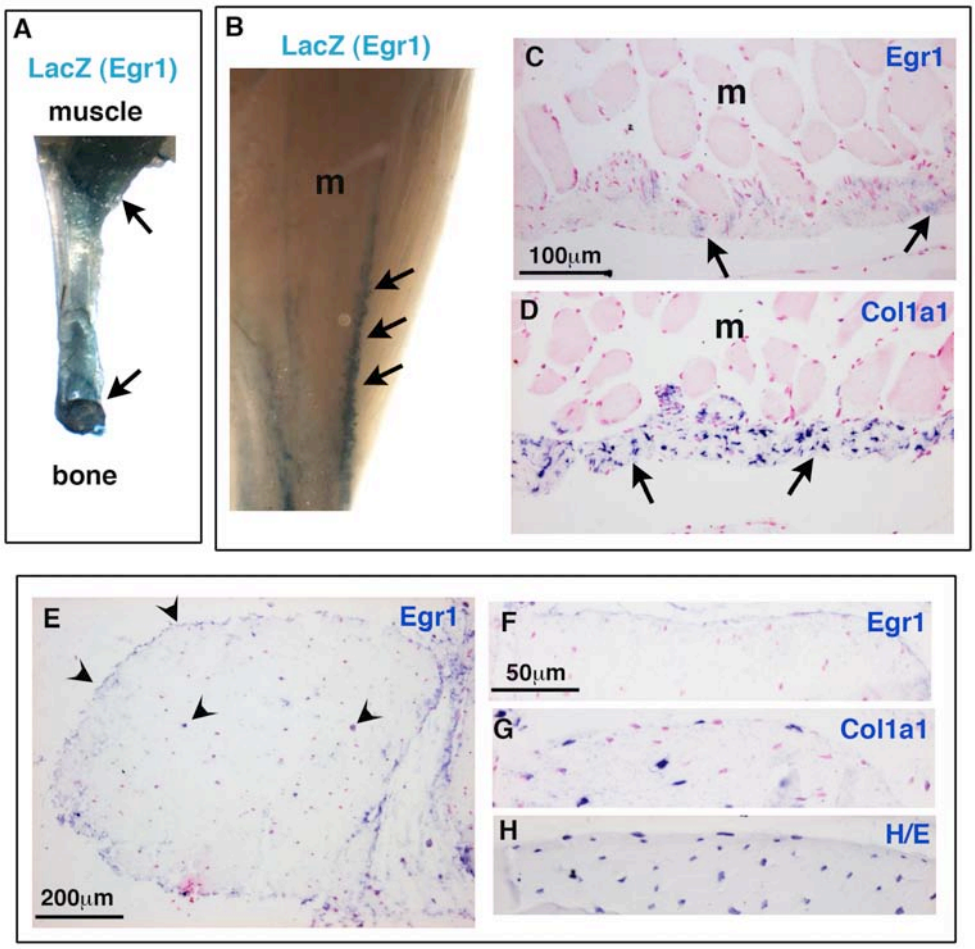
