Precision RNAi for Fibrodysplasia Ossificans Progressiva in Mice using a combinatorial unimolecular allele selective approach

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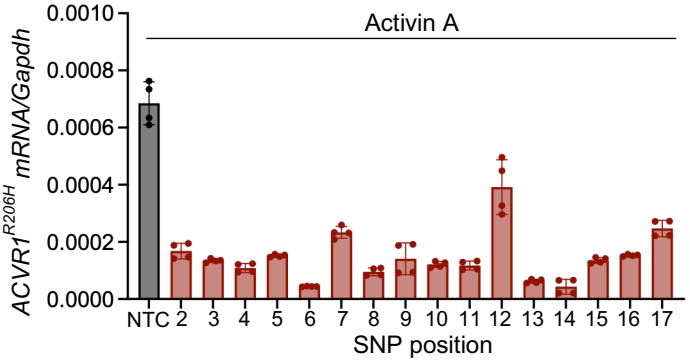
[+]These authors contributed equally.

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Jae-Hyuck Shim and Julia Alterman

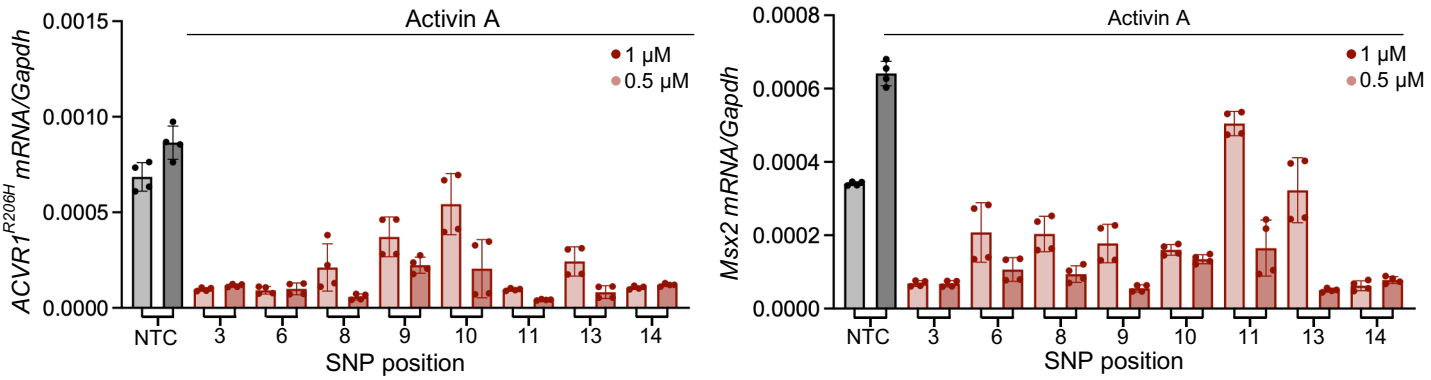
Supplemental information:

- 22 Supplementary Figures
- Uncropped western blot images
- 6 Supplementary Tables

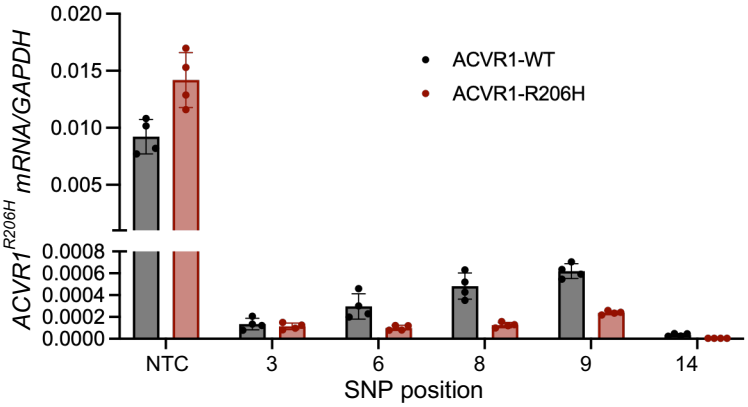
a Silencing Efficacy of *ACVR1*^{R206H} After Activin A Stimulation



b Silencing Efficacy of *ACVR1*^{R206H} and *Msx2* After Activin A Stimulation at Two Different Doses



c Primary Mismatch Screening in Human FOP iPSCs

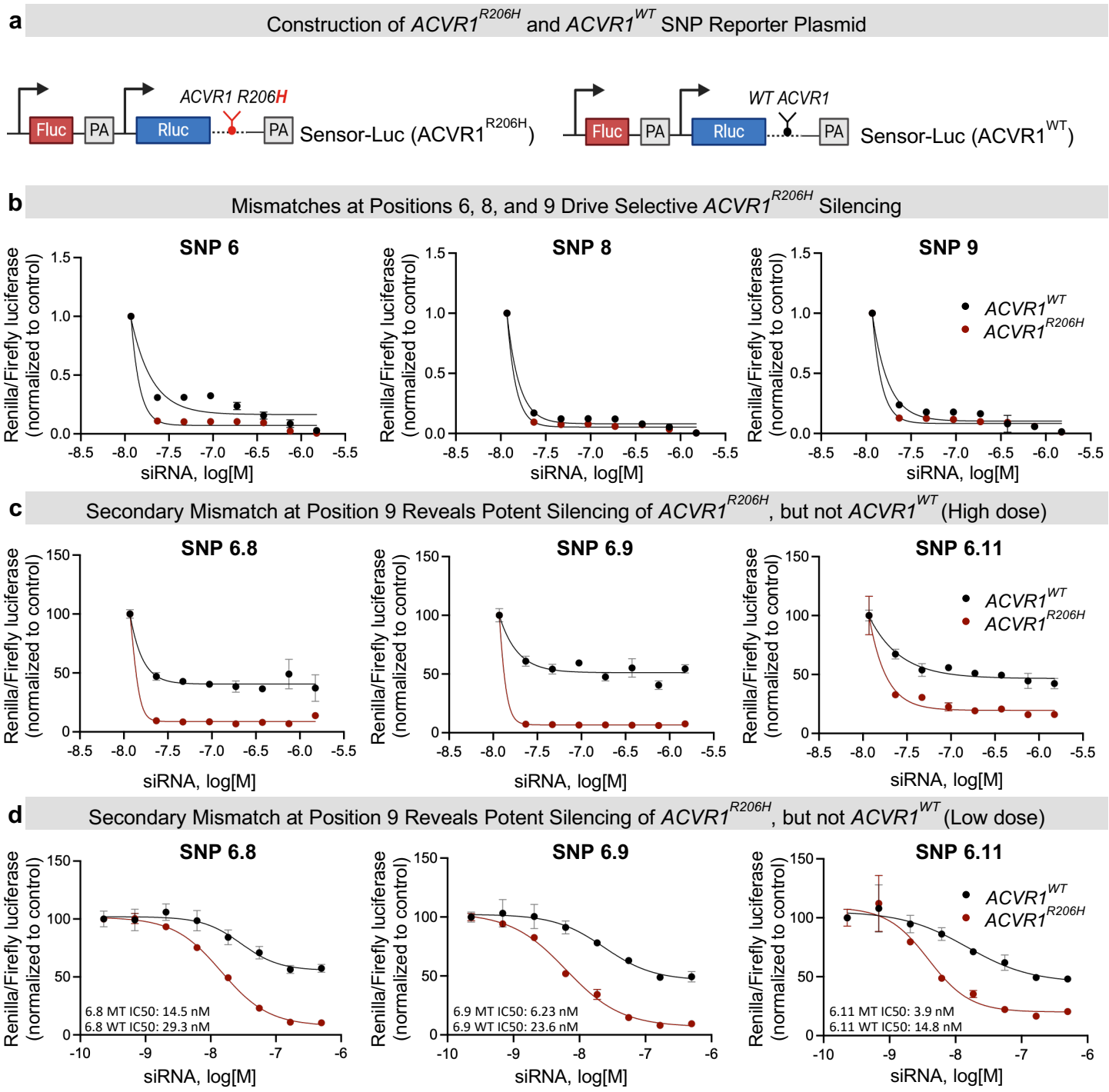


Supplementary Figure 1. Screening of siRNA candidates targeting human *ACVR1^{R206H}* mRNA (Primary mismatch).

a. Mouse bone marrow-derived stromal cells expressing human *ACVR1^{R206H}* (*ACVR1$^{(R206H)Fl}$;Prrx1-cre* BMSCs) were treated with a panel of 16 siRNAs (1 μM) and three days later, cells were stimulated with Activin A (50 ng/ml) for twelve hours. mRNA levels of *ACVR1^{R206H}* were measured by RT-PCR and normalized to *Gapdh* (n = 4 wells). NTC: non-targeting control.

b. *ACVR1$^{(R206H)Fl}$;Prrx1-cre* BMSCs were treated with each siRNA at 1.0 and 0.5 μM and three days later, cells were stimulated with Activin A (50 ng/ml) for twelve hours. mRNA levels of *ACVR1^{R206H}* and *Msx2* were measured by RT-PCR and normalized to *Gapdh* (n = 4 wells).

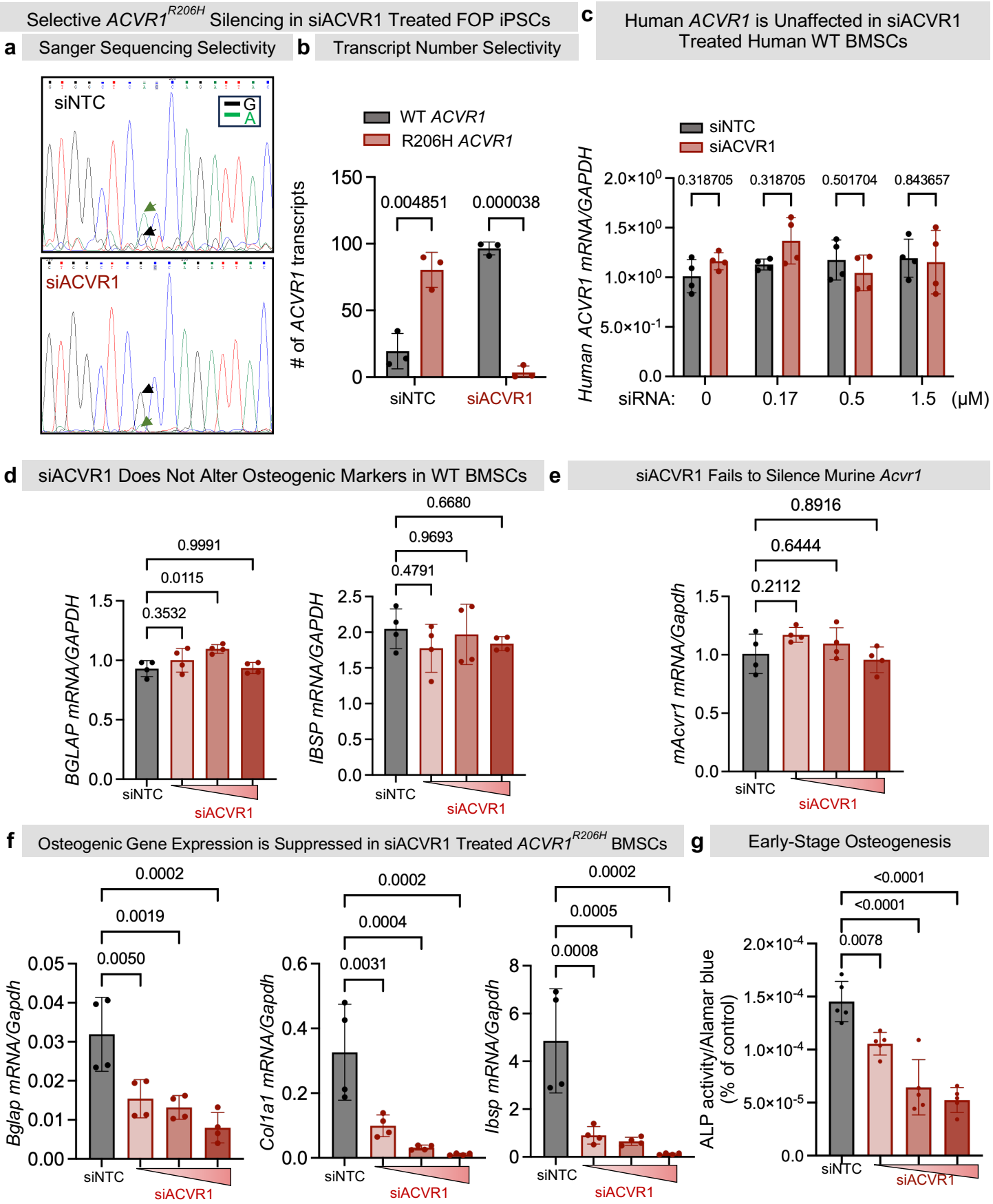
c. Human FOP iPSCs were treated with 1 μM siNTC or siACVR1 and cultured under osteogenic conditions for four days. mRNA levels of *ACVR1$^{+/+}$* and *ACVR1^{R206H}* were measured by RT-PCR and normalized to *GAPDH* (n = 4 wells). Data are representative of three independent experiments. Values represent mean ± SD.


a
Construction of ACVR1R206H and ACVR1WT SNP Reporter Plasmid
ACVR1 R206H
Fluc
PA
Rluc
PA
Sensor-Luc (ACVR1R206H)
WT ACVR1
Fluc
PA
Rluc
PA
Sensor-Luc (ACVR1WT)
b
Mismatches at Positions 6, 8, and 9 Drive Selective ACVR1R206H Silencing
SNP 6
SNP 8
SNP 9
Renilla/Firefly luciferase (normalized to control)
siRNA, log[M]
ACVR1WT
ACVR1R206H
c
Secondary Mismatch at Position 9 Reveals Potent Silencing of ACVR1R206H, but not ACVR1WT (High dose)
SNP 6.8
SNP 6.9
SNP 6.11
Renilla/Firefly luciferase (normalized to control)
siRNA, log[M]
ACVR1WT
ACVR1R206H
d
Secondary Mismatch at Position 9 Reveals Potent Silencing of ACVR1R206H, but not ACVR1WT (Low dose)
SNP 6.8
6.8 MT IC50: 14.5 nM
6.8 WT IC50: 29.3 nM
SNP 6.9
6.9 MT IC50: 6.23 nM
6.9 WT IC50: 23.6 nM
SNP 6.11
6.11 MT IC50: 3.9 nM
6.11 WT IC50: 14.8 nM
Renilla/Firefly luciferase (normalized to control)
siRNA, log[M]
ACVR1WT
ACVR1R206H

Supplementary Figure 2. Screening of siRNA candidates targeting human *ACVR1*^{R206H} mRNA in 7-point dose response (Primary and secondary mismatch).

a. Schematic diagram showing the reporter plasmids that contain firefly luciferase (Fluc), *Renilla* luciferase (RLuc), with complementary sequences of human *ACVR1*^{R206H} or *ACVR1*^{WT} incorporated into the 3' UTR of RLuc.

b-d. 1 day after siRNA treatment, HEK293 cells were transiently transfected with the reporter plasmids in 7-point dose response. Two days later, a luciferase assay was performed to measure RLuc and normalized to Fluc. Lower activities indicate higher silencing efficacy of siRNAs (n = 3 wells). Data are representative of three independent experiments. Values represent mean ± SD.


Selective ACVR1R206H Silencing in siACVR1 Treated FOP iPSCs
a
Sanger Sequencing Selectivity
siNTC
G
A
siACVR1
b
Transcript Number Selectivity
WT ACVR1
R206H ACVR1
of ACVR1 transcripts
150
100
50
0
0.004851
0.000038
siNTC
siACVR1
c
Human ACVR1 is Unaffected in siACVR1 Treated Human WT BMSCs
siNTC
siACVR1
Human ACVR1 mRNA/GAPDH
2.0×10^0
1.5×10^0
1.0×10^0
5.0×10^-1
0.0
0.318705
0.318705
0.501704
0.843657
siRNA:
0
0.17
0.5
1.5
(μM)
d
siACVR1 Does Not Alter Osteogenic Markers in WT BMSCs
BGLAP mRNA/GAPDH
0.9991
0.0115
0.3532
IBSP mRNA/GAPDH
0.6680
0.9693
0.4791
siNTC
siACVR1
e
siACVR1 Fails to Silence Murine Acvr1
mAcvr1 mRNA/Gapdh
0.8916
0.6444
0.2112
siNTC
siACVR1
f
Osteogenic Gene Expression is Suppressed in siACVR1 Treated ACVR1R206H BMSCs
Bglap mRNA/Gapdh
0.0002
0.0019
0.0050
Col1a1 mRNA/Gapdh
0.0002
0.0004
0.0031
Ibsp mRNA/Gapdh
0.0002
0.0005
0.0008
siNTC
siACVR1
g
Early-Stage Osteogenesis
ALP activity/Alamar blue (% of control)
<0.0001
<0.0001
0.0078
siNTC
siACVR1

Supplementary Figure 3. siACVR1 treatment inhibits osteogenic development in FOP cells, but not in WT cells.

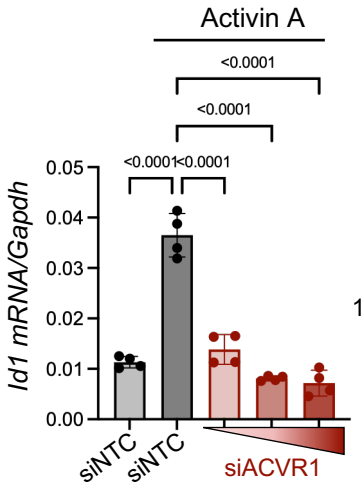
a, b. Human FOP iPSCs were treated with 1 μM siNTC or siACVR1, cultured under osteogenic conditions for four days, and subjected to Sanger sequencing (n = 4 wells). Black (Guanine, G) and green (Adenine, A) indicate wild type and R206H mutation in *ACVR1* gene, respectively **(a)**. Alternatively, extracted RNA was subjected to next-generation sequencing (NGS) to quantify human $ACVR1^{R206H}$ and $ACVR1^{WT}$ transcripts **(b)**.

c, d. Human bone marrow-derived stromal cells (BMSCs) were treated with siNTC or siACVR1 in a 3-point dose response and cultured under osteogenic conditions for four days. mRNA levels of human *ACVR1* **(c)** and osteogenic marker genes **(d)** were measured by RT-PCR and normalized to *GAPDH* (n = 4 wells).

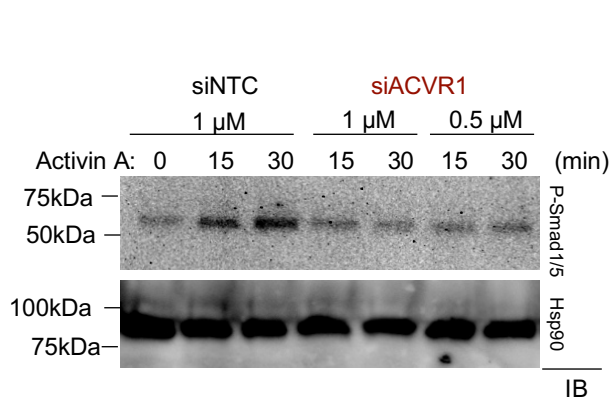
e-g. $ACVR1^{(R206H)Fl}$*;Prrx1-cre* BMSCs were treated with siNTC or siACVR1 in a 3-point dose response and cultured under osteogenic conditions for four days. mRNA levels of mouse *Acvr1* **(e)** and osteogenic marker genes **(f)** were measured by RT-PCR and normalized to *Gapdh* (n = 4 wells). Alternatively, osteogenic differentiation and cell proliferation were assessed by alkaline phosphatase activity (ALP) and alamar blue staining, respectively (n = 5 wells, **g**). Data are representative of two to three independent experiments. Values represent mean ± SD by two-sided multiple unpaired t-tests **(b, c)** and one-way ANOVA with Dunnett's multiple comparisons test **(d, e, f, g)**.

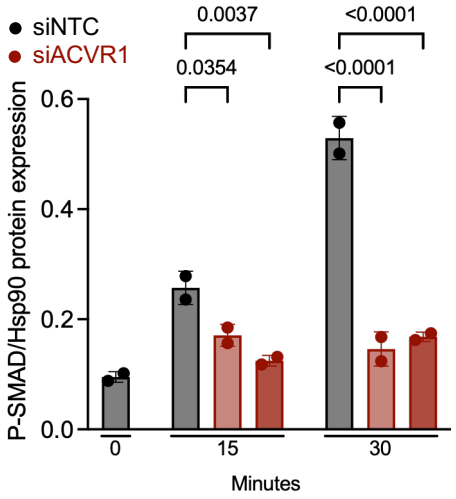
siACVR1 Inhibits Activin A Signaling in Murine ACVR1^{R206H} BMSCs

a Activin A-Induced *Id1*



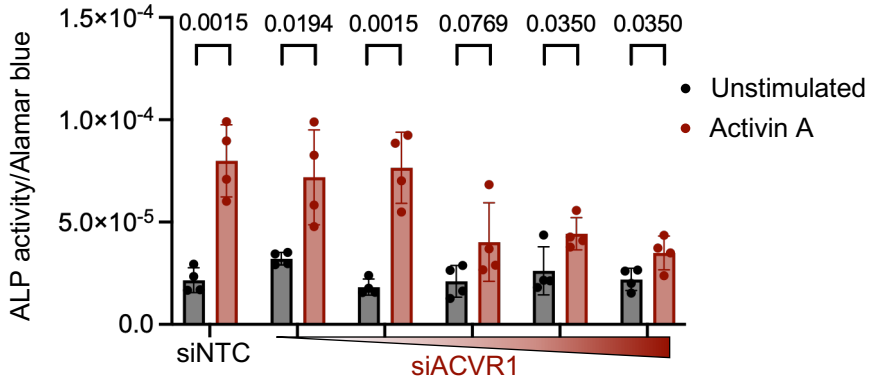
b Activin A-Induced SMAD1/5 Phosphorylation



