Supplementary Figure1-14 and captions

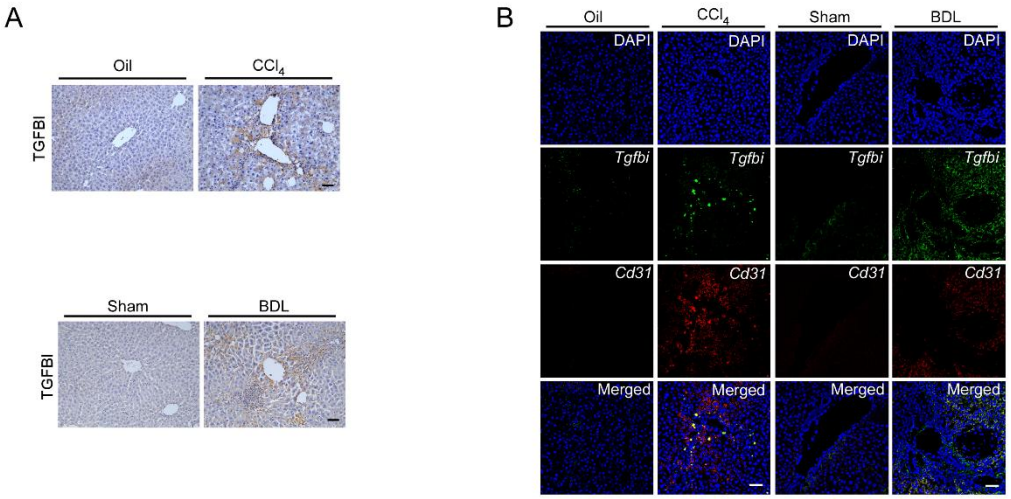


Fig S1. TGFBI is significantly upregulated in nonparenchymal cells of fibrotic livers. A IHC staining of TGFBI in mouse livers. **B** FISH analysis of coexpression of *Tgfbi* with *Cd31* in mouse livers, respectively. Mice samples (n = 4-6 per group). Data were presented as the mean ± SDs; scale bars, 50 μm.

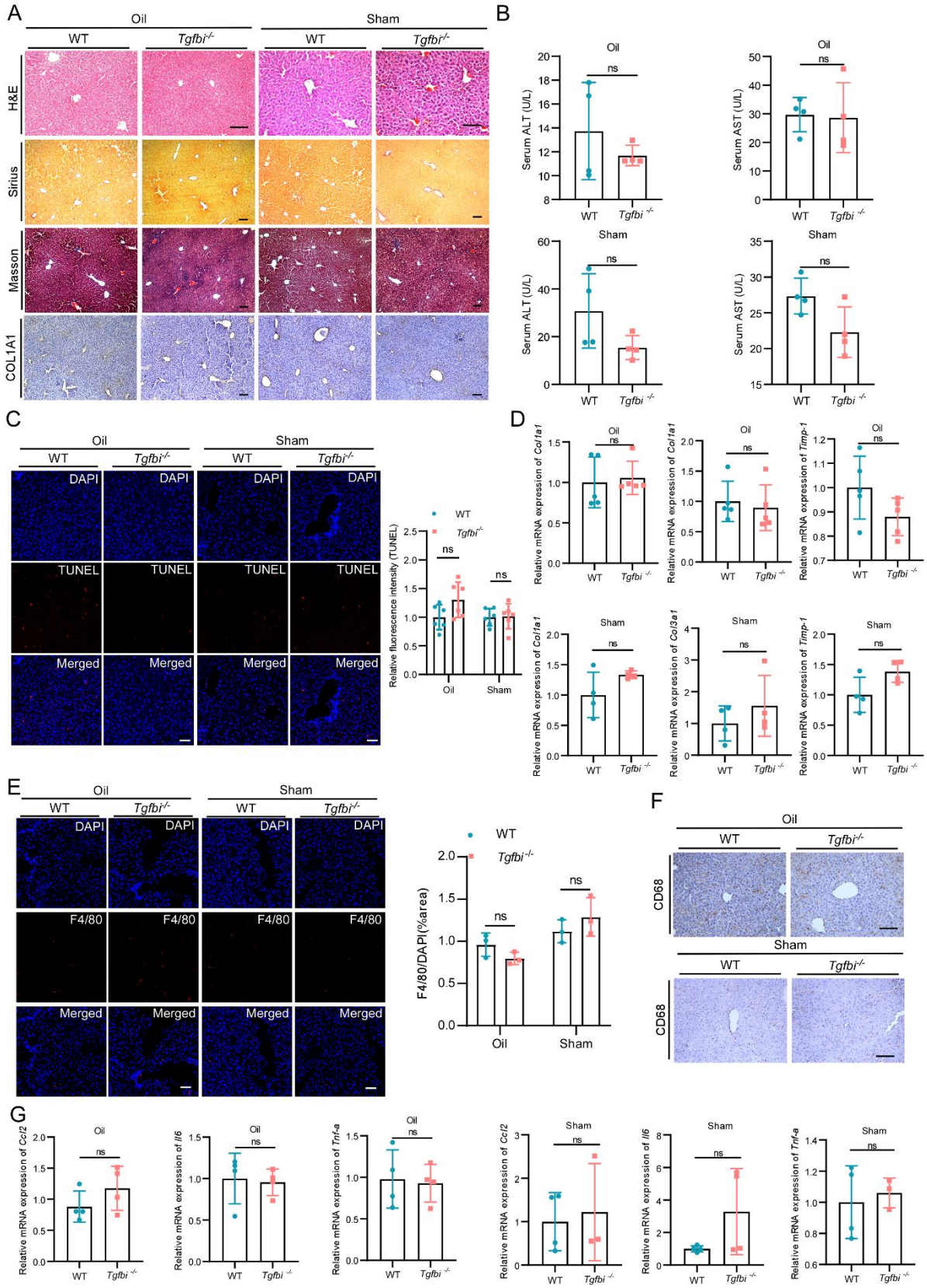

A
Oil
Sham
WT
Tgfbi-/-
H&E
Sirius
Masson
COL1A1
B
Oil
Sham
Serum ALT (U/L)
Serum AST (U/L)
ns
WT
Tgfbi -/-
C
DAPI
TUNEL
Merged
Relative fluorescence intensity (TUNEL)
D
Relative mRNA expression of Col1a1
Relative mRNA expression of Col3a1
Relative mRNA expression of Timp-1
E
F4/80
F4/80/DAPI(%area)
F
CD68
G
Relative mRNA expression of Ccl2
Relative mRNA expression of Il6
Relative mRNA expression of Tnf-a

Fig S2. TGFBI deficiency remarkably alleviates mice liver inflammation and fibrosis. A H&E, Sirius, Masson staining and IHC staining of COL1A1 in the livers of WT and *Tgfbi* $^{-/-}$ mice of control group. **B** The measurement of serum ALT and AST in mice of control group. **C** TUNEL staining and quantitative analysis of apoptosis in mice of control group. **D** RT-qPCR analysis of *Col1a1*, *Col3a1* and *Timp-1* expression in mice of control group. **E** IF staining of F4/80 in mouse fibrotic livers and statistical analysis of IF staining of F4/80. **F** IHC staining of CD68 in mouse livers of CCl_4 and BDL models. **G** RT-qPCR analysis of *Ccl2*, *Il6* and *Tnf-a* expression in mice of control group. Mice samples (n = 4-6 per group). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

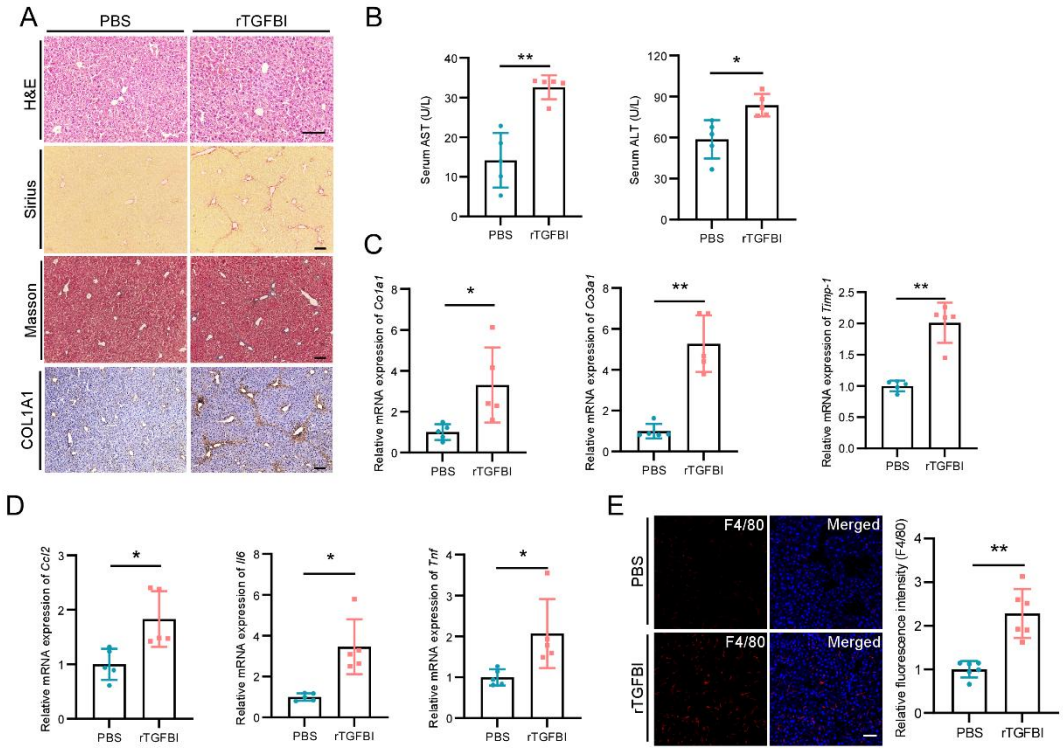

A
PBS
rTGFBI
H&E
Sirius
Masson
COL1A1
B
Serum AST (U/L)
Serum ALT (U/L)
C
Relative mRNA expression of Col1a1
Relative mRNA expression of Col3a1
Relative mRNA expression of Timp-1
D
Relative mRNA expression of Ccl2
Relative mRNA expression of Il6
Relative mRNA expression of Tnf
E
F4/80
Merged
Relative fluorescence intensity (F4/80)

Fig S3. Overexpression of TGFBI can induce liver fibrosis in mice.

A H&E, Sirius, Masson staining and IHC staining of COL1A1 in mouse livers treated with or without rTGFBI. **B** The measurement of serum ALT and AST in mice. **C** RT-qPCR analysis of *Acta2, Col1a1* and *Col3a1* expression. **D** RT-qPCR analysis of *Ccl2*, *Il6* and *Tnf-a* expression. **E** IF staining of F4/80 in mouse fibrotic livers. Mice samples (n = 4-6 per group). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001.

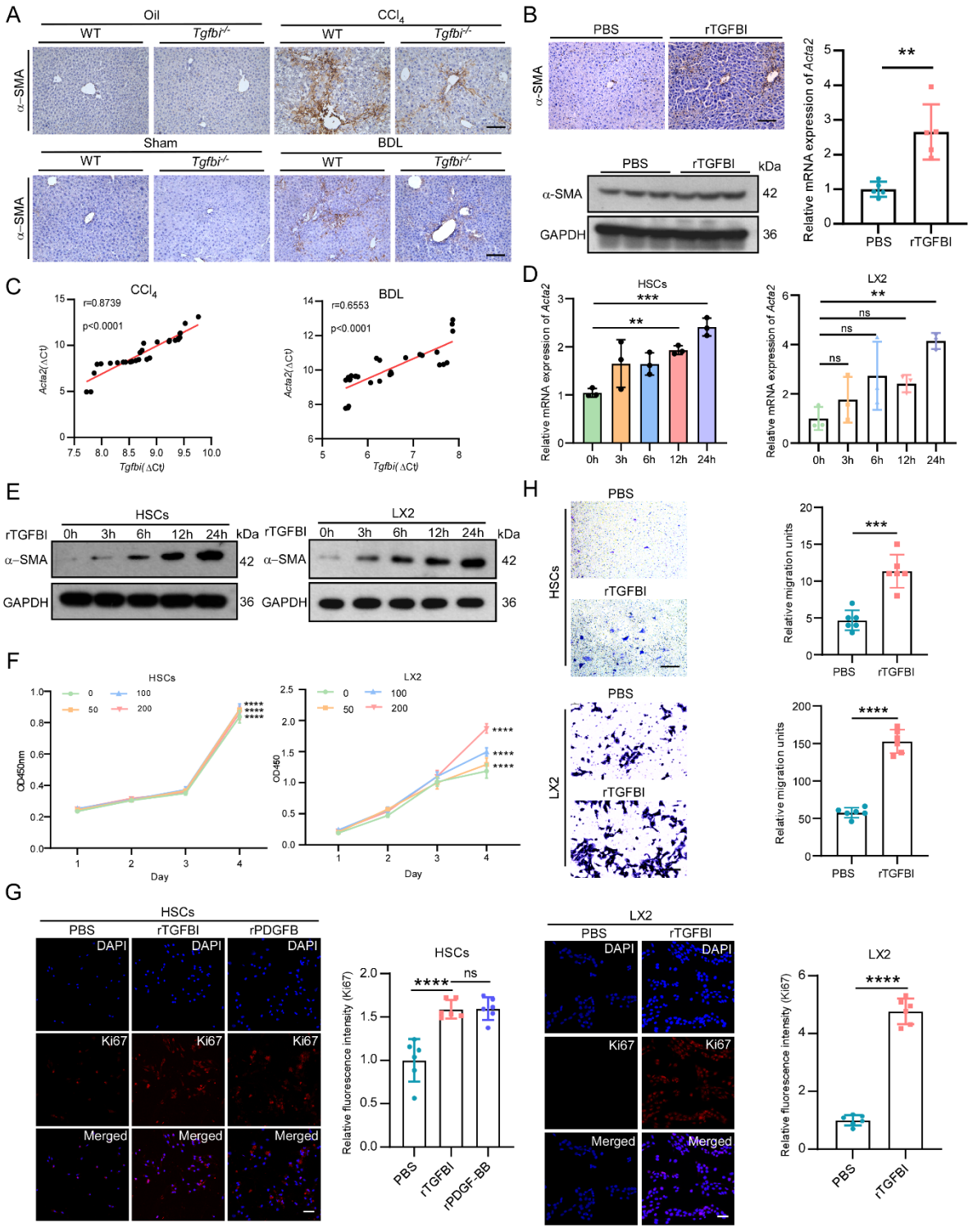

A
Oil
CCl4
WT
Tgfbi-/-
α–SMA
Sham
BDL
B
PBS
rTGFBI
α-SMA
GAPDH
kDa
42
36
Relative mRNA expression of Acta2
C
CCl4
BDL
r=0.8739
p<0.0001
r=0.6553
p<0.0001
Acta2(ΔCt)
Tgfbi(ΔCt)
D
HSCs
LX2
Relative mRNA expression of Acta2
0h
3h
6h
12h
24h
ns
E
HSCs
LX2
rTGFBI
F
HSCs
LX2
OD450nm
Day
G
PBS
rTGFBI
rPDGFB
DAPI
Ki67
Merged
Relative fluorescence intensity (Ki67)
rPDGF-BB
H
HSCs
LX2
Relative migration units

Fig S4. TGFBI promotes HSCs proliferation, migration and activation. **A** IHC staining of α-SMA in WT and *Tgfbi* $^{-/-}$ mouse livers of CCl_4 and BDL models. **B** IHC staining of α-SMA, Western blot analysis of α-SMA and RT-qPCR analysis of *Acta2* in mouse livers treated with or without rTGFBI. **C** Correlation analysis of *Tgfbi* and *Acta2* mRNA levels in mouse fibrotic livers (n = 12 independent samples). **D** RT-qPCR analysis of α-SMA in HSCs or LX2 treated with rTGFBI (200ng/mL) with the indicated times (n = 3 independent experiments). **E** Western blot analysis of α-SMA in HSCs or LX2 treated with rTGFBI (200ng/mL) with the indicated times (n = 3 independent experiments). **F** CCK8 assay of HSCs or LX2 treated with rTGFBI (200ng/mL) (n = 3 independent experiments). **G** IF staining of Ki67 in HSCs or LX2 treated with rTGFBI (200 ng/mL) for 6 h (n = 3 independent experiments). **H** Transwell assay of HSCs or LX2 treated with rTGFBI (200ng/mL) (n = 3 independent experiments). Mice samples (n = 4-6 per group). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