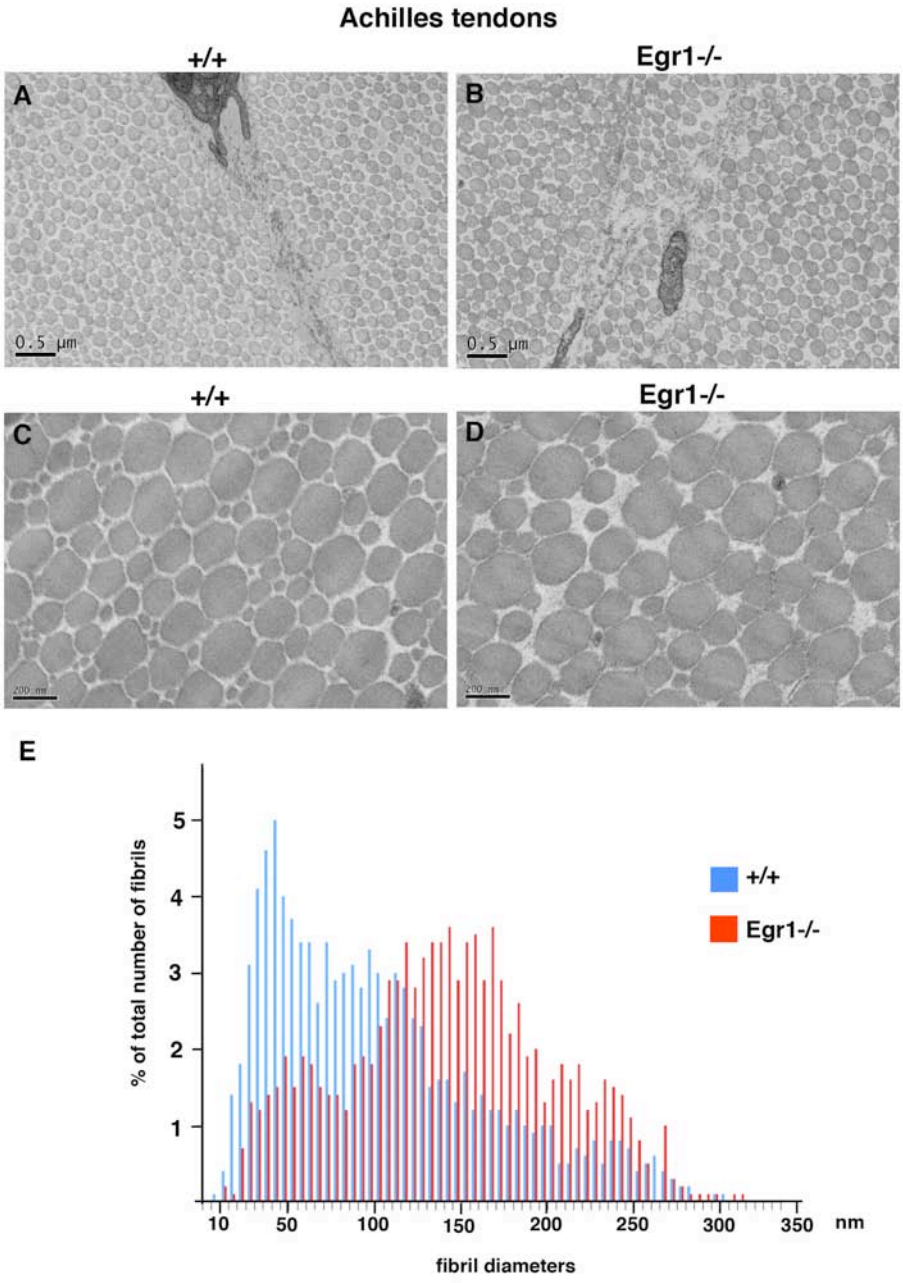