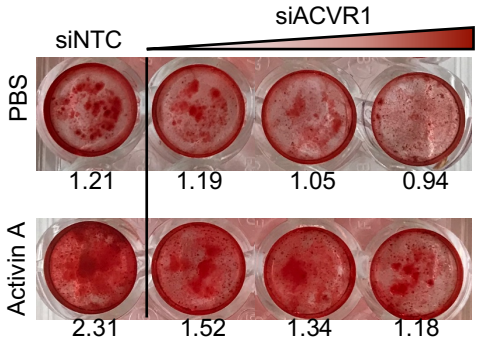


siACVR1 Attenuates Activin A-induced Osteogenesis in ACVR1^{R206H} BMSCs

c Activin A Induced Osteogenesis

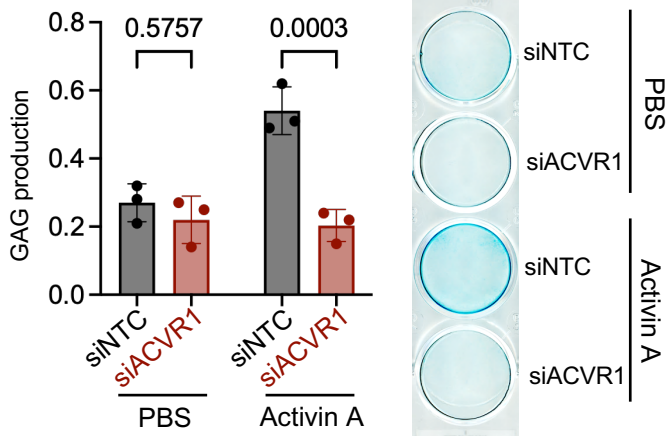


d Mineralization Activity

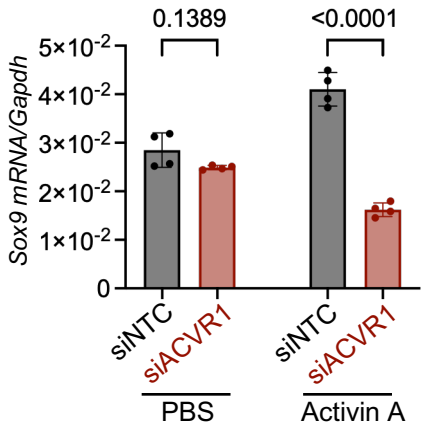


siACVR1 Mitigates Activin A-Induced Chondrogenesis in ACVR1^{R206H} Chondroprogenitors

e Glycosaminoglycan (GAG) Extracellular Production



f Chondrocyte Differentiation Via *Sox9* mRNA

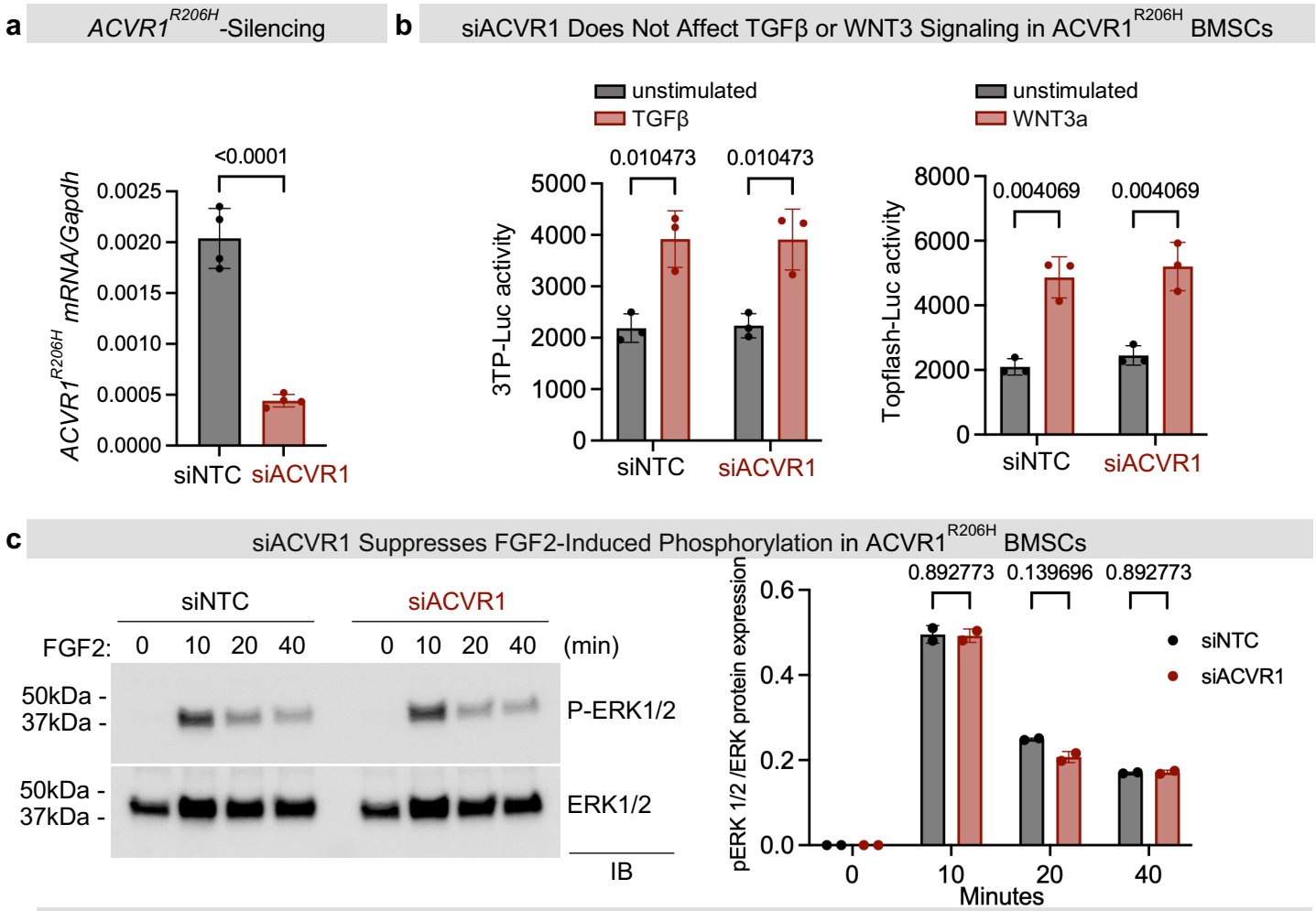


Supplementary Figure 4. siACVR1 treatment inhibits Activin A-induced signaling, osteogenesis, and chondrogenesis in FOP cells.

a, b. *ACVR1*$^{(R206H)Fl}$*;Prrx1-cre* BMSCs were treated with siNTC or siACVR1 in a 3-point dose response and three days later, stimulated with Activin A (50 ng/ml). Twelve hours later, *Id1* mRNA expression were evaluated by RT-PCR (n = 4 wells, **a**). Alternatively, siRNA-treated cells were stimulated with Activin A (100 ng/ml) for 15 or 30 min and immunoblotted for phospho-Smad1/5. Hsp90 was used as a loading control. Representative immunoblot images and relative quantification are displayed **(**n = 2 wells, **b)**.

c, d. *ACVR1*$^{(R206H)Fl}$*;Prrx1-cre* BMSCs were treated with siNTC or siACVR1 in a 3- or 5-point dose response and cultured under osteogenic conditions in the presence or absence of Activin A (50 ng/ml). Early and late osteogenic differentiation was assessed by measuring ALP activity at day 4 **(c)** and extracellular matrix mineralization at day 14 **(d)**.

e, f. *ACVR1*$^{(R206H)Fl}$*;Prrx1-cre* chondroprogenitors were treated with siNTC or siACVR1 and cultured under chondrogenic conditions in the presence or absence of Activin A (50 ng/ml). Chondrocyte differentiation was assessed by alcian blue staining **(e)** and expression of chondrogenic gene *Sox9* **(f)**. Representative images of Alcian Blue staining and relative quantification are displayed (**e,** n = 3 wells). Data are representative of two to three independent experiments. Values represent mean ± SD by two-sided multiple unpaired t-tests **(b)**, one-way ANOVA with Dunnett's multiple comparisons test **(a, c)**, and one-way ANOVA with Sidak's multiple comparisons test **(e, f)**.


a
ACVR1R206H-Silencing
b
siACVR1 Does Not Affect TGFβ or WNT3 Signaling in ACVR1R206H BMSCs
<0.0001
ACVR1R206H mRNA/Gapdh
0.0025
0.0020
0.0015
0.0010
0.0005
0.0000
siNTC
siACVR1
unstimulated
TGFβ
0.010473
0.010473
3TP-Luc activity
5000
4000
3000
2000
1000
0
siNTC
siACVR1
unstimulated
WNT3a
0.004069
0.004069
Topflash-Luc activity
8000
6000
4000
2000
0
siNTC
siACVR1
c
siACVR1 Suppresses FGF2-Induced Phosphorylation in ACVR1R206H BMSCs
siNTC
siACVR1
FGF2: 0 10 20 40 0 10 20 40 (min)
50kDa -
37kDa -
P-ERK1/2
50kDa -
37kDa -
ERK1/2
IB
0.892773
0.139696
0.892773
pERK 1/2 /ERK protein expression
0.6
0.4
0.2
0.0
0
10
20
40
Minutes
siNTC
siACVR1
d
siACVR1 Does Not Affect Other Activin Receptors (ACVR) in ACVR1R206H BMSCs
siNTC
siACVR1
0.1960
Alk4 mRNA/Actb
0.0010
0.0008
0.0006
0.0004
0.0002
0.0000
0.0626
Alk3 mRNA/Actb
0.000015
0.000010
0.000005
0.000000
0.8060
Alk6 mRNA/Actb
0.00025
0.00020
0.00015
0.00010
0.00005
0.00000

Supplementary Figure 5. siACVR1 treatment does not affect other osteogenic signaling in FOP cells.

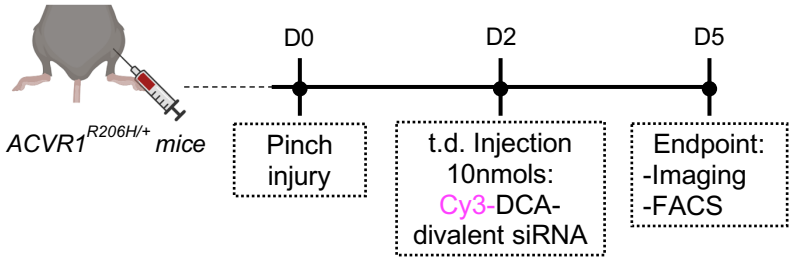
a. *ACVR1*$^{(R206H)Fl}$*;Prrx1-cre* (*ACVR1*^{R206H}) BMSCs were treated with 1 μM siNTC or siACVR1 and three days later, knockdown efficiency of *ACVR1*^{R206H} was assessed by RT-PCR (n = 4 wells).

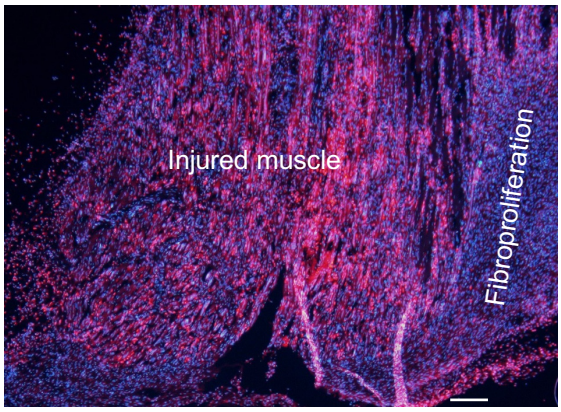
b. siRNA-treated cells were transfected with 3TP-Luc or Topflash-Luc reporter gene and one day later, the cells were stimulated with TGFβ (10 ng/ml) and WNT3a (50 ng/ml), respectively. Luciferase activity was measured one day post-stimulation (n = 3 wells).

c. siRNA-treated cells were stimulated with FGF2 (20 ng/ml) for 10, 20, or 40 min and immunoblotted for phospho-ERK1/2. ERK1/2 was used as a loading control. Representative immunoblot images and relative quantification are displayed (n = 2 wells).

d. *ACVR1*^{R206H} BMSCs were treated with 1 μM siNTC or siACVR1 and three days later, mRNA levels of the closely related paralogs *Alk3*, *Alk4*, and *Alk6* were measured by qRT-PCR, indicating no detectable off-target silencing of these receptors (n = 10 wells). Data are representative of two independent experiments. Values represent mean ± SD by two-sided unpaired t-test **(a)**, two-sided multiple unpaired t-tests **(b)**, one-way ANOVA with Sidak's multiple comparisons test **(c)**, and two-sided Welch's t-test **(d)**.

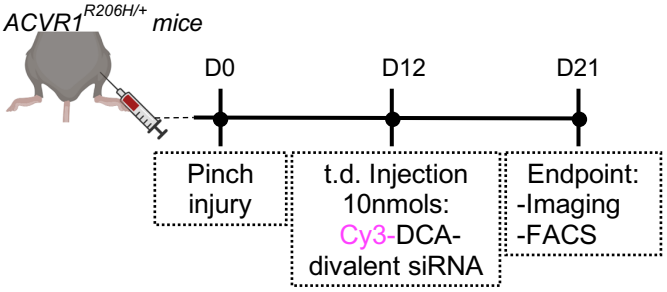
a DCA-Conjugated siRNA Accumulates in Injured Muscle at the Early Stage of HO

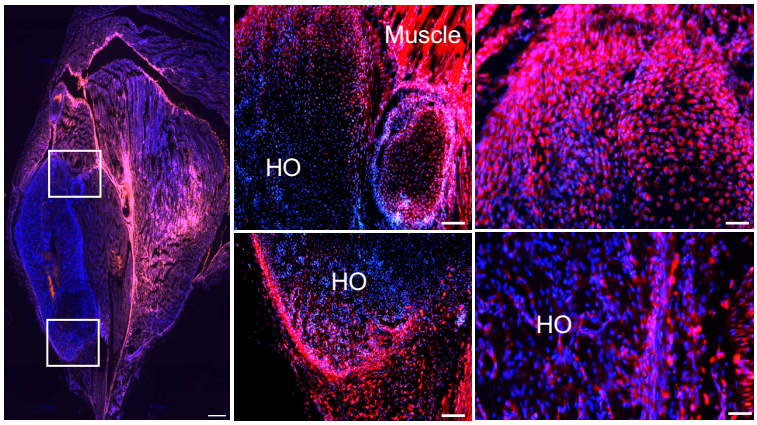




DCA-monovalent siRNA.Cy3/DAPI

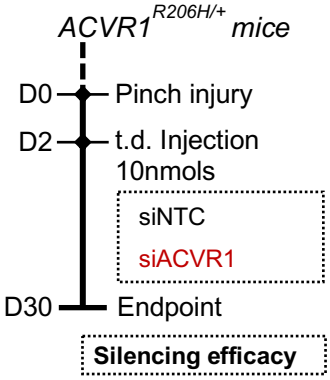
b DCA-Conjugated siRNA Accumulates in Regenerating Muscle and Heterotopic Bone at the Late Stage of HO



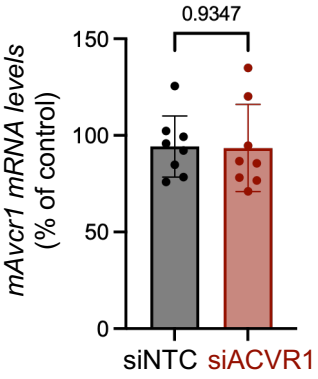


DCA-monovalent siRNA.Cy3/DAPI

c *In vivo* Study Design



d No Significant Mouse *Acvr1* Silencing



Supplementary Figure 6. Biodistribution of DCA-conjugated monovalent siRNA in injured muscle of FOP mice.

a. Schematic diagram showing study design for the early stage of HO progression (five day post-injury, **left**). A single dose of Cy3-labeled, DCA-conjugated monovalent siRNA was injected transdermally (t.d.) into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$ mice two days post-injury. Three days later, siRNA-targeted cells in the cryo-sectioned muscle were visualized by fluorescent microscopy (n = 3 mice, **right**). Scale bars: 100 μm.

b. Schematic diagram showing study design for late stage of HO progression (21 day post-injury, **left**). A single dose of Cy3-labeled, DCA-conjugated monovalent siRNA was injected t.d. into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$ mice twelve days post-injury. Nine days later, siRNA-targeted cells in the cryo-sectioned muscle were visualized by fluorescent microscopy (n = 3 mice, **right**). HO: heterotopic ossification. Scale bars: 200 μm **(left)**, 100 μm **(middle)**, 50 μm **(right)**.

c, d. Schematic diagram showing study design **(c)**. A single dose of siNTC or siACVR1 (10 nmol) was injected t.d. into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$ mice two days post-injury. 28 days later, mRNA levels of endogenous mouse *Acvr1* in HO lesions were assessed using Quantigene 2.0 assay (n = 8 mice, **d**). Data are representative of two independent experiments. Values represent mean ± SD by two-sided unpaired t-test (**d**). Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

a *In vivo* Study Design



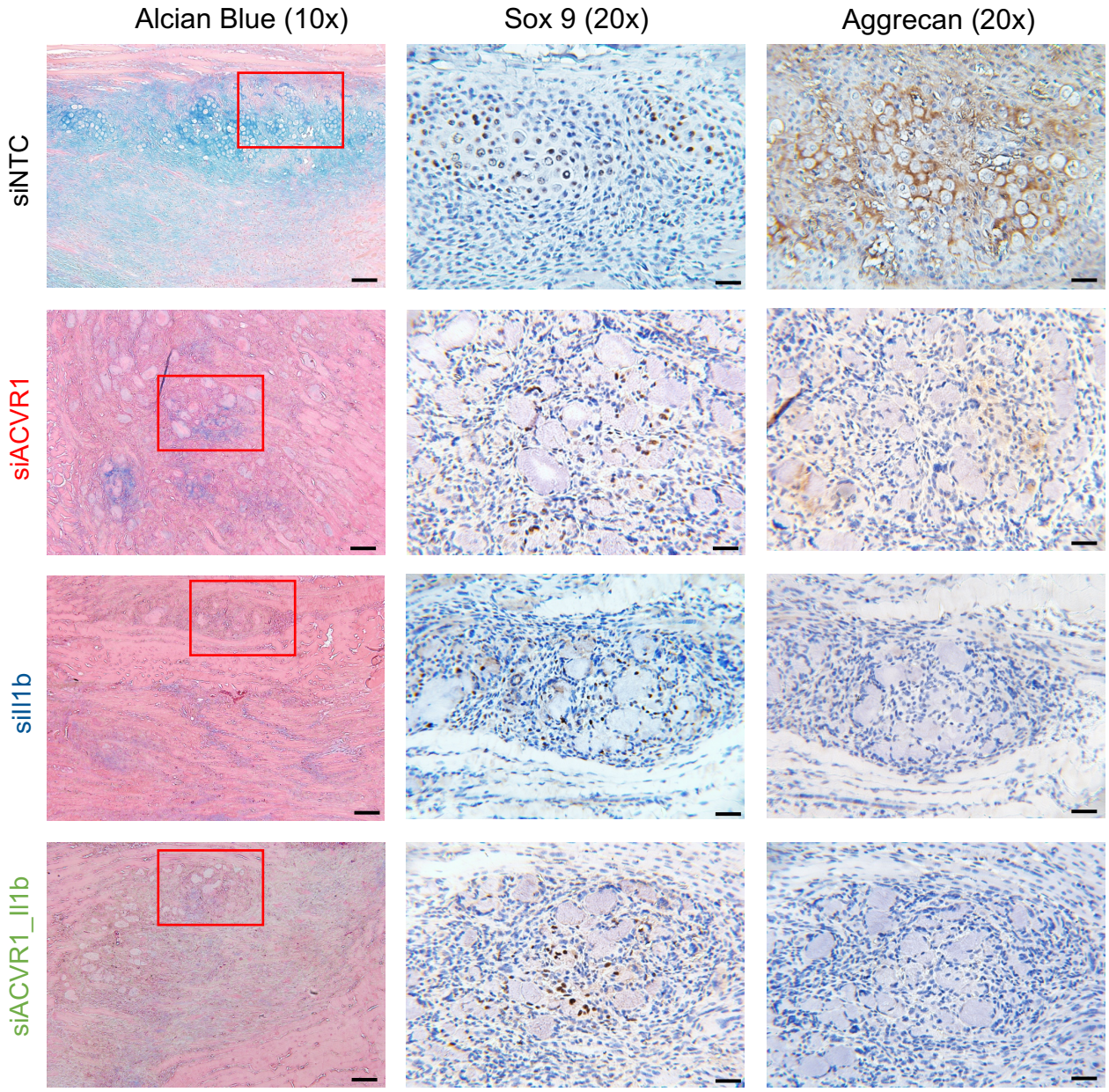
ACVR1$^{R206H/+}$ *mice*

D0 — Pinch injury

D1 — t.d. injection 10nmol: siNTC, siACVR1, siIl1b, siACVR1_Il1b

D7 — Endpoint: Alcian Blue, Sox9 and Aggrecan IHC

b siACVR1, siIl1b, and siACVR1_Il1b Suppress Chondrogenic Anlagen Formation

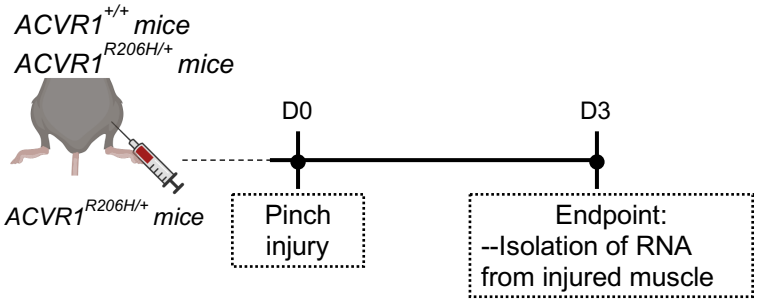


Supplementary Figure 7. Local delivery of DCA-conjugated siRNA targeting *ACVR1*^{R206H} and/or *Il1b* suppresses chondrogenic anlagen formation in injured muscle of FOP mice.

a. Schematic diagram showing study design.

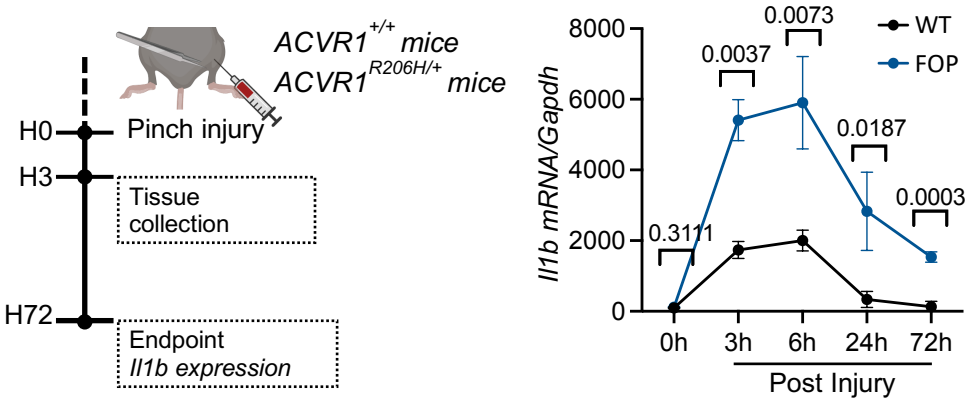
b. 10 nmol DCA monovalent siRNAs were injected t.d. into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$ mice two day after pinch injury (n = 3 mice). Five days later, injured muscles were harvested, paraffin-sectioned, and stained with alcian blue for histopathologic analysis (left). Alternatively, immunohistochemistry was performed to examine the expression of early (Sox9, middle) and late (Aggrecan, right) chondrogenic genes in the injured muscle of FOP mice. Scale bars: 100 μm (left) and 50 μm (middle, right). Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

a *Il1b* Expression is Significantly Upregulated in Injured Muscle (FOP vs WT)

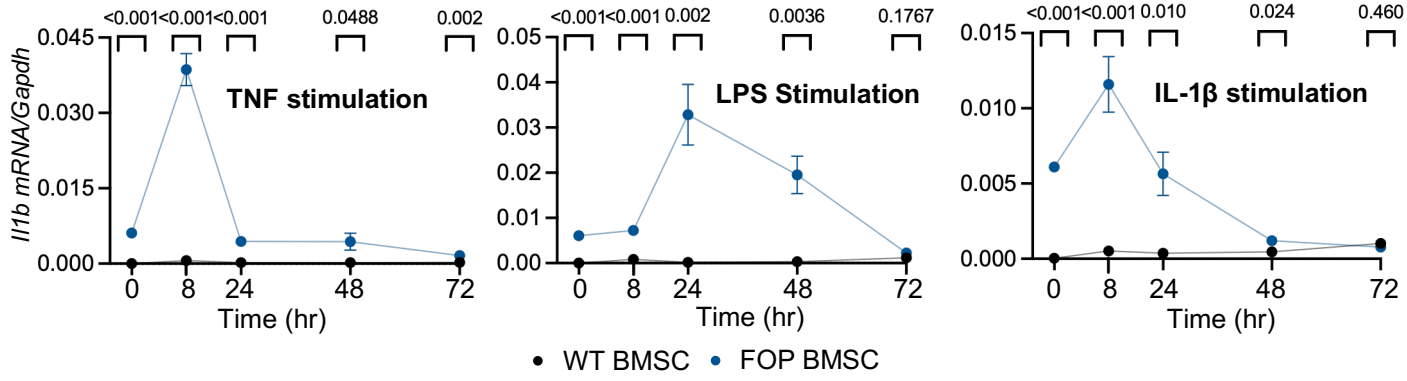


Position	Gene	Fold Change	p Value	q Value
A05	*Ccl12*	4.54	0.047385	0.159214
B01	*Ccl4*	2.78	0.031127	0.153804
B04	*Ccl7*	5.51	0.00518	0.134652
C04	*Csf1*	3.1	0.022442	0.134652
C09	*Cxcl10*	5.13	0.015512	0.118455
D09	*Il10ra*	4.22	0.046363	0.159248
E04	*Il17b*	2.57	0.038532	0.159248
E07	*Il1b*	9.1	0.000446	0.009366
E08	*Il1r1*	2.19	0.046101	0.159348
E09	*Il1rn*	4.73	0.018493	0.119493
G03	*Pf4*	5.1	0.024994	0.13996

