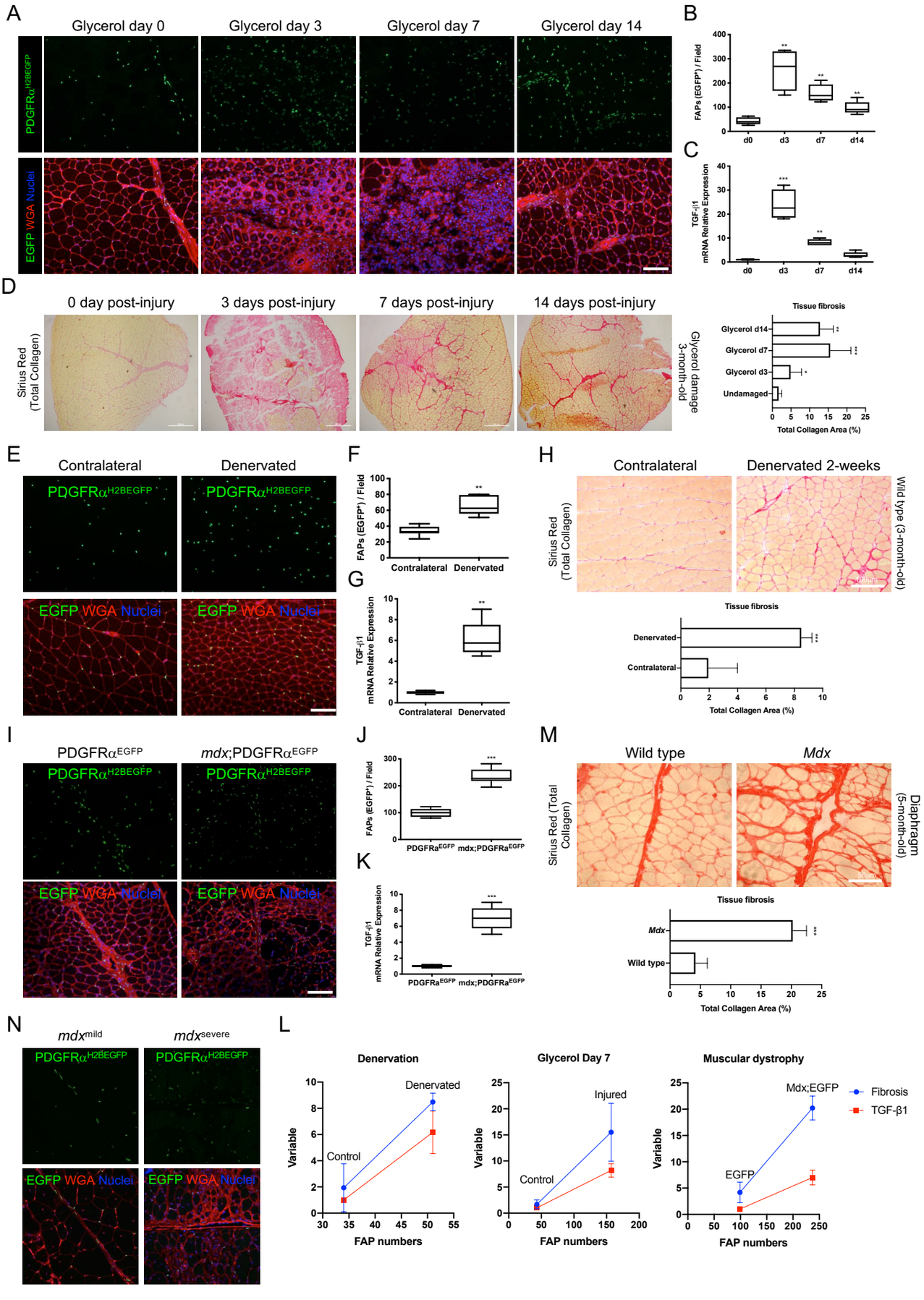

**Fig. S1. FAPs number correlates with TGF-β expression and fibrosis in several skeletal muscle injury models.**

(A) Representative fluorescent images of damaged (3, 7, and 14 days after glycerol injection (50% v/v)) and undamaged (day 0) tibialis anterior (TA) sections from PDGFRα$^{H2BEGFP}$ mice. Wheat germ agglutinin (WGA) staining (*red*) and nuclei/Höechst (*blue*) staining are also shown. (B) Quantification of the number of EGFP$^{+}$ TA FAPs per field in acute glycerol damage. (C) Quantification of TA *TGF-β1* mRNA expression determined by quantitative PCR in acute glycerol damage. (D) Sirius Red staining in TA sections of the glycerol damage time course. *Right*, quantification of tissue fibrosis as a percentage of total collagen (Sirius Red) stained area in acute glycerol damage. (E) Representative fluorescent images of gastrocnemius muscle 2-weeks post denervation. (F) Quantification of the number of EGFP$^{+}$ gastrocnemius FAPs per field after 2-weeks of denervation. (G) Quantification of *TGF-β1* mRNA expression in gastrocnemius determined by quantitative PCR after 2-weeks of denervation. (H) Sirius Red staining in gastrocnemius sections of contralateral or denervated muscle. *Right*, quantification of tissue fibrosis as a percentage of total collagen (Sirius Red) stained area. (I) Representative fluorescent images of 5-month-old PDGFRα$^{H2BEGFP}$ and *mdx*;PDGFRα$^{H2BEGFP}$ diaphragm muscle. (J) Quantification of the number of EGFP$^{+}$ diaphragm FAPs per field. (K) Quantification of *TGF-β1* mRNA expression in diaphragm