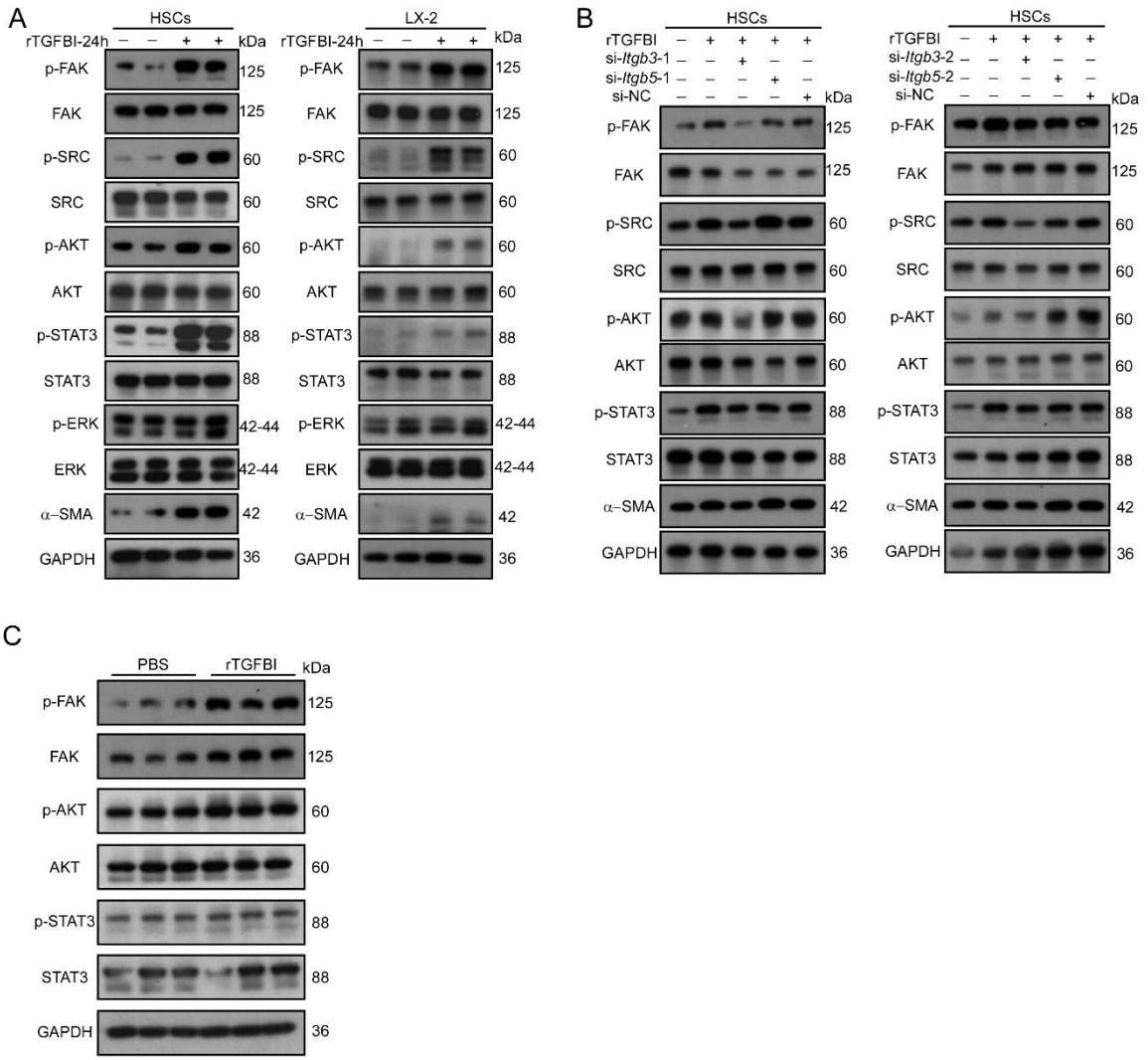

A
HSCs
rTGFBI-24h – – + +
kDa
p-FAK 125
FAK 125
p-SRC 60
SRC 60
p-AKT 60
AKT 60
p-STAT3 88
STAT3 88
p-ERK 42-44
ERK 42-44
α–SMA 42
GAPDH 36
LX-2
rTGFBI-24h – – + +
kDa
p-FAK 125
FAK 125
p-SRC 60
SRC 60
p-AKT 60
AKT 60
p-STAT3 88
STAT3 88
p-ERK 42-44
ERK 42-44
α–SMA 42
GAPDH 36
B
HSCs
rTGFBI – + + + +
si-Itgb3-1 – – + – –
si-Itgb5-1 – – – + –
si-NC – – – – +
kDa
p-FAK 125
FAK 125
p-SRC 60
SRC 60
p-AKT 60
AKT 60
p-STAT3 88
STAT3 88
α–SMA 42
GAPDH 36
HSCs
rTGFBI – + + + +
si-Itgb3-2 – – + – –
si-Itgb5-2 – – – + –
si-NC – – – – +
kDa
p-FAK 125
FAK 125
p-SRC 60
SRC 60
p-AKT 60
AKT 60
p-STAT3 88
STAT3 88
α–SMA 42
GAPDH 36
C
PBS rTGFBI
kDa
p-FAK 125
FAK 125
p-AKT 60
AKT 60
p-STAT3 88
STAT3 88
GAPDH 36

Fig S5. TGFBI activates HSCs through the integrin avβ3-FAK-STAT3 signaling pathway. A Western blot analysis of the indicated proteins in HSCs treated with rTGFBI (200ng/mL) for 24 h (n = 3 independent experiments). **B** Western blotting analysis of indicator proteins in HSCS treated alone with rTGFBI (200ng/mL) or in combination with *Itgb*3 or *Itgb5* siRNA (n = 3 independent experiments). **C** Western blot analysis of the indicated proteins in mouse livers treated with or without rTGFBI. Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

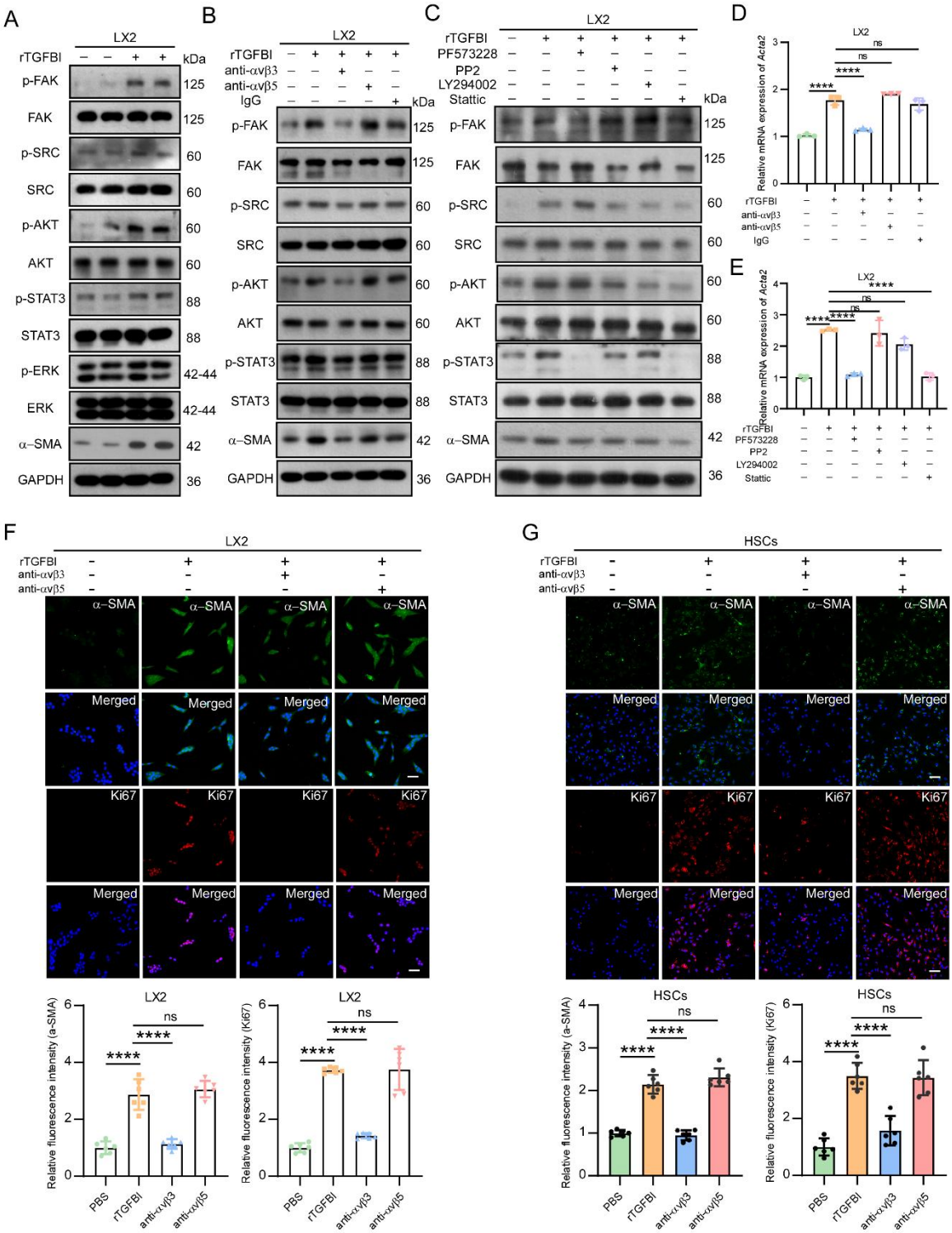

A
LX2
rTGFBI
kDa
p-FAK
FAK
p-SRC
SRC
p-AKT
AKT
p-STAT3
STAT3
p-ERK
ERK
α–SMA
GAPDH
125
60
88
42-44
42
36
B
LX2
rTGFBI
anti-αvβ3
anti-αvβ5
IgG
C
LX2
rTGFBI
PF573228
PP2
LY294002
Stattic
D
LX2
Relative mRNA expression of Acta2
ns
****
E
LX2
F
LX2
α–SMA
Merged
Ki67
Relative fluorescence intensity (a-SMA)
Relative fluorescence intensity (Ki67)
PBS
rTGFBI
anti-αvβ3
anti-αvβ5
G
HSCs

Fig S6. TGFBI activates HSCs through the integrin avβ3-FAK-STAT3 signaling pathway. A Western blot analysis of the indicated proteins in LX2 treated with rTGFBI (200ng/mL) for 6 h (n = 3 independent experiments). **B** Western blot analysis of the indicated proteins in LX2 treated with rTGFBI (200ng/mL) alone or in combination with integrin αvβ3 or αvβ5 neutralizing antibody (n = 3 independent experiments). **C** Western blot analysis of the indicated proteins in HSCs or LX2 treated with rTGFBI (200ng/mL) or in combination with the indicated inhibitors for 6 h (n = 3 independent experiments). **D** RT-qPCR analysis of *Acta2* in LX2 treated with rTGFBI (200ng/mL) alone or in combination with integrin αvβ3 or αvβ5 neutralizing antibody (n = 3 independent experiments). **E** RT-qPCR analysis of *Acta2* in HSCs or LX2 treated with rTGFBI (200ng/mL) alone or in combination with the indicated inhibitors for 6 h (n = 3 independent experiments). **F-G** IF staining and statistical graph of α-SMA in HSCS or LX2 treated with rTGFBI (200ng/mL) alone or in combination with integrin αvβ3 or αvβ5 neutralizing antibodies (n = 3 independent experiments). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

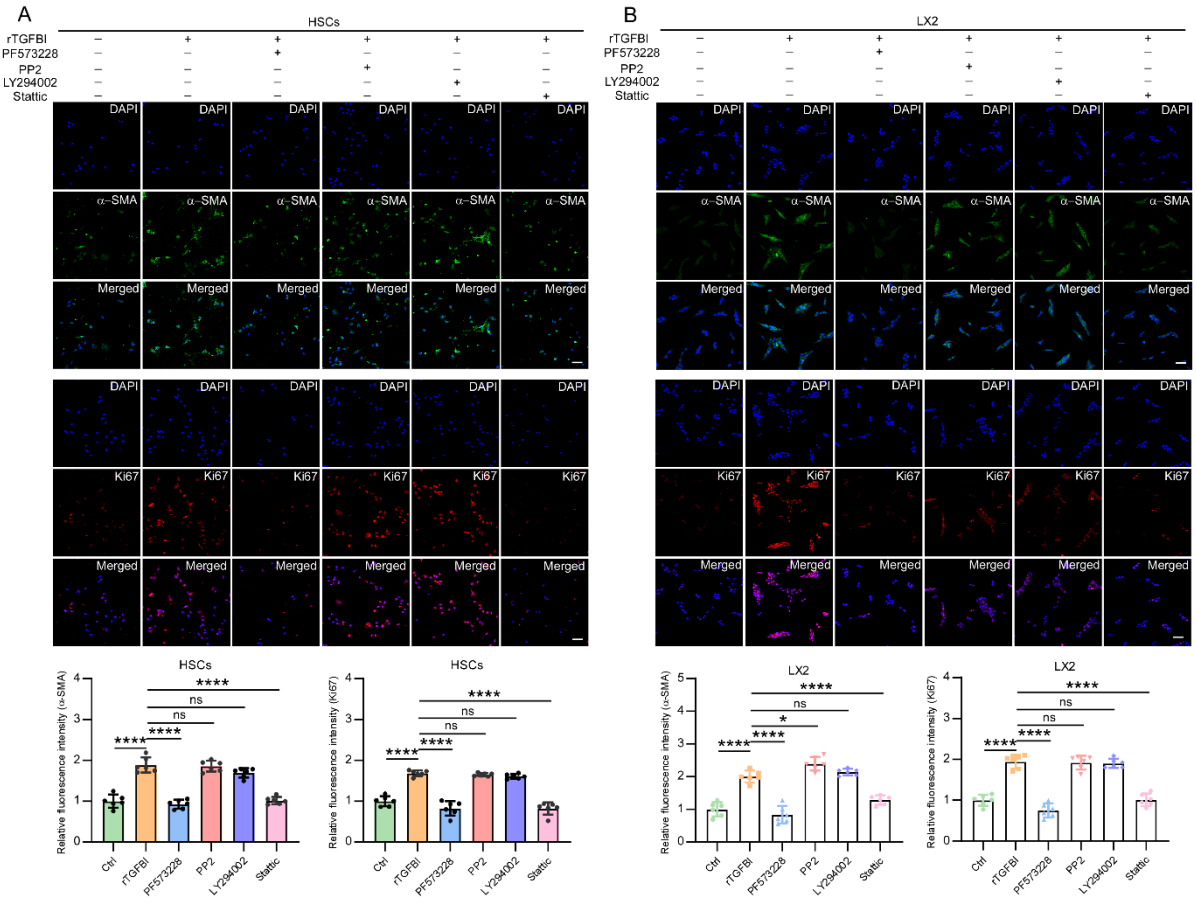


Fig S7. TGFBI activates HSCs through the integrin avβ3-FAK-STAT3 signaling pathway. A-B IF staining of α-SMA in HSC or LX2 treated with rTGFBI (200ng/mL) alone or in combination with indicated inhibitors for 6 h (n = 3 independent experiments) and statistical plots of relative fluorescence intensity. Scale bars, 50 μm. *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

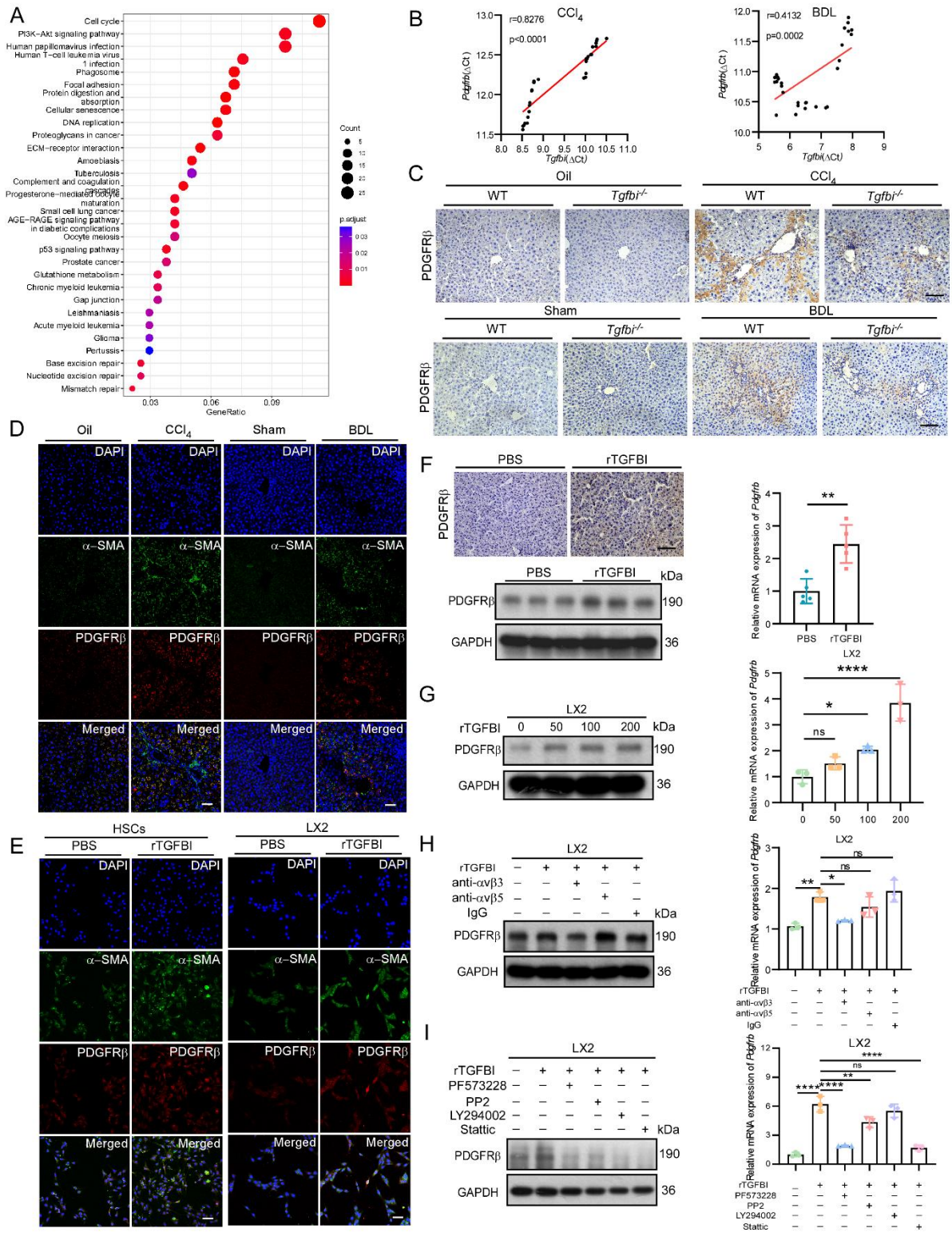

A
Cell cycle
PI3K−Akt signaling pathway
Human papillomavirus infection
Human T−cell leukemia virus 1 infection
Phagosome
Focal adhesion
Protein digestion and absorption
Cellular senescence
DNA replication
Proteoglycans in cancer
ECM−receptor interaction
Amoebiasis
Tuberculosis
Complement and coagulation cascades
Progesterone−mediated oocyte maturation
Small cell lung cancer
AGE−RAGE signaling pathway in diabetic complications
Oocyte meiosis
p53 signaling pathway
Prostate cancer
Glutathione metabolism
Chronic myeloid leukemia
Gap junction
Leishmaniasis
Acute myeloid leukemia
Glioma
Pertussis
Base excision repair
Nucleotide excision repair
Mismatch repair
0.03
0.06
0.09
GeneRatio
Count
p.adjust
B
CCl4
r=0.8276
p<0.0001
Pdgfrb(ΔCt)
Tgfbi(ΔCt)
BDL
r=0.4132
p=0.0002
C
Oil
CCl4
Sham
BDL
WT
Tgfbi-/-
PDGFRβ
D
Oil
CCl4
Sham
BDL
DAPI
α−SMA
PDGFRβ
Merged
E
HSCs
LX2
PBS
rTGFBI
F
PBS
rTGFBI
PDGFRβ
kDa
190
GAPDH
36
Relative mRNA expression of Pdgfrb
G
LX2
rTGFBI
0
50
100
200
H
anti-αvβ3
anti-αvβ5
IgG
I
PF573228
PP2
LY294002
Stattic