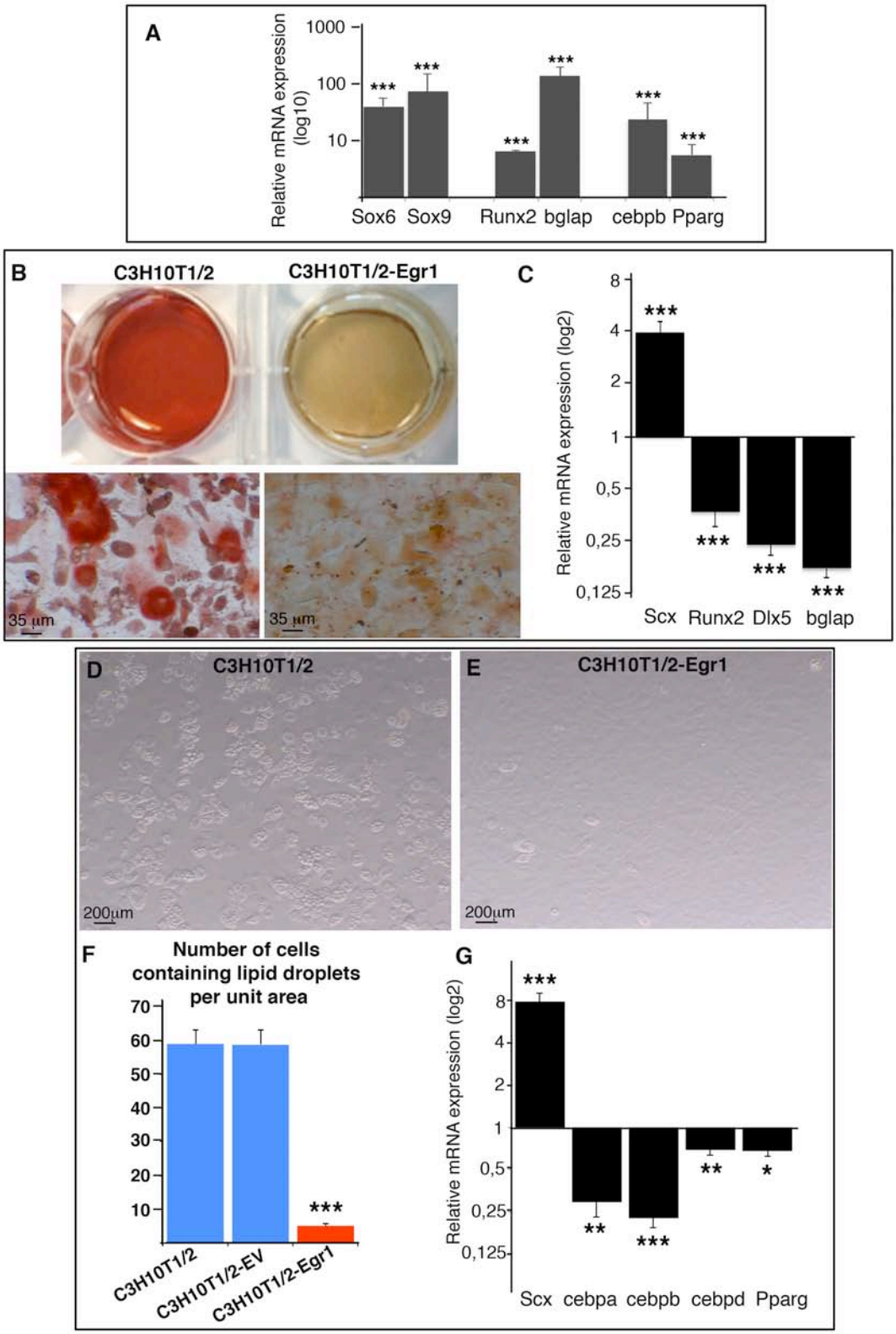