determined by quantitative PCR. (M) Sirius Red staining in diaphragm sections. *Below*, quantification of tissue fibrosis as a percentage of total collagen (Sirius Red) stained area. (N) Representative fluorescent images of mdx mild and severe dystrophic phenotypes of diaphragm sections from 5-month-old PDGFRα$^{EGFP}$ and *mdx*;PDGFRα$^{EGFP}$ mice. (L) Fibro/adipogenic progenitors number correlate positively with TGF-β1 expression and the severity of fibrosis. Scale bars: 50μm. Glycerol (A), denervation (E), and *mdx* mice (I). ***P < 0.001, **P < 0.005, *P < 0.05, n.s not significant; n = 3. One-Way ANOVA with Dunnett post-test and two-tailed Student's t-test.

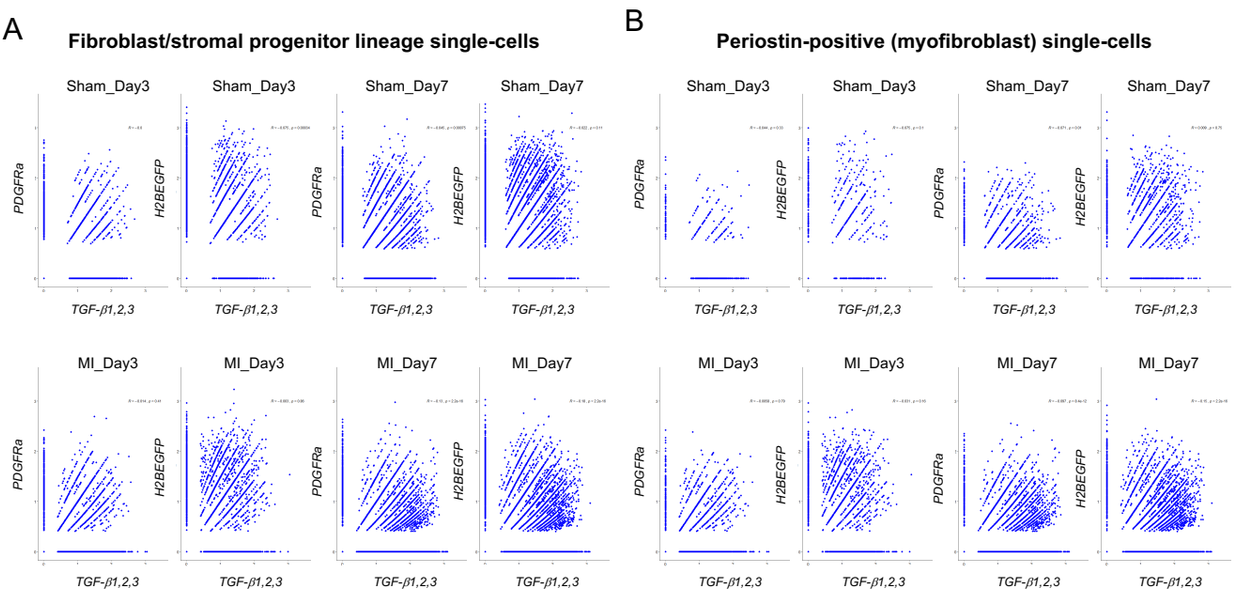


**Fig. S2. Damage and TGF-β-induced cell state negatively correlate with PDGFRα expression in cardiac fibroblast/stromal progenitors.**

(A) Single-cell RNA sequencing expression values, showing the relationship between PDGFRα and TGF-β cytokine (1, 2 and 3 ligands) expression in the *Pdgfra*EGFP$^{+}$ cardiac fibroblast/stromal progenitor lineage from murine hearts at days 3 and 7 post-sham or myocardial infarction (MI) surgery. (B) This time, only the cells that express at least one count of Postn (Periostin) are kept. PDGFRα expression negatively correlates with TGF-β expression at day 7 of MI, which corresponds with myofibroblast differentiation (Periostin-expressing cells) occurring at that time point.