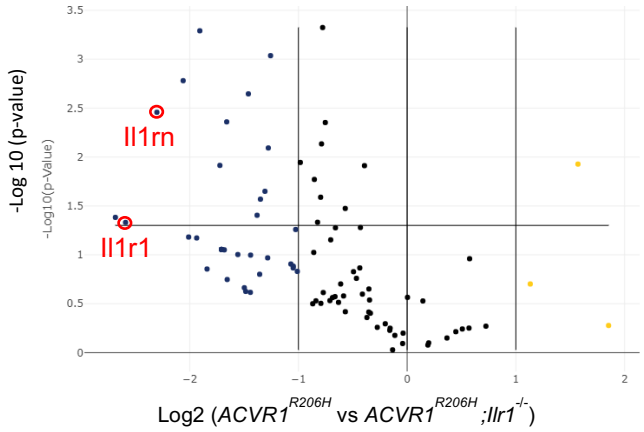
b *Il1b* Expression is Significantly Upregulated in Injured Muscle (FOP vs WT)



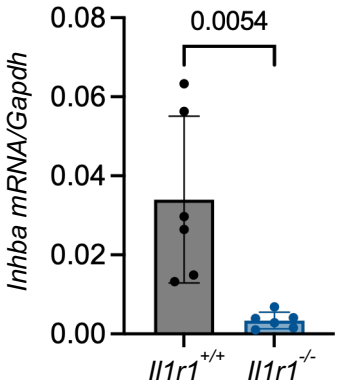
c Elevated and Persistent Expression of *Il1b* in ACVR1^{R206H} BMSCs Following Inflammatory Stimuli



d Reduced IL-1 Signaling in Injured Muscle of *ACVR1*^{R206H}*;Il1r1*$^{-/-}$ mice



e Reduced Expression of Activin A



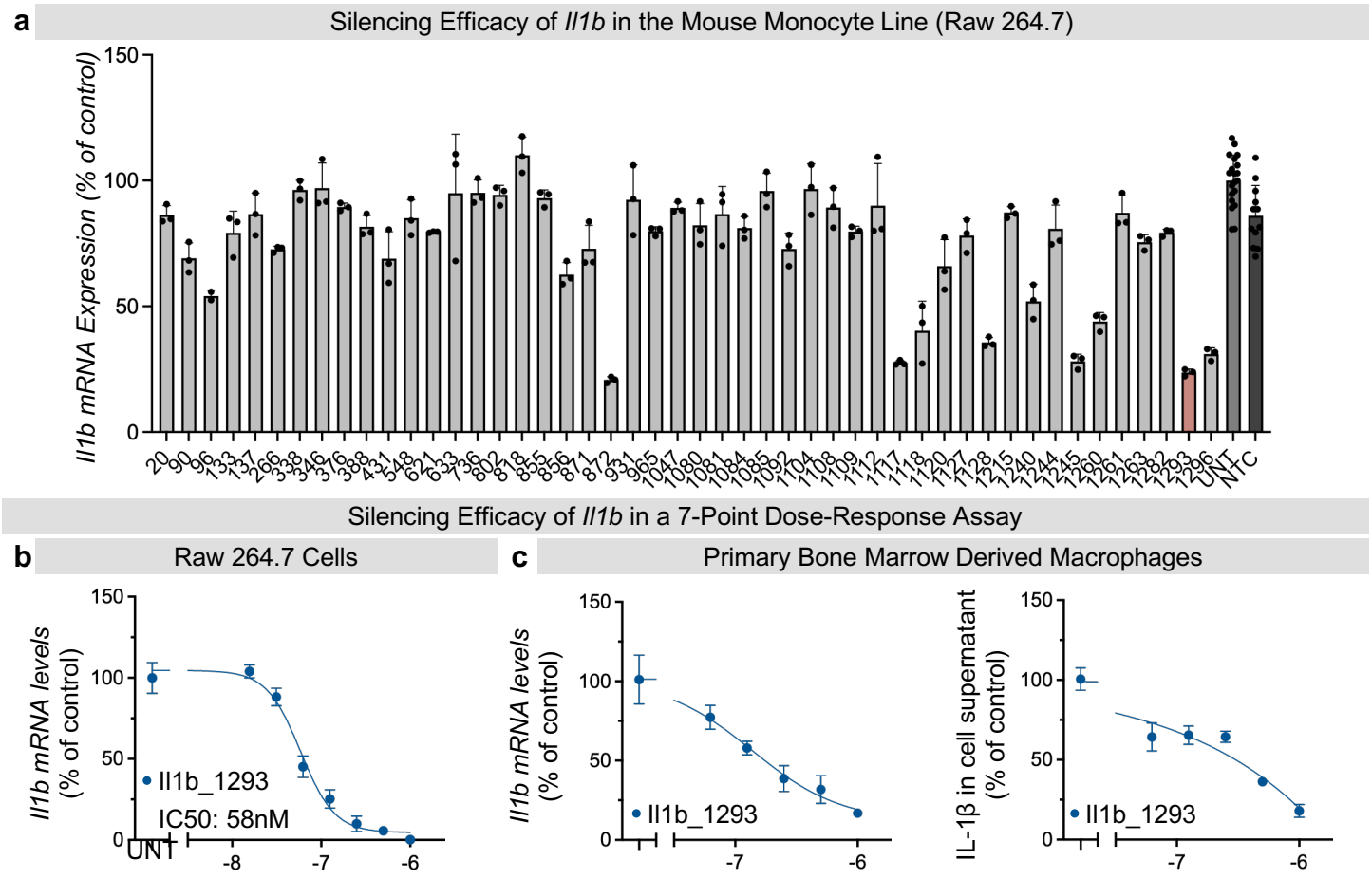
Supplementary Figure 8. IL-1 signaling mediates trauma-induced HO in FOP mice.

a. Schematic diagram showing study design **(left)**. 8-week-old WT *(ACVR1$^{+/+}$)* and FOP *(ACVR1$^{R206H/+}$)* mice underwent pinch injury on the tibial muscle and injured tissues were collected three days post-injury. RT_2 profiler PCR array demonstrates that *Il1b* is the most highly expressed gene in injured muscle of FOP mice among 84 inflammatory genes tested (*n* = 3 mice, **right**). Among the 84 genes tested, *Il1b* showed the largest fold change and the most statistically significant differential expression ($p = 0.0004$, $q = 0.0094$ by Benjamini-Hochberg FDR correction).

b. Schematic diagram showing study design **(left)**. 8-week-old WT and FOP mice underwent pinch injury on the tibial muscle and injured tissues were collected 0, 3, 6, 24, and 72 hr post-injury. mRNA levels of *Il1b* were measured by RT-PCR and normalized to *Gapdh* (*n* = 4 mice, **right**).

c. *ACVR1$^{(R206H)Fl}$* (black) and *ACVR1$^{(R206H)Fl}$;Prrx1-cre* (blue) BMSCs were stimulated with TNF (10 ng/ml), LPS (1 μg/ml), or IL-1β (20 ng/ml) for 8, 24, 48, and 72 hrs and mRNA levels of *Il1b* were measured by RT-PCR and normalized to *Gapdh* (*n* = 4 wells).

d, e. 8-week-old *ACVR1$^{R206H/+}$* and *ACVR1$^{R206H/+}$;Il1r1$^{-/-}$* mice underwent pinch injury on the tibial muscle and injured tissues were collected three days post-injury. RT_2 profiler PCR array was performed to assess inflammatory gene expression (n = 3 mice, **d**). Alternatively, mRNA levels of *Inhba* were measured by RT-PCR and normalized to *Gapdh* (n = 6 mice, **e**). Data are representative of three independent experiments. Values represent mean ± SD by two-sided multiple unpaired t-tests **(b, c)** and two-sided unpaired t-test **(e)**. Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

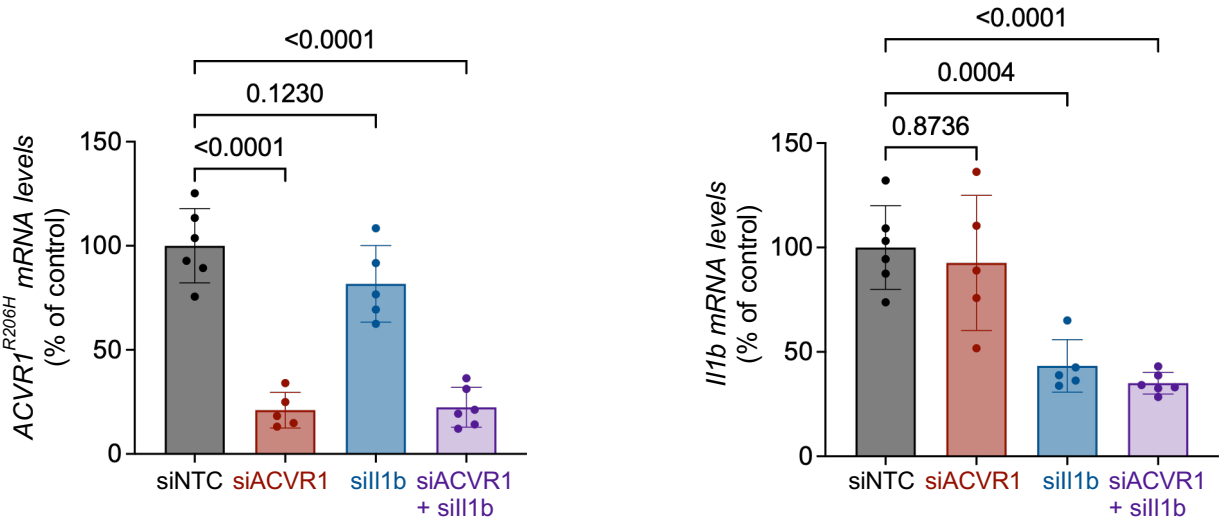


Supplementary Figure 9. Development of the siRNA targeting mouse *Il1b* mRNA.

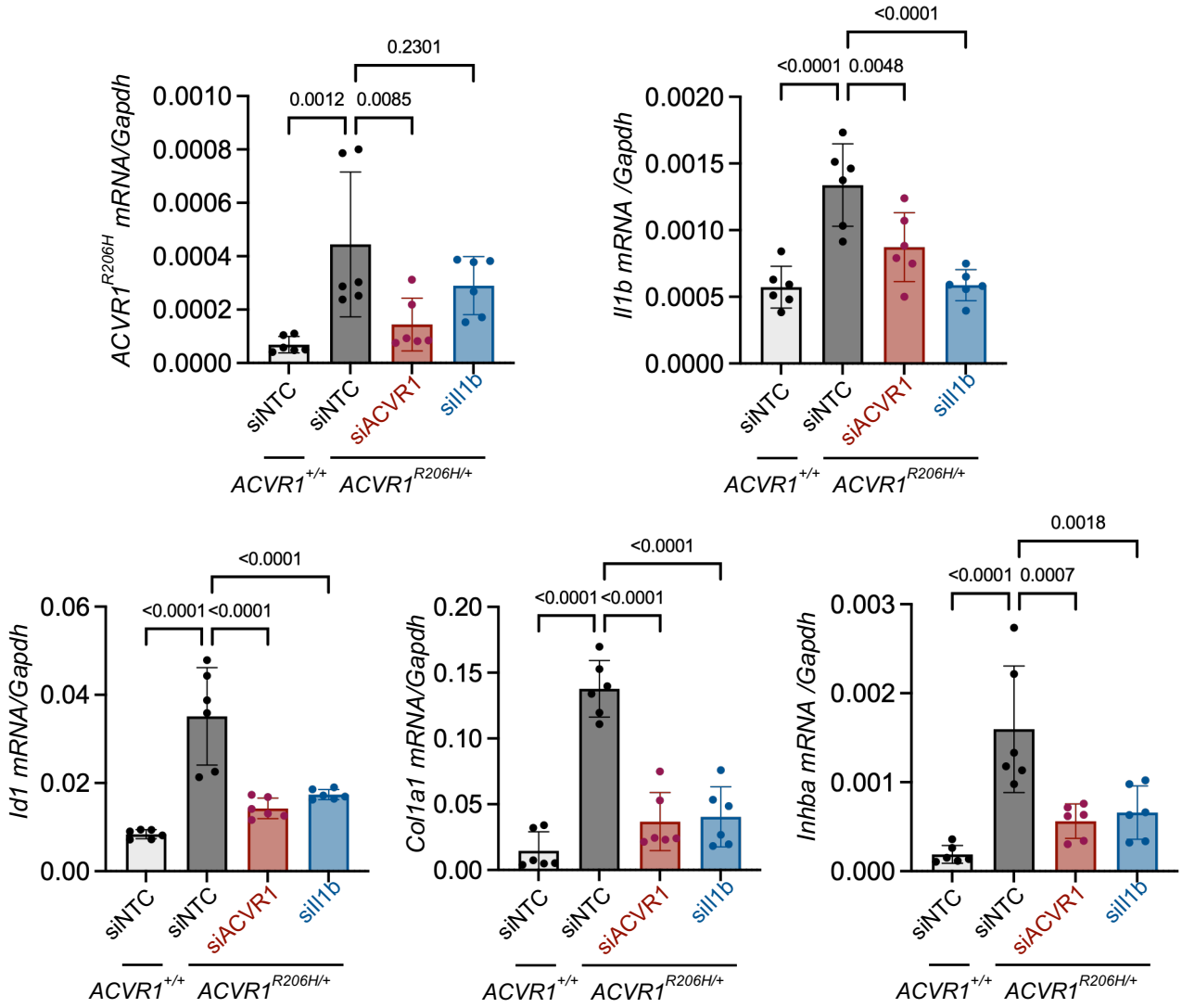
a, b. The mouse monocyte line (Raw264.7) was treated with a panel of 48 siRNAs targeting mouse *Il1b* mRNA, UNT, and siNTC. 3 days later, cells were stimulated with LPS (25 ng/mL) for 8 hrs and mRNA levels of *Il1b* were measured using the Quantigene 2.0 assay (n = 3 wells). UNT: untreated control, siNTC: non-targeting control siRNA **(a)**. Alternatively, Raw264.7 cells were treated with the lead siRNA_1293 in 7-point dose response, stimulated with LPS, and mRNA levels of *Il1b* were measured **(**n = 3 wells, **b).**

c. Mouse bone marrow-derived monocytes (BMMs) were cultured for six days in the presence of M-CSF (50 ng/ml) to differentiate into macrophages (BMDMs). The cells were treated with the lead siRNA_1293 in 7-point dose response and stimulated with LPS for 8 hrs. mRNA levels of *Il1b* **(left)** and protein levels of IL-1β in the cell supernatant **(right)** were measured by the Quantigene 2.0 and ELISA assays, respectively (n = 3 wells). Data are representative of three independent experiments. Values represent mean ± SD.

a Silencing Efficacy of *ACVR1*^{R206H} and *Il1b* in FOP Muscle After Single or Dual Treatment of siACVR1 and siIl1b



b Single Silencing of *ACVR1*^{R206H} or *Il1b* Suppresses Activin A and Osteo-Chondrogenic Gene Expression

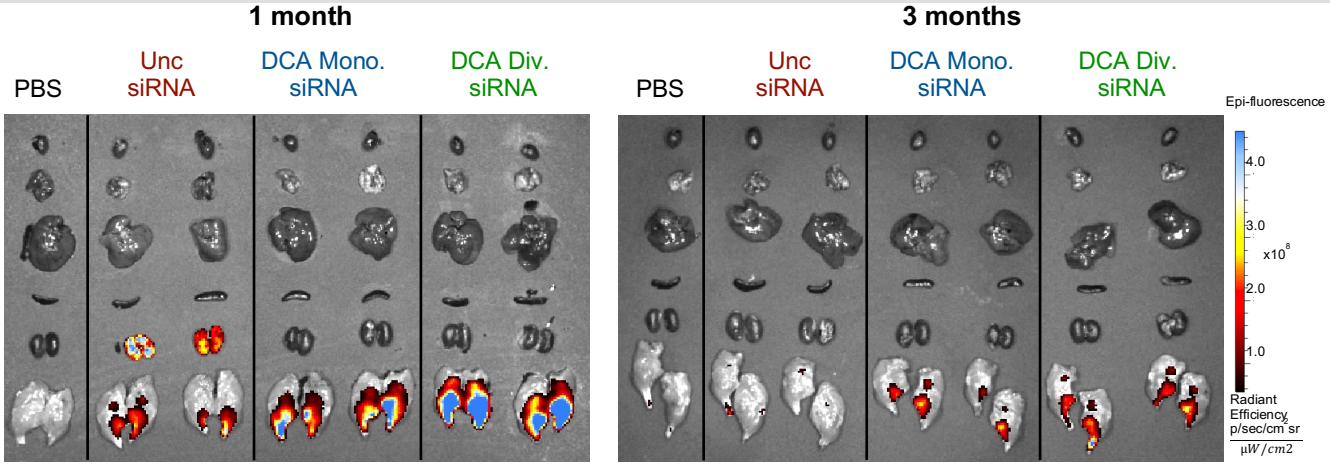


Supplementary Figure 10. Gene expression in injured muscle tissues of siRNA-treated FOP mice.

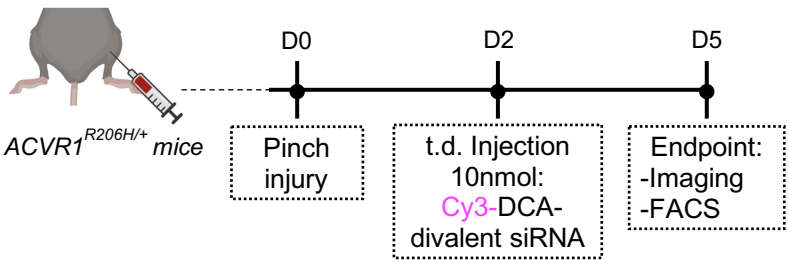
a. A single dose of siNTC, siACVR1, siIl1b, and siACVR1+siIl1b (10 nmol) was injected t.d. into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$ mice 2 days post-injury. Four weeks later, mRNA levels of *ACVR1*^{R206H} and *Il1b* were measured by the Quantigene 2.0 assay (n = 5-6 mice). This is the same experiment of **Figure 3c**.

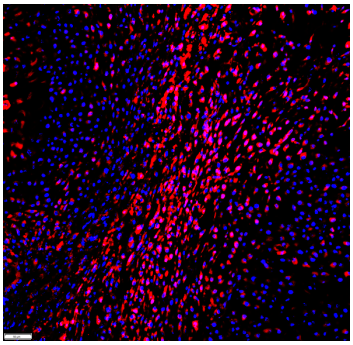
b. A single dose of siNTC, siACVR1, and siIl1b (10 nmol) was injected t.d. into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$ mice two days post-injury. Three days later, mRNA levels of the indicated genes in injured muscle tissues were measured by RT-PCR (n = 6 mice). Data are representative of two to three independent experiments. Values represent mean ± SD by one-way ANOVA with Sidak's multiple comparisons test (**a,b**).

a Muscle Accumulation of Different siRNA Scaffolds 1 and 3 Months After Transdermal Injection



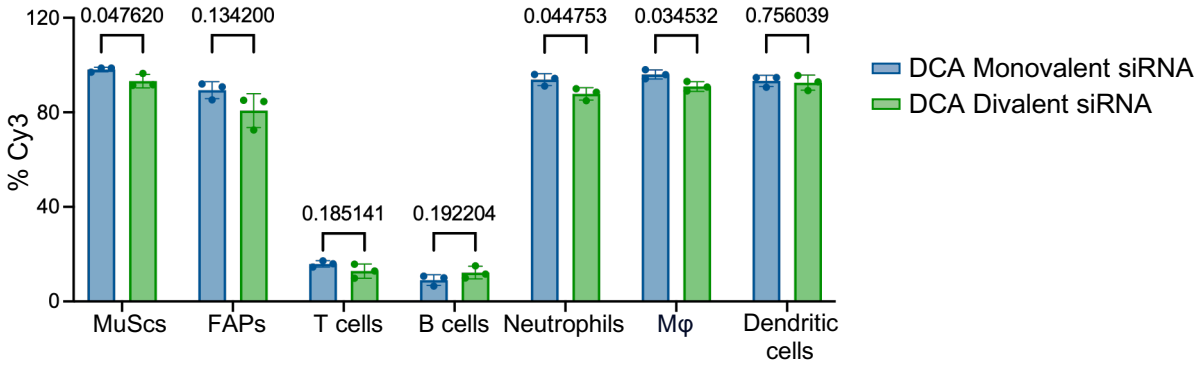
b DCA-Divalent siRNA Accumulates in Injured Muscle at the Early Stage of HO Progression



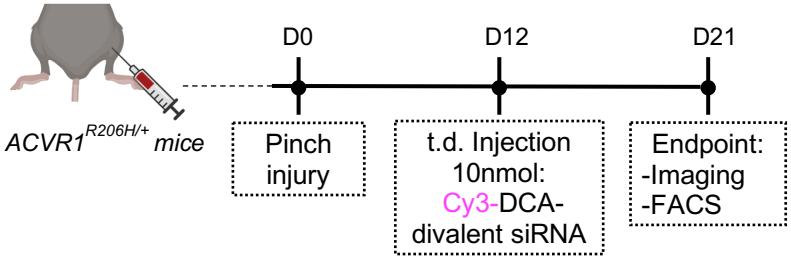


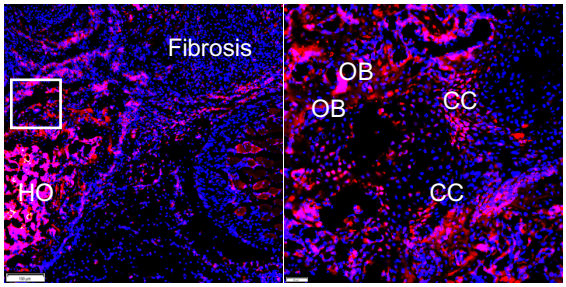
DCA-Divalent siRNA.Cy3/DAPI

c Cellular Update of DCA-Monovalent vs Divalent siRNAs in Immune Cells at the Early Stage of HO Progression



d DCA-Divalent siRNA Accumulates in HO Lesions at the Late Stage of HO Progression



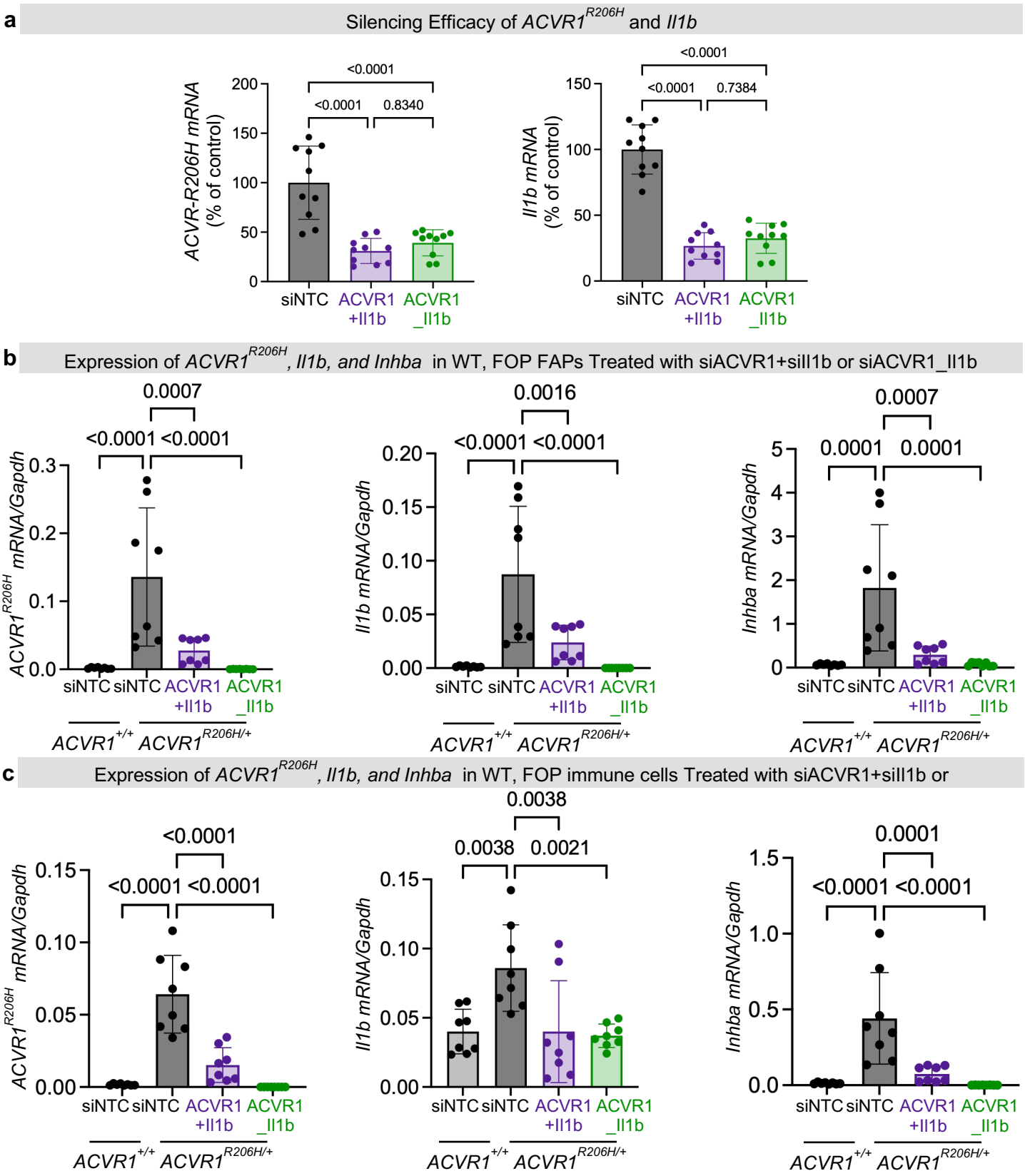


DCA Divalent siRNA.Cy3/DAPI

Supplementary Figure 11. Biodistribution of DCA-conjugated divalent siRNA in FOP mice.

a. A single dose of Cy3-labeled, unconjugated monovalent (Unc) siRNA, DCA-conjugated monovalent (DCA Mono) siRNA, or DCA-conjugated divalent (DCA Div) siRNA (10 nmol) was injected t.d. into the tibial muscle of 8-week-old wildtype mice. One- and three-months later, Cy3 fluorescence in individual tissues was visualized via IVIS-100 optical imaging (n = 5 mice). This is the same experiment of **Figures 4a and b**. **b, c.** A single dose of Cy3-labeled DCA-conjugated divalent (DCA Div) siRNA (10 nmol) was injected t.d. into the tibial muscle of *ACVR1*$^{R206H/+}$ mice two days post-injury. Three days later, Cy3-labeled cells in cryo-sectioned muscle was visualized by fluorescence microscopy (n = 3 mice, **b**). Scale bars: 50 μm. Alternatively, cells were isolated from digested muscle near the site of injury and subjected for FACS analysis to assess the frequency of Cy3-labeled cell populations **(**n = 3 mice, **c)**.