Supplemental Figure 1. *Egr1* expression in adult Achilles tendons. **(A,B)** Achilles tendons were isolated from 2 month-old *Egr1*$^{+/-}$ mice and stained for LacZ activity, which reflects *Egr1* expression. (A) Low magnification of one Achilles tendon, showing enhanced *Egr1* expression at tendon extremities close to bone and muscle attachments (arrows). (B) Highlight of the insertion of the Achilles tendon in the Gastrocnemius muscle. Arrows point to the LacZ expression in tendons close to muscle. **(C,D)** Adjacent transverse sections of Achilles tendons were hybridized with *Egr1* or *Col1a1* probes (blue labelling), followed by nuclear fast red staining. Arrows indicated *Egr1* and *Col1a2* expression in the myotendinous junction. **(E)** *Egr1* expression in one of the three Achilles tendon fascicles in transverse sections. Arrowheads indicate examples of *Egr1*-positive cells (blue labelling) at the periphery or centre of the tendon **(F-H)** Adjacent transverse sections of Achilles tendons were hybridized with *Egr1* (F) or *Col1a1* (G) probes followed by nuclear fast red staining, or H&E stained (H). m, muscle.

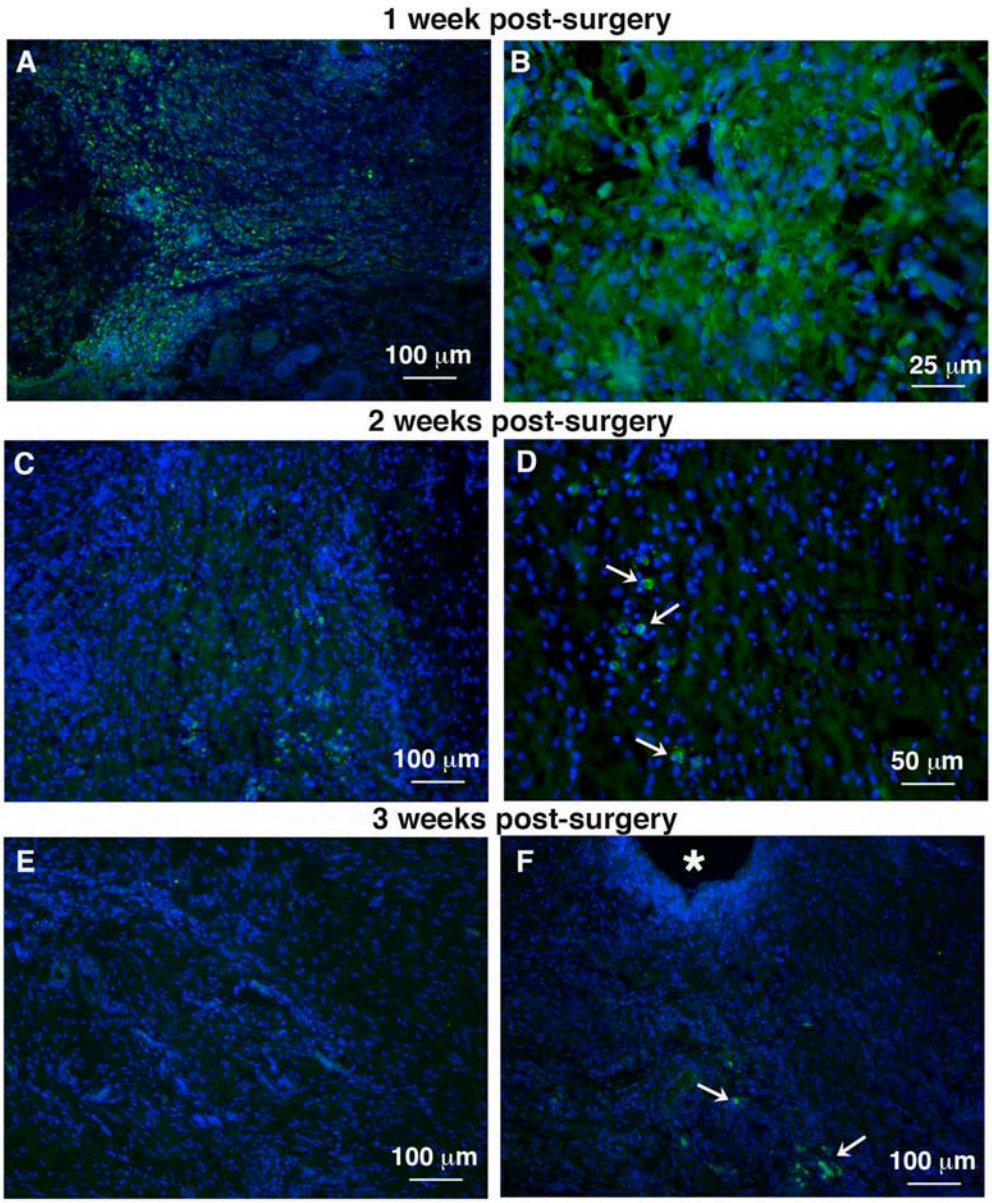


Supplemental Figure 2. Effects of *Egr1*-deficiency on collagen fibril diameter repartition of Achilles tendons. **(A-D)** Electron microscopy photographs at different scales of Achilles tendons from 4 month *wt* (A,C) and *Egr1*$^{-/-}$ (B,D) mice. (**E**) Histograms showing the frequency of collagen fibril diameters from 4 month *wt* versus *Egr1*$^{-/-}$ mice. For *wt* tendons: Mean of diameters = 106 nm, SD = 58,1. For *Egr1*$^{-/-}$ tendons: Mean of diameters = 131,8 nm, SD = 44,3. Electron microscopy analyses of Achilles tendons of adult *Egr1*$^{-/-}$ mutant mice showed a shift of the collagen fibril diameters towards highest values.