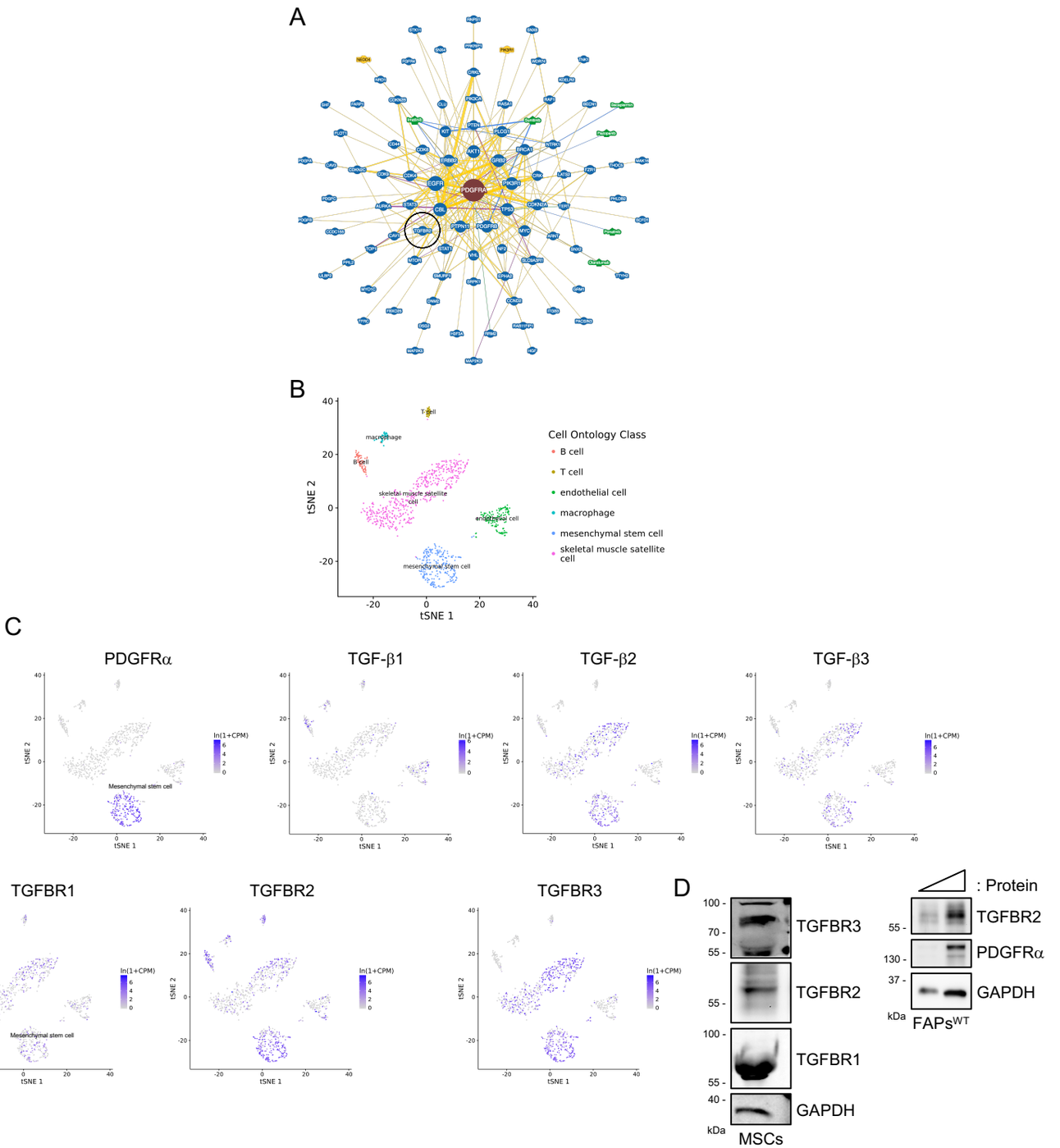

**Fig. S3. TGF-β ligands and TGF-BRs are expressed by skeletal muscle stromal mesenchymal progenitors.**

(A) BioGRID interactome analysis of the human PDGFRα. Black circle marks the protein-protein interaction between TGF-BR2 and PDGFRα. (B) A t-SNE plot of all cells collected using the microfluidic-droplet method, colored by the predominant cell type that composes each cluster. Cells were colored by cell type for limb muscle and visualized with t-SNE. Cell types were determined by differential gene expression of known markers between clusters. (C) t-SNE visualization of select genes (PDGFRα, TGF-β1, TGF-β2, TGF-β3, TGF-BR1, TGF-BR2, and TGF-BR3) (from *grey*, low expression, to *blue*, high expression). (D) Western blot analysis of C3H/10T1/2 MSCs and wild type FAPs total lysate, showing TGF-BR1, TGF-BR2, TGF-BR3, PDGFRα, and GAPDH levels.