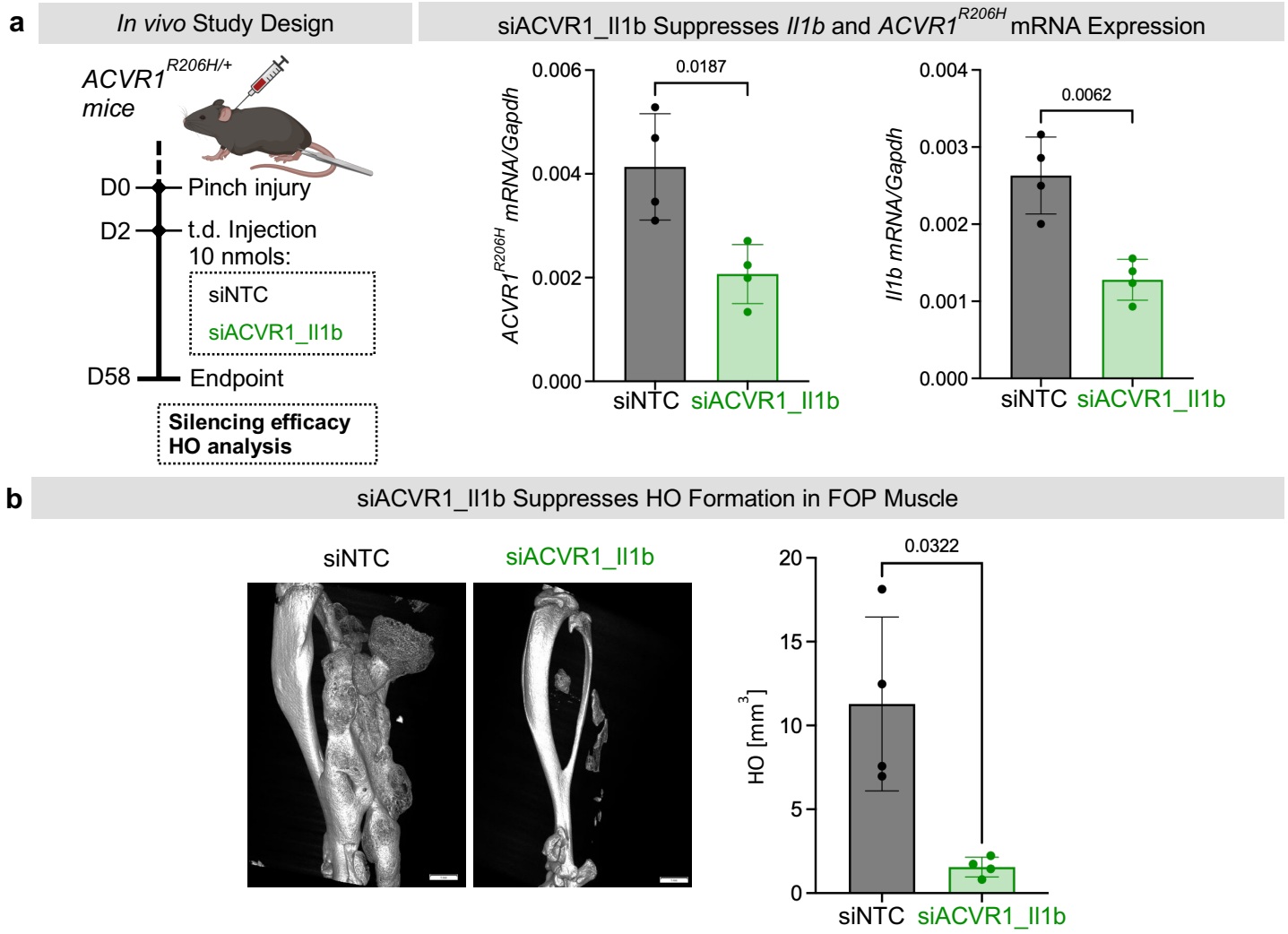
d. Schematic diagram showing study design for late stage of HO progression (**left**). A single dose of Cy3-labeled DCA-conjugated divalent siRNA (10 nmol) was injected t.d. into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$ mice twelve days post-injury. 9 days later, Cy3-labeled cells in cryo-sectioned muscle was visualized by fluorescence microscopy (n = 3 mice, **right**). HO: heterotopic ossification, OB: osteoblast, CC: chondrocyte. Scale bars: 100 μm **(left)**, 50 μm **(right)**. Data are representative of two independent experiments. Values represent mean ± SD by two-sided multiple unpaired t-tests (**c**). Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.


a
Silencing Efficacy of ACVR1R206H and Il1b
ACVR-R206H mRNA (% of control)
<0.0001
<0.0001
0.8340
siNTC
ACVR1 +Il1b
ACVR1 _Il1b
Il1b mRNA (% of control)
<0.0001
<0.0001
0.7384
b
Expression of ACVR1R206H, Il1b, and Inhba in WT, FOP FAPs Treated with siACVR1+siIl1b or siACVR1_Il1b
ACVR1R206H mRNA/Gapdh
0.0007
<0.0001 <0.0001
Il1b mRNA/Gapdh
0.0016
<0.0001 <0.0001
Inhba mRNA/Gapdh
0.0007
0.0001 0.0001
siNTC siNTC ACVR1 +Il1b ACVR1 _Il1b
ACVR1+/+ ACVR1R206H/+
c
Expression of ACVR1R206H, Il1b, and Inhba in WT, FOP immune cells Treated with siACVR1+siIl1b or
ACVR1R206H mRNA/Gapdh
<0.0001
<0.0001 <0.0001
Il1b mRNA/Gapdh
0.0038
0.0038 0.0021
Inhba mRNA/Gapdh
0.0001
<0.0001 <0.0001
siNTC siNTC ACVR1 +Il1b ACVR1 _Il1b
ACVR1+/+ ACVR1R206H/+

Supplementary Figure 12. Gene expression in injured muscle tissues, FAPs, and immune cells of siRNA-treated FOP mice.

a. A single dose of siNTC, siACVR1+Il1b, or siACVR1_Il1b (10 nmol) was injected t.d. into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$ mice 2 days post-injury. 4 weeks later, mRNA levels of *ACVR1*^{R206H} and *Il1b* were measured by the Quantigene 2.0 assay (n = 10 mice, **a**). This is the same experiment of **Figure 4c**.

b, c. A single dose of siNTC, siACVR1+Il1b, or siACVR1_Il1b (10 nmol) was injected t.d. into the tibial muscle of *ACVR1*$^{+/+}$*;PDGFRα-GFP* (WT) and *ACVR1*$^{R206H/+}$*;PDGFRα-GFP* (FOP) mice 2 days post-injury. 3 days later, GFP^{+}Sca1^{+}CD31^{-}CD45^{-} FAPs (b) and GFP^{-}Sca1^{-}CD31^{-}CD45^{+} immune cells (**c**) were FACS-sorted from digested muscle near the site of injury. mRNA levels of *ACVR1*^{R206H}*, Il1b,* and *Inhba* were measured by RT-PCR and normalized to *Gapdh* (n = 8 mice). Data are representative of two independent experiments. Values represent mean ± SD by one-way ANOVA with Sidak's multiple comparisons test (**a**) and Dunnett's multiple comparisons test (**b, c**).



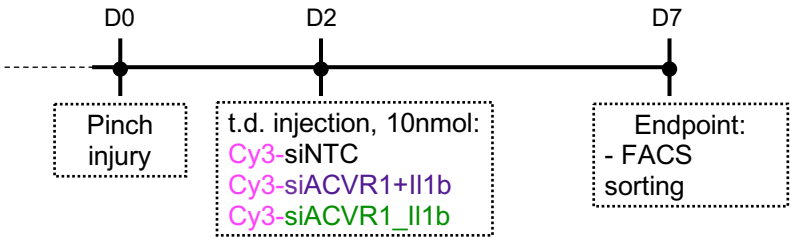
Supplementary Figure 13. DCA-conjugated siRNA targeting *ACVR1*^{R206H} and *Il1b* suppresses HO in FOP mice for up to 8 weeks.

Schematic diagram showing study design (**a, left**). A single dose of siNTC and siACVR1_Il1b (10 nmol) was injected t.d. into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$ mice two days post-injury. Eight weeks later, silencing efficiency of *ACVR1*^{R206H} and *Il1b* in HO lesions and HO formation were assessed by RT-PCR **(**n = 4 mice, **a, right)** and microCT imaging and quantification (n = 4 mice, **b**), respectively. Values represent mean ± SD by two-sided Welch's t-test. Data are representative of two independent experiments. Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

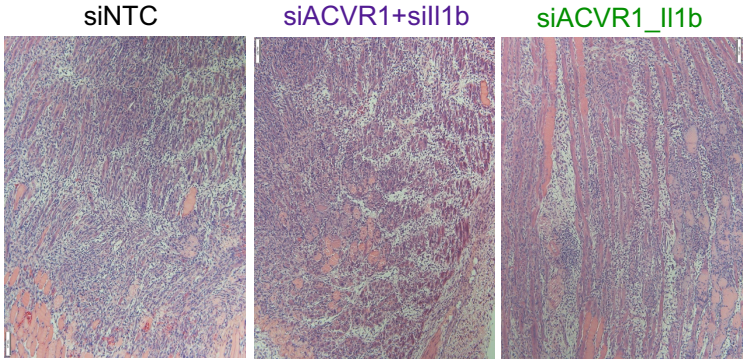
a *In vivo* Study Design



PDGFRα-GFP;ACVR1$^{R206H/+}$ *mice*

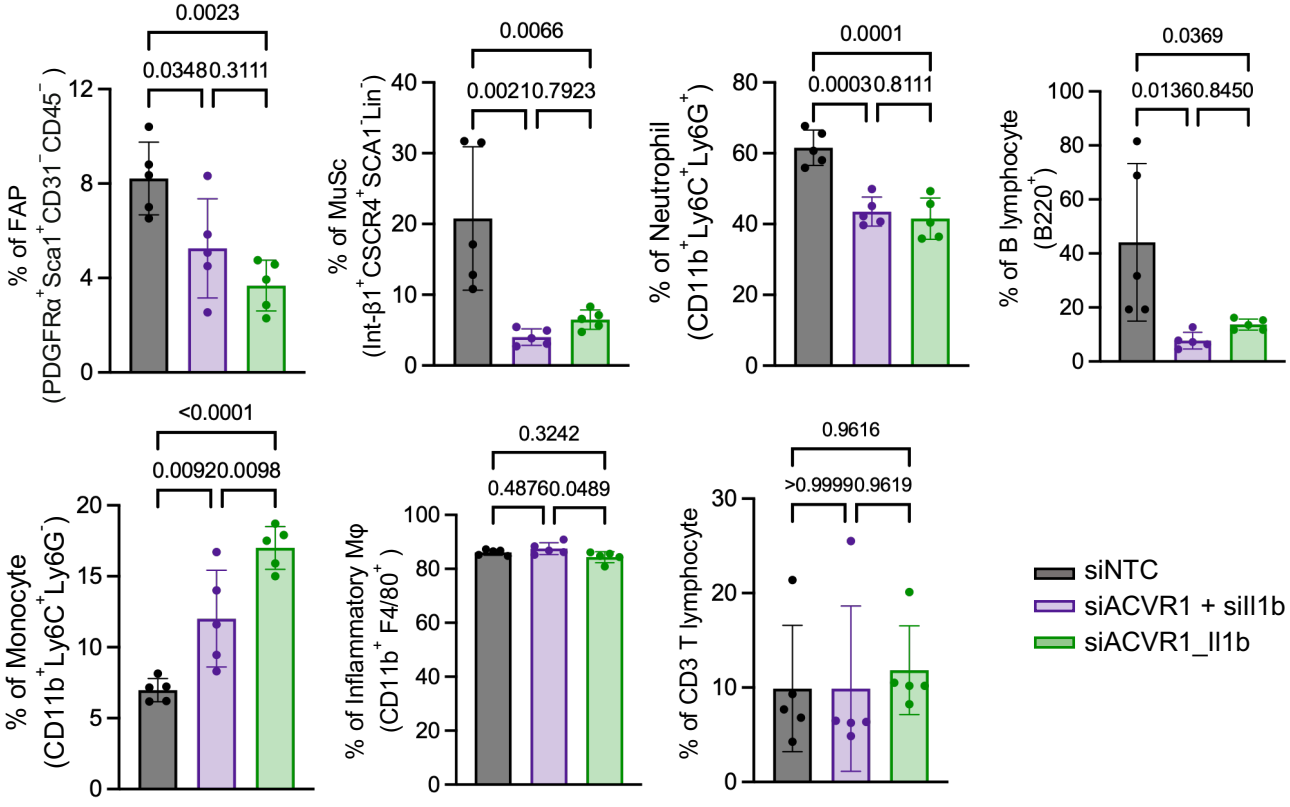


b FOP Muscle Tissue 4 Days Post Injury (t.d. injection)



H&E

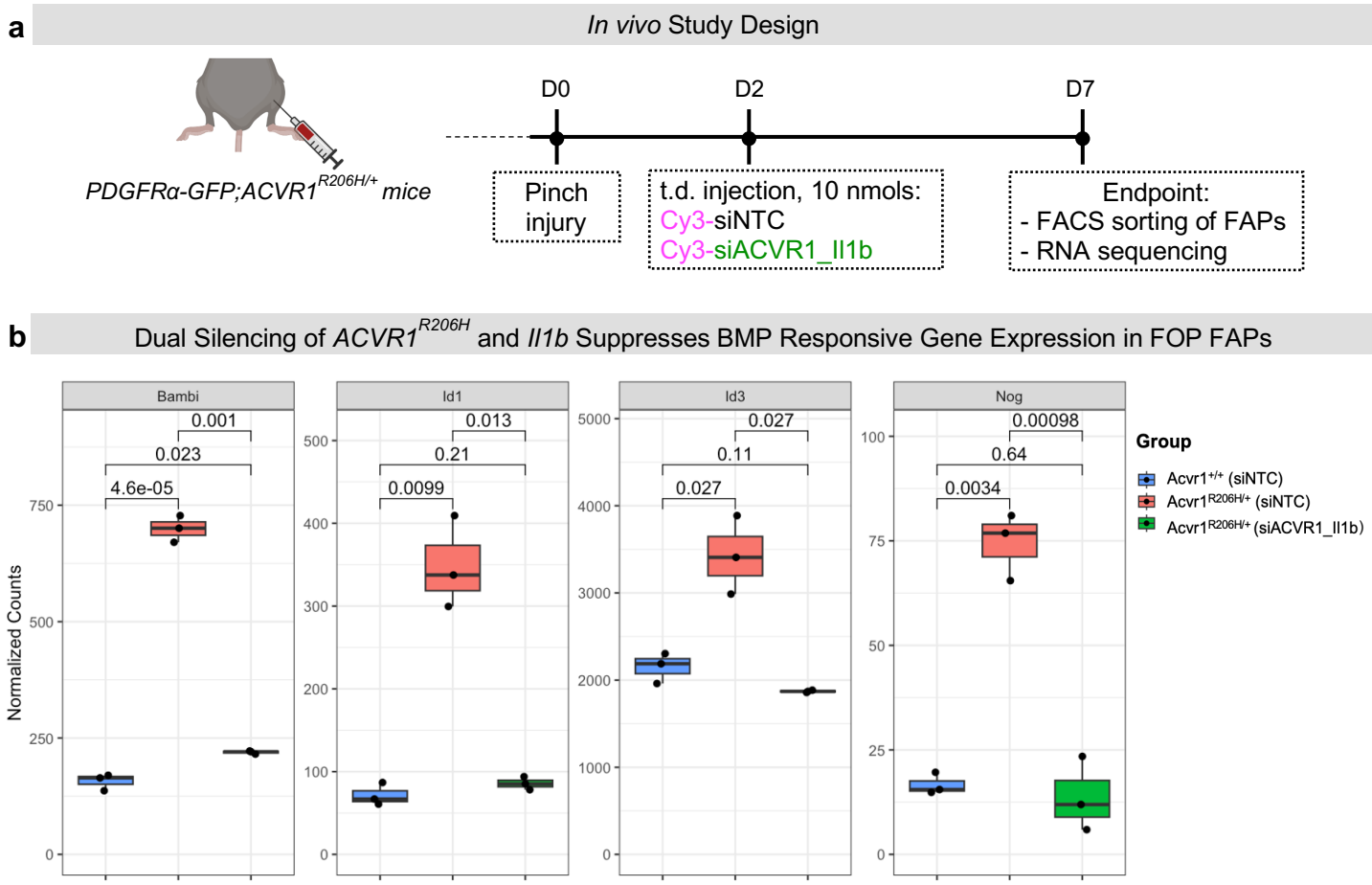
c Alteration of Cell Frequency in Injured FOP Muscle After Treatment of siACVR1+siIl1b or siACVR1_Il1b



Supplementary Figure 14. Characterization of cell populations in injured muscle of siRNA-treated FOP mice.

a. Schematic diagram showing study design for the early stage of HO progression.

b, c. A single dose of siNTC, siACVR1+Il1b, or siACVR1_Il1b (10 nmol) was injected t.d. into the tibial muscle of 8-week-old *ACVR1*$^{R206H/+}$*;PDGFRα-GFP* mice two days post-injury. Two days later, injured muscles were stained with hematoxylin and eosin (H&E), demonstrating little to no difference in siRNA-treated muscles (n = 3 mice, **b**). Scale bars: 100 μm. Seven days after injury, cells were isolated from digested muscle near the site of injury and subjected for FACS analysis to assess the frequency of Cy3-labeled cell types (n = 5 mice, **c**). Data are representative of two independent experiments. Values represent mean ± SD by one-way ANOVA with Tukey's multiple comparisons test (**c**). Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

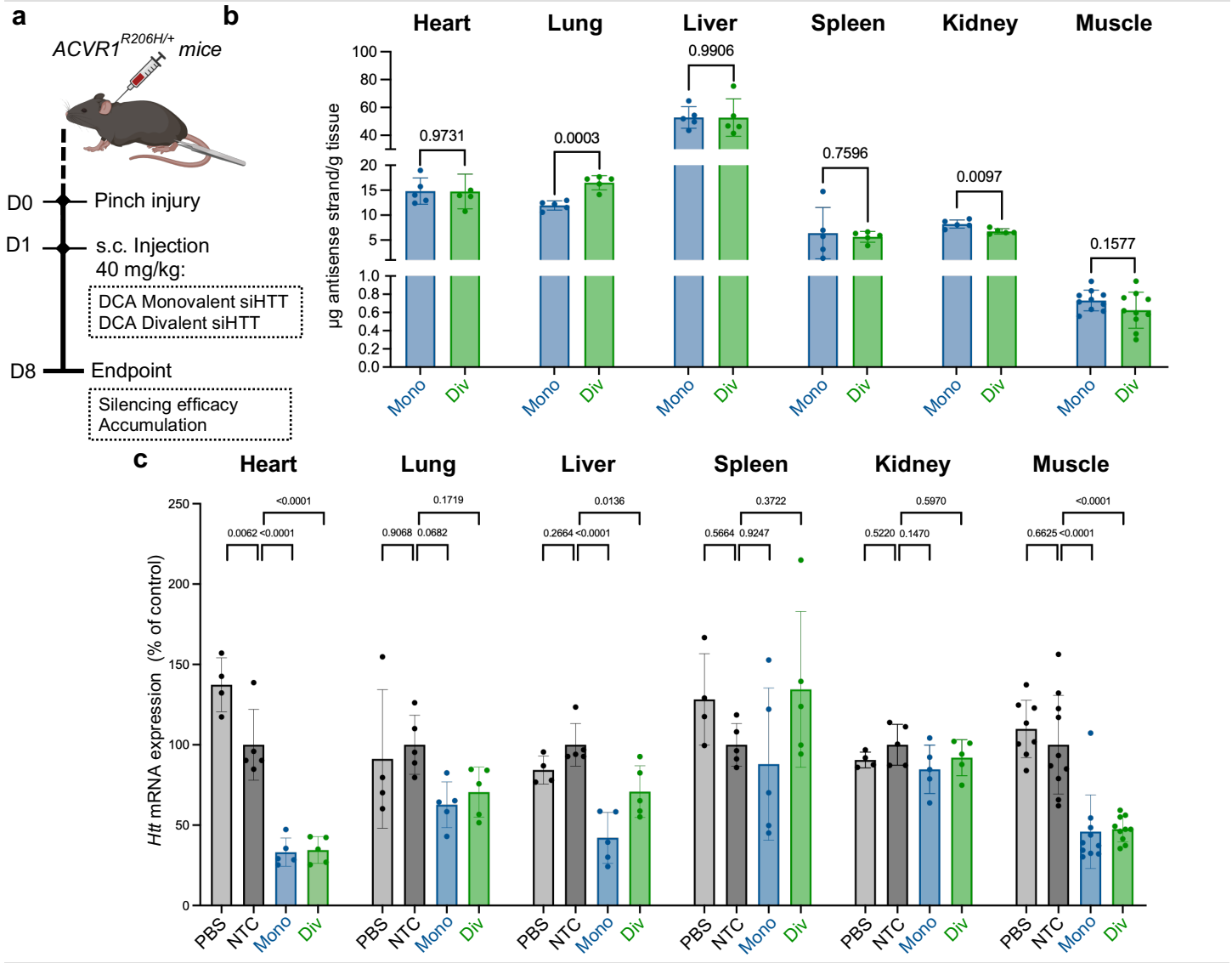


Supplementary Figure 15. BMP-responsive gene expression in siRNA-treated WT and FOP FAPs.