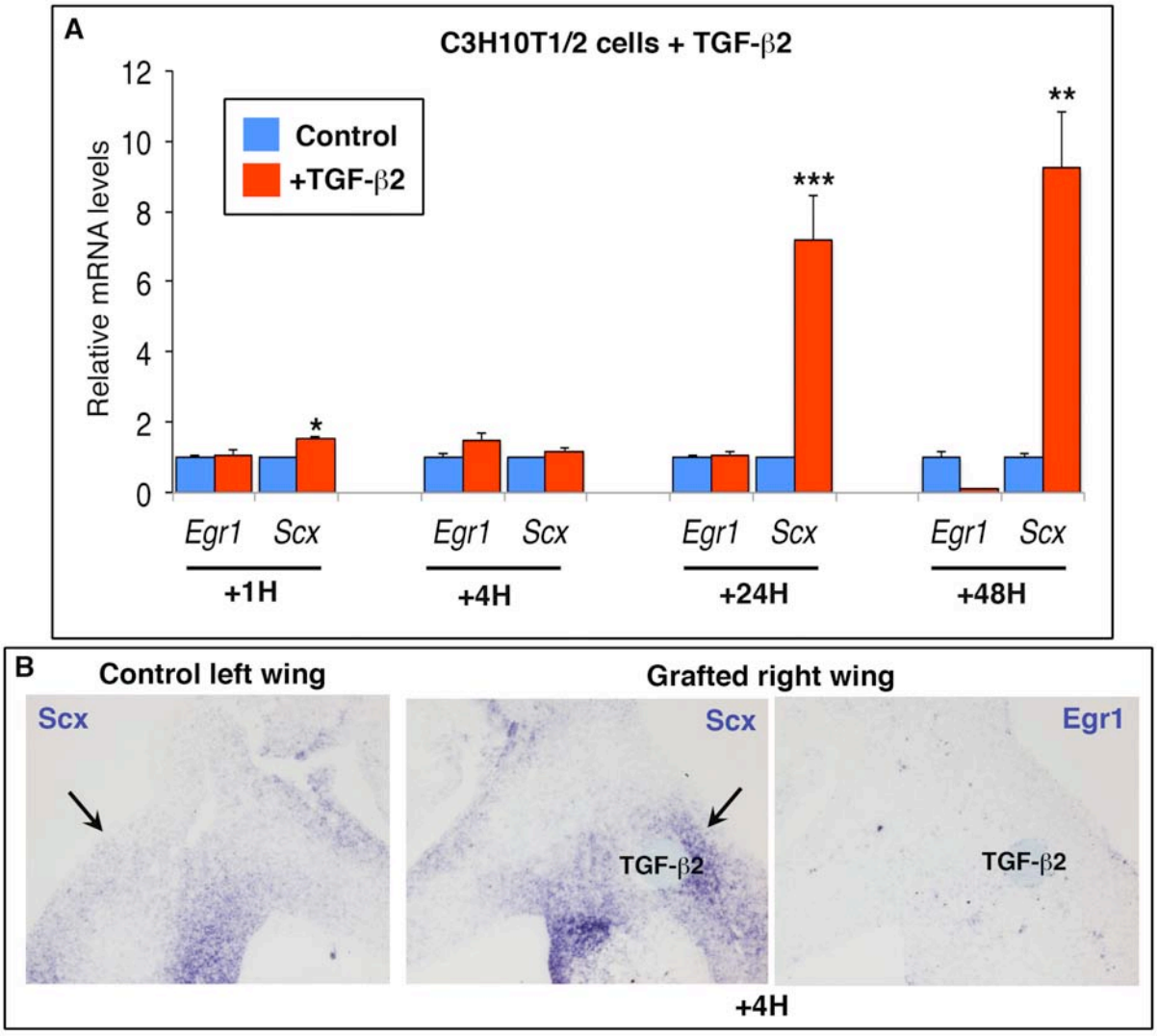


Supplemental Figure 3. Egr1 abolishes the capacity of C3H10T1/2 cells to differentiate into bone and fat lineages. (**A**) Q-PCR analysis of the mRNA expression levels of chondrocyte (*Sox6, Sox9*), osteocyte (*Runx2, bglap*) and adipocyte (*cebpb, Pparg*) markers in C3H10T1/2 cells cultured in chondrogenic, osteogenic and adipogenic differentiation media, respectively. There is a drastic increase of mRNA expression levels of differentiation markers upon