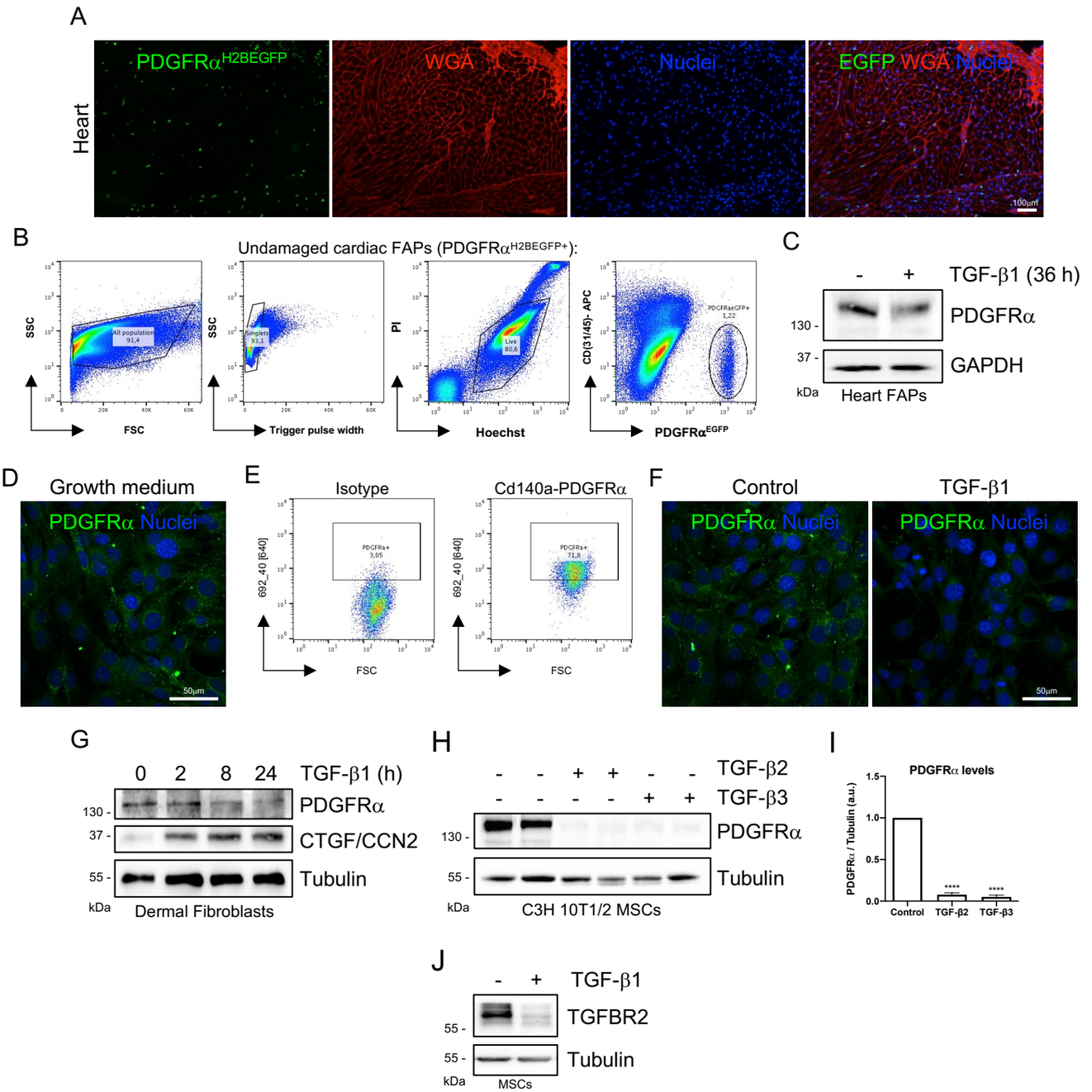

**Fig. S4. TGF-β downregulates PDGFRα in heart FAPs and C3H 10T1/2 MPs.**

(A) Representative fluorescent images of heart sections from PDGFRα$^{H2BEGFP}$ mice stained for WGA (*red*). (B) The sequential gating strategy used to isolate EGFP$^{+}$ cardiac FAPs/fibroblasts from the reporter mice PDGFRα $^{H2BEGFP}$. (C) PDGFRα and GAPDH levels were analyzed by western blot in heart FAPs isolated by FACS and cultured with TGF-β1 (5 ng/ml) for 36 h. (**d**) Confocal image of PDGFRα immunofluorescence in proliferating C3H/10T1/2 MSCs. (E) Flow cytometry analysis of plasma membrane-bound CD140a (PDGFRα) in C3H/10T1/2 MSCs. (F) Confocal images of PDGFRα immunofluorescence, showing its cytoplasmic and plasma membrane distribution in control and TGF-β1-treated (5ng/ml) C3H/10T1/2 MSCs for 24 h. (A, D, F) Nuclei are stained with Hoechst (*blue*). (G) Representative western blot analysis showing PDGFRα and CTGF/CCN2 expression levels in primary mouse dermal fibroblasts (MDFs) after treatment with TGF-β1 (5 ng/ml) at different time points (0, 2, 8, and 24 h). Tubulin was used