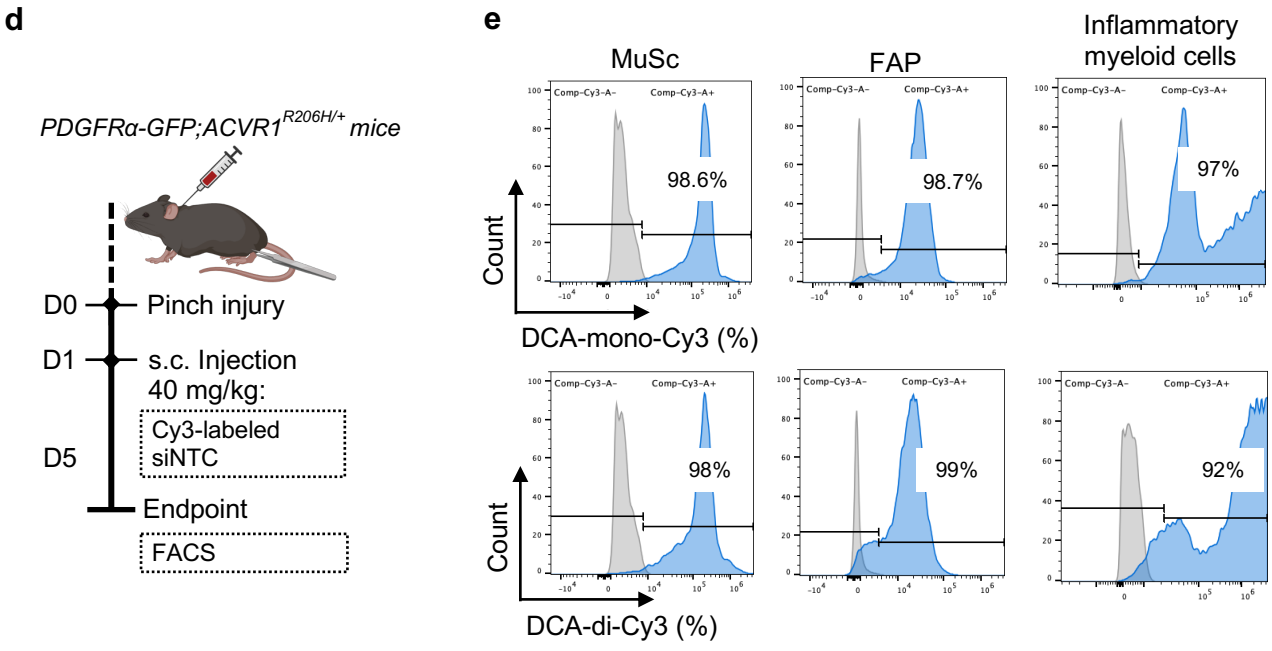
a. Schematic diagram showing study design for the early stage of HO progression.

b. A single dose of siNTC or siACVR1_Il1b (10 nmol) was injected t.d. into the tibial muscle of *ACVR1*$^{+/+}$*;PDGFRα-GFP* and *ACVR1*$^{R206H/+}$*;PDGFRα-GFP* mice two days post-injury. Five days later, GFP^{+}Sca1^{+}CD31^{-}CD45^{-} FAPs were FACS-sorted from digested muscle near the site of injury and then, subjected to RNA sequencing. Normalized transcript numbers of the indicated BMP-responsive genes are displayed (n = 3 mice). This is the same experiment of **Figures 5b-e**. Data are representative of two independent experiments. Values represent mean ± SD by one-way ANOVA with Tukey's multiple comparisons test (**b**). Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

In vivo study design, silencing efficiency, and siRNA accumulation in individual tissues



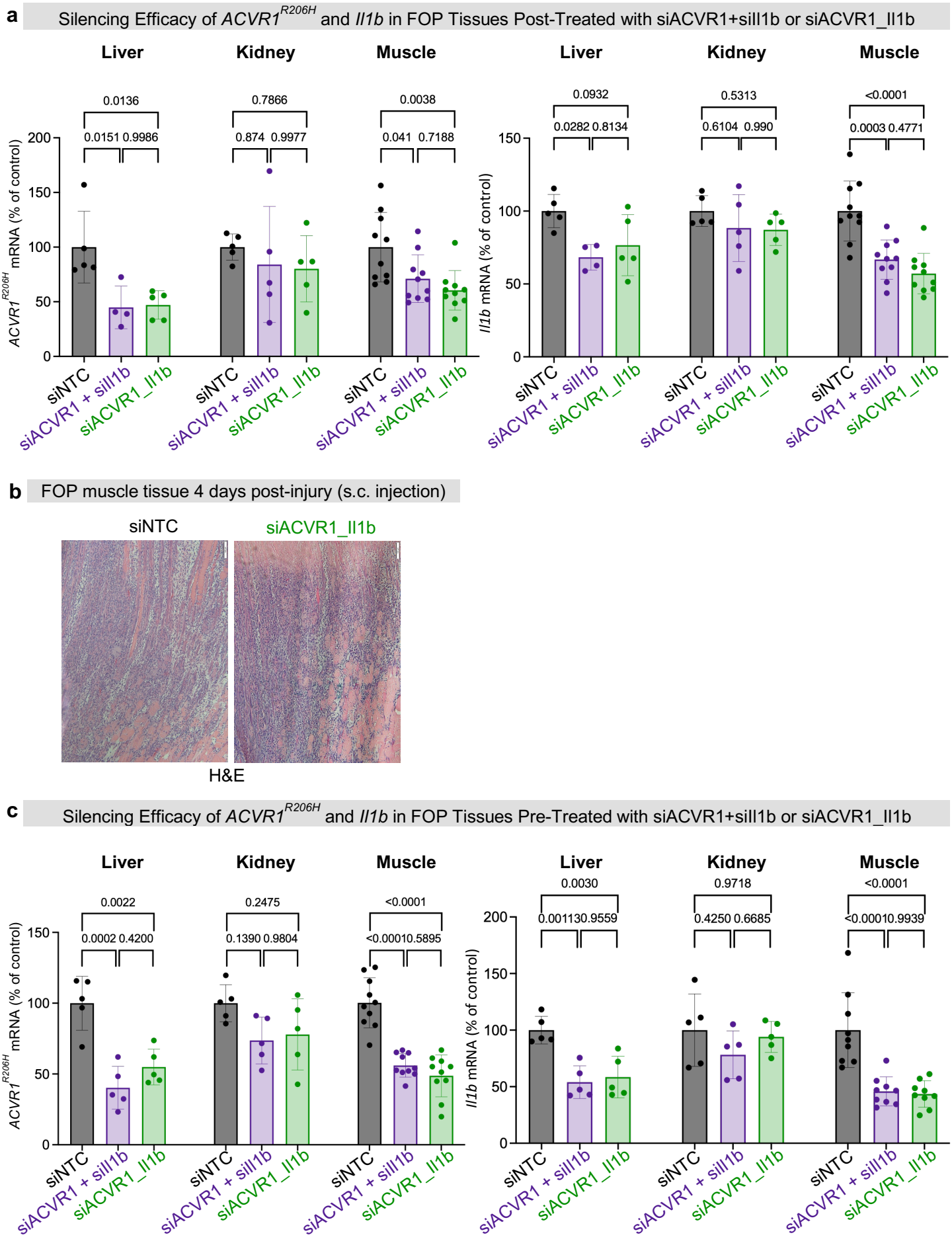
DCA-siRNA uptake in FOP-relevant cell types (FACS)



Supplementary Figure 16. Biodistribution and silencing efficiency in individual tissues following systemic delivery of siRNAs.

a-c. Schematic diagram showing study design **(a)**. A single dose of DCA-conjugated monovalent (Mono) or DCA-conjugated divalent (Div) siHTT (40 mg/kg) was injected subcutaneously (s.c.) into 8-week-old *ACVR1*$^{R206H/+}$ mice one day post-injury. Seven days later, antisense accumulation **(b)** and knockdown efficiency **(c)** in heart, lung, liver, spleen, kidney, and muscle were quantified by the Quantigene 2.0 assay (n = 4 mice).

d, e. Schematic diagram showing study design **(d)**. A single dose of Cy3-labeled, DCA-conjugated monovalent or divalent siNTC (40 mg/kg) was injected s.c. into 8-week-old *ACVR1*$^{R206H/+}$*;PDGFRα-GFP* mice one day post-injury. Four days later, cells were isolated from digested muscle near the site of injury and subjected for FACS analysis to assess the frequency of the indicated cell types (n = 6 mice, **e**). FAP (fibroadipogenic progenitor): GFP^{+}Sca1^{+}CD31^{-}CD45^{-}, MuSc (muscle satellite cells): Sca1^{-} Ter119^{-}Cxcr4^{-} Intβ1^{+}, Inflammatory myeloid cells: F4/80^{+}CD45^{+}CD11b^{+}CD11c^{-}. Data are representative of two independent experiments. Values represent mean ± SD by two-sided multiple unpaired t-tests (**b**) and one-way ANOVA with Dunnett's multiple comparisons test (**c**). Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

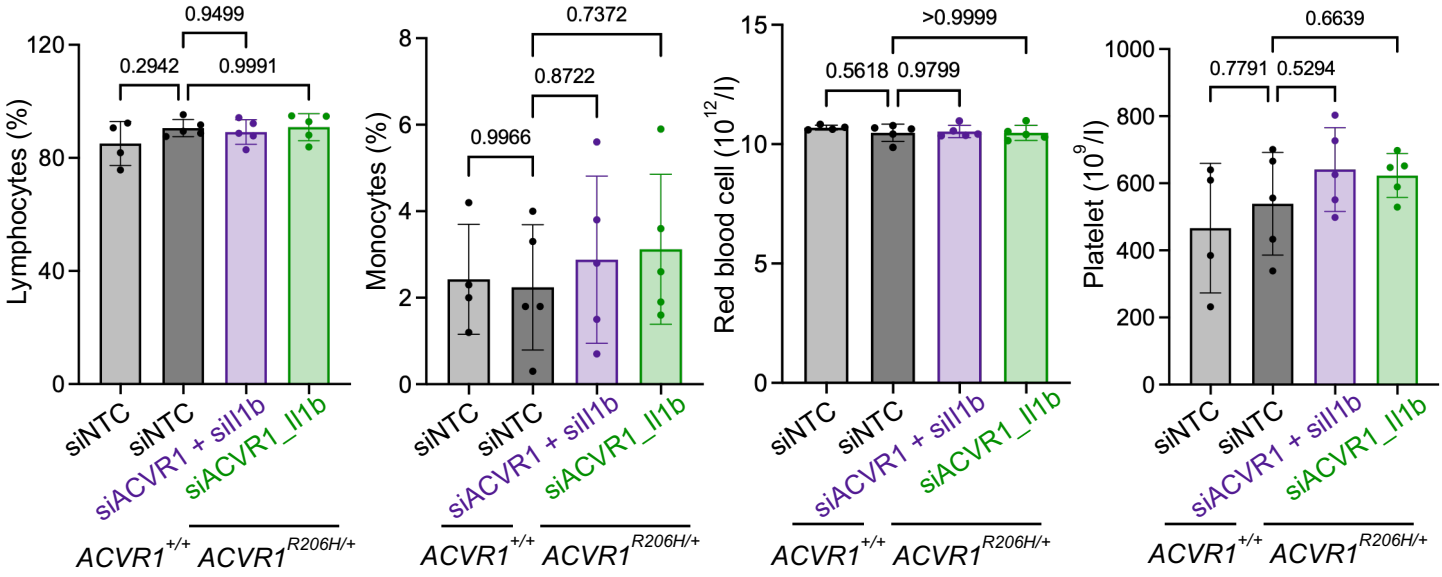

a
Silencing Efficacy of ACVR1R206H and Il1b in FOP Tissues Post-Treated with siACVR1+siIl1b or siACVR1_Il1b
Liver
Kidney
Muscle
ACVR1R206H mRNA (% of control)
0.0136
0.0151 0.9986
0.7866
0.874 0.9977
0.0038
0.041 0.7188
Il1b mRNA (% of control)
0.0932
0.0282 0.8134
0.5313
0.6104 0.990
<0.0001
0.0003 0.4771
siNTC
siACVR1 + siIl1b
siACVR1_Il1b
b
FOP muscle tissue 4 days post-injury (s.c. injection)
siNTC
siACVR1_Il1b
H&E
c
Silencing Efficacy of ACVR1R206H and Il1b in FOP Tissues Pre-Treated with siACVR1+siIl1b or siACVR1_Il1b
Liver
Kidney
Muscle
ACVR1R206H mRNA (% of control)
0.0022
0.0002 0.4200
0.2475
0.1390 0.9804
<0.0001
<0.0001 0.5895
Il1b mRNA (% of control)
0.0030
0.0011 0.9559
0.9718
0.4250 0.6685
<0.0001
<0.0001 0.9939
siNTC
siACVR1 + siIl1b
siACVR1_Il1b

Supplementary Figure 17. Silencing efficiency of *ACVR1*^{R206H} and *Il1b* in various tissues after systemic delivery of siRNAs.

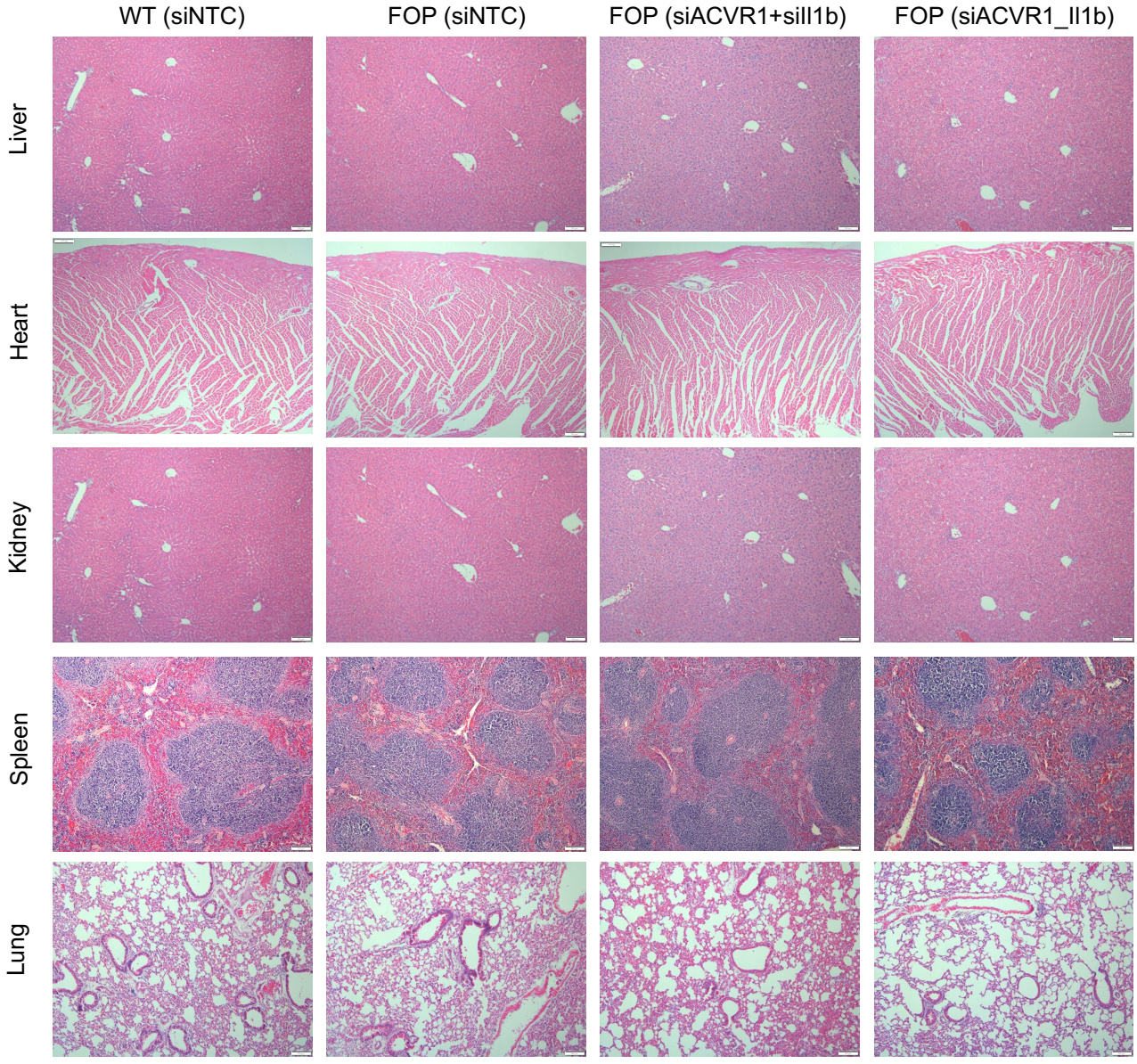
a. A single dose of siNTC, siACVR1+siIl1b, or siACVR1_Il1b (40 mg/kg) was injected subcutaneously (s.c.) into 8-week-old *ACVR1*$^{R206H/+}$ mice one day post-injury. Four weeks later, mRNA levels of *ACVR1*^{R206H} and *Il1b* in liver, kidney, and muscle were quantified by the Quantigene 2.0 assay (n = 5 mice). This is the same experiment of **Figure 6a**.

b, c. A single dose of siNTC, siACVR1+siIl1b, or siACVR1_Il1b (40 mg/kg) was injected s.c. into 8-week-old *ACVR1*$^{R206H/+}$ mice 10 days prior to pinch injury. Injured muscles were stained with H&E four days post-injury, demonstrating little to no difference in siRNA-treated muscles (n = 3 mice, **b**). Scale bars: 100 μm. Four weeks later, mRNA levels of *ACVR1*^{R206H} and *Il1b* in liver, kidney, and muscle were quantified by the Quantigene 2.0 assay (n = 5 mice, **c**). This is the same experiment of **Figures 6b and c**. Data are representative of two independent experiments. Values represent mean ± SD by one-way ANOVA with Sidak's multiple comparisons test (**a, c**).

a No Effects of siRNA Treatments on Circulating Lymphocytes, Monocytes, or Red Blood Cells: CBC Test



b Little to No Histological Changes in siRNA-Treated Tissues: H&E Staining

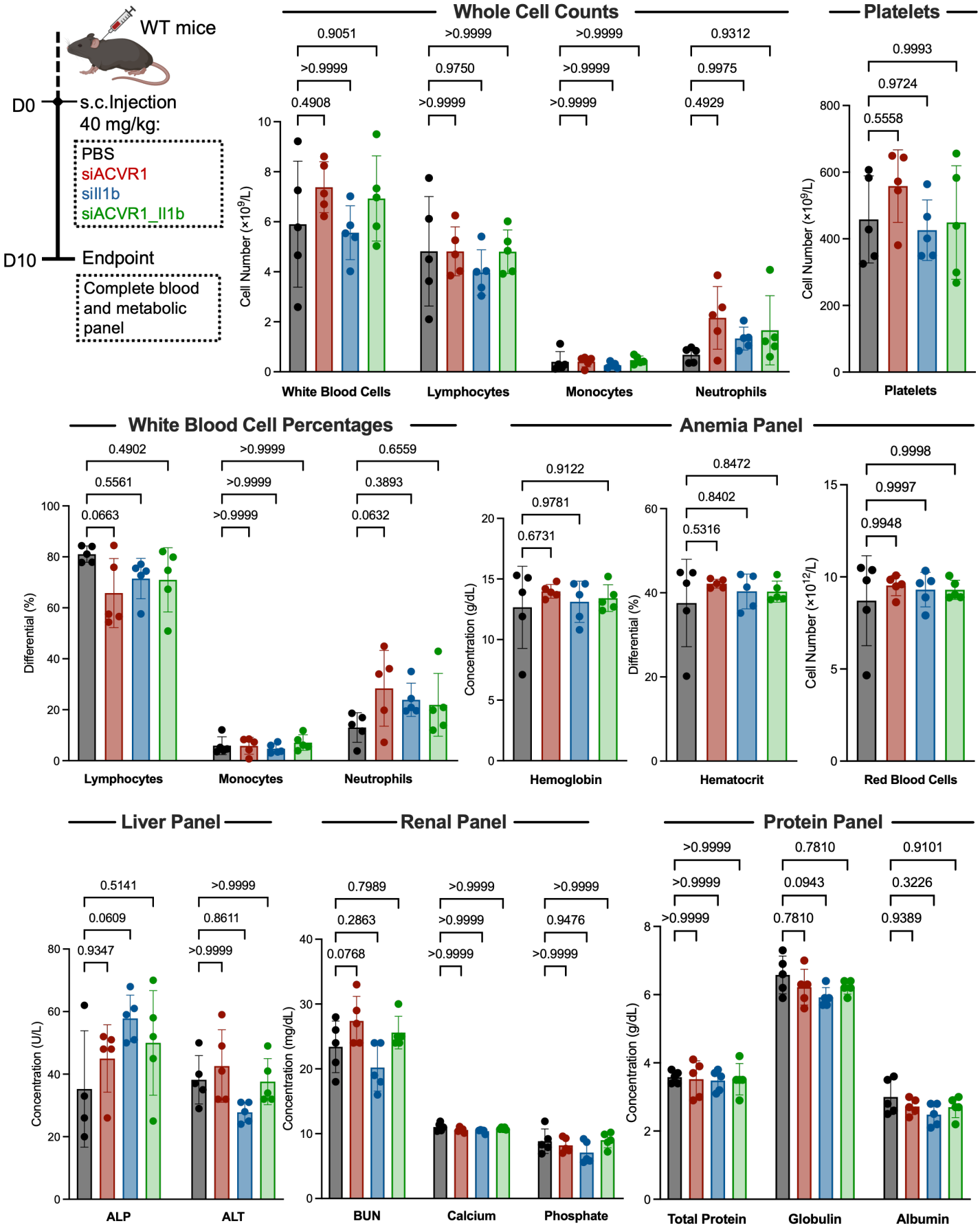


Supplementary Figure 18. No adverse effects of systemically delivered siRNAs in FOP mice.

a. A single dose of siNTC, siACVR1+siIl1b, or siACVR1_Il1b (40 mg/kg) was injected s.c. into 8-week-old WT (*ACVR1*$^{+/+}$) and FOP (*ACVR1*$^{R206H/+}$) mice 1 day post-injury. Four weeks later, peripheral blood was collected via cheek bleeding and then, subjected to complete blood count (CBC) test (n = 4-5 mice).

b. Alternatively, multiple tissues, including liver, heart, kidney, spleen, and lung, were harvested, paraffin-sectioned, and stained with hematoxylin and eosin (H&E) for histopathologic analysis (n = 5 mice, **b**). Scale bars: 100 μm. This is the same experiment of **Figure 6a.** Data are representative of two independent experiments. Values represent mean ± SD by one-way ANOVA with Dunnett's multiple comparisons test **(a)**.