Fig S8. TGFBI significantly enhances PDGFRβ expression in HSCs. **A** KEGG pathway analysis of differentially expressed genes from liver tissues of CCl_4-induced WT, and *Tgfbi*$^{-/-}$ mice. **B** Correlation analysis of *Tgfbi* mRNA with *Pdgfrb* mRNA in mouse fibrotic livers (n = 12 independent samples). **C** IHC staining of PDGFRβ in mouse livers. **D** IF co-staining of PDGFRβ with α-SMA in mouse livers of CCl_4 and BDL models. **E** IF co-staining of PDGFRβ with α-SMA in HSCs or LX2 treated with rTGFBI. **F** IHC staining of in mouse livers treated with or without rTGFBI, Western blot analysis of PDGFRβ and RT-qPCR analysis of *Pdgfrb* in mouse livers treated with or without rTGFBI. **G** Western blot and RT-qPCR analysis of PDGFRβ in LX2 treated with rTGFBI (ng/mL) with the indicated concentrations for 6 h (n = 3 independent experiments). **H** Western blot and RT-qPCR analyses of PDGFRβ in LX2 treated with rTGFBI (200ng/mL) alone or in combination with integrin αvβ3 or αvβ5 neutralizing antibody for 6 h (n = 3 independent experiments). **I** RT-qPCR and Western blot analyses of PDGFRβ in LX2 treated with rTGFBI (200ng/mL) alone or in combination with the indicated inhibitors for 6 h (n = 3 independent experiments). Mice samples (n = 4-6 per group). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

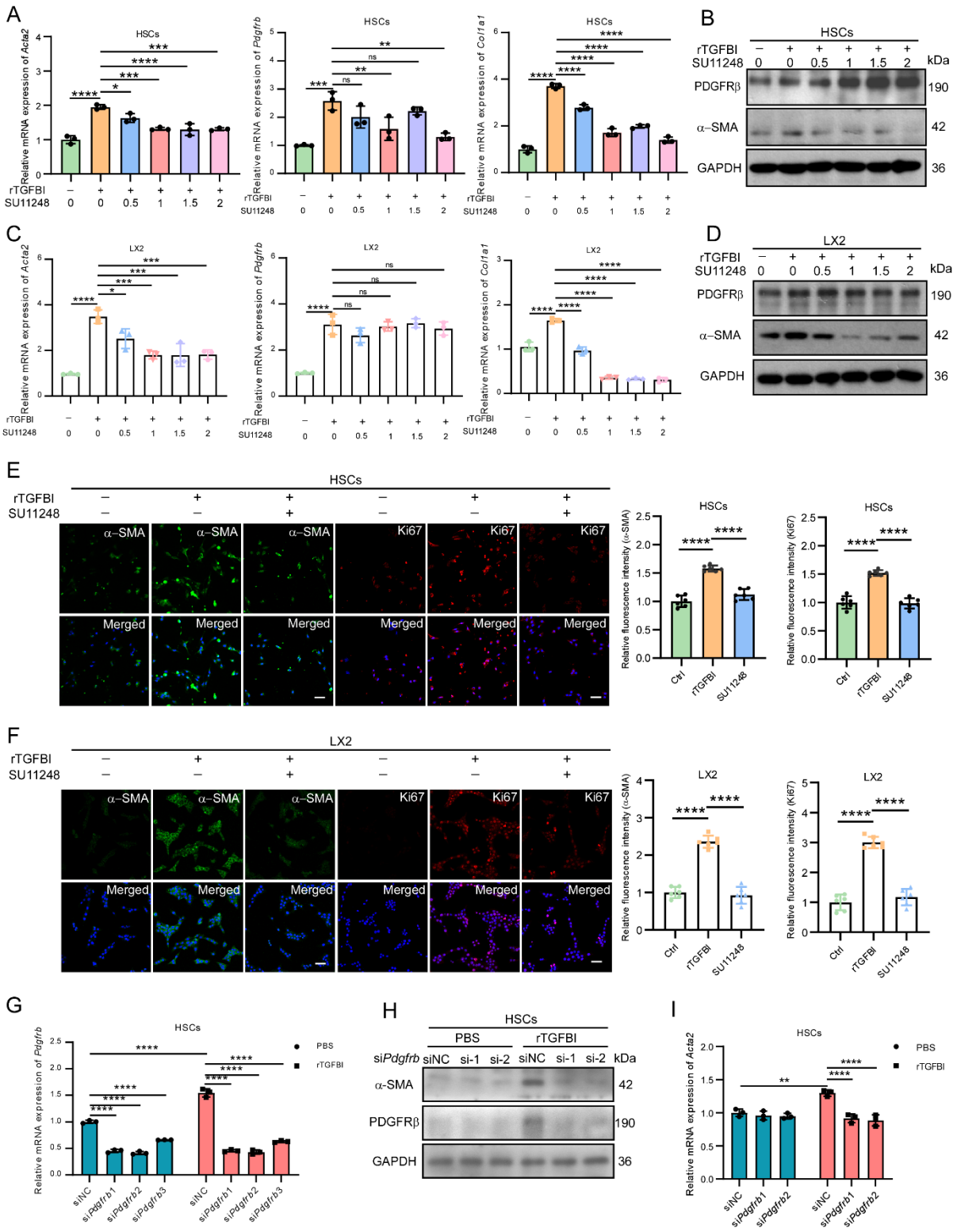

A
HSCs
Relative mRNA expression of Acta2
Relative mRNA expression of Pdgfrb
Relative mRNA expression of Col1a1
rTGFBI
SU11248
B
HSCs
kDa
PDGFRβ
α–SMA
GAPDH
190
42
36
C
LX2
D
LX2
E
HSCs
α–SMA
Ki67
Merged
Relative fluorescence intensity (α-SMA)
Relative fluorescence intensity (Ki67)
Ctrl
F
LX2
G
HSCs
Relative mRNA expression of Pdgfrb
PBS
rTGFBI
siNC
siPdgfrb1
siPdgfrb2
siPdgfrb3
H
HSCs
PBS
rTGFBI
siPdgfrb
siNC
si-1
si-2
I
HSCs
Relative mRNA expression of Acta2

Fig S9. Blocking PDGFRβ can effectively reduce HSCs activation. A and C RT-qPCR analysis of *Acta2*, *Pdgfrb* and *Col1a1* in HSCs or LX2 treated with rTGFBI (200ng/mL) alone or in combination with SU11248 (μM) for 6h (n = 3 independent experiments). **B and D** Western blot analysis of α-SMA and PDGFRβ in HSCs or LX2 treated with rTGFBI (200ng/mL) alone or in combination with SU11248 (μM) for 6h (n = 3 independent experiments). **E-F** IF staining and statistical graph of α-SMA and Ki67 in HSCs or LX2 treated with rTGFBI (200ng/mL) alone or in combination with SU11248 (μM) (n = 3). **G** RT-qPCR analysis of *Pdgfrb* in HSCs transfected with indicated siRNAs for 24h and treated with or without rTGFBI (200ng/mL) for 24 h (n = 3 independent experiments). **H** Western blot analyses of α-SMA in HSCs transfected with the indicated siRNAs for 24h and treated with or without rTGFBI (200ng/mL) for 24 h (n = 3 independent experiments). **I** RT-qPCR analyses of α-SMA in HSCs transfected with the indicated siRNAs for 24h and treated with or without rTGFBI (200ng/mL) for 24 h (n = 3 independent experiments). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

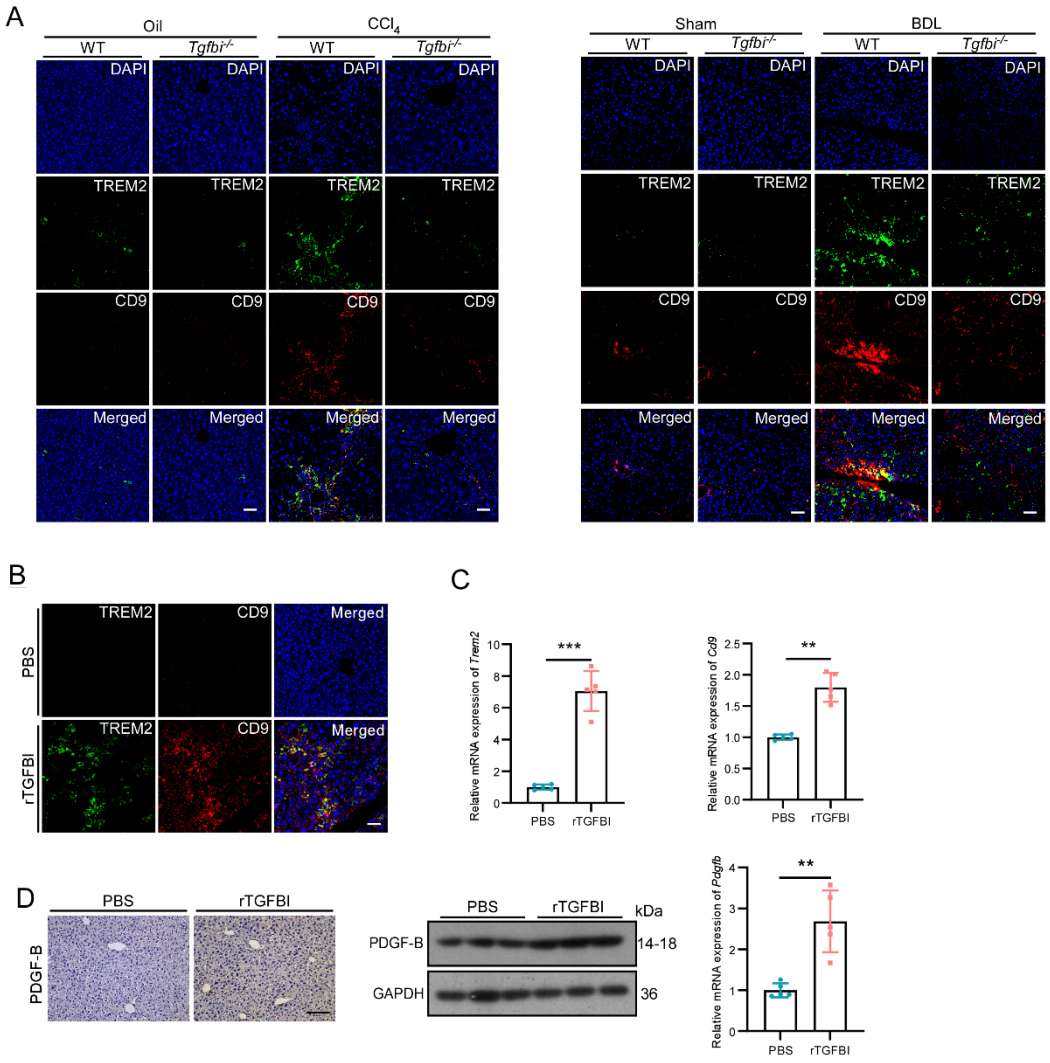

A
Oil
CCl4
Sham
BDL
WT
Tgfbi-/-
DAPI
TREM2
CD9
Merged
B
PBS
rTGFBI
C
Relative mRNA expression of Trem2
Relative mRNA expression of Cd9
Relative mRNA expression of Pdgfb
***
**
D
PDGF-B
GAPDH
kDa
14-18
36

Fig S10. TGFBI regulates the expression of TREM2, CD9 and PDGF-B in macrophages. A IF co-staining of PDGFRB with α-SMA in WT and *Tgfbi* $^{-/-}$ mice livers of CCl_4 and BDL models. Mice samples (n = 4-6 per group). Scale bars, 50 μm. **B** IF co-staining of α-SMA with TREM2 and CD9 in mouse livers treated with or without rTGFBI. **C** RT-qPCR analysis of *Trem2* and *Cd9* expression in mouse livers treated with or without rTGFBI. Mice samples (n = 5-6 per group). **D** IHC staining of PDGF-B, Western blot analysis of PDGF-B and RT-qPCR analysis of *Pdgfb* in mouse livers treated with or without rTGFBI. Mice samples (n = 4-6 per group). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

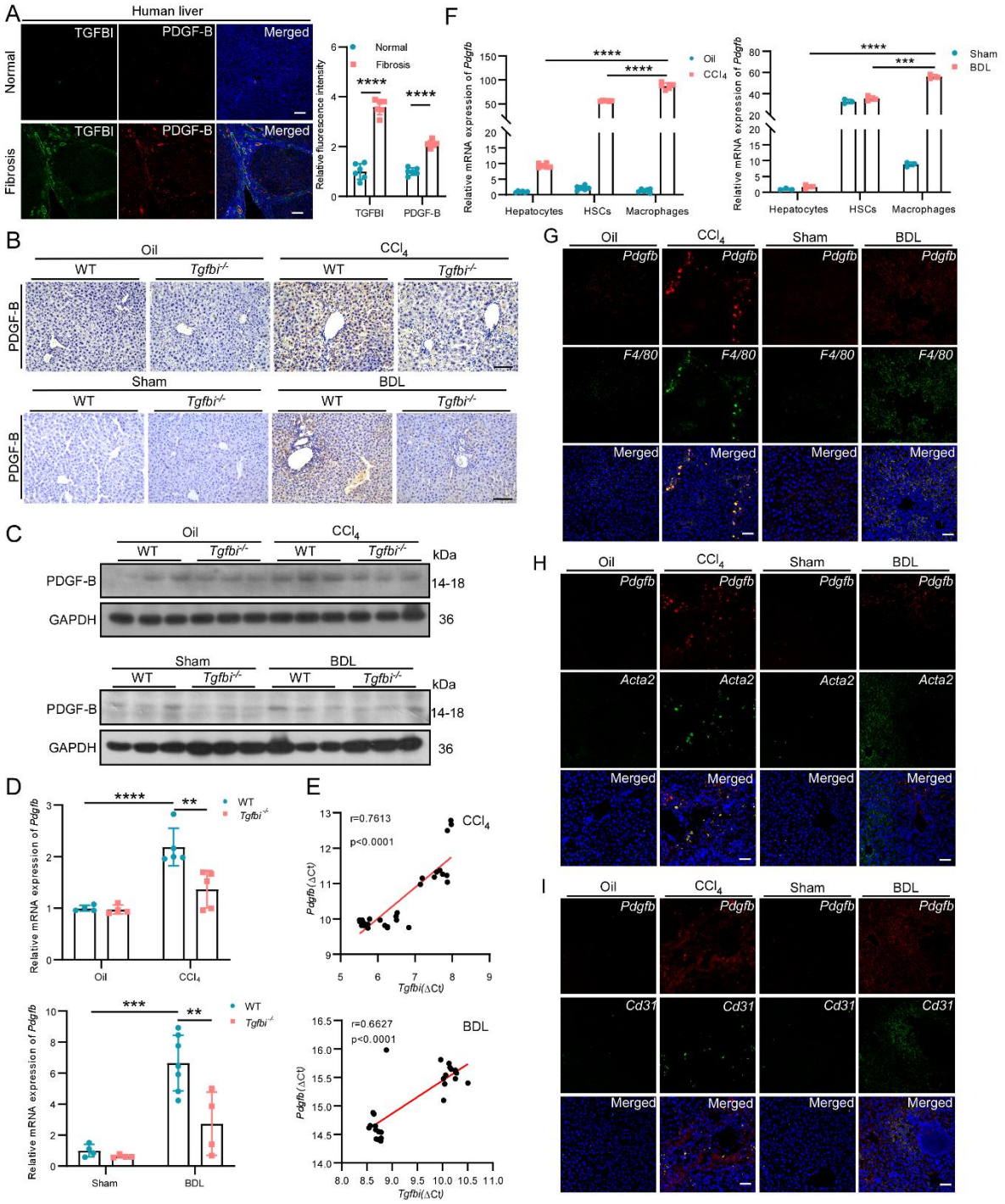

A
Human liver
TGFBI
PDGF-B
Merged
Normal
Fibrosis
Relative fluorescence intensity
Normal
Fibrosis
****
TGFBI
PDGF-B
B
Oil
CCl4
WT
Tgfbi-/-
PDGF-B
Sham
BDL
C
kDa
PDGF-B
14-18
GAPDH
36
D
Relative mRNA expression of Pdgfb
Oil
CCl4
Sham
BDL
E
r=0.7613
p<0.0001
r=0.6627
p<0.0001
Pdgfb (ΔCt)
Tgfbi(ΔCt)
F
Relative mRNA expression of Pdgfb
Hepatocytes
HSCs
Macrophages
G
Pdgfb
F4/80
Merged
H
Acta2
I
Cd31

Fig S11. TGFBI orchestrates macrophages through enhancing PDGF-B expression. A IF staining of TGFBI and PDGFRβ in human fibrotic liver tissue. **B** IHC staining of PDGFB in WT and *Tgfbi* $^{-/-}$ mice livers of CCl_4 and BDL models. **C** Western blot analysis of PDGFB expression in mouse livers of CCl_4 and BDL models. **D** RT-qPCR analysis of PDGF-B expression in mouse livers of CCl_4 and BDL models. **E** Correlation analysis of *Tgfbi* mRNA with *Pdgfb* mRNA in mouse fibrotic livers (n = 12 independent samples). **F** RT-qPCR analysis of PDGFRB in primary liver parenchymal cells, HSCs and macrophages isolated from mice livers of CCl_4 and BDL models (n = 3 independent experiments). **G-I** FISH analysis of co-expression of *Pdgfb* with *F4/80, Acta2* and *CD31* in mouse livers, respectively. Mice samples (n = 4-6 per group). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