as the loading control. (H) Representative western blot from three independent experiments, showing PDGFRα protein levels after stimulation with TGF- β2 and TGF- β3 for 24 h at a final concentration of 5 ng/ml in MSCs. Tubulin was used as the loading control. (I) Quantification of PDGFRα expression after treatment with TGF- β2 and TGF- β3. N=3; ****P < 0.0001; One-Way ANOVA with Dunnett post-test. (J) TGF-b1 reduces TGF-b receptor type II expression. Representative western blot analysis showing TGF-BR2 expression levels in C3H/10T1/2 cells after TGF-b1 (5 ng/ml) treatment for 24 h. Tubulin was used as the loading control.

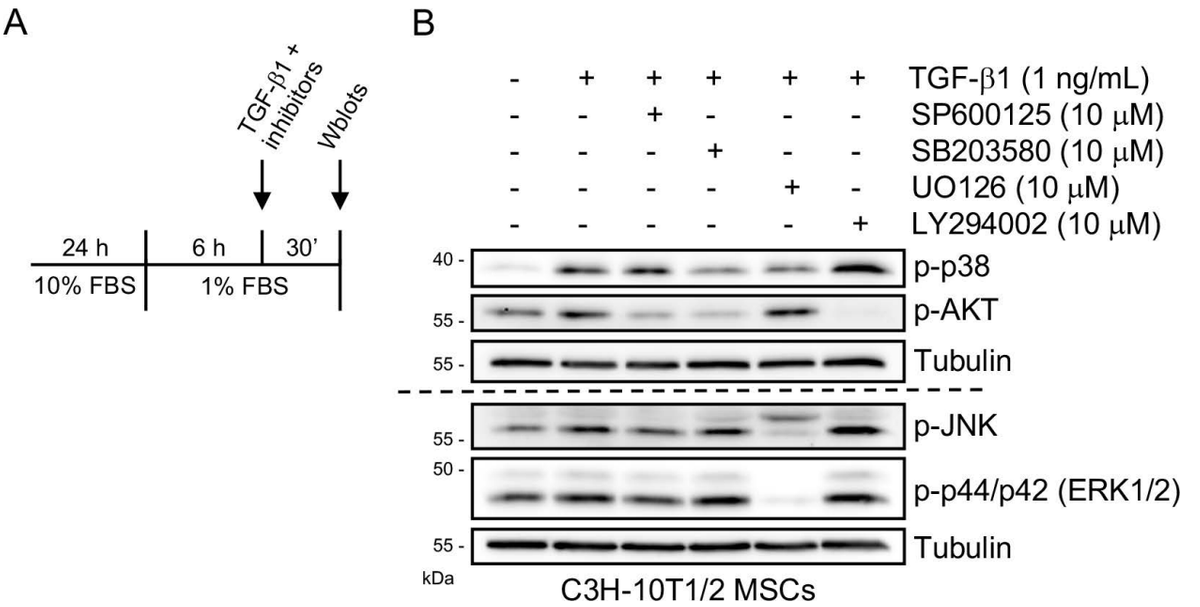


**Fig. S5. TGF-β1-mediated signaling pathways in mesenchymal progenitors.**

(A) Outline of C3H/10T1/2 MSCs, TGF-β signaling pathway inhibitors, and TGF-β1 treatment (1 ng/ml) protocol. (B) Representative western blot of phosphorylated (p-) p38, p-AKT, p-JNK, p-ERK1/2, and tubulin from C3H/10T1/2 MSCs treated with TGF- β1 and SP600125 (JNK), SB203580 (p38), UO126 (ERK1/2), LY294002 (PI3K/AKT) inhibitors. Tubulin was used as the loading control.