differentiation for each lineage, showing that C3H10T1/2 cells differentiate towards the 3 lineages. The mRNA levels of C3H10T1/2 cells were normalized to 1. (**B**) Alizarin S red staining of C3H10T1/2 and C3H10T1/2-Egr1 cells, 16 days after bone differentiation medium, application shows an absence of osteocyte differentiation in C3H10T1/2-Egr1 cells compared to C3H10T1/2 cells. (**C**) Q-PCR analysis showed a very significant diminution of the relative transcript levels of the osteocyte markers, *Runx2, Dlx5* and *bglap* in the presence of Egr1. The mRNA levels of C3H10T1/2 cells under bone differentiation medium were normalized to 1 (**D,E**) C3H10T1/2 (D) and C3H10T1/2-Egr1 (E) cells, 7 days after fat differentiation medium application. (**F**) Numbers of cells per unit area displaying lipid accumulation in C3H10T1/2, C3H10T1/2-EV and C3H10T1/2-Egr1 cells. (**G**) Q-PCR analysis showed a significant diminution of the relative transcript levels of the fat markers, *cebpa, cebpb, cebpd* and *Pparg* in the presence of Egr1. The mRNA levels of C3H10T1/2 cells under fat differentiation medium were normalized to 1. The error bars represent standard deviation (SD). The asterisks in the histograms indicate p values, *<0.05, **<0.01, ***<0.001 in unpaired student's t-test.



Supplemental Figure 4. MSCs do not persist long after transplantation into host tendons. Achilles tendons from adult rats were separated from the Plantaris and Soleus tendons. A total transverse section of Achilles tendon was created and immediately both ends sutured back together with surgical sutures. Primary GFP-MSCs were then implanted in the injured/sutured tendons. Sections of Achilles tendons, 1 (**A-B**), 2 (**C-D**) and 3 (**D-F**) weeks after manipulation. The GFP fluorescence (green) allowed us to follow transplanted cells over time. One week after surgery, GFP cells were observed in the manipulated tendons (A,B). From 1 week after transplantation, we observed a drastic reduction in the number of transplanted MSCs (C-E). (F) However, some transplanted MSCs persisted up to 3 weeks (White arrows) around the suture scar (asterisk).



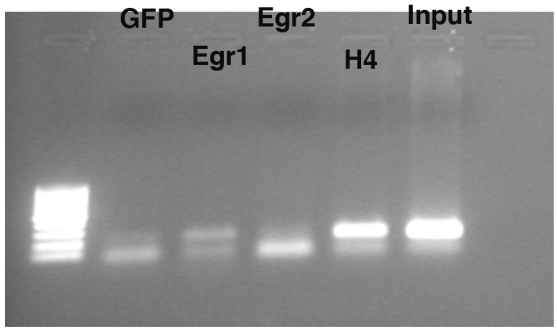
Supplemental Figure 5. TGF-β2 does not induce *Egr1* expression in MSCs or in chick limb buds. (**A**) C3H10T1/2 cells were cultured in the presence of absence of TGF-β2 recombinant protein, during 1, 4, 24 or 48 hours. The relative expression levels of *Egr1* or *Scx* transcripts were assayed by q-PCR. In the presence of TGF-β2, the expression of *Scx* was increased after 1 hour in culture, while that of *Egr1* was unchanged. The asterisks in the histograms indicate p values, * <0.05, **<0.01, ***<0.001. (**B**) Beads were soaked with human TGF-β2 recombinant protein (RD systems) at 500ng/ml for 1 hour, on ice. TGF-β2 beads were grafted into the right wings of normal embryos at E3 (Embryonic day 3). Four hours after grafting, embryos were harvested and processed for in situ hybridization to adjacent tissue sections with *Scx* or *Egr1* probes. TGF-β2 activates the expression of *Scx* (arrow) but not that of *Egr1* in grafted right wings.