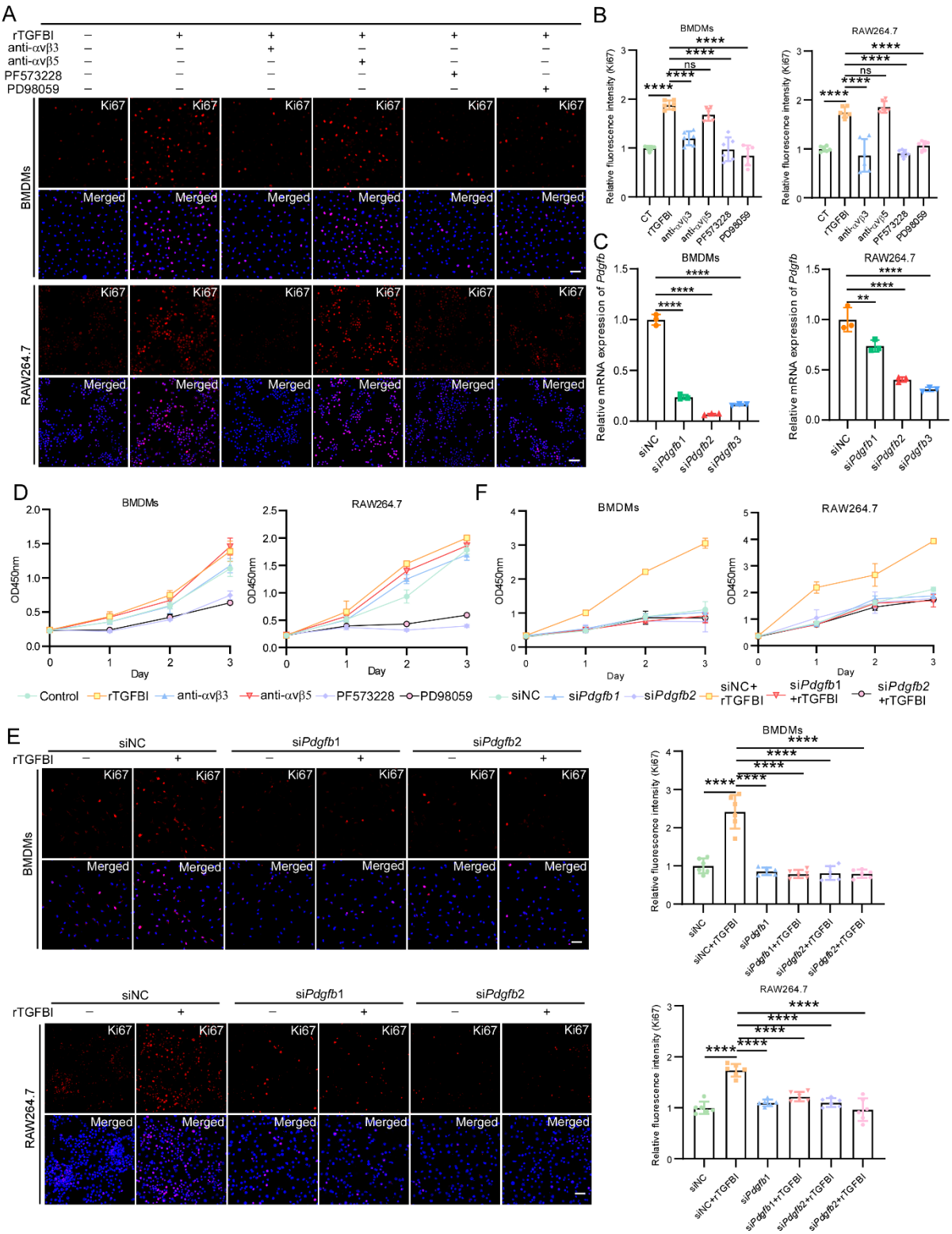

A
rTGFBI
anti-αvβ3
anti-αvβ5
PF573228
PD98059
BMDMs
RAW264.7
Ki67
Merged
B
BMDMs
RAW264.7
Relative fluorescence intensity (Ki67)
CT
rTGFBI
anti-αvβ3
anti-αvβ5
PF573228
PD98059
C
Relative mRNA expression of Pdgfb
siNC
siPdgfb1
siPdgfb2
siPdgfb3
D
OD450nm
Day
Control
rTGFBI
anti-αvβ3
anti-αvβ5
PF573228
PD98059
F
siNC
siPdgfb1
siPdgfb2
siNC+ rTGFBI
siPdgfb1 +rTGFBI
siPdgfb2 +rTGFBI
E
siNC
siPdgfb1
siPdgfb2
rTGFBI
siNC+rTGFBI
siPdgfb1+rTGFBI
siPdgfb2+rTGFBI

Fig S12. TGFBI promotes the proliferation of macrophages. A IF staining of Ki67 in BMDM or RAW264.7 treated with rTGFBI (200ng/mL) alone or in combination with the indicated inhibitors for 6h (n = 3 independent experiments). **B** Statistics of relative fluorescence intensity of Ki67. **C** RT-qPCR analysis of *Pdgfb* in BMDM or RAW264.7 transfected with indicated siRNAs for 24h (n = 3 independent experiments). **D** CCK8 assay of BMDM or RAW264.7 treated with rTGFBI (200ng/mL) alone or in combination with the indicated inhibitors (n = 3 independent experiments). **E** IF staining of Ki67 in BMDM or RAW264.7 transfected with the indicated siRNAs for 24 h and treated with or without rTGFBI (200ng/mL) for 24 h (n = 3 independent experiments). **F** CCK8 assay of BMDM or RAW264.7 transfected with the indicated siRNAs for 24 h and treated with or without rTGFBI (200ng/mL) for 24 h (n = 3 independent experiments). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

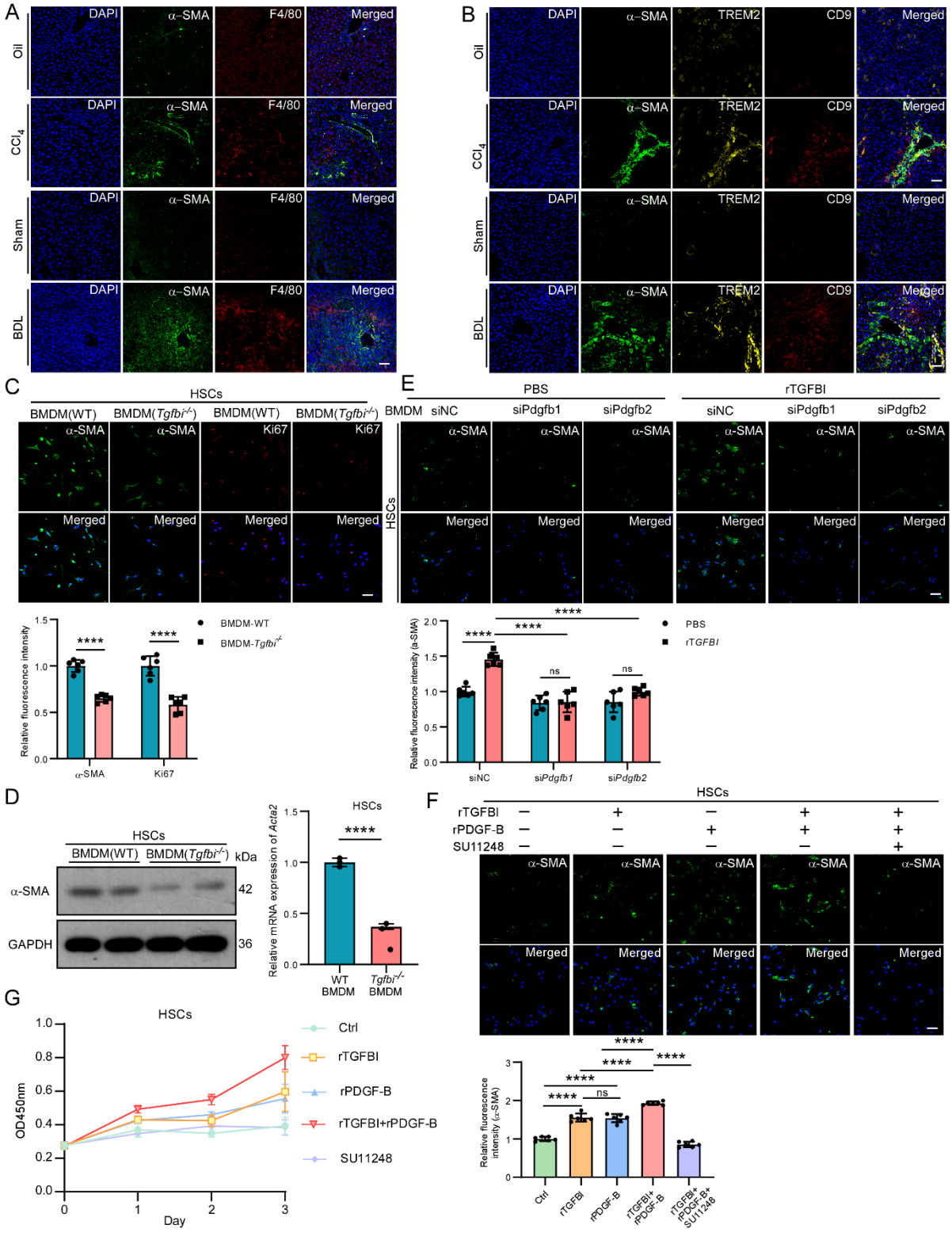

A
Oil
CCl4
Sham
BDL
DAPI
α-SMA
F4/80
Merged
B
TREM2
CD9
C
HSCs
BMDM(WT)
BMDM(Tgfbi-/-)
Ki67
Relative fluorescence intensity
BMDM-WT
BMDM-Tgfbi-/-
α-SMA
Ki67
D
kDa
GAPDH
42
36
Relative mRNA expression of Acta2
WT BMDM
Tgfbi-/- BMDM
E
PBS
rTGFBI
BMDM
siNC
siPdgfb1
siPdgfb2
Relative fluorescence intensity (α-SMA)
rTGFBI
siPdgfb1
siPdgfb2
F
rTGFBI
rPDGF-B
SU11248
Relative fluorescence intensity (α-SMA)
Ctrl
rTGFBI
rPDGF-B
rTGFBI+rPDGF-B
rTGFBI+rPDGF-B+SU11248
G
OD450nm
Day
Ctrl
rTGFBI
rPDGF-B
rTGFBI+rPDGF-B
SU11248

Fig S13. Macrophages promote HSCs activation. A IF co-staining of α-SMA with F4/80 in mouse livers of CCl4 and BDL models. **B** IF co-staining of α-SMA with TREM2 and CD9 in mouse livers of CCl4 and BDL models. **C** IF staining and quantitative analysis of α-SMA and Ki67 in HSCs cocultured with WT or *Tgfbi*$^{-/-}$ BMDMs (n = 3 independent experiments). **D** RT-qPCR and Western blot analyses of α-SMA in HSCs cocultured with WT or *Tgfbi*$^{-/-}$ BMDMs (n = 3 independent experiments). **E** IF staining and quantitative analysis of α-SMA in HSCs cocultured with BMDMs transfected the indicated siRNAs for 24 h and treated with or without rTGFB I (200ng/mL) (n = 3 independent experiments). **F** IF staining and quantitative analysis of α-SMA in HSCs treated with rTGFBI (200ng/mL) alone or in combination with rPDGF-B (200ng/mL) or SU11248 (1μM) for 6h (n = 3 independent experiments). **G** CCK8 assay of HSCs treated with treated with rTGFBI (200ng/mL) alone or in combination with rPDGF-B (200ng/mL) or SU11248 (1μM) (n = 6 independent experiments). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

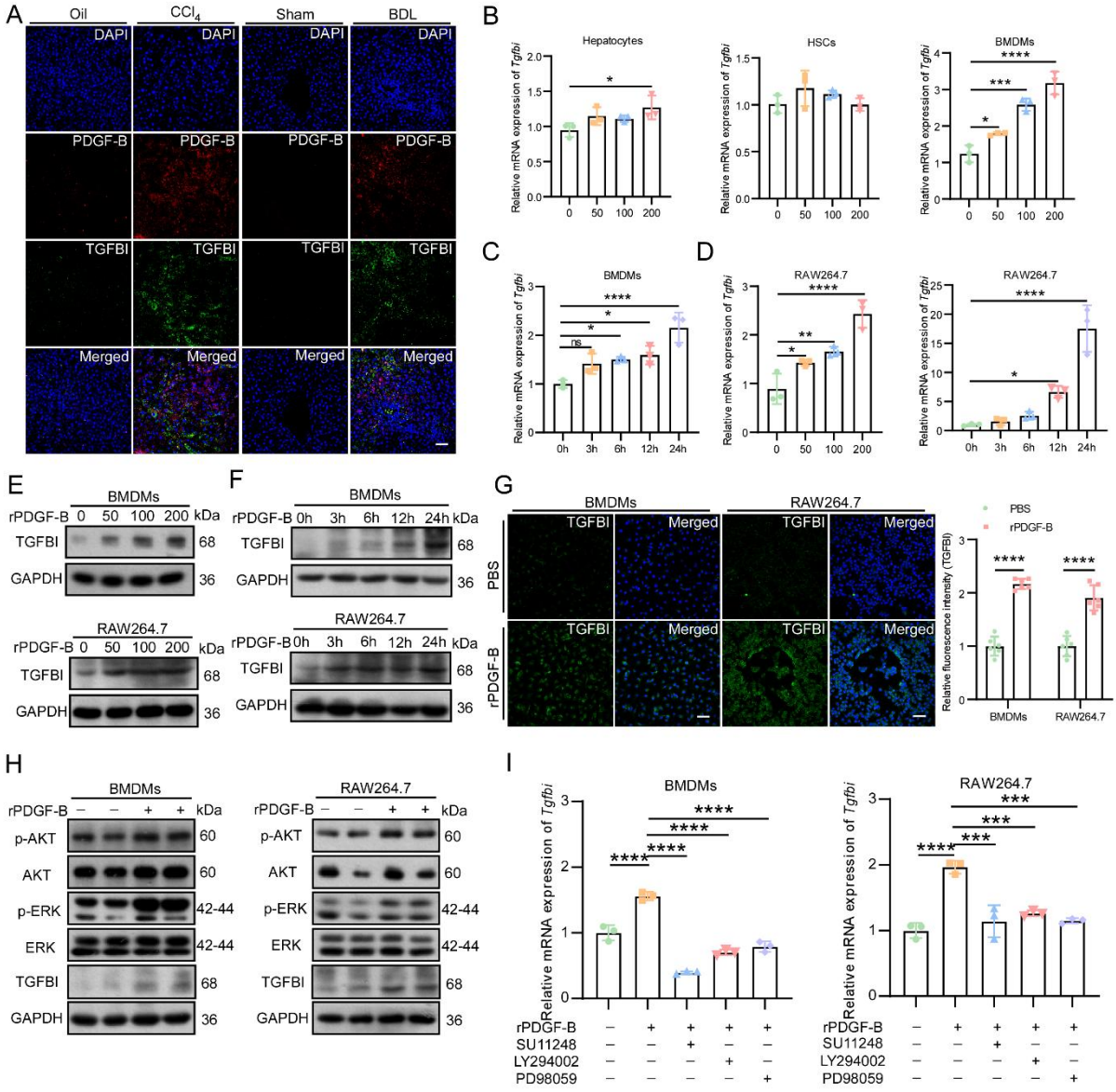
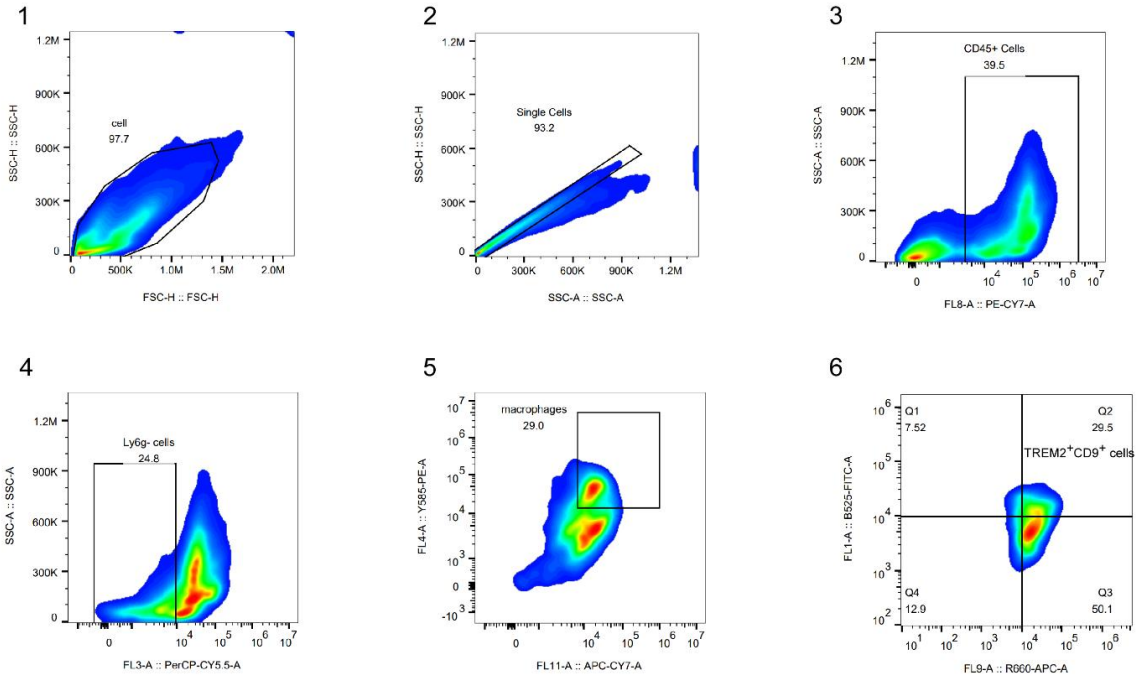

A
Oil
CCl4
Sham
BDL
DAPI
PDGF-B
TGFBI
Merged
B
Hepatocytes
HSCs
BMDMs
Relative mRNA expression of Tgfbi
C
BMDMs
D
RAW264.7
E
BMDMs
rPDGF-B 0 50 100 200 kDa
TGFBI 68
GAPDH 36
RAW264.7
F
BMDMs
rPDGF-B 0h 3h 6h 12h 24h kDa
TGFBI 68
GAPDH 36
RAW264.7
G
BMDMs
RAW264.7
PBS
rPDGF-B
Relative fluorescence intensity (TGFBI)
H
BMDMs
RAW264.7
rPDGF-B – – + + kDa
p-AKT 60
AKT 60
p-ERK 42-44
ERK 42-44
TGFBI 68
GAPDH 36
I
BMDMs
RAW264.7
Relative mRNA expression of Tgfbi
rPDGF-B – + + + +
SU11248 – – + – –
LY294002 – – – + –
PD98059 – – – – +

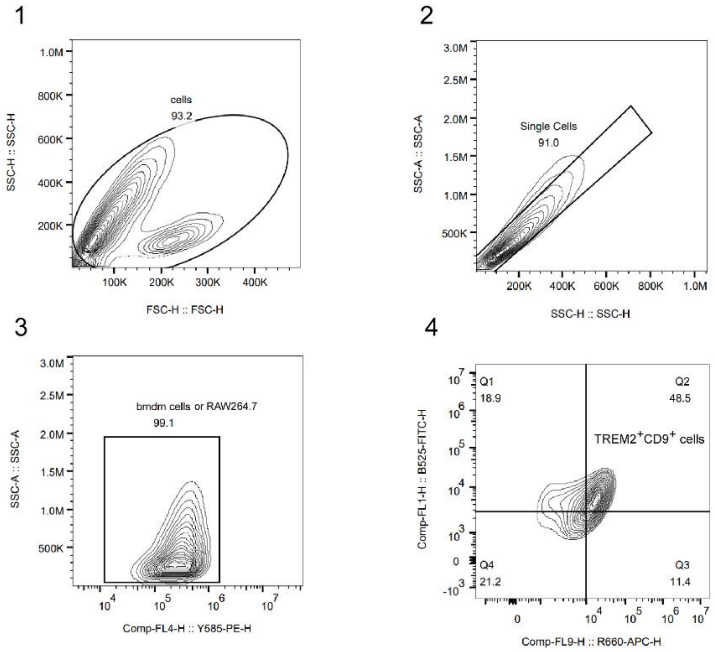
Fig S14. The up-regulation of TGFBI is attributed to PDGF-B positive feedback. A IF co-staining of TGFBI with PDGF-B in mouse livers of CCl_4 and BDL models. **B** RT-qPCR analysis of *Tgfbi* in primary liver parenchymal cells, HSCs and BMDM treated with rPDGF-B (200ng/mL) with the indicated concentrations for 6h (n = 3 independent experiments). **C** RT-qPCR analysis of *Tgfbi* in BMDM treated with rPDGF-B (200ng/mL) with the indicated times. **D** RT-qPCR analysis of *Tgfbi* in RAW264.7 treated with rPDGF-B (200ng/mL) for 6h (n = 3 independent experiments). **E-F** Western blot analysis of TGFBI in BMDM or RAW264.7 treated with or without rPDGF-B (200ng/mL) for 6h (n = 3 independent experiments). **G** IF staining and quantitative analysis of TGFBI in BMDM or RAW264.7 treated with or without rPDGF-B (200ng/mL) for 6h (n = 3 independent experiments).**H** Western blot analysis of the indicated proteins in BMDM or RAW264.7 treated with or without rPDGF-B (200ng/mL) for 6h (n = 3 independent experiments). **I** RT-qPCR analysis of *Tgfbi* expression in BMDM or RAW264.7 treated with rPDGF-B (200ng/mL) alone or in combination with the indicated inhibitors for for 6h (n = 3 independent experiments). Mice samples (n = 4-6 per group). Data were presented as the mean ± SDs; scale bars, 50 μm; *p<0.05 **p<0.01, ***p<0.001, ****p<0.0001; ns, not significant (Student's t test).