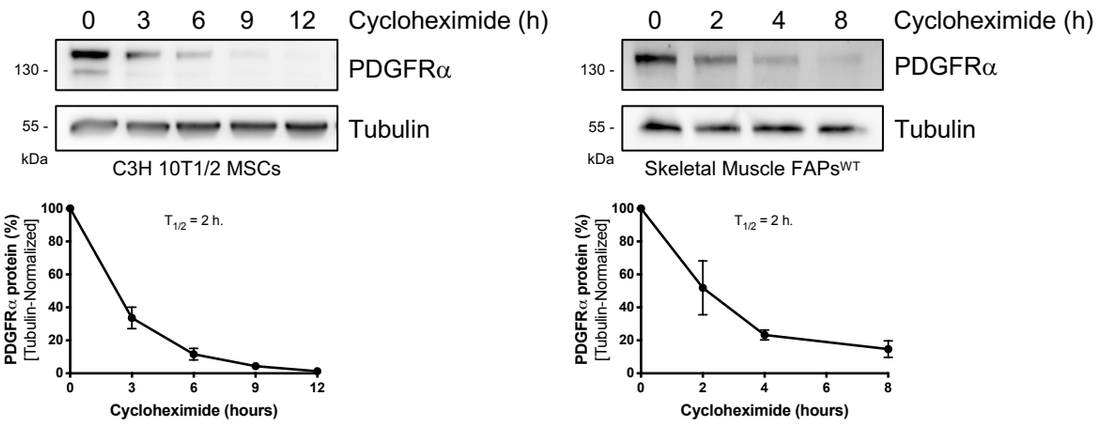


**Fig. S6. Evaluation of PDGFRα protein half-life in mesenchymal stromal cells and fibro/adipogenic progenitors.**

Representative western blot of PDGFRα and tubulin in C3H/10T1/2 MSCs (*left*) and skeletal muscle FAPs (*right*) after a time course treatment with cycloheximide 30 μg/ml. Quantifications of PDGFRα protein levels (tubulin-normalized) during the cycloheximide time course (*lower graphs*).

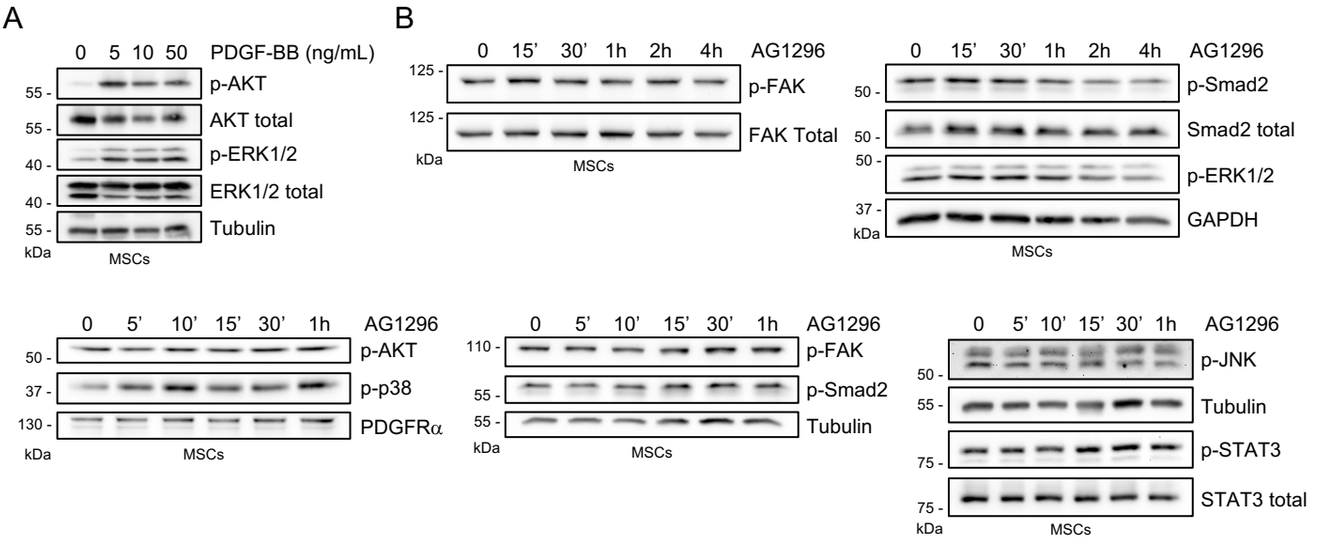


**Fig. S7. Evaluation of signaling pathways activated by PDGF-BB stimulation and AG1296 inhibitory effects in mesenchymal stromal cells.**