gene	Forward primers	Reverse primers	Accession No.
bglap	5′-GCCTTCATGTCCAAGCAGGA-3′	5′-GCGCCGGAGTCTGTTCACTA-3′	NM_007541.2
Bgn	5′-TTTCTGAGCTTCGCAAGGATG-3′	5′-GGGCGTAGAGGTGCTGGAG-3′	NM_007542.4
cebpa	5′-CAAGAACAGCAACGAGTACCG-3′	5′-GTCACTGGTCAACTCCAGCAC-3′	NM_007678
cebpb	5′-CGCCTTTAGACCCATGGAAG-3′	5′-AGGCAGTCGGGCTCGTAGTAG-3′	NM_009883
cebpd	5′-CGACTTCAGCGCCTACATTGA-3′	5′-CTAGCGACAGACCCCACAC-3′	NM_007679
cebpg	5′-CAGCACGGAAACTACAGCGA-3′	5′-ACTGCCCTGGGTTATCAGAAT-3′	NM_009884
Col1a1	5′-TGGAGAGAGCATGACCGATG-3′	5′-GAGCCCTCGCTTCCGTACT-3′	NM_007742
Col1a1(r.n)	5′- CACCTACAGCACGCTTGTGG -3′	5′- CCCCAAGTTCCGGTGTGAC-3′	NM_053304.1
Col1a2	5′-CCAGCGAAGAACTCATACAGC-3′	5′-GGACACCCCTTCTACGTTGT-3′	NM_007743
Col1a2 (r.n)	5′- ACCCCAGCCAAGAATGCATAC -3′	5′- CCAGACATGCTTGTTGGCCT -3′	NM_053356.1
Col2a1	5′-TTCCACTTCAGCTATGGCGA-3′	5′-GACGTTAGCGGTGTTGGGAG-3′	NM_001113515.2
Col3a1	5′-CTAAAATTCTGCCACCCCGAA-3′	5′-AGGATCAACCCAGTATTCTCCACTC-3′	NM_009930
Col5a1	5′-CCTGGCATCAACTTGTCCGATGG-3′	5′-GTGGTCACTGCGGCTGAGGAACTTC-3	NM_015734
Col6a1	5′-CTACACCGACTGCGCCATTA-3′	5′- CCCCCTATGAGCAGCTCCT-3′	NM_009933
Col12a1	5′-CCGTGTTGTGTATCGCCCT-3′	5′-CACCTTAGCAACCATCTGCCTC-3′	NM_007730
Col14a1	5′-GAGCAGAGACCACATTGGCC-3′	5′-CGTACAGCTCGAGGTCGGAA-3′	NM_181277
Dcn	5′-CTATGTGCCCCTACCGATGC-3′	5′-CAGAACACTGCACCACTCGAAG-3′	NM_001190451.1
Dlx5	5′-CGTCTCAGGAATCGCCAACT-3′	5′-AGTCAGAATCGGTGGCCG-3′	NM_198854
Egr1	5′-CAGCGCCTTCAATCCTCAAG-3′	5′-GCGATGTCAGAAAAGGACTCTGT-3′	NM_007913
Eln	5′-CAAGTCGGAGCTGGCATCGG-3′	5′-GTGGGAACTCCAGGGAGCAC-3′	NM_007925.3
Fbn1	5′-GGACACGATGCGCTGAAAGG-3′	5′- CAGGAATGCCGGCAAATGGG-3′	NM_007993.2
Fn1	5′-CACGTACCTCTTCAAAGTCTTTGC-3′	5′- GGATTGCTTTCCCTGCCCT-3′	NM_010233.1
Gapdh	5′-TTGTGGAAGGGCTCATGACC-3′	5′-TCTTCTGGGTGGCAGTGATG-3′	NM_008084.2
Mhk	5′-AGTAAAGACAGTCAAGCTGCCACTG-3′	5′-TCCTGGCCACTCTAGAAGCG3′	NM_177595
Osx	5′-CCAGCCTCTGGCTATGCAAA-3′	5′-AGGAAATGAGTGAGGGAAGGGT-3′	NM_130458
Pparg	5′-TCGCTGATGCACTGCCTATG-3′	5′-GAGAGGTCCACAGAGCTGATT-3′	NM_011146
Runx2	5′-GGTCCCCGGGAACCAA-3′	5′-GGCGATCAGAGAACAAACTAGGTTT-3′	NM_001145920
Scx	5′-CCTTCTGCCTCAGCAACCAG-3′	5′-GGTCCAAAGTGGGGCTCTCCGTGACT-3′	NM_198885.3
Scx (r.n.)	5′- GCACCTTCTGCCTCAGCAAC -3′	5′- TTCTGTCACGGTCTTTGCTCA -3′	NM_001130508.1
Smad7	5′-CAGCACTGCCAAGCATGGT-3′	5′-ACCGAAACGCTGATCCAAAG-3′	NM_001042660.1
Sox5	5′-TGATCCCAACCACTATGGCA-3′	5′-GGCCTAAGCCTGGTGTTGC-3′	NM_001113559
Sox6	5′-CTGCCTCTGCACCCCATAATG-3′	5′-TTGCTGAGATGACAGAACGCT-3′	NM_001025560
Tgfb1	5′-GGTGTCAGAGCCTCACCGCG-3′	5′-AGAGCGGGAACCCTCGGCAA-3′	NM_011577.1
Tgfb2	5′-GAATAAAAGCGAAGAGCTCGAGG-3′	5′-GAGGTGCCATCAATACCTGCA-3′	NM_009367
Tgfb3	5′-CGGAGCACAATGAACTGGC-3′	5′-AAACCTTAGAGGTAATTCCTTTGGG-3′	NM_009368.3
Tgfbr1	5′-CCCGGGGGCGAAGGCATTAC-3′	5′-GCTGCCAGCTCCACAGGACC-3′	NM_009370.2
Tgfbr2	5′-CGTCCCGCTGCAATGC-3′	5′-CGCACCTTGGAACCAAATG-3′	NM_029575.3
Tnc	5′-AACCATCAATGCGGCCAC-3′	5′-TGTCGTCCAGAAAAACGTCAGA-3′	NM_011607
Tnmd	5′-AACACTTCTGGCCCGAGGTAT-3′	5′-AAGTGTGCTCCATGTCATAGGTTTT-3’	NM_022322.2