Supplementary Figure 15

Gating strategy for flow cytometry analysis in CCl_4- and BDL-induced models.



Gating strategy for flow cytometry in BMDM and RAW264.7 cell models



Supplementary Figure 16

Fig 1D

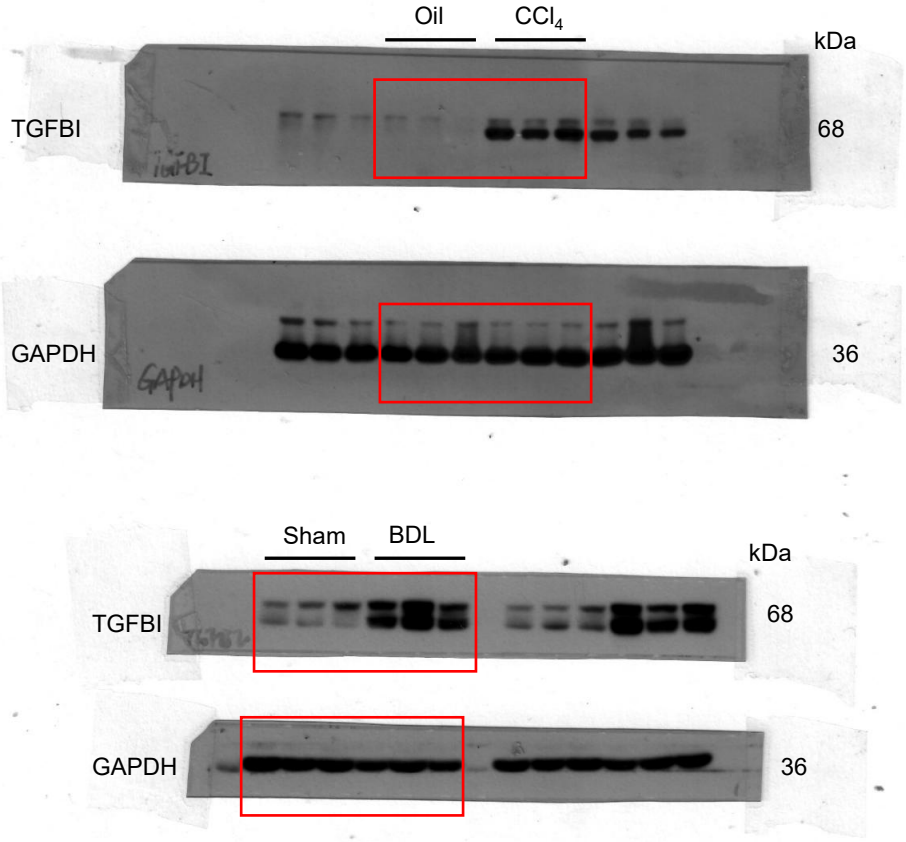


Fig 3B

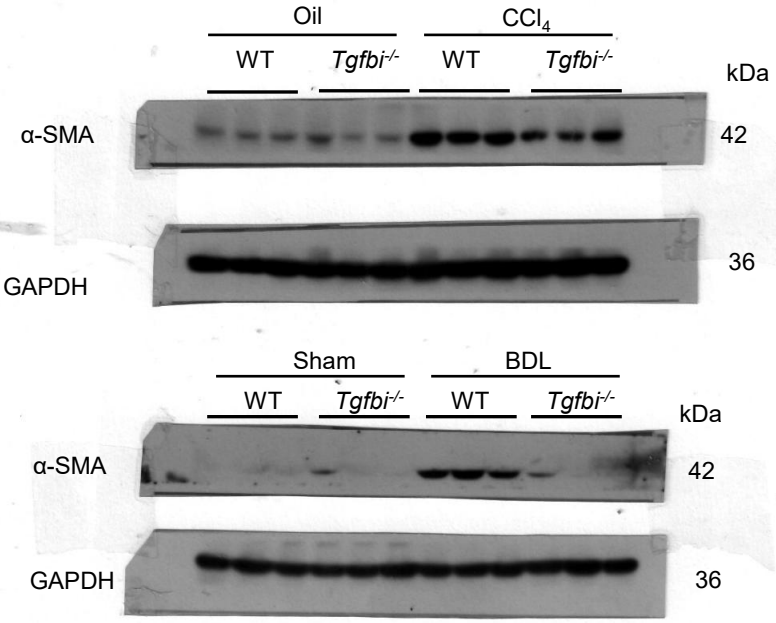

Oil
CCl4
WT
Tgfbi-/-
WT
Tgfbi-/-
kDa
α-SMA
42
GAPDH
36
Sham
BDL
WT
Tgfbi-/-
WT
Tgfbi-/-
kDa
α-SMA
42
GAPDH
36

Fig 3E

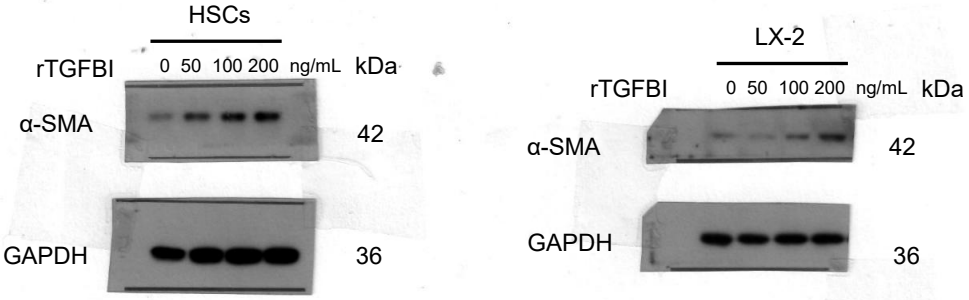

HSCs
rTGFBI
0 50 100 200 ng/mL
kDa
α-SMA
42
GAPDH
36
LX-2
rTGFBI
0 50 100 200 ng/mL
kDa
α-SMA
42
GAPDH
36

Fig 3G

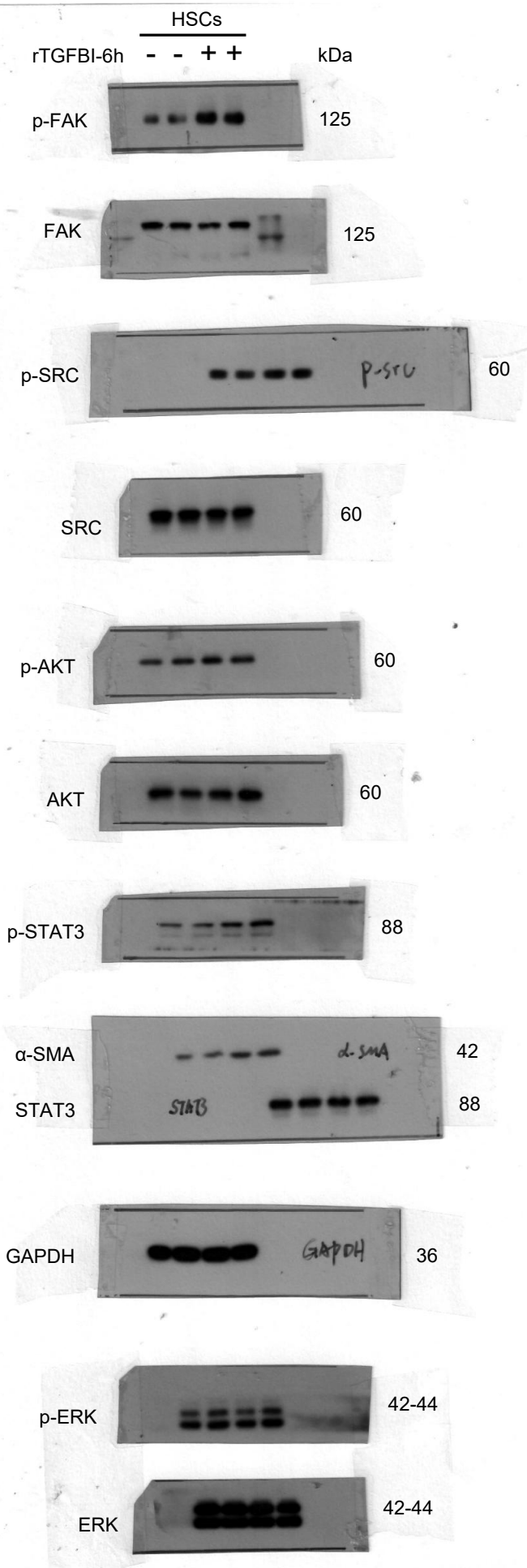

HSCs
rTGFBI-6h - - + +
kDa
p-FAK
125
FAK
125
p-SRC
p-SRC
60
SRC
60
p-AKT
60
AKT
60
p-STAT3
88
α-SMA
α-SMA
42
STAT3
STAT3
88
GAPDH
GAPDH
36
p-ERK
42-44
ERK
42-44

Fig 3H

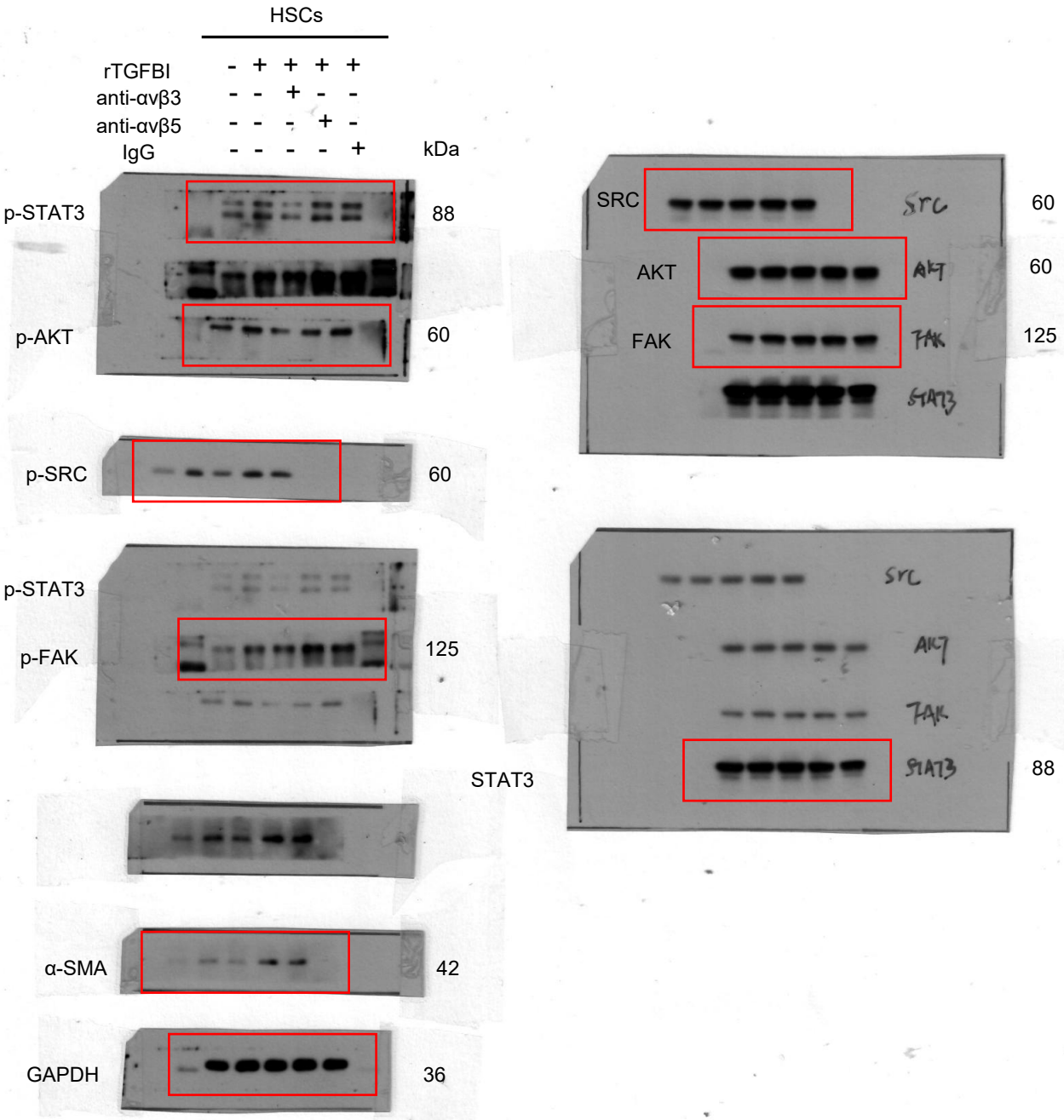

HSCs
rTGFBI - + + + +
anti-αvβ3 - - + - -
anti-αvβ5 - - - + -
IgG - - - - +
kDa
p-STAT3
p-AKT
88
60
p-SRC
60
p-STAT3
p-FAK
125
STAT3
α-SMA
42
GAPDH
36
SRC
AKT
FAK
STAT3
60
60
125
88

Fig 3I

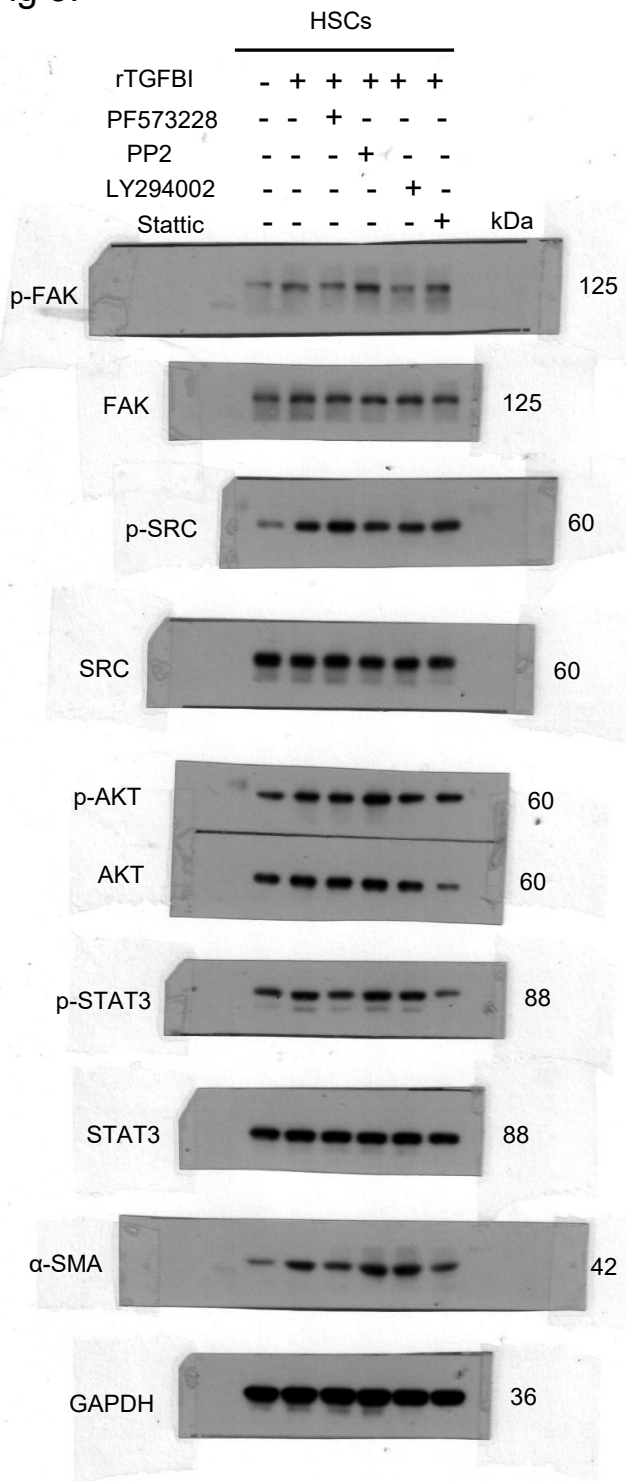

HSCs
rTGFBI - + + + + +
PF573228 - - + - - -
PP2 - - - + - -
LY294002 - - - - + -
Stattic - - - - - +
kDa
p-FAK
125
FAK
125
p-SRC
60
SRC
60
p-AKT
60
AKT
60
p-STAT3
88
STAT3
88
α-SMA
42
GAPDH
36