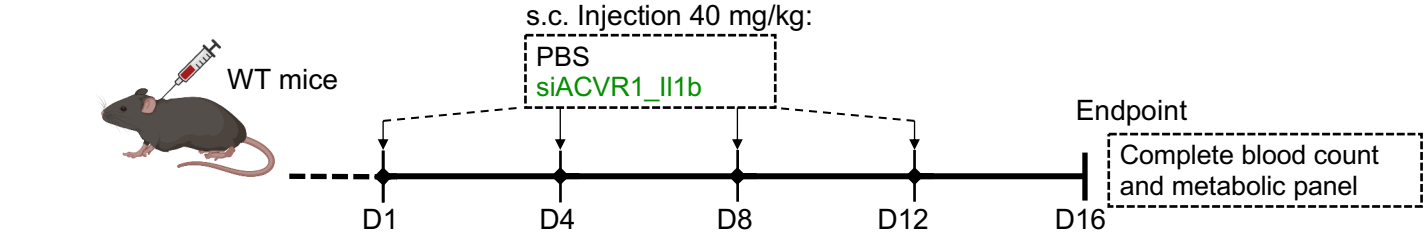
No Adverse Effects of Single Dose siRNA Treatment on Complete Blood Count or Metabolic Panel

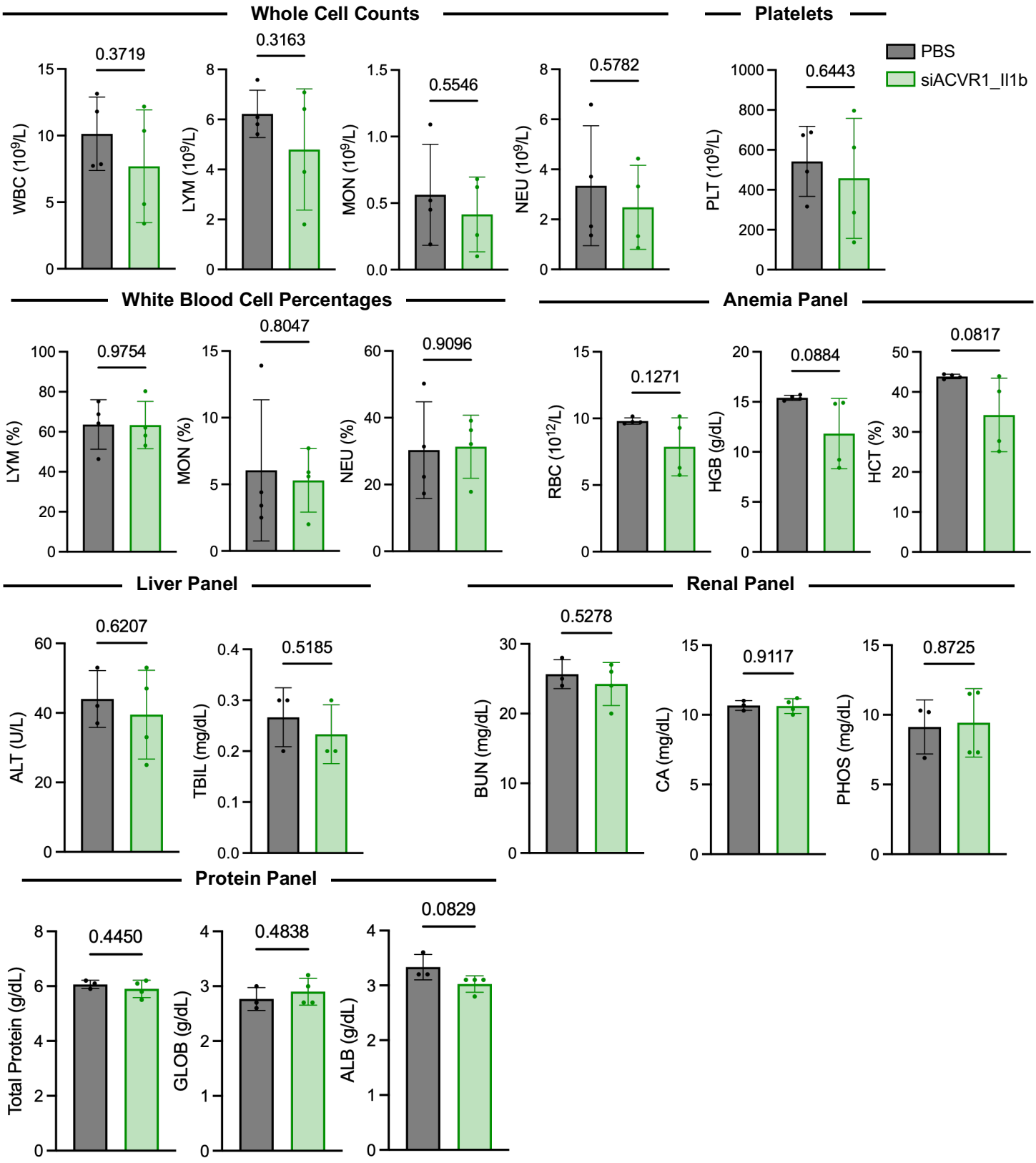


Supplementary Figure 19. Toxicology study shows no adverse effects of systemically delivered siRNAs in WT mice.

A single dose of PBS, siACVR1, siIl1b, or siACVR1_Il1b (40 mg/kg) was injected s.c. into 8-week-old WT mice (n = 4-5 mice). One week later, peripheral blood was collected via cheek bleeding and then, subjected to complete blood count (CBC) test to assess circulating immune cells, red blood cells, and levels of platelets, hemoglobin, and hematocrit. Alternatively, blood levels of globulin and albumin proteins, alkaline phosphatase (ALP) and alanine aminotransferase (ALT), and Bun, Calcium, and Phosphate were measured to assess blood, liver, and renal toxicities, respectively. Values represent mean ± SD by one-way ANOVA with Dunnett's multiple comparisons test. Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

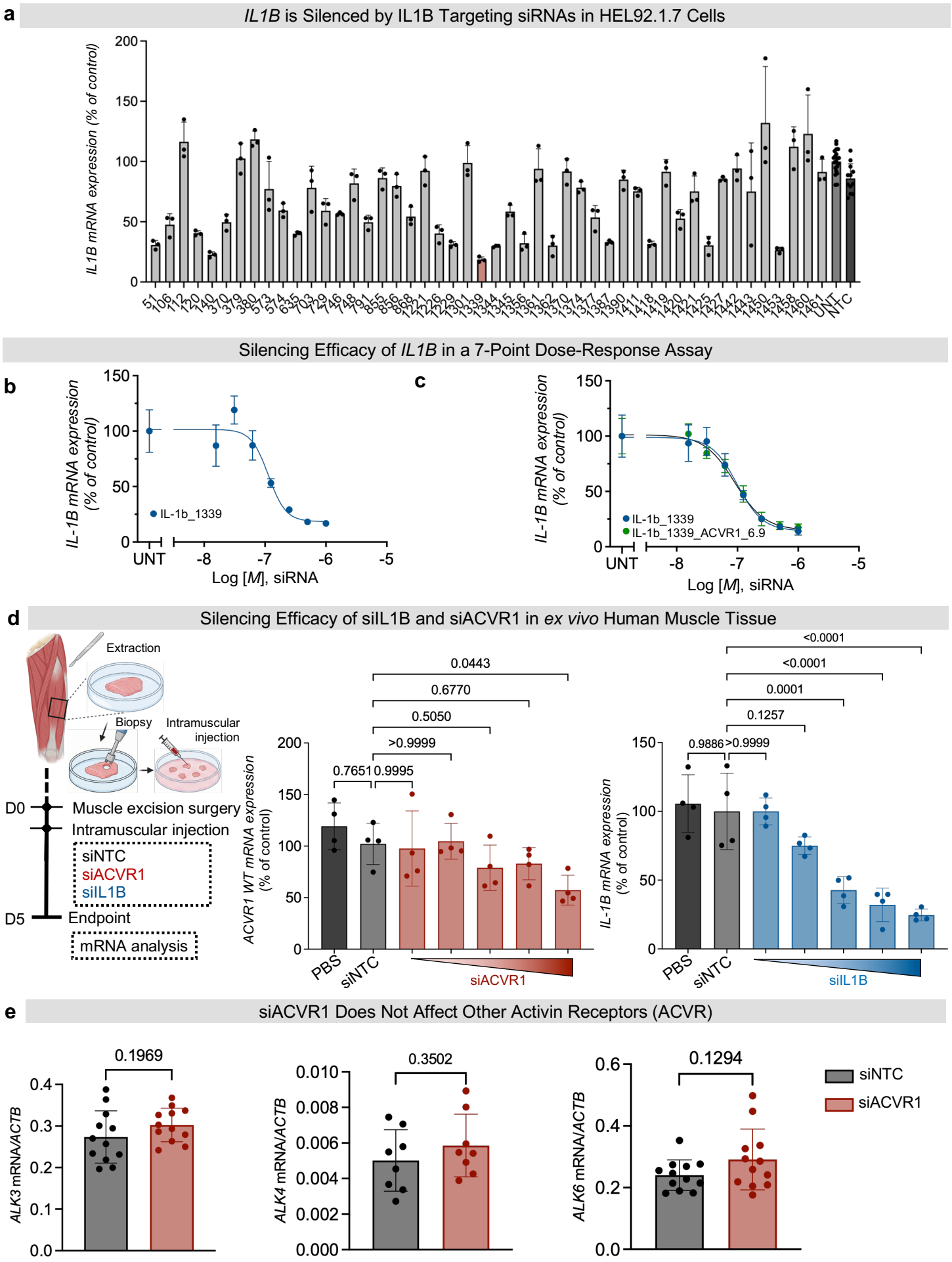
No Adverse Effects of siRNA Treatments on Complete Blood Count or Comprehensive Metabolic Panel





Supplementary Figure 20. Repeat-dose tolerability of siACVR1_Il1b in WT mice.

PBS or siACVR1_Il1b (40 mg/kg) was administered s.c. into 8-week-old WT mice (n = 4 mice) every 4 days for 16 days (4 doses total). Peripheral blood was collected via cheek bleeding and then, subjected to CBC test to assess circulating immune cells, red blood cells (RBC), platelets (PLT), hemoglobin (HGB), and hematocrit (HCT). Additionally, a comprehensive metabolic panel was performed to assess blood levels of total protein, globulin (GLOB), albumin (ALB), total bilirubin (TBL), alanine aminotransferase (ALT), blood-urea-nitrogen (BUN), calcium (CA), and phosphate (PHOS). No treatment-related changes were observed in any hematologic or metabolic parameter. Values represent mean ± SD by two-sided multiple unpaired t-tests. Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

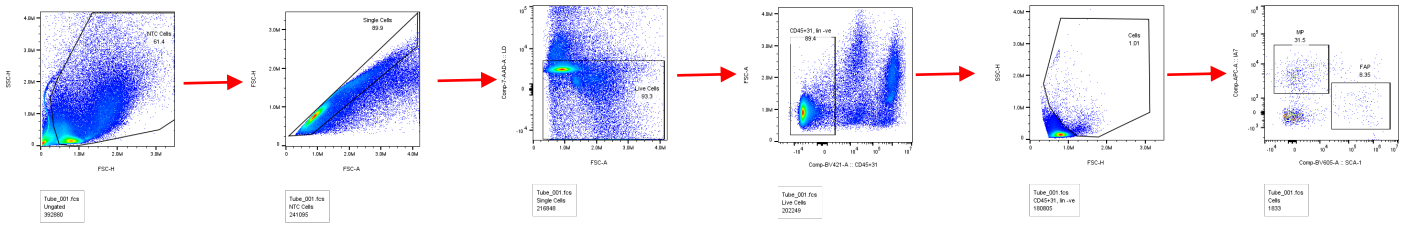

a
IL1B is Silenced by IL1B Targeting siRNAs in HEL92.1.7 Cells
IL1B mRNA expression (% of control)
200
150
100
50
0
51 106 112 120 140 370 379 380 573 514 635 703 729 746 748 791 855 856 868 1221 1226 1229 1301 1339 1344 1345 1356 1361 1362 1370 1374 1377 1387 1390 1411 1418 1419 1420 1421 1425 1427 1442 1443 1450 1453 1458 1460 1461 UNT NTC
Silencing Efficacy of IL1B in a 7-Point Dose-Response Assay
b
IL-1B mRNA expression (% of control)
150
100
50
0
IL-1b_1339
UNT -8 -7 -6 -5
Log [M], siRNA
c
IL-1B mRNA expression (% of control)
150
100
50
0
IL-1b_1339
IL-1b_1339_ACVR1_6.9
UNT -8 -7 -6 -5
Log [M], siRNA
d
Silencing Efficacy of siIL1B and siACVR1 in ex vivo Human Muscle Tissue
Extraction
Biopsy
Intramuscular injection
D0
Muscle excision surgery
Intramuscular injection
siNTC
siACVR1
siIL1B
D5
Endpoint
mRNA analysis
ACVR1 WT mRNA expression (% of control)
0.0443
0.6770
0.5050
>0.9999
0.7651
0.9995
200
150
100
50
0
PBS
siNTC
siACVR1
IL-1B mRNA expression (% of control)
<0.0001
<0.0001
0.0001
0.1257
0.9886
>0.9999
150
100
50
0
PBS
siNTC
siIL1B
e
siACVR1 Does Not Affect Other Activin Receptors (ACVR)
ALK3 mRNA/ACTB
0.1969
0.4
0.3
0.2
0.1
0.0
ALK4 mRNA/ACTB
0.3502
0.010
0.008
0.006
0.004
0.002
0.000
ALK6 mRNA/ACTB
0.1294
0.6
0.4
0.2
0.0
siNTC
siACVR1

Supplementary Figure 21. Development of the siRNA targeting human *IL1B* mRNA.

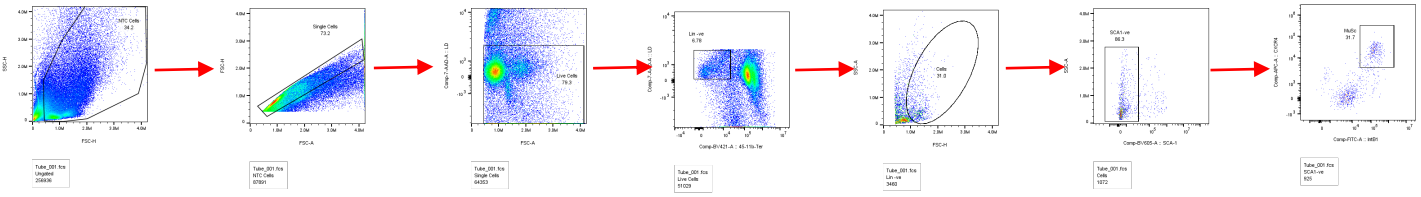
a-c. The human lymphoblastic cell line HEL92.1.7 was treated with a panel of 48 siRNAs targeting human *IL1B* mRNA and siNTC. Three days later, mRNA levels of *IL-1B* were measured using the Quantigene 2.0 assay (n = 3 wells, **a**). UNT: untreated control, siNTC: non-targeting control siRNA. HEL92.1.7 cells were treated with the lead siRNA, IL1B_1339 in a 7-point dose response, and mRNA levels of *IL1B* were measured (n = 3 wells, **b**). Alternatively, a unimolecular structure comprising of both lead compound IL1B_1339 and ACVR1_6.9 were tested in human peripheral blood mononuclear cells (PBMCs) in a 7-point dose response, and mRNA levels of *IL1B* were measured (n = 3 wells, **c**).

d, e. Schematic of administering siRNAs into human muscle biopsies (8 mm) in a 5-point dose response following intramuscular injection of siRNAs (50 uL of 200 uM siRNA/biopsy, 10 nmol top dose/biopsy). Both WT *ACVR1* and *IL-1B* mRNA silencing four days post intramuscular injection (n = 4 biopsies, **d**). Alternatively, mRNA levels of the closely related paralogs *ALK3*, *ALK4*, and *ALK6* were assessed by qRT-PCR (n = 8-13 biopsies). Expression of all three paralogs remained comparable between siNTC- and siACVR1-treated tissues (**e**). Values represent mean ± SD by one-way ANOVA with Dunnett's multiple comparisons test (**d**) and two-sided Welch's t-test (**e**). Created in BioRender. Gross, K. (2026) https://BioRender.com/ybyow46.

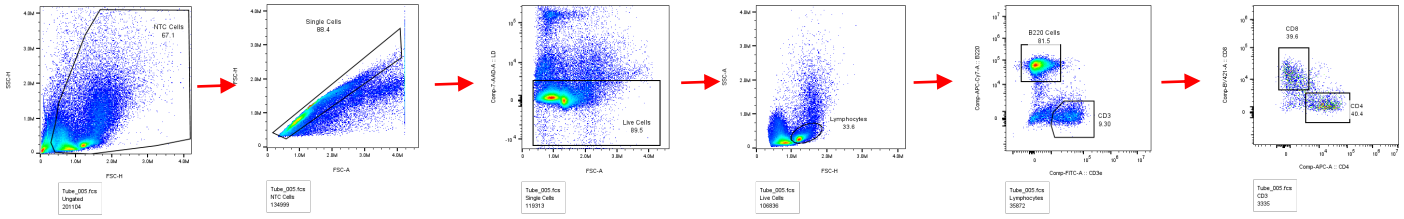
a FAP Cells (Lin$^-$Int-α7$^-$Sca-1$^+$)



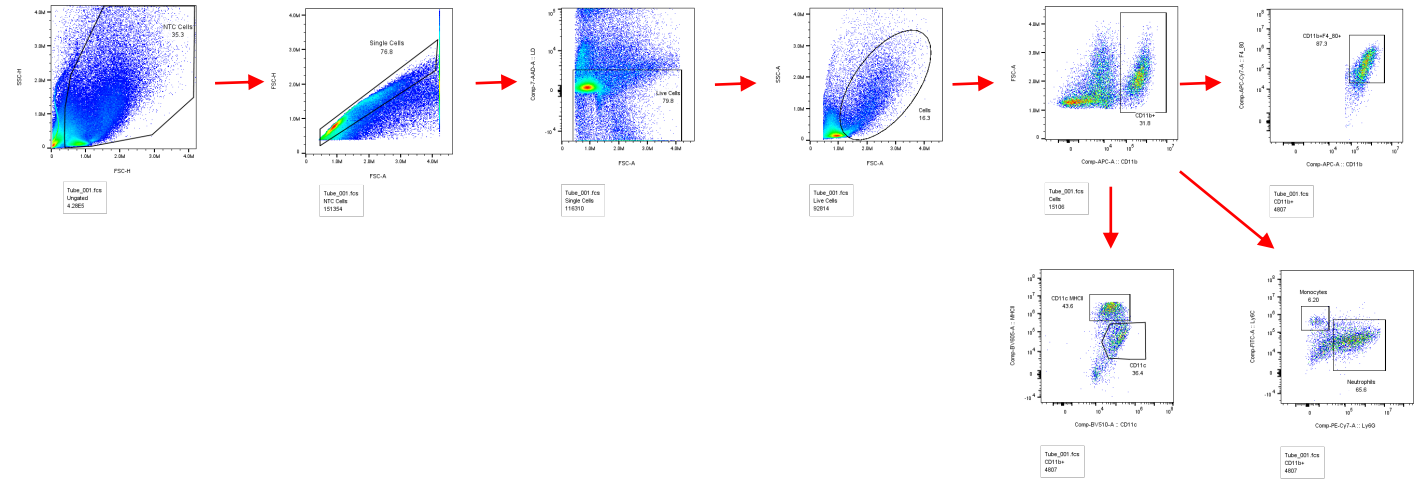
b Satellite Cells (Lin$^-$Sca-1$^-$ Int-β1$^+$CXCR4$^+$)



c T cells (CD3$^+$CD4$^+$, CD3$^+$CD8$^+$), B cells (B220$^+$)



d Macrophages (CD11b$^+$F4/80$^+$), Dendritic cells (CD11c$^+$MHCII$^+$)
Monocytes (CD11b$^+$Ly6c$^+$Ly6g$^-$), Neutrophils (CD11b$^+$Ly6c$^+$Ly6g$^+$),



Supplementary Figure 22. Gating strategy for flow cytometric analysis and sorting of muscle-resident cell populations.

Cells were isolated from digested tibial muscle near the site of injury. In all panels, debris was excluded on FSC-H versus SSC-H, doublets were excluded on FSC-A versus FSC-H, and dead cells were excluded as 7-AAD$^+$.

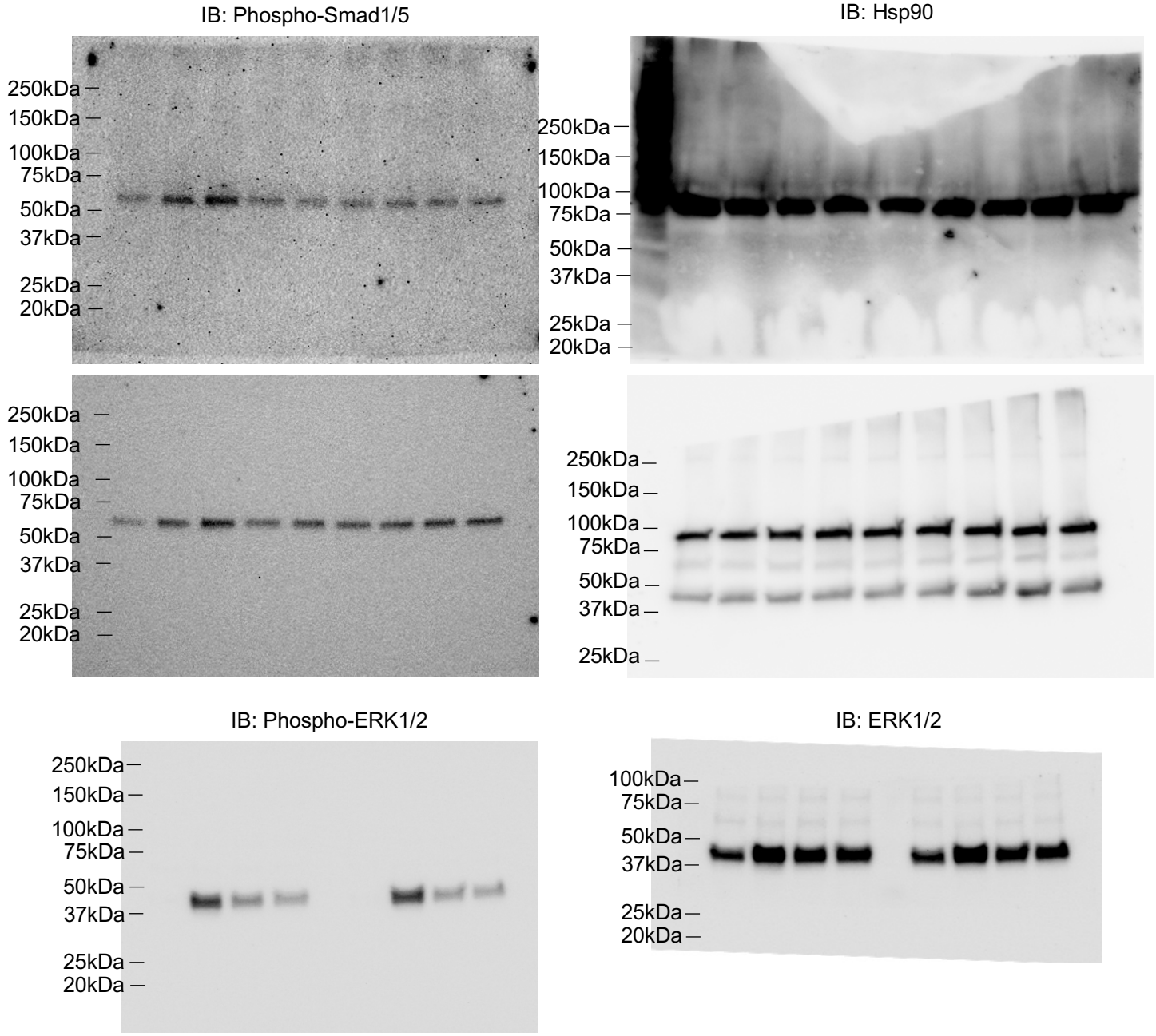
a. Fibro-adipogenic progenitors (FAPs). Lineage-positive cells were excluded using a combined CD45 and CD31 gate (Lin−), and Lin− cells were resolved on SCA-1 versus α7-integrin. FAPs were gated as Lin$^-$α7-integrin$^-$SCA-1$^+$ and myogenic progenitors (MP) as Lin$^-$α7-integrin$^+$SCA-1$^-$. In PDGFRα-GFP mice this FAP population is GFP$^+$.

b. Muscle satellite cells (MuSc). Lin$^-$SCA-1$^-$ cells were resolved on integrin-β1 versus CXCR4, and MuScs were gated as integrin-β1$^+$CXCR4$^+$.

c. T and B lymphocytes. Live cells were gated on lymphocyte forward and side scatter, then resolved on CD3 versus B220. B cells were gated as B220$^+$ and T cells as CD3$^+$, and CD3$^+$ cells were further resolved into CD4$^+$ and CD8$^+$ subsets.

d. Myeloid populations. Live cells were resolved on CD11b, and CD11b$^+$ cells were further gated as macrophages (F4/80$^+$), dendritic cells (CD11c$^+$MHCII$^+$), monocytes (Ly6C$^+$Ly6G$^-$) and neutrophils (Ly6C$^+$Ly6G$^+$).

Numbers adjacent to each gate indicate the percentage of the parent population. Representative plots are shown.



Uncropped Western Blot Images. Top and middle rows, phospho-Smad1/5 (left) and Hsp90 (right) corresponding to Supplementary Figure 4b, shown for two independent experiments. Bottom row, phospho-ERK1/2 (left) and ERK1/2 (right) corresponding to Supplementary Figure 5c. In each case the loading control was probed on the same membrane as the target protein.

Supplementary Table 1. Sequences and chemical modification patterns of human *ACVR1*^{R206H} siRNAs (Primary mismatch).