(A) Representative western blot analysis showing phosphorylated levels of AKT and ERK1/2 after PDGF-BB treatment (20 ng/ml). AKT and ERK1/2 were used as total proteins. Tubulin was used as the loading control. (B) Representative western blot analysis showing phosphorylated levels of FAK, Smad2, and ERK1/2 after AG1296 treatment (10 μM). FAK, Smad2, and GAPDH were used as total proteins. (C) Representative western blot analysis showing phosphorylated levels of AKT, p38, FAK, Smad2, JNK, and STAT3 after AG1296 treatment (10 μM). PDGFRa, tubulin, and STAT3 were used as total proteins.

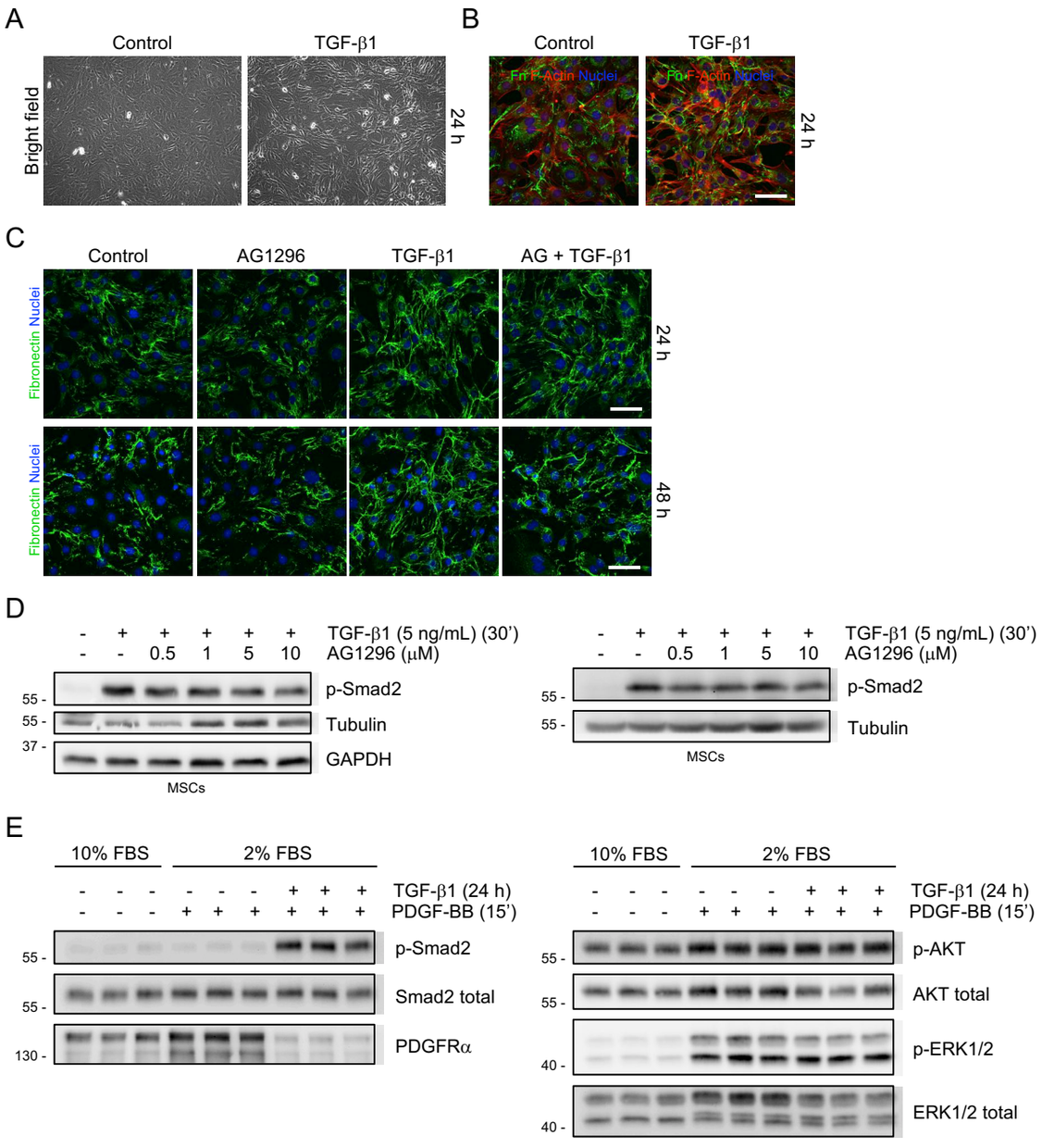

**Fig. S8. The PDGFRα pharmacological inhibitor AG1296 impairs TGF-β-mediated ECM remodeling and Smad2 signaling.**

(A) Bright-field images showing TGF-β1-induced myofibroblast differentiation of C3H/10T1/2 MSCs after 24 h of treatment. (B) Z-stack confocal images showing the ECM organization of fibronectin (Fn) and filamentous actin (F-actin) in control and TGF-β1-induced myofibroblast differentiation. (C) Z-stack confocal images showing the ECM organization of fibronectin (Fn) and filamentous actin (F-actin) in control, AG1296, TGF-β1, and AG1296 + TGF-β1 treated C3H 10T1/2 cells. Scar bars: 50 μm. Nuclei are stained with Höechst (*blue*). (D) Representative western blot analyses showing phosphorylated levels of the TGF-β canonical effector Smad2 after TGF-β1 and AG1296 treatments (different concentrations) at 30 minutes. Tubulin and GAPDH were used as the loading controls. (E) Representative western blot analyses showing phosphorylated levels of the TGF-β canonical effector Smad2, AKT, and ERK1/2 after TGF-β1 and PDGF-BB treatments. Total protein forms were used as the loading controls. PDGFRα protein levels were used as a positive control of TGF-β-mediated effects.