Fig 4E

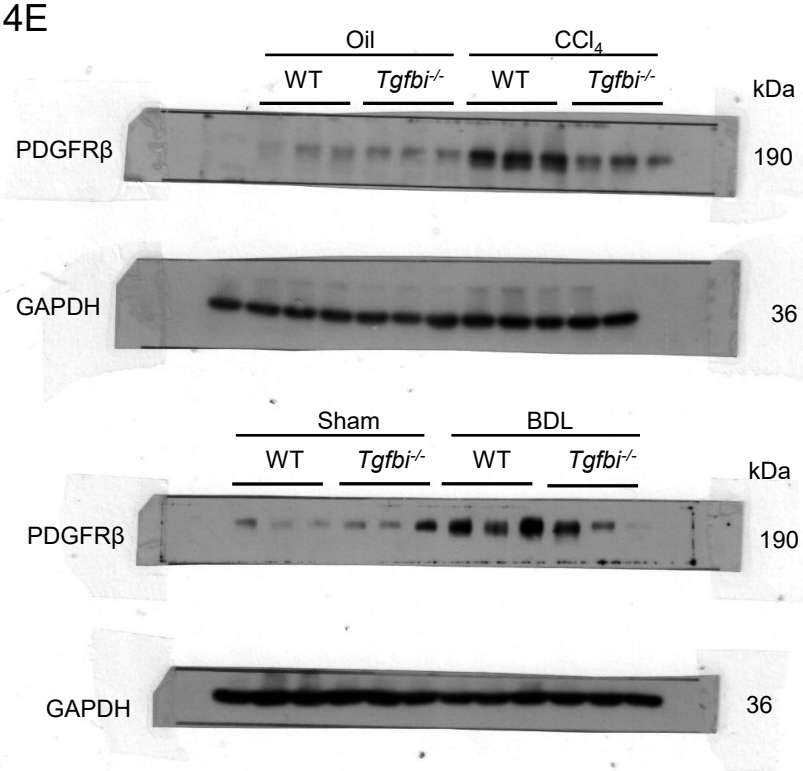


Fig 4H

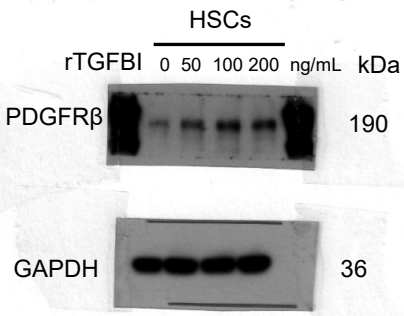


Fig 4I

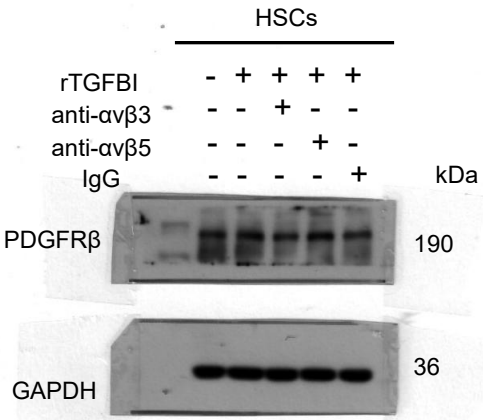


Fig 4J

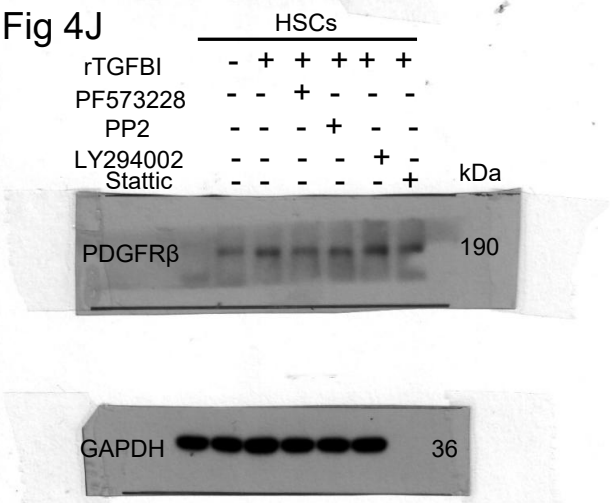


Fig 6A

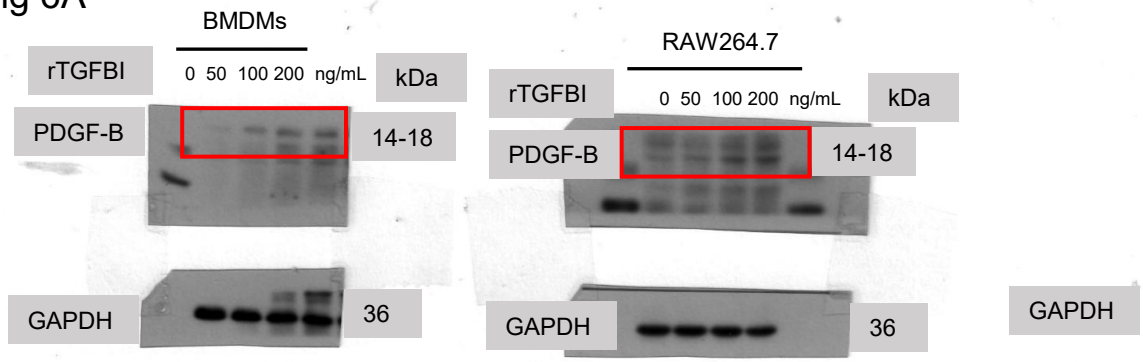
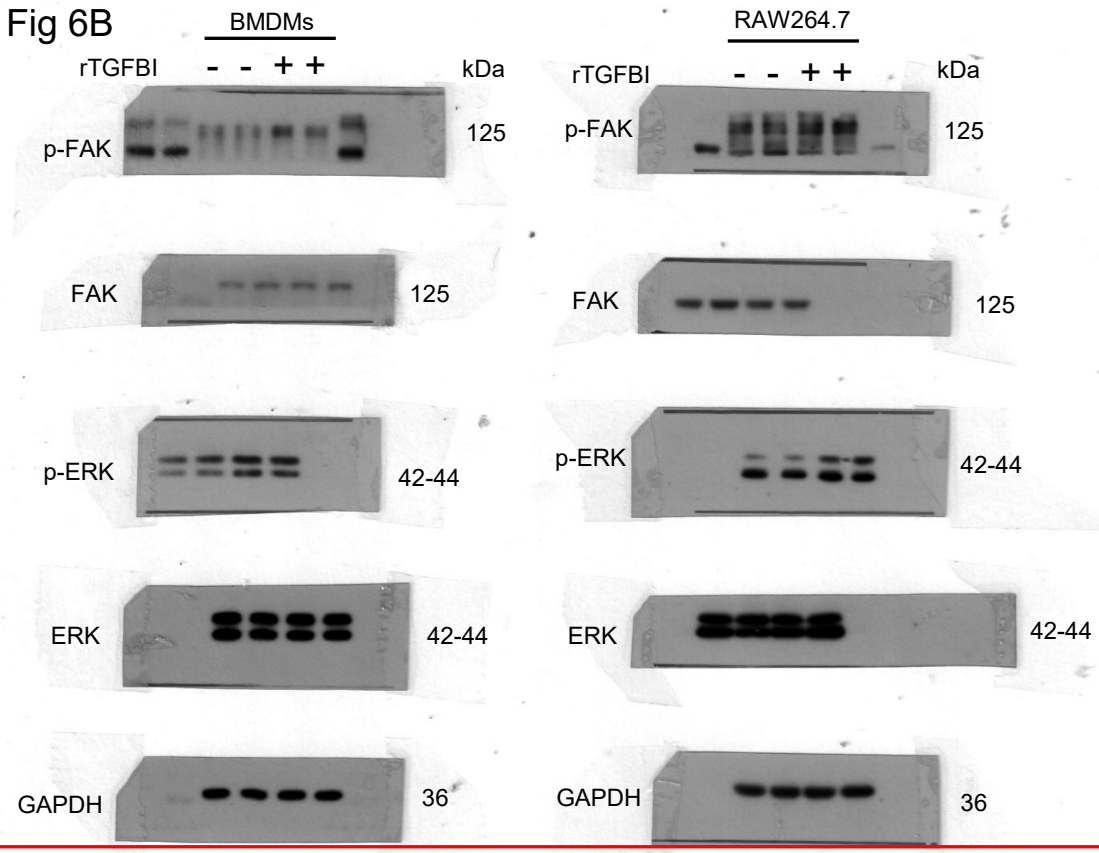


Fig 6B



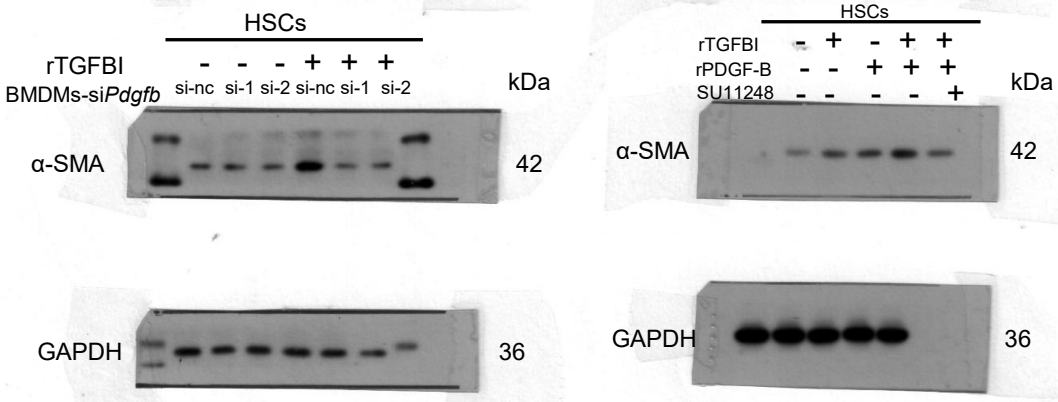


Fig 6F

Fig 6G

Fig S4B

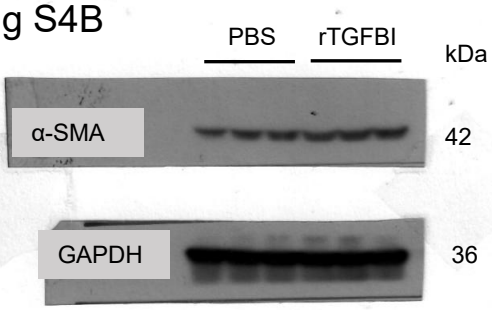


Fig S4E

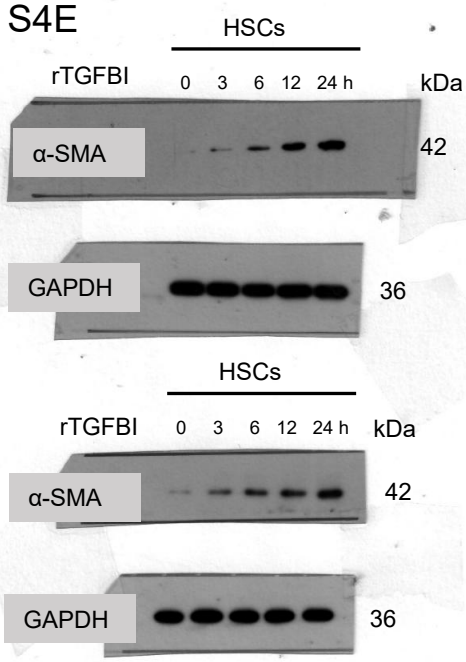


Fig S5A

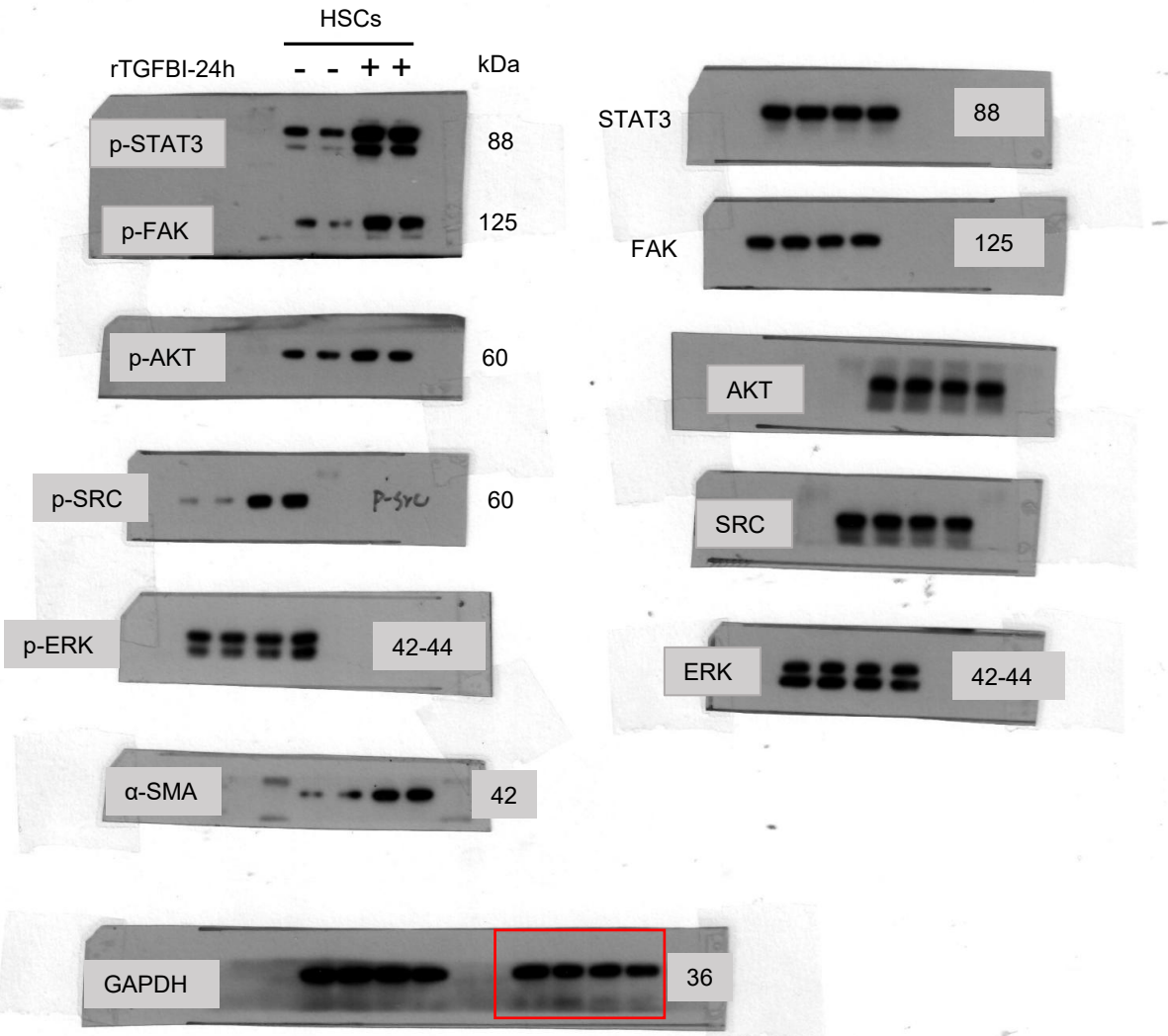

HSCs
rTGFBI-24h - - + +
kDa
p-STAT3
88
p-FAK
125
p-AKT
60
p-SRC
60
p-ERK
42-44
α-SMA
42
GAPDH
36
STAT3
88
FAK
125
AKT
SRC
ERK
42-44

Fig S5A

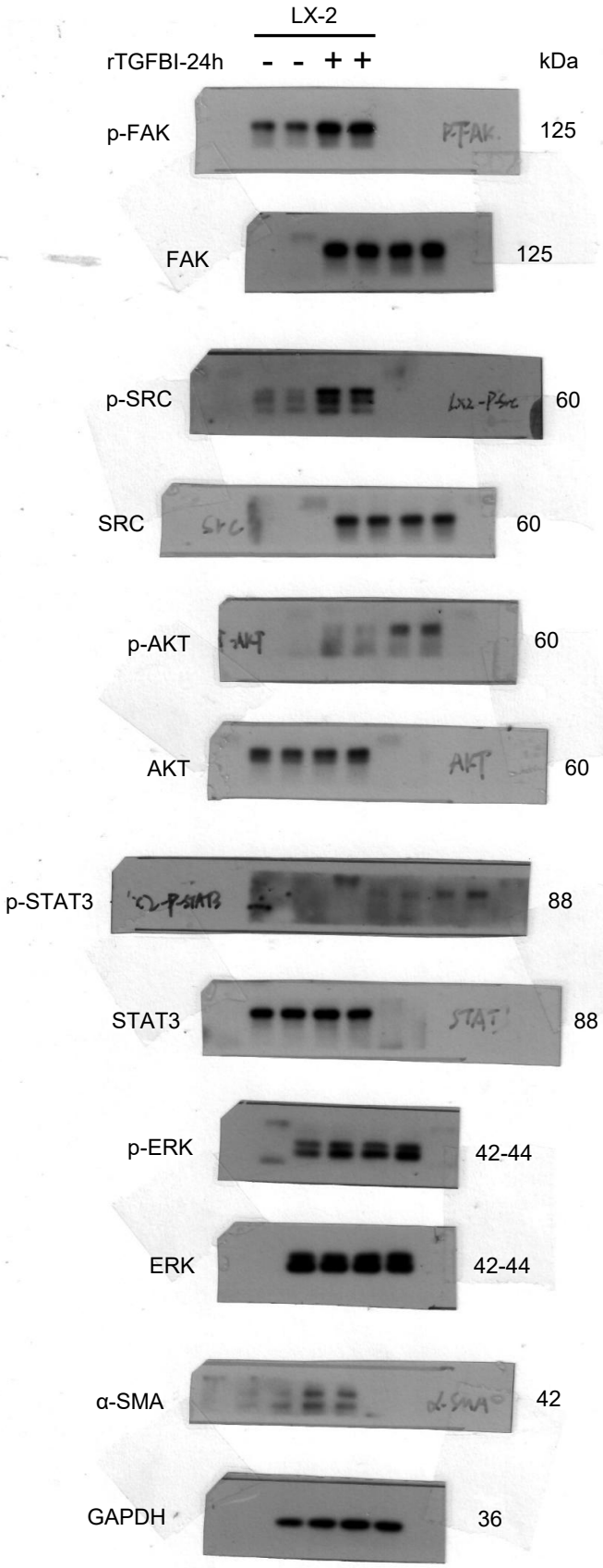

LX-2
rTGFBI-24h - - + +
kDa
p-FAK
125
FAK
125
p-SRC
60
SRC
60
p-AKT
60
AKT
60
p-STAT3
88
STAT3
88
p-ERK
42-44
ERK
42-44
α-SMA
42
GAPDH
36