Oligo Name	Sequence
ACVR1_2	P(mU)#(fU)#(mG)(fA)(fG)(fC)(mC)(fA)(mC)(fU)(mG)(fU)(mU)(fC)#(mU)#(fU)#(mU)#(mG)#(mU)#(mA)#(fA)
	(mA)#(mA)#(mG)(fA)(mA)(fC)(mA)(fG)(mU)(fG)(mG)(mC)(mU)(fC)#(mA)#(mA)-TegChol
ACVR1_3	P(mU)#(fG)#(mU)(fG)(fA)(fG)(mC)(fC)(mA)(fC)(mU)(fG)(mU)(fU)#(mC)#(fU)#(mU)#(mU)#(mG)#(mU)#(fA)
	(mA)#(mG)#(mA)(fA)(mC)(fA)(mG)(fU)(mG)(fG)(mC)(mU)(mC)(fA)#(mC)#(mA)-TegChol
ACVR1_4	P(mU)#(fG)#(mG)(fU)(fG)(fA)(mG)(fC)(mC)(fA)(mC)(fU)(mG)(fU)#(mU)#(fC)#(mU)#(mU)#(mU)#(mG)#(fA)
	(mG)#(mA)#(mA)(fC)(mA)(fG)(mU)(fG)(mG)(fC)(mU)(mC)(mA)(fC)#(mC)#(mA)-TegChol
ACVR1_5	P(mU)#(fU)#(mG)(fG)(fU)(fG)(mA)(fG)(mC)(fC)(mA)(fC)(mU)(fG)#(mU)#(fU)#(mC)#(mU)#(mU)#(mU)#(fA)
	(mA)#(mA)#(mC)(fA)(mG)(fU)(mG)(fG)(mC)(fU)(mC)(mA)(mC)(fC)#(mA)#(mA)-TegChol
ACVR1_6	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_7	P(mU)#(fU)#(mC)(fU)(fG)(fG)(mU)(fG)(mA)(fG)(mC)(fC)(mA)(fC)#(mU)#(fG)#(mU)#(mU)#(mC)#(mU)#(fA)
	(mC)#(mA)#(mG)(fU)(mG)(fG)(mC)(fU)(mC)(fA)(mC)(mC)(mA)(fG)#(mA)#(mA)-TegChol
ACVR1_8	P(mU)#(fA)#(mU)(fC)(fU)(fG)(mG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)#(mC)#(fU)#(mG)#(mU)#(mU)#(mC)#(fA)
	(mA)#(mG)#(mU)(fG)(mG)(fC)(mU)(fC)(mA)(fC)(mC)(mA)(mG)(fA)#(mU)#(mA)-TegChol
ACVR1_9	P(mU)#(fA)#(mA)(fU)(fC)(fU)(mG)(fG)(mU)(fG)(mA)(fG)(mC)(fC)#(mA)#(fC)#(mU)#(mG)#(mU)#(mU)#(fA)
	(mG)#(mU)#(mG)(fG)(mC)(fU)(mC)(fA)(mC)(fC)(mA)(mG)(mA)(fU)#(mU)#(mA)-TegChol
ACVR1_10	P(mU)#(fU)#(mA)(fA)(fU)(fC)(mU)(fG)(mG)(fU)(mG)(fA)(mG)(fC)#(mC)#(fA)#(mC)#(mU)#(mG)#(mU)#(fA)
	(mU)#(mG)#(mG)(fC)(mU)(fC)(mA)(fC)(mC)(fA)(mG)(mA)(mU)(fU)#(mA)#(mA)-TegChol
ACVR1_11	P(mU)#(fG)#(mU)(fA)(fA)(fU)(mC)(fU)(mG)(fG)(mU)(fG)(mA)(fG)#(mC)#(fC)#(mA)#(mC)#(mU)#(mG)#(fA)
	(mG)#(mG)#(mC)(fU)(mC)(fA)(mC)(fC)(mA)(fG)(mA)(mU)(mU)(fA)#(mC)#(mA)-TegChol
ACVR1_12	P(mU)#(fU)#(mG)(fU)(fA)(fA)(mU)(fC)(mU)(fG)(mG)(fU)(mG)(fA)#(mG)#(fC)#(mC)#(mA)#(mC)#(mU)#(fA)
	(mG)#(mC)#(mU)(fC)(mA)(fC)(mC)(fA)(mG)(fA)(mU)(mU)(mA)(fC)#(mA)#(mA)-TegChol
ACVR1_13	P(mU)#(fG)#(mU)(fG)(fU)(fA)(mA)(fU)(mC)(fU)(mG)(fG)(mU)(fG)#(mA)#(fG)#(mC)#(mC)#(mA)#(mC)#(fA)
	(mC)#(mU)#(mC)(fA)(mC)(fC)(mA)(fG)(mA)(fU)(mU)(mA)(mC)(fA)#(mC)#(mA)-TegChol
ACVR1_14	P(mU)#(fA)#(mG)(fU)(fG)(fU)(mA)(fA)(mU)(fC)(mU)(fG)(mG)(fU)#(mG)#(fA)#(mG)#(mC)#(mC)#(mA)#(fA)
	(mU)#(mC)#(mA)(fC)(mC)(fA)(mG)(fA)(mU)(fU)(mA)(mC)(mA)(fC)#(mU)#(mA)-TegChol
ACVR1_15	P(mU)#(fC)#(mA)(fG)(fU)(fG)(mU)(fA)(mA)(fU)(mC)(fU)(mG)(fG)#(mU)#(fG)#(mA)#(mG)#(mC)#(mC)#(fA)

	(mC)#(mA)#(mC)(fC)(mA)(fG)(mA)(fU)(mU)(fA)(mC)(mA)(mC)(fU)#(mG)#(mA)-TegChol
ACVR1_16	P(mU)#(fA)#(mC)(fA)(fG)(fU)(mG)(fU)(mA)(fA)(mU)(fC)(mU)(fG)#(mG)#(fU)#(mG)#(mA)#(mG)#(mC)#(fA)
	(mA)#(mC)#(mC)(fA)(mG)(fA)(mU)(fU)(mA)(fC)(mA)(mC)(mU)(fG)#(mU)#(mA)-TegChol
ACVR1_17	P(mU)#(fA)#(mA)(fC)(fA)(fG)(mU)(fG)(mU)(fA)(mA)(fU)(mC)(fU)#(mG)#(fG)#(mU)#(mG)#(mA)#(mG)#(fA)
	(mC)#(mC)#(mA)(fG)(mA)(fU)(mU)(fA)(mC)(fA)(mC)(mU)(mG)(fU)#(mU)#(mA)-TegChol

Supplementary Table 2. Sequences and chemical modification patterns of human *ACVR1*^{R206H} siRNAs (Secondary mismatch).

Oligo Name	Sequence
ACVR1_6_2	P(mU)#(fU)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mA)#(mA)-TegChol
ACVR1_6_3	P(mU)#(fC)#(mA)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fU)#(mG)#(mA)-TegChol
ACVR1_6_4	P(mU)#(fC)#(mU)(fU)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mA)(fA)#(mG)#(mA)-TegChol
ACVR1_6_5	P(mU)#(fC)#(mU)(fG)(fU)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mA)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_7	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mU)(fA)(mG)(fC)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mG)(fC)(mU)(fA)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_8	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fU)(mG)(fC)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mG)(fC)(mA)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_9	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mU)(fC)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mG)(fA)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_10	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fA)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mU)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_11	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mA)(fA)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fU)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_12	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fU)(mC)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mA)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_13	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mA)(fU)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fU)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_14	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mC)(fA)#(mG)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mU)(fG)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_15	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mC)(fU)#(mU)#(fU)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mA)#(mA)(fG)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_16	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mC)(fU)#(mG)#(fA)#(mU)#(mC)#(mU)#(mU)#(fA)
	(mU)#(mC)#(mA)(fG)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
ACVR1_6_17	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fA)(mG)(fC)(mC)(fA)(mC)(fU)#(mG)#(fU)#(mA)#(mC)#(mU)#(mU)#(fA)
	(mA)#(mC)#(mA)(fG)(mU)(fG)(mG)(fC)(mU)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol

Supplementary Table 3. Sequences and chemical modification patterns of mouse *Il1b* siRNAs.

Oligo Name	Sequence
Il1b_NM_008361_1293	P(mU)#(fA)#(mA)(fA)(fG)(fC)(mA)(fA)(mU)(fG)(mU)(fG)(mC)(fU)#(mG)#(fG)#(mU)#(mG)#(mC)#(mU)#(fU)
	(mC)#(mC)#(mA)(fG)(mC)(fA)(mC)(fA)(mU)(fU)(mG)(mC)(mU)(fU)#(mU)#(mA)-TegChol
Il1b_NM_008361_1263	P(mU)#(fA)#(mA)(fG)(fU)(fC)(mU)(fC)(mA)(fU)(mC)(fC)(mA)(fU)#(mA)#(fU)#(mU)#(mA)#(mU)#(mU)#(fU)
	(mA)#(mU)#(mA)(fU)(mG)(fG)(mA)(fU)(mG)(fA)(mG)(mA)(mC)(fU)#(mU)#(mA)-TegChol
Il1b_NM_008361_856	P(mU)#(fU)#(mG)(fA)(fA)(fG)(mU)(fC)(mA)(fA)(mU)(fU)(mA)(fU)#(mG)#(fU)#(mC)#(mC)#(mU)#(mU)#(fU)
	(mA)#(mC)#(mA)(fU)(mA)(fA)(mU)(fU)(mG)(fA)(mC)(mU)(mU)(fC)#(mA)#(mA)-TegChol
Il1b_NM_008361_1245	P(mU)#(fA)#(mG)(fG)(fA)(fA)(mC)(fC)(mU)(fA)(mU)(fU)(mU)(fA)#(mU)#(fU)#(mC)#(mU)#(mC)#(mU)#(fU)
	(mA)#(mA)#(mU)(fA)(mA)(fA)(mU)(fA)(mG)(fG)(mU)(mU)(mC)(fC)#(mU)#(mA)-TegChol
Il1b_NM_008361_1092	P(mU)#(fU)#(mA)(fA)(fA)(fU)(mA)(fA)(mA)(fU)(mA)(fG)(mG)(fU)#(mA)#(fA)#(mG)#(mU)#(mG)#(mU)#(fU)
	(mU)#(mU)#(mA)(fC)(mC)(fU)(mA)(fU)(mU)(fU)(mA)(mU)(mU)(fU)#(mA)#(mA)-TegChol
Il1b_NM_008361_1117	P(mU)#(fA)#(mU)(fA)(fG)(fA)(mU)(fC)(mA)(fA)(mC)(fC)(mA)(fA)#(mU)#(fC)#(mA)#(mA)#(mU)#(mU)#(fU)
	(mG)#(mA)#(mU)(fU)(mG)(fG)(mU)(fU)(mG)(fA)(mU)(mC)(mU)(fA)#(mU)#(mA)-TegChol
Il1b_NM_008361_1108	P(mU)#(fC)#(mC)(fA)(fA)(fU)(mC)(fA)(mA)(fU)(mA)(fA)(mA)(fU)#(mA)#(fC)#(mA)#(mU)#(mA)#(mU)#(fU)
	(mG)#(mU)#(mA)(fU)(mU)(fU)(mA)(fU)(mU)(fG)(mA)(mU)(mU)(fG)#(mG)#(mA)-TegChol
Il1b_NM_008361_1118	P(mU)#(fA)#(mA)(fU)(fA)(fG)(mA)(fU)(mC)(fA)(mA)(fC)(mC)(fA)#(mA)#(fU)#(mC)#(mA)#(mA)#(mU)#(fU)
	(mA)#(mU)#(mU)(fG)(mG)(fU)(mU)(fG)(mA)(fU)(mC)(mU)(mA)(fU)#(mU)#(mA)-TegChol
Il1b_NM_008361_1244	P(mU)#(fG)#(mG)(fA)(fA)(fC)(mC)(fU)(mA)(fU)(mU)(fU)(mA)(fU)#(mU)#(fC)#(mU)#(mC)#(mA)#(mU)#(fU)
	(mG)#(mA)#(mA)(fU)(mA)(fA)(mA)(fU)(mA)(fG)(mG)(mU)(mU)(fC)#(mC)#(mA)-TegChol
Il1b_NM_008361_1080	P(mU)#(fU)#(mA)(fA)(fG)(fU)(mG)(fG)(mU)(fU)(mG)(fC)(mC)(fC)#(mA)#(fU)#(mC)#(mA)#(mG)#(mU)#(fU)
	(mA)#(mU)#(mG)(fG)(mG)(fC)(mA)(fA)(mC)(fC)(mA)(mC)(mU)(fU)#(mA)#(mA)-TegChol
Il1b_NM_008361_1127	P(mU)#(fA)#(mU)(fC)(fA)(fA)(mC)(fU)(mU)(fA)(mA)(fA)(mU)(fA)#(mG)#(fA)#(mU)#(mC)#(mA)#(mU)#(fU)
	(mU)#(mC)#(mU)(fA)(mU)(fU)(mU)(fA)(mA)(fG)(mU)(mU)(mG)(fA)#(mU)#(mA)-TegChol
Il1b_NM_008361_1081	P(mU)#(fG)#(mU)(fA)(fA)(fG)(mU)(fG)(mG)(fU)(mU)(fG)(mC)(fC)#(mC)#(fA)#(mU)#(mC)#(mA)#(mU)#(fU)
	(mU)#(mG)#(mG)(fG)(mC)(fA)(mA)(fC)(mC)(fA)(mC)(mU)(mU)(fA)#(mC)#(mA)-TegChol
Il1b_NM_008361_266	P(mU)#(fA)#(mG)(fU)(fG)(fA)(mU)(fA)(mC)(fU)(mG)(fC)(mC)(fU)#(mG)#(fC)#(mC)#(mU)#(mG)#(mU)#(fU)
	(mG)#(mC)#(mA)(fG)(mG)(fC)(mA)(fG)(mU)(fA)(mU)(mC)(mA)(fC)#(mU)#(mA)-TegChol
Il1b_NM_008361_1282	P(mU)#(fC)#(mU)(fG)(fG)(fU)(mG)(fC)(mU)(fU)(mC)(fA)(mU)(fU)#(mC)#(fA)#(mU)#(mA)#(mA)#(mU)#(fU)
	(mU)#(mG)#(mA)(fA)(mU)(fG)(mA)(fA)(mG)(fC)(mA)(mC)(mC)(fA)#(mG)#(mA)-TegChol
Il1b_NM_008361_1296	P(mU)#(fA)#(mU)(fC)(fA)(fA)(mA)(fG)(mC)(fA)(mA)(fU)(mG)(fU)#(mG)#(fC)#(mU)#(mG)#(mG)#(mU)#(fU)
	(mG)#(mC)#(mA)(fC)(mA)(fU)(mU)(fG)(mC)(fU)(mU)(mU)(mG)(fA)#(mU)#(mA)-TegChol
Il1b_NM_008361_1085	P(mU)#(fA)#(mU)(fA)(fG)(fG)(mU)(fA)(mA)(fG)(mU)(fG)(mG)(fU)#(mU)#(fG)#(mC)#(mC)#(mC)#(mU)#(fU)
	(mC)#(mA)#(mA)(fC)(mC)(fA)(mC)(fU)(mU)(fA)(mC)(mC)(mU)(fA)#(mU)#(mA)-TegChol
Il1b_NM_008361_133	P(mU)#(fA)#(mC)(fA)(fG)(fG)(mU)(fC)(mA)(fU)(mU)(fC)(mU)(fC)#(mA)#(fU)#(mC)#(mA)#(mC)#(mU)#(fU)
	(mA)#(mU)#(mG)(fA)(mG)(fA)(mA)(fU)(mG)(fA)(mC)(mC)(mU)(fG)#(mU)#(mA)-TegChol
Il1b_NM_008361_137	P(mU)#(fA)#(mA)(fG)(fA)(fA)(mC)(fA)(mG)(fG)(mU)(fC)(mA)(fU)#(mU)#(fC)#(mU)#(mC)#(mA)#(mU)#(fU)

	(mG)#(mA)#(mA)(fU)(mG)(fA)(mC)(fC)(mU)(fG)(mU)(mU)(mC)(fU)#(mU)#(mA)-TegChol
Il1b_NM_008361_431	P(mU)#(fC)#(mU)(fA)(fA)(fU)(mG)(fG)(mG)(fA)(mA)(fC)(mG)(fU)#(mC)#(fA)#(mC)#(mA)#(mC)#(mU)#(fU)
	(mU)#(mG)#(mA)(fC)(mG)(fU)(mU)(fC)(mC)(fC)(mA)(mU)(mU)(fA)#(mG)#(mA)-TegChol
Il1b_NM_008361_1128	P(mU)#(fA)#(mA)(fU)(fC)(fA)(mA)(fC)(mU)(fU)(mA)(fA)(mA)(fU)#(mA)#(fG)#(mA)#(mU)#(mC)#(mU)#(fU)
	(mC)#(mU)#(mA)(fU)(mU)(fU)(mA)(fA)(mG)(fU)(mU)(mG)(mA)(fU)#(mU)#(mA)-TegChol
Il1b_NM_008361_1215	P(mU)#(fA)#(mG)(fA)(fC)(fC)(mU)(fC)(mA)(fG)(mU)(fG)(mC)(fG)#(mG)#(fG)#(mC)#(mU)#(mA)#(mU)#(fU)
	(mC)#(mC)#(mC)(fG)(mC)(fA)(mC)(fU)(mG)(fA)(mG)(mG)(mU)(fC)#(mU)#(mA)-TegChol
Il1b_NM_008361_802	P(mU)#(fC)#(mU)(fG)(fC)(fU)(mU)(fG)(mU)(fG)(mA)(fG)(mG)(fU)#(mG)#(fC)#(mU)#(mG)#(mA)#(mU)#(fU)
	(mG)#(mC)#(mA)(fC)(mC)(fU)(mC)(fA)(mC)(fA)(mA)(mG)(mC)(fA)#(mG)#(mA)-TegChol
Il1b_NM_008361_871	P(mU)#(fA)#(mC)(fA)(fC)(fG)(mG)(fA)(mU)(fU)(mC)(fC)(mA)(fU)#(mG)#(fG)#(mU)#(mG)#(mA)#(mU)#(fU)
	(mC)#(mC)#(mA)(fU)(mG)(fG)(mA)(fA)(mU)(fC)(mC)(mG)(mU)(fG)#(mU)#(mA)-TegChol
Il1b_NM_008361_90	P(mU)#(fG)#(mA)(fG)(fU)(fU)(mC)(fA)(mG)(fG)(mA)(fA)(mC)(fA)#(mG)#(fU)#(mU)#(mG)#(mC)#(mU)#(fU)
	(mA)#(mC)#(mU)(fG)(mU)(fU)(mC)(fC)(mU)(fG)(mA)(mA)(mC)(fU)#(mC)#(mA)-TegChol
Il1b_NM_008361_388	P(mU)#(fA)#(mU)(fG)(fA)(fG)(mU)(fC)(mA)(fC)(mA)(fG)(mA)(fG)#(mG)#(fA)#(mU)#(mG)#(mG)#(mU)#(fU)
	(mU)#(mC)#(mC)(fU)(mC)(fU)(mG)(fU)(mG)(fA)(mC)(mU)(mC)(fA)#(mU)#(mA)-TegChol
Il1b_NM_008361_376	P(mU)#(fG)#(mG)(fA)(fU)(fG)(mG)(fG)(mC)(fU)(mC)(fU)(mU)(fC)#(mU)#(fU)#(mC)#(mA)#(mA)#(mU)#(fU)
	(mA)#(mA)#(mG)(fA)(mA)(fG)(mA)(fG)(mC)(fC)(mC)(mA)(mU)(fC)#(mC)#(mA)-TegChol
Il1b_NM_008361_548	P(mU)#(fG)#(mA)(fG)(fA)(fA)(mU)(fA)(mU)(fC)(mA)(fC)(mU)(fU)#(mG)#(fU)#(mU)#(mG)#(mG)#(mU)#(fU)
	(mA)#(mC)#(mA)(fA)(mG)(fU)(mG)(fA)(mU)(fA)(mU)(mU)(mC)(fU)#(mC)#(mA)-TegChol
Il1b_NM_008361_96	P(mU)#(fA)#(mC)(fA)(fG)(fU)(mU)(fG)(mA)(fG)(mU)(fU)(mC)(fA)#(mG)#(fG)#(mA)#(mA)#(mC)#(mU)#(fU)
	(mC)#(mC)#(mU)(fG)(mA)(fA)(mC)(fU)(mC)(fA)(mA)(mC)(mU)(fG)#(mU)#(mA)-TegChol
Il1b_NM_008361_346	P(mU)#(fA)#(mG)(fA)(fA)(fG)(mG)(fU)(mG)(fC)(mU)(fC)(mA)(fU)#(mG)#(fU)#(mC)#(mC)#(mU)#(mU)#(fU)
	(mA)#(mC)#(mA)(fU)(mG)(fA)(mG)(fC)(mA)(fC)(mC)(mU)(mU)(fC)#(mU)#(mA)-TegChol
Il1b_NM_008361_1261	P(mU)#(fG)#(mU)(fC)(fU)(fC)(mA)(fU)(mC)(fC)(mA)(fU)(mA)(fU)#(mU)#(fA)#(mU)#(mA)#(mG)#(mU)#(fU)
	(mU)#(mA)#(mA)(fU)(mA)(fU)(mG)(fG)(mA)(fU)(mG)(mA)(mG)(fA)#(mC)#(mA)-TegChol
Il1b_NM_008361_1104	P(mU)#(fU)#(mC)(fA)(fA)(fU)(mA)(fA)(mA)(fU)(mA)(fC)(mA)(fU)#(mA)#(fA)#(mA)#(mU)#(mA)#(mU)#(fU)
	(mU)#(mU)#(mA)(fU)(mG)(fU)(mA)(fU)(mU)(fU)(mA)(mU)(mU)(fG)#(mA)#(mA)-TegChol
Il1b_NM_008361_338	P(mU)#(fC)#(mU)(fC)(fA)(fU)(mG)(fU)(mC)(fC)(mU)(fC)(mA)(fU)#(mC)#(fC)#(mU)#(mG)#(mG)#(mU)#(fU)
	(mG)#(mG)#(mA)(fU)(mG)(fA)(mG)(fG)(mA)(fC)(mA)(mU)(mG)(fA)#(mG)#(mA)-TegChol
Il1b_NM_008361_1112	P(mU)#(fU)#(mC)(fA)(fA)(fC)(mC)(fA)(mA)(fU)(mC)(fA)(mA)(fU)#(mA)#(fA)#(mA)#(mU)#(mA)#(mU)#(fU)
	(mU)#(mU)#(mA)(fU)(mU)(fG)(mA)(fU)(mU)(fG)(mG)(mU)(mU)(fG)#(mA)#(mA)-TegChol
Il1b_NM_008361_855	P(mU)#(fG)#(mA)(fA)(fG)(fU)(mC)(fA)(mA)(fU)(mU)(fA)(mU)(fG)#(mU)#(fC)#(mC)#(mU)#(mG)#(mU)#(fU)
	(mG)#(mA)#(mC)(fA)(mU)(fA)(mA)(fU)(mU)(fG)(mA)(mC)(mU)(fU)#(mC)#(mA)-TegChol
Il1b_NM_008361_621	P(mU)#(fU)#(mA)(fG)(fA)(fU)(mU)(fC)(mU)(fU)(mU)(fC)(mC)(fU)#(mU)#(fU)#(mG)#(mA)#(mG)#(mU)#(fU)
	(mA)#(mA)#(mA)(fG)(mG)(fA)(mA)(fA)(mG)(fA)(mA)(mU)(mC)(fU)#(mA)#(mA)-TegChol
Il1b_NM_008361_736	P(mU)#(fC)#(mU)(fU)(fC)(fU)(mA)(fU)(mC)(fU)(mU)(fG)(mU)(fU)#(mG)#(fA)#(mA)#(mG)#(mA)#(mU)#(fU)
	(mU)#(mC)#(mA)(fA)(mC)(fA)(mA)(fG)(mA)(fU)(mA)(mG)(mA)(fA)#(mG)#(mA)-TegChol
Il1b_NM_008361_965	P(mU)#(fU)#(mG)(fG)(fA)(fG)(mA)(fU)(mU)(fG)(mA)(fG)(mC)(fU)#(mG)#(fU)#(mC)#(mU)#(mG)#(mU)#(fU)