**Table S1. The expression of the PDGFRα immediate early gene *Txnip* decreases during skeletal muscle regeneration.**

*In-silico* analysis from microarray data obtained from Lukjanenko et al., 2013. Skeletal muscle *Txnip* expression decreases at days 3 and 7 after acute damage.

| Probe set ID | Gene Symbol | Gene Name | Glycerol 3 days - Sham 14 days_logFC | Glycerol 3 days - Sham 14 days_log.adj.P.Val |
|---|---|---|---|---|
| 1415997_at | *Txnip* | thioredoxin interacting protein | -1.73 | 4.51 |
| Probe set ID | Gene Symbol | Gene Name | Glycerol 7 days - Sham 14 days_logFC | Glycerol 7 days - Sham 14 days_log.adj.P.Val |
| 1415997_at | *Txnip* | thioredoxin interacting protein | -1.2 | 2.54 |
| Probe set ID | Gene Symbol | Gene Name | Cardiotoxin 3 days - Sham 14 days_logFC | Cardiotoxin 3 days - Sham 14 days_log.adj.P.Val |
| 1415997_at | *Txnip* | thioredoxin interacting protein | -1.63 | 3.45 |
| Probe set ID | Gene Symbol | Gene Name | Cardiotoxin 7 days - Sham 14 days_logFC | Cardiotoxin 7 days - Sham 14 days_log.adj.P.Val |
| 1415997_at | *Txnip* | thioredoxin interacting protein | -1.79 | 4.17 |

**Table S2: Primers used in RT-qPCR**

| **Gene** | **Forward primer (5′-3′)** | **Reverse primer (5′-3′)** |
|---|---|---|
| *Txnip* | ACGACTCTCAAGACAGCCC | GGAGTTCAAGCAGAGAGGCA |
| *Tiparp* | CAGTTGCGGCTTTCAGCGCTCAG | CTCAAGGATCTCAGGGTTCCAGTTC |
| *Axud1* | GTCTGTCCTCGGCTGTTGGAACC | CCACCTCAGCATCTCCAGCTTC |
| *Arid5b* | CAGTACTGTCGGTACCGGTCCATG | GTTCCATCTGCCCTGCATTCTTCGCC |
| *Schip1* | GCACAATGGCAACGTGGTGGTAGC | CCGTCTTACTGTCATCTGCATCGCTG |
| *Tgfb1* | CTCCACCTGCAAGACCAT | CTTAGTTTGGACAGGATCTGG |
| *Adiponectin* | GGAACTTGTGCAGGTTGGAT | TCTCCAGGAGTGCCATCTCT |
| *Pparg* | AGGCGAGGGCGATCTTGACAG | AATTCGGATGGCCACCTCTTTG |
| *18S* | TGACGGAAGGGCACCACCAG | CACCACCACCCACGGAATCG |