Fig S5B

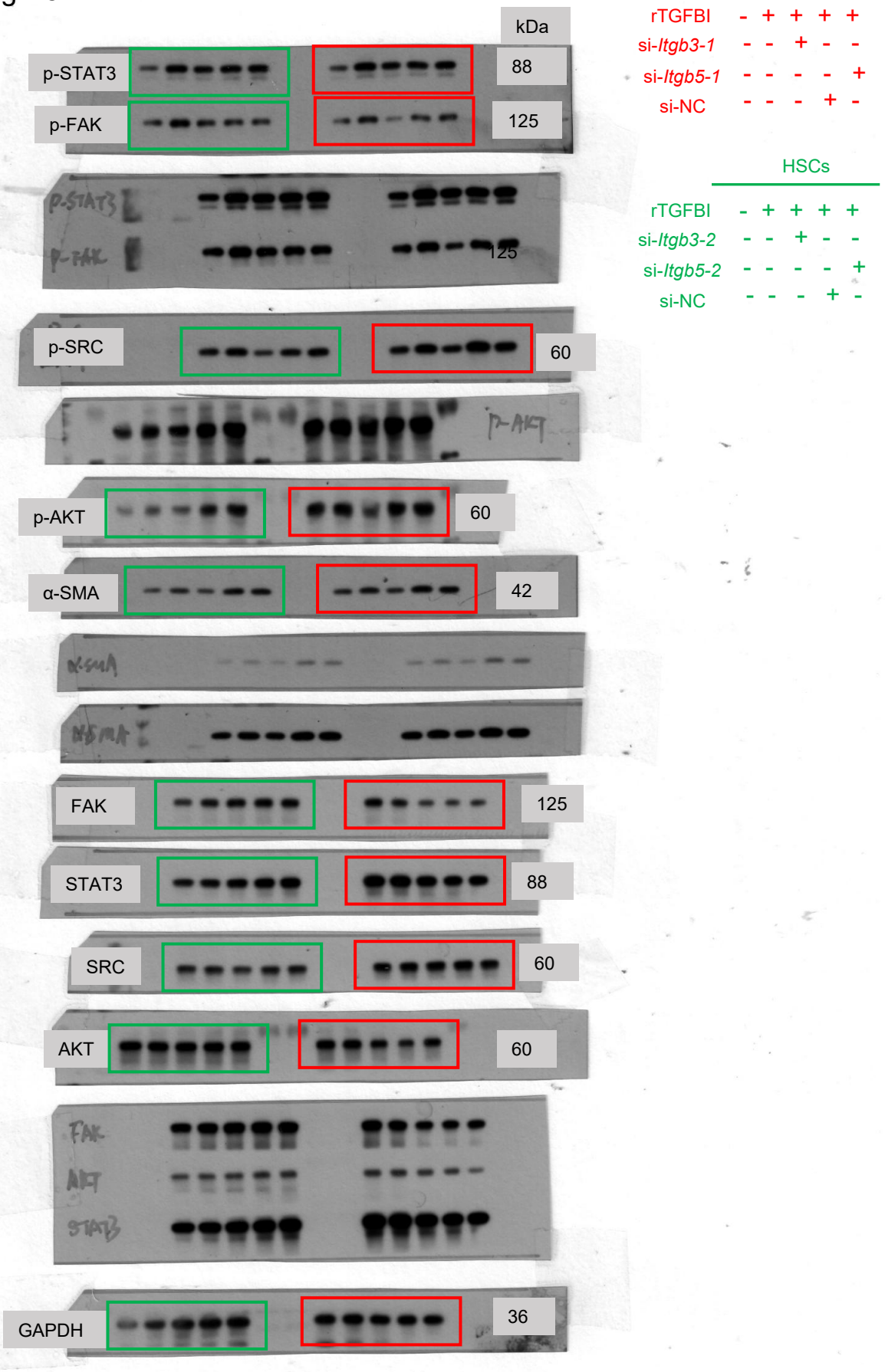

kDa
p-STAT3
88
p-FAK
125
p-SRC
60
p-AKT
60
α-SMA
42
FAK
125
STAT3
88
SRC
60
AKT
60
GAPDH
36
HSCs
rTGFBI - + + + +
si-Itgb3-1 - - + - -
si-Itgb5-1 - - - - +
si-NC - - - + -
HSCs
rTGFBI - + + + +
si-Itgb3-2 - - + - -
si-Itgb5-2 - - - - +
si-NC - - - + -

Fig S5C

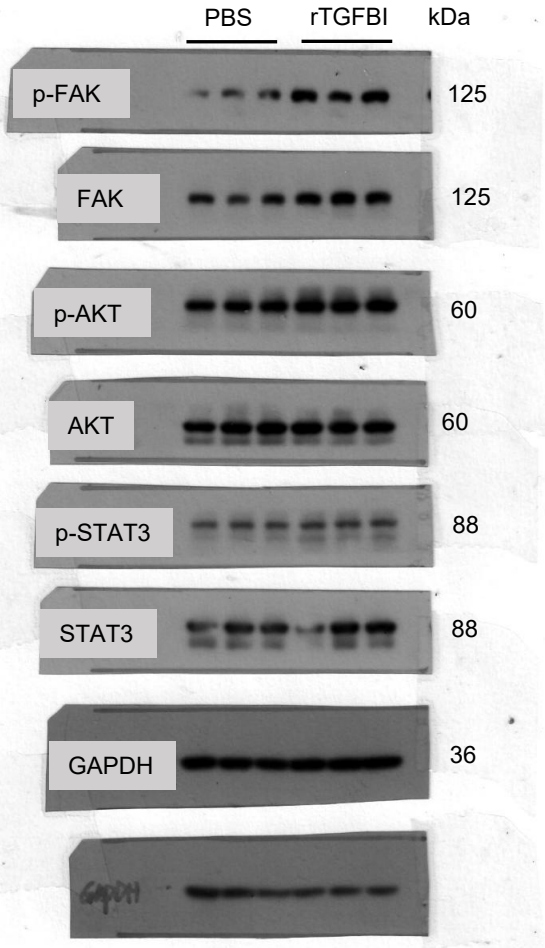

PBS
rTGFBI
kDa
p-FAK
125
FAK
125
p-AKT
60
AKT
60
p-STAT3
88
STAT3
88
GAPDH
36

Fig S6A

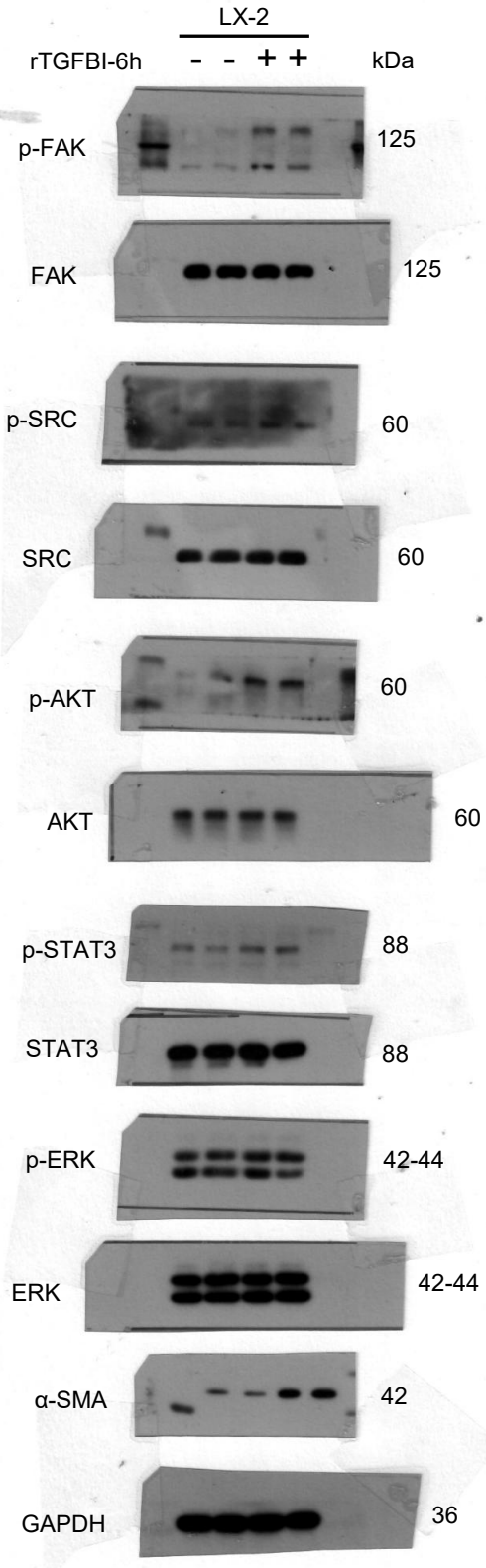

LX-2
rTGFBI-6h
- - + +
kDa
p-FAK
125
FAK
125
p-SRC
60
SRC
60
p-AKT
60
AKT
60
p-STAT3
88
STAT3
88
p-ERK
42-44
ERK
42-44
α-SMA
42
GAPDH
36

Fig S6B

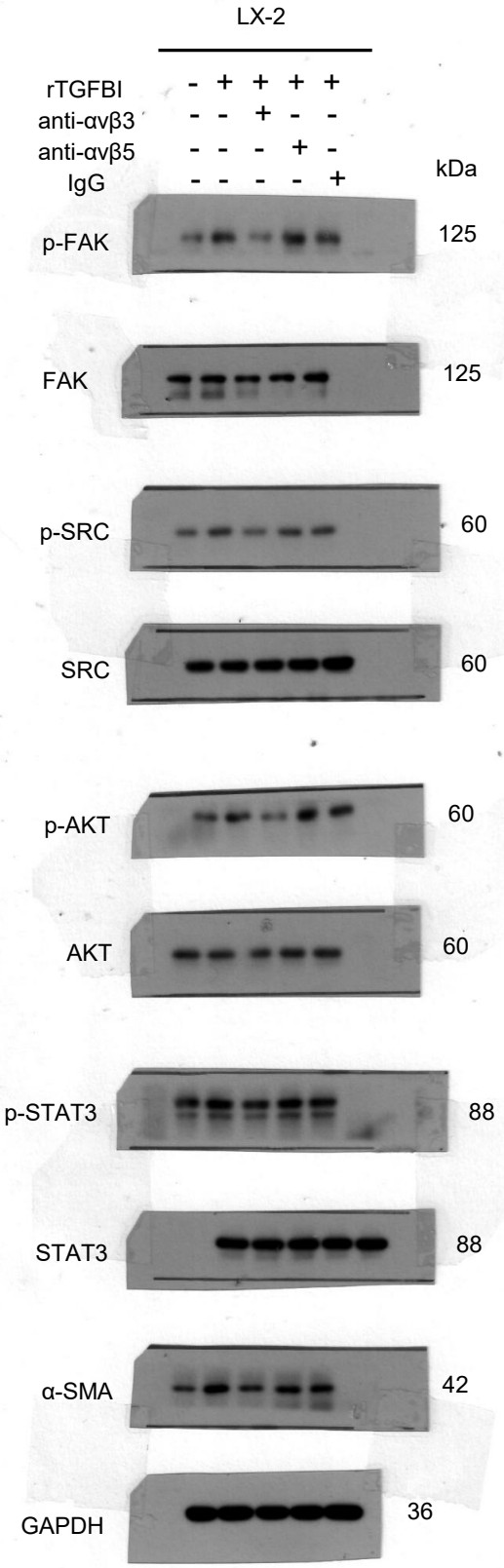

LX-2
rTGFBI - + + + +
anti-αvβ3 - - + - -
anti-αvβ5 - - - + -
IgG - - - - +
kDa
p-FAK
125
FAK
125
p-SRC
60
SRC
60
p-AKT
60
AKT
60
p-STAT3
88
STAT3
88
α-SMA
42
GAPDH
36

Fig S6C

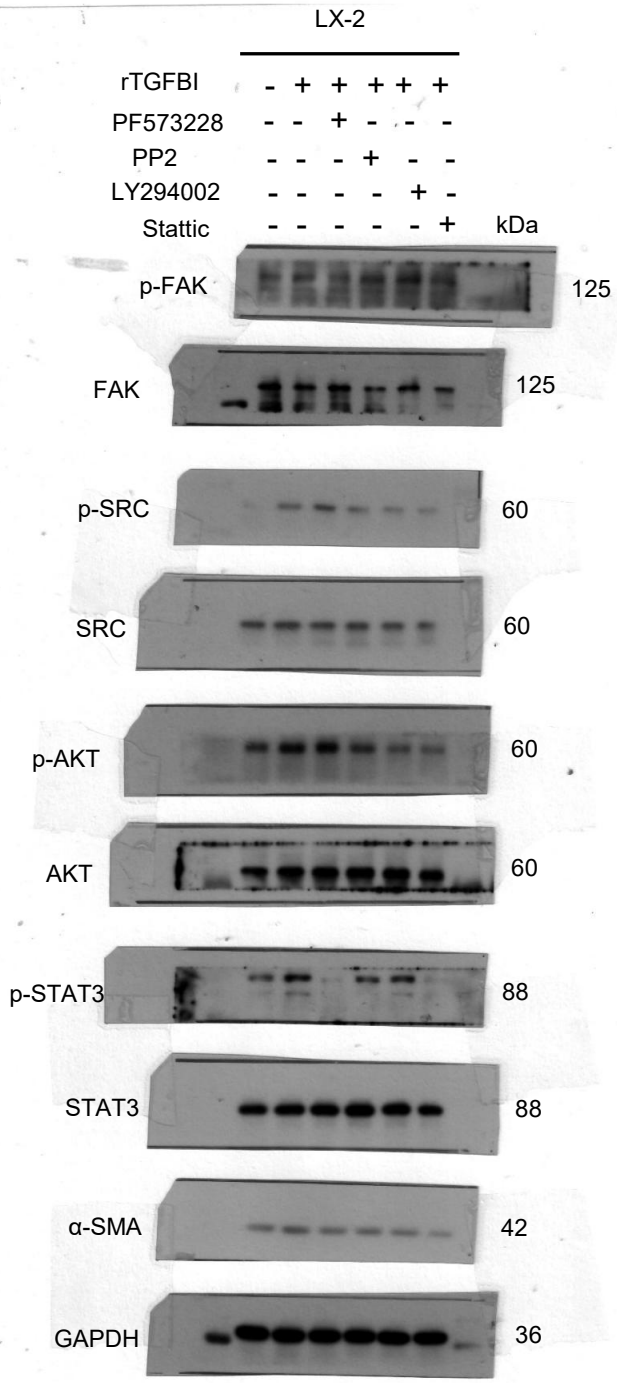

LX-2
rTGFBI - + + + + +
PF573228 - - + - - -
PP2 - - - + - -
LY294002 - - - - + -
Stattic - - - - - +
kDa
p-FAK
125
FAK
125
p-SRC
60
SRC
60
p-AKT
60
AKT
60
p-STAT3
88
STAT3
88
α-SMA
42
GAPDH
36