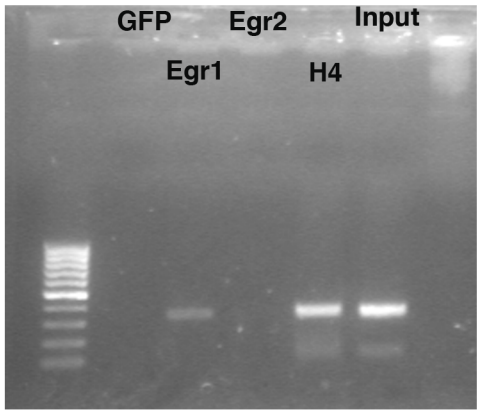
Supplemental Table 1. Primers used for quantitative real-time PCR. All primers were designed from *mus musculus* genome. *Col1a1, Col1a2* and *Scx* primers were also designed from *rattus norvegicus* (*r.n*) genome. It has to be noted that *mus musculus* and *rattus norvegicus* primers cross-reacted with each others and gave similar results in mouse or rat tissues.

Col1a1 (Figure 2D)

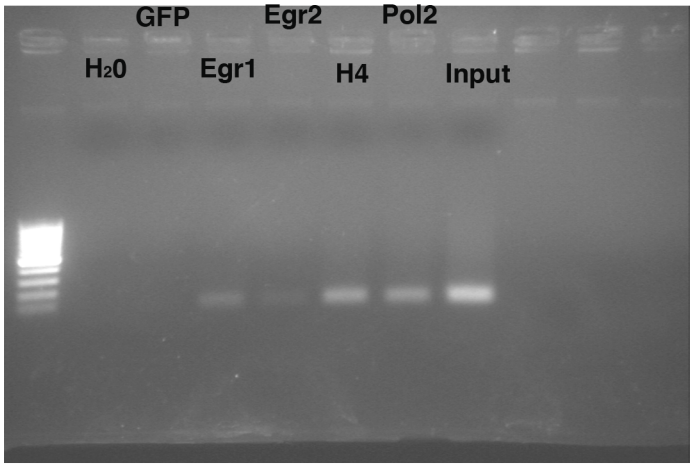
Fragment A (230b)



Fragment B (330b)



Col1a2 (Figure 2E)



Tgfb2 (Figure 9E)