Fig S8F

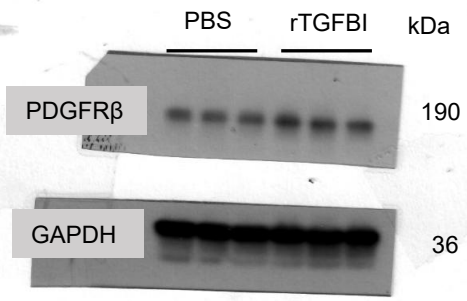


Fig S8G

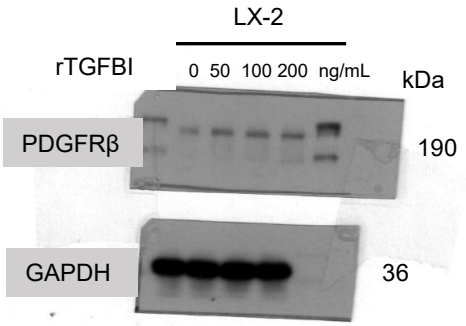


Fig S8H

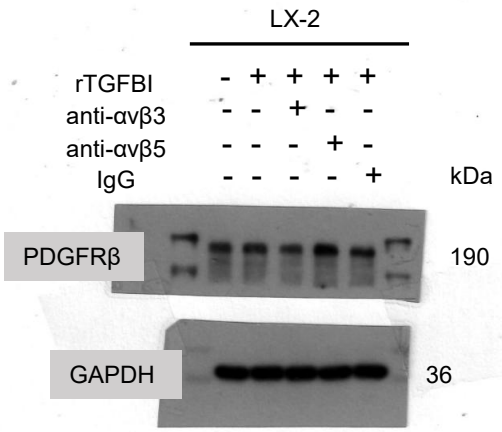


Fig S8I

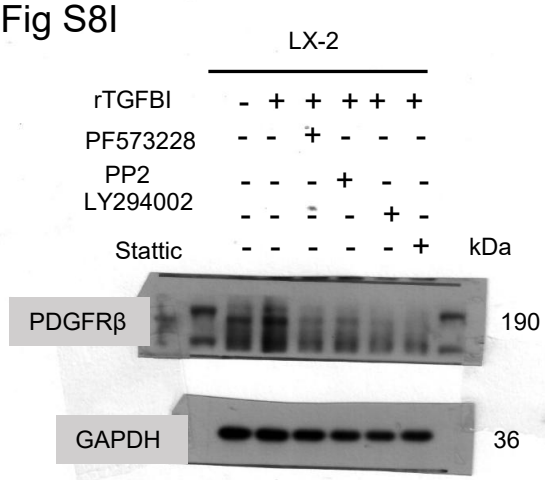


Fig S9B

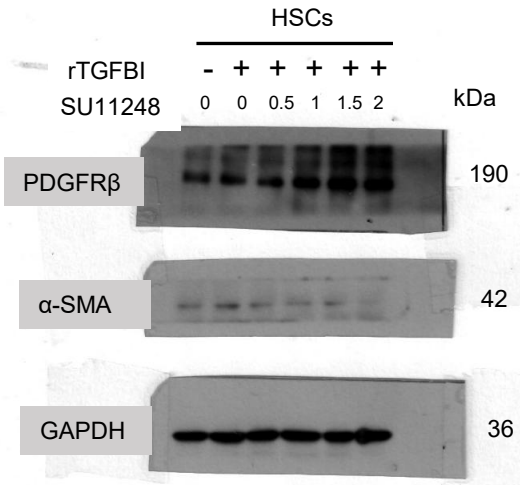


Fig S9D

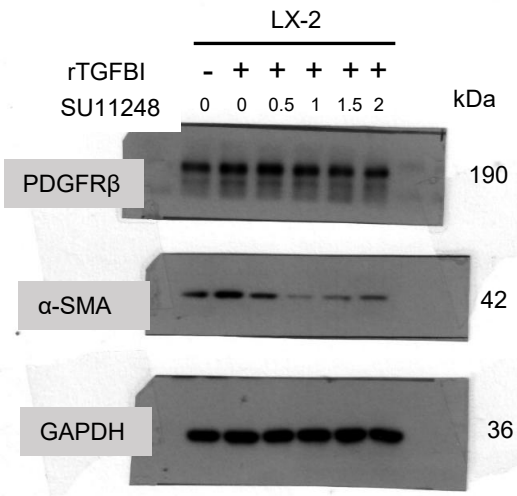


Fig S9H

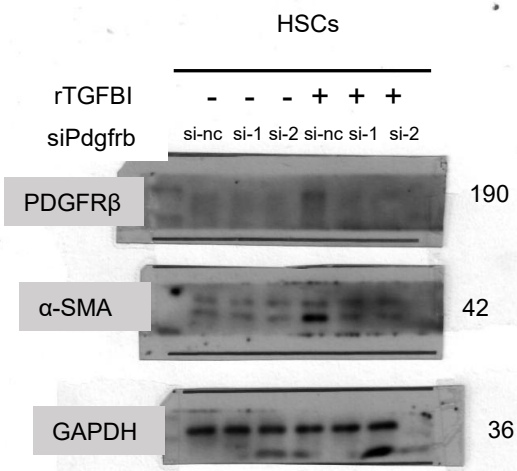


Fig S10D

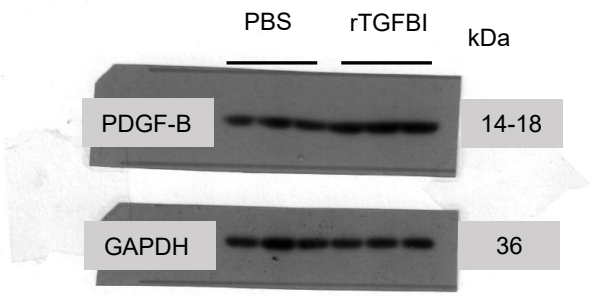


Fig S11C

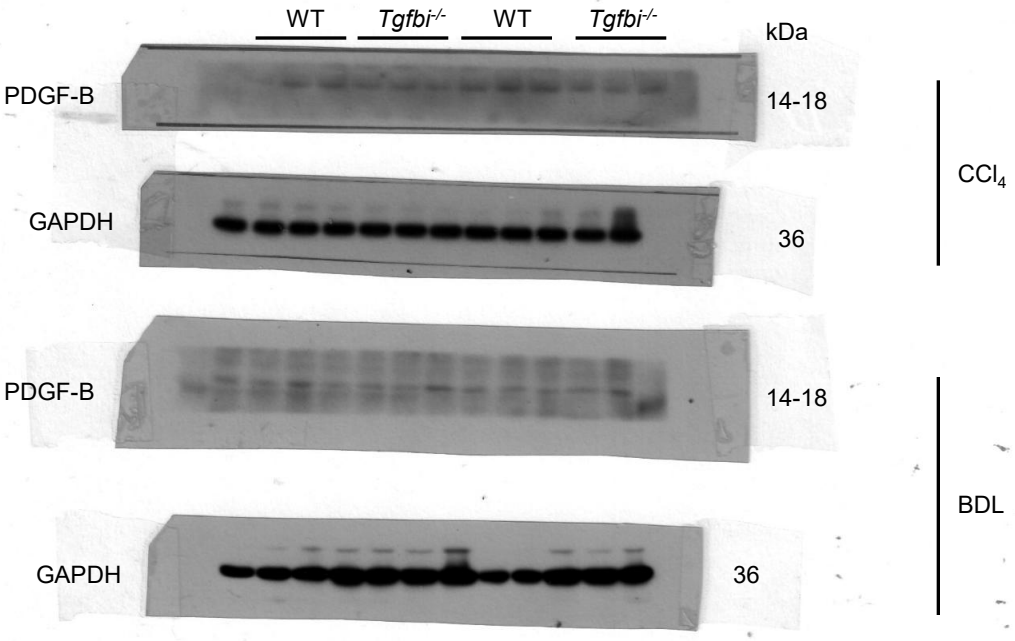

WT
Tgfbi-/-
WT
Tgfbi-/-
kDa
PDGF-B
14-18
GAPDH
36
CCl4
PDGF-B
14-18
GAPDH
36
BDL

Fig S13D

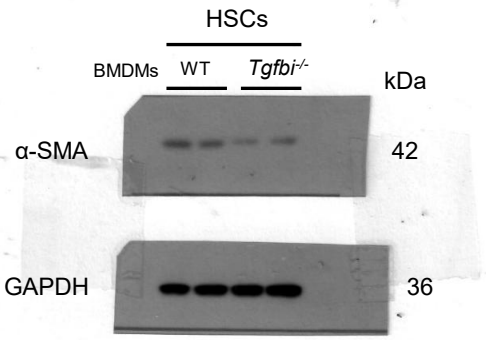


Fig S14E

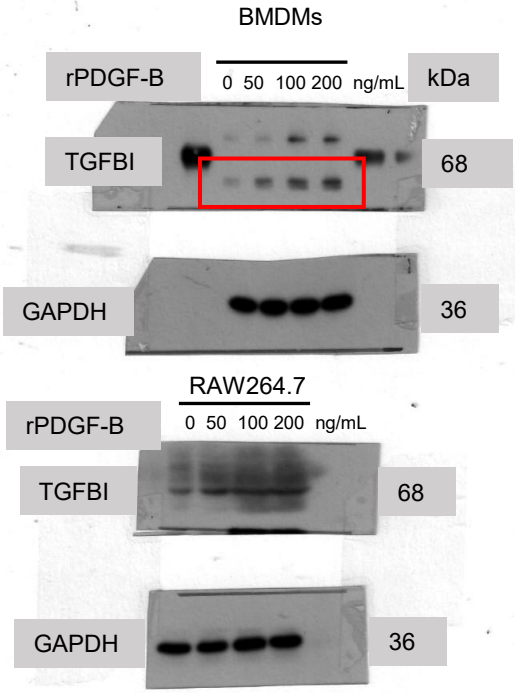


Fig S14F

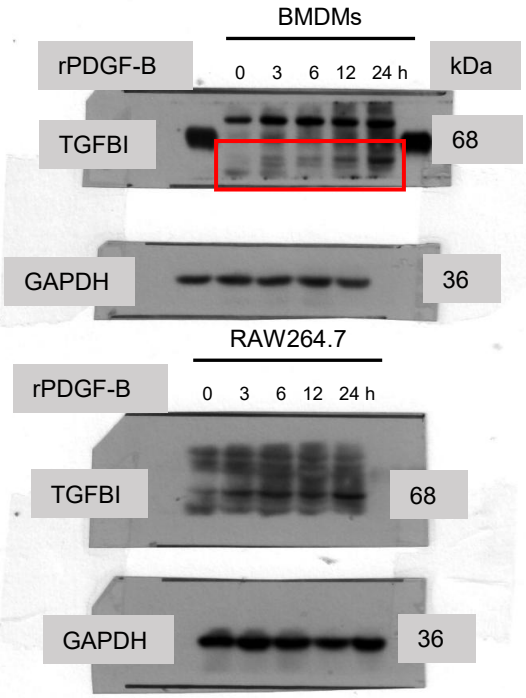
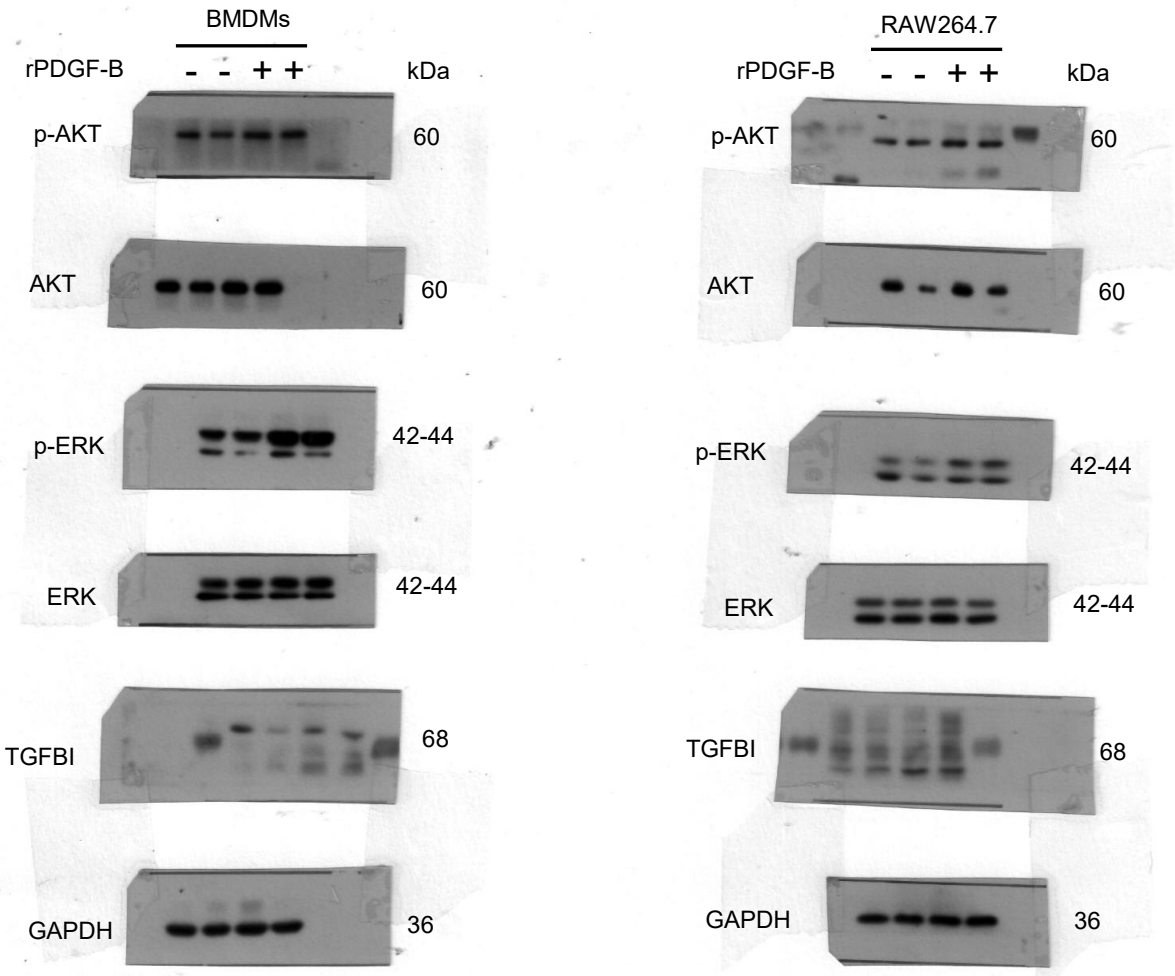


Fig S14H



Supplementary Table 1

Summary of Antibodies

Antibody Target	Company	Catalog Number	Dilution Concentration	Application
TGFBI	abcam	ab99562	1:2000 1:200	Western Blot IHC/IF
COL1A1	CST	72026T	1:2000 1:200	Western Blot IHC/IF
α-SMA	CST	19245S	1:2000 1:200	Western Blot IHC/IF
PDGFRβ	CST	3169T	1:2000 1:200	Western Blot IHC/IF
PDGF-B	Biodragon	BD-PT3631	1:1000 1:100	Western Blot IHC/IF
TREM2	CST	91068T	1:100	IF
CD9	abmart	T55337	1:100 1:100	IF FACS
F4/80	Abcam	ab300421	1:100	IHC/IF
Ki67	Abcam	ab15580	1:200	IHC/IF
GAPDH	CST	2118S	1:3000	Western Blot
p-FAK	CST	3283s	1:2000	Western Blot
FAK	CST	3285s	1:2000	Western Blot
p-AKT	CST	4060S	1:2000	Western Blot
AKT	CST	4691S	1:2000	Western Blot
p-SRC	CST	2105T	1:2000	Western Blot
SRC	CST	2123T	1:2000	Western Blot

p-ERK1/2	CST	4695S	1:2000	Western Blot
ERK1/2	CST	4695S	1:2000	Western Blot
p-STAT3	CST	9145S	1:2000	Western Blot
STAT3	CST	30835S	1:2000	Western Blot
PE CD11b	Biolegend	101207	1:100	FACS
PE/Cyanine7 CD45	Biolegend	103113	1:100	FACS
APC/Cyanine7 F4/80	Biolegend	123117	1:100	FACS
Ly-6G/Ly-6C PerCP-Cyanine5.5	Thermo Fisher	45-5931-80	1:100	FACS
TREM2	Abcam	ab252876	1:10000	FACS
Goat anti-rabbit IgG，HRP	Thermo Fisher	31460	1:10000	Western Blot
Goat anti-mouse IgG，HRP	Thermo Fisher	31430	1:10000	Western Blot
Goat anti-mouse lgG (Alexa Fluor R 488)	Abcam	ab150117	1:400	IF
Donkey anti-rabbit lgG (Alexa Fluor R 647)	Abcam	ab150075	1:400	IF
Donkey anti-Rat lgG (Alexa Fluor R 568)	Abcam	ab175475	1:400	IF

Supplementary Table 2

Primers sequence

Gene Name	Forward	Reverse
Mouse		
Gapdh	TGTGTCCGTCGTGGATCTGA	TTGCTGTTGAAGTCGCAGGAG
Tgfbi	GGGACCTTTTCATATCCAGGACA	CAGCACGGCCCCAATGTAT
Col1a1	GAGGGCCAAGACGAAGACATC	CAGATCACGTCATCGCACAAC
Col3a1	CCTGGCTCAAATGGCTCAC	CAGGACTGCCGTTATTCCCG
Timp1	TCTTGGTTCCCTGGCGTACTCT	GTGAGTGTCACTCTCCAGTTTGC
Ccl2	TTAAAAACCTGGATCGGAACCAA	GCATTAGCTTCAGATTTACGGGT
Il6	GCTAAGGACCAAGACCATCCAAT	GGCATAACGCACTAGGTTTGC
Tnf-a	GCCAACGGCATGGATCTC	GCAGCCTTGTCCCTTGAAGAG
Acta2	GTCCCAGACATCAGGGAGTAA	TCGGATACTTCAGCGTCAGGA
Pdgfrb	CAGAAGTAGCGAGAAGCAA	ATCACCGTATCGGCAGTA
Pdgfb	CACCAACGCCAACTTCCT	TTCGCACAATCTCAATCTTTCT
Trem2	CTGGAACCGTCACCATCACTC	CGAAACTCGATGACTCCTCGG
Cd9	ATGCCGGTCAAAGGAGGTAG	GCCATAGTCCAATAGCAAGCA
Human		
Gapdh	GAAAGCCTGCCGGTGACTAA	GCCCAATACGACCAAATCAGAG A
Acta2	CTATGAGGGCTATGCCTTGCC	GCTCAGCAGTAGTAACGAAGGA

Col1a1	TCCAAACCACTGAAACCTCTG	CCCCTGGAAAGAATGGAGATG
Pdgfrb	AGCACCTTCGTTCTGACCTG	TATTCTCCCGTGTCTAGCCCA
siRNA	Sense	Anti-sense
si*Pdgfrb-1*	/rC//rC//rU//rU//rC//rA//rA//rG//rC//rU//rG//rC//rA//rG//rG//rU//rC//rA//rA/TT	/rU//rU//rG//rA//rC//rC//rU//rG//rC//rA//rG//rC//rU//rU//rG//rA//rA//rG//rG/TT
si*Pdgfrb-2*	/rG//rG//rU//rG//rC//rA//rU//rU//rG//rU//rG//rA//rU//rG//rG//rG//rC//rA//rA/TT	/rU//rU//rG//rC//rC//rC//rA//rU//rC//rA//rC//rA//rA//rU//rG//rC//rA//rC//rC/TT
si*Pdgfrb-3*	/rG//rG//rA//rU//rG//rU//rC//rA//rC//rU//rG//rA//rG//rA//rC//rG//rA//rC//rA/TT	/rU//rG//rU//rC//rG//rU//rC//rU//rC//rA//rG//rU//rG//rA//rC//rA//rU//rC//rC/TT
si*Pdgfb-1*	/rG//rG//rC//rA//rA//rG//rC//rA//rC//rC//rG//rA//rA//rA//rG//rU//rU//rU//rA/TT	/rU//rA//rA//rA//rC//rU//rU//rU//rC//rG//rG//rU//rG//rC//rU//rU//rG//rC//rC/TT
si*Pdgfb-2*	/rA//rG//rA//rU//rU//rG//rA//rG//rA//rU//rU//rG//rU//rG//rC//rG//rA//rA//rA/TT	/rU//rU//rU//rC//rG//rC//rA//rC//rA//rA//rU//rC//rU//rC//rA//rA//rU//rC//rU/TT
si*Pdgfb-3*	/rC//rA//rG//rA//rG//rA//rC//rU//rC//rC//rG//rU//rA//rG//rA//rU//rG//rA//rA/TT	/rU//rU//rC//rA//rU//rC//rU//rA//rC//rG//rG//rA//rG//rU//rC//rU//rC//rU//rG/TT
si*Itgb3-1*	GGCGGGCGUUGUUGUUGGA/dT//dT/	UCCAACAACAACGCCCGCC/dT//dT/
si*Itgb3-2*	GGAGAGUCCAACAUCUGUA/dT//dT/	UACAGAUGUUGGACUCUCC/dT//dT/
si*Itgb3-3*	GAAGGACAAUUGUGCUCCA/dT//dT/	UGGAGCACAAUUGUCCUUC/dT//dT/
si*Itgb5-1*	GGUGUGACCUGAAGGCAAA/dT//dT/	UUUGCCUUCAGGUCACACC/dT//dT/
si*Itgb5-2*	GUGUAUUGGUUACAAGUUA/dT//dT/	UAACUUGUAACCAAUACAC/dT//dT/
si*Itgb5-3*	GGUGGAGGACUACCCUGUA/dT//dT/	UACAGGGUAGUCCUCCACC/dT//dT/