	(mA)#(mC)#(mA)(fG)(mC)(fU)(mC)(fA)(mA)(fU)(mC)(mU)(mC)(fC)#(mA)#(mA)-TegChol
Il1b_NM_008361_1109	(mU)#(mA)#(mU)(fU)(mU)(fA)(mU)(fU)(mG)(fA)(mU)(mU)(mG)(fG)#(mU)#(mA)-TegChol
	P(mU)#(fA)#(mC)(fC)(fA)(fA)(mU)(fC)(mA)(fA)(mU)(fA)(mA)(fA)#(mU)#(fA)#(mC)#(mA)#(mU)#(mU)#(fU)
Il1b_NM_008361_20	(mG)#(mC)#(mC)(fU)(mA)(fA)(mU)(fA)(mG)(fG)(mC)(mU)(mC)(fA)#(mU)#(mA)-TegChol
	P(mU)#(fA)#(mU)(fG)(fA)(fG)(mC)(fC)(mU)(fA)(mU)(fU)(mA)(fG)#(mG)#(fC)#(mC)#(mU)#(mC)#(mU)#(fU)
Il1b_NM_008361_1047	(mC)#(mA)#(mA)(fA)(mG)(fA)(mG)(fA)(mG)(fC)(mC)(mU)(mG)(fU)#(mG)#(mA)-TegChol
	P(mU)#(fC)#(mA)(fC)(fA)(fG)(mG)(fC)(mU)(fC)(mU)(fC)(mU)(fU)#(mU)#(fG)#(mA)#(mA)#(mC)#(mU)#(fU)
Il1b_NM_008361_1120	(mU)#(mG)#(mG)(fU)(mU)(fG)(mA)(fU)(mC)(fU)(mA)(mU)(mU)(fU)#(mA)#(mA)-TegChol
	P(mU)#(fU)#(mA)(fA)(fA)(fU)(mA)(fG)(mA)(fU)(mC)(fA)(mA)(fC)#(mC)#(fA)#(mA)#(mU)#(mC)#(mU)#(fU)
Il1b_NM_008361_1260	(mA)#(mU)#(mA)(fA)(mU)(fA)(mU)(fG)(mG)(fA)(mU)(mG)(mA)(fG)#(mA)#(mA)-TegChol
	P(mU)#(fU)#(mC)(fU)(fC)(fA)(mU)(fC)(mC)(fA)(mU)(fA)(mU)(fU)#(mA)#(fU)#(mA)#(mG)#(mG)#(mU)#(fU)
Il1b_NM_008361_931	(mC)#(mA)#(mU)(fG)(mU)(fU)(mA)(fA)(mG)(fG)(mA)(mG)(mC)(fU)#(mC)#(mA)-TegChol
	P(mU)#(fG)#(mA)(fG)(fC)(fU)(mC)(fC)(mU)(fU)(mA)(fA)(mC)(fA)#(mU)#(fG)#(mC)#(mC)#(mC)#(mU)#(fU)
Il1b_NM_008361_872	(mC)#(mA)#(mU)(fG)(mG)(fA)(mA)(fU)(mC)(fC)(mG)(mU)(mG)(fU)#(mC)#(mA)-TegChol
	P(mU)#(fG)#(mA)(fC)(fA)(fC)(mG)(fG)(mA)(fU)(mU)(fC)(mC)(fA)#(mU)#(fG)#(mG)#(mU)#(mG)#(mU)#(fU)
Il1b_NM_008361_633	(mC)#(mU)#(mA)(fU)(mA)(fC)(mC)(fU)(mG)(fU)(mC)(mC)(mU)(fG)#(mU)#(mA)-TegChol
	P(mU)#(fA)#(mC)(fA)(fG)(fG)(mA)(fC)(mA)(fG)(mG)(fU)(mA)(fU)#(mA)#(fG)#(mA)#(mU)#(mU)#(mU)#(fU)
Il1b_NM_008361_1084	(mG)#(mC)#(mA)(fA)(mC)(fC)(mA)(fC)(mU)(fU)(mA)(mC)(mC)(fU)#(mA)#(mA)-TegChol
	P(mU)#(fU)#(mA)(fG)(fG)(fU)(mA)(fA)(mG)(fU)(mG)(fG)(mU)(fU)#(mG)#(fC)#(mC)#(mC)#(mA)#(mU)#(fU)
Il1b_NM_008361_1240	(mC)#(mU)#(mG)(fA)(mG)(fA)(mA)(fU)(mA)(fA)(mA)(mU)(mA)(fG)#(mG)#(mA)-TegChol
	P(mU)#(fC)#(mC)(fU)(fA)(fU)(mU)(fU)(mA)(fU)(mU)(fC)(mU)(fC)#(mA)#(fG)#(mC)#(mU)#(mU)#(mU)#(fU)
Il1b_NM_008361_818	(mG)#(mC)#(mA)(fC)(mA)(fA)(mG)(fC)(mC)(fU)(mG)(mU)(mC)(fU)#(mU)#(mA)-TegChol
	P(mU)#(fA)#(mA)(fG)(fA)(fC)(mA)(fG)(mG)(fC)(mU)(fU)(mG)(fU)#(mG)#(fC)#(mU)#(mC)#(mU)#(mU)#(fU)

Supplementary Table 4. Sequences and chemical modification patterns of human *IL1B* siRNAs.

Oligo Name	Sequence
IL1B_NM_000576_856	P(mU)#(fU)#(mG)(fA)(fA)(fG)(mU)(fC)(mA)(fG)(mU)(fU)(mA)(fU)#(mA)#(fU)#(mC)#(mC)#(mU)#(mU)#(fU)
	(mA)#(mU)#(mA)(fU)(mA)(fA)(mC)(fU)(mG)(fA)(mC)(mU)(mU)(fC)#(mA)#(mA)-TegChol
IL1B_NM_000576_1370	P(mU)#(fU)#(mU)(fG)(fA)(fU)(mU)(fU)(mA)(fA)(mA)(fG)(mA)(fG)#(mA)#(fG)#(mC)#(mA)#(mC)#(mU)#(fU)
	(mC)#(mU)#(mC)(fU)(mC)(fU)(mU)(fU)(mA)(fA)(mA)(mU)(mC)(fA)#(mA)#(mA)-TegChol
IL1B_NM_000576_1427	P(mU)#(fU)#(mA)(fA)(fA)(fU)(mA)(fU)(mU)(fC)(mC)(fC)(mA)(fU)#(mU)#(fU)#(mA)#(mA)#(mA)#(mU)#(fU)
	(mA)#(mA)#(mA)(fU)(mG)(fG)(mG)(fA)(mA)(fU)(mA)(mU)(mU)(fU)#(mA)#(mA)-TegChol
IL1B_NM_000576_1411	P(mU)#(fA)#(mA)(fU)(fA)(fA)(mU)(fC)(mU)(fG)(mA)(fG)(mC)(fU)#(mU)#(fA)#(mU)#(mA)#(mU)#(mU)#(fU)
	(mU)#(mA)#(mA)(fG)(mC)(fU)(mC)(fA)(mG)(fA)(mU)(mU)(mA)(fU)#(mU)#(mA)-TegChol
IL1B_NM_000576_1390	P(mU)#(fU)#(mU)(fC)(fA)(fG)(mU)(fC)(mU)(fU)(mA)(fA)(mU)(fU)#(mA)#(fA)#(mA)#(mG)#(mG)#(mU)#(fU)
	(mU)#(mU)#(mA)(fA)(mU)(fU)(mA)(fA)(mG)(fA)(mC)(mU)(mG)(fA)#(mA)#(mA)-TegChol
IL1B_NM_000576_112	P(mU)#(fA)#(mA)(fU)(fA)(fA)(mG)(fC)(mC)(fA)(mU)(fC)(mA)(fU)#(mU)#(fU)#(mC)#(mA)#(mC)#(mU)#(fU)

	(mA)#(mA)#(mA)(fU)(mG)(fA)(mU)(fG)(mG)(fC)(mU)(mU)(mA)(fU)#(mU)#(mA)-TegChol
IL1B_NM_000576_1374	P(mU)#(fG)#(mG)(fA)(fC)(fU)(mU)(fG)(mA)(fU)(mU)(fU)(mA)(fA)#(mA)#(fG)#(mA)#(mG)#(mA)#(mU)#(fU)
	(mC)#(mU)#(mU)(fU)(mA)(fA)(mA)(fU)(mC)(fA)(mA)(mG)(mU)(fC)#(mC)#(mA)-TegChol
IL1B_NM_000576_1443	P(mU)#(fG)#(mA)(fU)(fA)(fU)(mU)(fU)(mG)(fC)(mU)(fC)(mA)(fU)#(mU)#(fU)#(mA)#(mU)#(mA)#(mU)#(fU)
	(mA)#(mA)#(mA)(fU)(mG)(fA)(mG)(fC)(mA)(fA)(mA)(mU)(mA)(fU)#(mC)#(mA)-TegChol
IL1B_NM_000576_1460	P(mU)#(fG)#(mA)(fA)(fC)(fC)(mA)(fU)(mU)(fG)(mA)(fA)(mC)(fA)#(mG)#(fU)#(mA)#(mU)#(mG)#(mU)#(fU)
	(mA)#(mC)#(mU)(fG)(mU)(fU)(mC)(fA)(mA)(fU)(mG)(mG)(mU)(fU)#(mC)#(mA)-TegChol
IL1B_NM_000576_1442	P(mU)#(fA)#(mU)(fA)(fU)(fU)(mU)(fG)(mC)(fU)(mC)(fA)(mU)(fU)#(mU)#(fA)#(mU)#(mA)#(mA)#(mU)#(fU)
	(mU)#(mA)#(mA)(fA)(mU)(fG)(mA)(fG)(mC)(fA)(mA)(mA)(mU)(fA)#(mU)#(mA)-TegChol
IL1B_NM_000576_703	P(mU)#(fC)#(mC)(fA)(fU)(fC)(mU)(fU)(mC)(fU)(mU)(fC)(mU)(fU)#(mU)#(fG)#(mG)#(mG)#(mU)#(mU)#(fU)
	(mC)#(mA)#(mA)(fA)(mG)(fA)(mA)(fG)(mA)(fA)(mG)(mA)(mU)(fG)#(mG)#(mA)-TegChol
IL1B_NM_000576_1421	P(mU)#(fU)#(mU)(fC)(fC)(fC)(mA)(fU)(mU)(fU)(mA)(fA)(mA)(fU)#(mA)#(fA)#(mU)#(mC)#(mU)#(mU)#(fU)
	(mU)#(mU)#(mA)(fU)(mU)(fU)(mA)(fA)(mA)(fU)(mG)(mG)(mG)(fA)#(mA)#(mA)-TegChol
IL1B_NM_000576_855	P(mU)#(fG)#(mA)(fA)(fG)(fU)(mC)(fA)(mG)(fU)(mU)(fA)(mU)(fA)#(mU)#(fC)#(mC)#(mU)#(mG)#(mU)#(fU)
	(mG)#(mA)#(mU)(fA)(mU)(fA)(mA)(fC)(mU)(fG)(mA)(mC)(mU)(fU)#(mC)#(mA)-TegChol
IL1B_NM_000576_380	P(mU)#(fA)#(mA)(fG)(fA)(fU)(mA)(fG)(mG)(fU)(mU)(fC)(mU)(fU)#(mC)#(fU)#(mU)#(mC)#(mA)#(mU)#(fU)
	(mA)#(mG)#(mA)(fA)(mG)(fA)(mA)(fC)(mC)(fU)(mA)(mU)(mC)(fU)#(mU)#(mA)-TegChol
IL1B_NM_000576_1361	P(mU)#(fA)#(mG)(fA)(fG)(fA)(mG)(fC)(mA)(fC)(mA)(fC)(mC)(fA)#(mG)#(fU)#(mC)#(mC)#(mA)#(mU)#(fU)
	(mA)#(mC)#(mU)(fG)(mG)(fU)(mG)(fU)(mG)(fC)(mU)(mC)(mU)(fC)#(mU)#(mA)-TegChol
IL1B_NM_000576_748	P(mU)#(fC)#(mC)(fA)(fG)(fC)(mU)(fU)(mG)(fU)(mU)(fA)(mU)(fU)#(mG)#(fA)#(mU)#(mU)#(mU)#(mU)#(fU)
	(mU)#(mC)#(mA)(fA)(mU)(fA)(mA)(fC)(mA)(fA)(mG)(mC)(mU)(fG)#(mG)#(mA)-TegChol
IL1B_NM_000576_1450	P(mU)#(fA)#(mC)(fA)(fG)(fU)(mA)(fU)(mG)(fA)(mU)(fA)(mU)(fU)#(mU)#(fG)#(mC)#(mU)#(mC)#(mU)#(fU)
	(mC)#(mA)#(mA)(fA)(mU)(fA)(mU)(fC)(mA)(fU)(mA)(mC)(mU)(fG)#(mU)#(mA)-TegChol
IL1B_NM_000576_1301	P(mU)#(fC)#(mA)(fG)(fA)(fC)(mA)(fC)(mU)(fG)(mC)(fU)(mA)(fC)#(mU)#(fU)#(mC)#(mU)#(mU)#(mU)#(fU)
	(mA)#(mA)#(mG)(fU)(mA)(fG)(mC)(fA)(mG)(fU)(mG)(mU)(mC)(fU)#(mG)#(mA)-TegChol
IL1B_NM_000576_1221	P(mU)#(fG)#(mA)(fA)(fG)(fC)(mG)(fG)(mU)(fU)(mG)(fC)(mU)(fC)#(mA)#(fU)#(mC)#(mA)#(mG)#(mU)#(fU)
	(mA)#(mU)#(mG)(fA)(mG)(fC)(mA)(fA)(mC)(fC)(mG)(mC)(mU)(fU)#(mC)#(mA)-TegChol
IL1B_NM_000576_379	P(mU)#(fA)#(mG)(fA)(fU)(fA)(mG)(fG)(mU)(fU)(mC)(fU)(mU)(fC)#(mU)#(fU)#(mC)#(mA)#(mA)#(mU)#(fU)
	(mA)#(mA)#(mG)(fA)(mA)(fG)(mA)(fA)(mC)(fC)(mU)(mA)(mU)(fC)#(mU)#(mA)-TegChol
IL1B_NM_000576_1461	P(mU)#(fA)#(mG)(fA)(fA)(fC)(mC)(fA)(mU)(fU)(mG)(fA)(mA)(fC)#(mA)#(fG)#(mU)#(mA)#(mU)#(mU)#(fU)
	(mC)#(mU)#(mG)(fU)(mU)(fC)(mA)(fA)(mU)(fG)(mG)(mU)(mU)(fC)#(mU)#(mA)-TegChol
IL1B_NM_000576_573	P(mU)#(fA)#(mC)(fU)(fU)(fU)(mC)(fU)(mU)(fC)(mU)(fC)(mC)(fU)#(mU)#(fG)#(mU)#(mA)#(mC)#(mU)#(fU)
	(mC)#(mA)#(mA)(fG)(mG)(fA)(mG)(fA)(mA)(fG)(mA)(mA)(mA)(fG)#(mU)#(mA)-TegChol
IL1B_NM_000576_1419	P(mU)#(fC)#(mC)(fC)(fA)(fU)(mU)(fU)(mA)(fA)(mA)(fU)(mA)(fA)#(mU)#(fC)#(mU)#(mG)#(mA)#(mU)#(fU)
	(mG)#(mA)#(mU)(fU)(mA)(fU)(mU)(fU)(mA)(fA)(mA)(mU)(mG)(fG)#(mG)#(mA)-TegChol
IL1B_NM_000576_1458	P(mU)#(fA)#(mC)(fC)(fA)(fU)(mU)(fG)(mA)(fA)(mC)(fA)(mG)(fU)#(mA)#(fU)#(mG)#(mA)#(mU)#(mU)#(fU)
	(mA)#(mU)#(mA)(fC)(mU)(fG)(mU)(fU)(mC)(fA)(mA)(mU)(mG)(fG)#(mU)#(mA)-TegChol
IL1B_NM_000576_120	P(mU)#(fG)#(mC)(fC)(fA)(fC)(mU)(fG)(mU)(fA)(mA)(fU)(mA)(fA)#(mG)#(fC)#(mC)#(mA)#(mU)#(mU)#(fU)

	(mG)#(mC)#(mU)(fU)(mA)(fU)(mU)(fA)(mC)(fA)(mG)(mU)(mG)(fG)#(mC)#(mA)-TegChol
IL1B_NM_000576_1387	P(mU)#(fA)#(mG)(fU)(fC)(fU)(mU)(fA)(mA)(fU)(mU)(fA)(mA)(fA)#(mG)#(fG)#(mA)#(mC)#(mU)#(mU)#(fU)
	(mC)#(mC)#(mU)(fU)(mU)(fA)(mA)(fU)(mU)(fA)(mA)(mG)(mA)(fC)#(mU)#(mA)-TegChol
IL1B_NM_000576_140	P(mU)#(fA)#(mA)(fG)(fA)(fA)(mC)(fA)(mA)(fG)(mU)(fC)(mA)(fU)#(mC)#(fC)#(mU)#(mC)#(mA)#(mU)#(fU)
	(mG)#(mG)#(mA)(fU)(mG)(fA)(mC)(fU)(mU)(fG)(mU)(mU)(mC)(fU)#(mU)#(mA)-TegChol
IL1B_NM_000576_635	P(mU)#(fA)#(mA)(fC)(fA)(fC)(mG)(fC)(mA)(fG)(mG)(fA)(mC)(fA)#(mG)#(fG)#(mU)#(mA)#(mC)#(mU)#(fU)
	(mC)#(mC)#(mU)(fG)(mU)(fC)(mC)(fU)(mG)(fC)(mG)(mU)(mG)(fU)#(mU)#(mA)-TegChol
IL1B_NM_000576_1418	P(mU)#(fC)#(mC)(fA)(fU)(fU)(mU)(fA)(mA)(fA)(mU)(fA)(mA)(fU)#(mC)#(fU)#(mG)#(mA)#(mG)#(mU)#(fU)
	(mA)#(mG)#(mA)(fU)(mU)(fA)(mU)(fU)(mU)(fA)(mA)(mA)(mU)(fG)#(mG)#(mA)-TegChol
IL1B_NM_000576_51	P(mU)#(fA)#(mG)(fC)(fA)(fA)(mU)(fG)(mA)(fA)(mG)(fA)(mU)(fU)#(mG)#(fG)#(mC)#(mU)#(mG)#(mU)#(fU)
	(mC)#(mC)#(mA)(fA)(mU)(fC)(mU)(fU)(mC)(fA)(mU)(mU)(mG)(fC)#(mU)#(mA)-TegChol
IL1B_NM_000576_1362	P(mU)#(fA)#(mA)(fG)(fA)(fG)(mA)(fG)(mC)(fA)(mC)(fA)(mC)(fC)#(mA)#(fG)#(mU)#(mC)#(mC)#(mU)#(fU)
	(mC)#(mU)#(mG)(fG)(mU)(fG)(mU)(fG)(mC)(fU)(mC)(mU)(mC)(fU)#(mU)#(mA)-TegChol
IL1B_NM_000576_1425	P(mU)#(fA)#(mA)(fU)(fA)(fU)(mU)(fC)(mC)(fC)(mA)(fU)(mU)(fU)#(mA)#(fA)#(mA)#(mU)#(mA)#(mU)#(fU)
	(mU)#(mU)#(mA)(fA)(mA)(fU)(mG)(fG)(mG)(fA)(mA)(mU)(mA)(fU)#(mU)#(mA)-TegChol
IL1B_NM_000576_1339	P(mU)#(fG)#(mA)(fA)(fU)(fU)(mG)(fA)(mU)(fU)(mC)(fC)(mA)(fU)#(mA)#(fG)#(mC)#(mU)#(mA)#(mU)#(fU)
	(mC)#(mU)#(mA)(fU)(mG)(fG)(mA)(fA)(mU)(fC)(mA)(mA)(mU)(fU)#(mC)#(mA)-TegChol
IL1B_NM_000576_106	P(mU)#(fC)#(mC)(fA)(fU)(fC)(mA)(fU)(mU)(fU)(mC)(fA)(mC)(fU)#(mG)#(fG)#(mC)#(mG)#(mA)#(mU)#(fU)
	(mC)#(mC)#(mA)(fG)(mU)(fG)(mA)(fA)(mA)(fU)(mG)(mA)(mU)(fG)#(mG)#(mA)-TegChol
IL1B_NM_000576_1377	P(mU)#(fA)#(mA)(fA)(fG)(fG)(mA)(fC)(mU)(fU)(mG)(fA)(mU)(fU)#(mU)#(fA)#(mA)#(mA)#(mG)#(mU)#(fU)
	(mU)#(mA)#(mA)(fA)(mU)(fC)(mA)(fA)(mG)(fU)(mC)(mC)(mU)(fU)#(mU)#(mA)-TegChol
IL1B_NM_000576_1420	P(mU)#(fU)#(mC)(fC)(fC)(fA)(mU)(fU)(mU)(fA)(mA)(fA)(mU)(fA)#(mA)#(fU)#(mC)#(mU)#(mG)#(mU)#(fU)
	(mA)#(mU)#(mU)(fA)(mU)(fU)(mU)(fA)(mA)(fA)(mU)(mG)(mG)(fG)#(mA)#(mA)-TegChol
IL1B_NM_000576_1229	P(mU)#(fU)#(mA)(fA)(fA)(fU)(mA)(fG)(mG)(fG)(mA)(fA)(mG)(fC)#(mG)#(fG)#(mU)#(mU)#(mG)#(mU)#(fU)
	(mC)#(mC)#(mG)(fC)(mU)(fU)(mC)(fC)(mC)(fU)(mA)(mU)(mU)(fU)#(mA)#(mA)-TegChol
IL1B_NM_000576_1453	P(mU)#(fU)#(mG)(fA)(fA)(fC)(mA)(fG)(mU)(fA)(mU)(fG)(mA)(fU)#(mA)#(fU)#(mU)#(mU)#(mG)#(mU)#(fU)
	(mA)#(mU)#(mA)(fU)(mC)(fA)(mU)(fA)(mC)(fU)(mG)(mU)(mU)(fC)#(mA)#(mA)-TegChol
IL1B_NM_000576_1344	P(mU)#(fA)#(mA)(fA)(fU)(fU)(mG)(fA)(mA)(fU)(mU)(fG)(mA)(fU)#(mU)#(fC)#(mC)#(mA)#(mU)#(mU)#(fU)
	(mG)#(mA)#(mA)(fU)(mC)(fA)(mA)(fU)(mU)(fC)(mA)(mA)(mU)(fU)#(mU)#(mA)-TegChol
IL1B_NM_000576_791	P(mU)#(fG)#(mA)(fG)(fG)(fU)(mG)(fC)(mU)(fG)(mA)(fU)(mG)(fU)#(mA)#(fC)#(mC)#(mA)#(mG)#(mU)#(fU)
	(mG)#(mU)#(mA)(fC)(mA)(fU)(mC)(fA)(mG)(fC)(mA)(mC)(mC)(fU)#(mC)#(mA)-TegChol
IL1B_NM_000576_1356	P(mU)#(fG)#(mC)(fA)(fC)(fA)(mC)(fC)(mA)(fG)(mU)(fC)(mC)(fA)#(mA)#(fA)#(mU)#(mU)#(mG)#(mU)#(fU)
	(mU)#(mU)#(mU)(fG)(mG)(fA)(mC)(fU)(mG)(fG)(mU)(mG)(mU)(fG)#(mC)#(mA)-TegChol
IL1B_NM_000576_1226	P(mU)#(fA)#(mU)(fA)(fG)(fG)(mG)(fA)(mA)(fG)(mC)(fG)(mG)(fU)#(mU)#(fG)#(mC)#(mU)#(mC)#(mU)#(fU)
	(mC)#(mA)#(mA)(fC)(mC)(fG)(mC)(fU)(mU)(fC)(mC)(mC)(mU)(fA)#(mU)#(mA)-TegChol
IL1B_NM_000576_1345	P(mU)#(fC)#(mA)(fA)(fA)(fU)(mU)(fG)(mA)(fA)(mU)(fU)(mG)(fA)#(mU)#(fU)#(mC)#(mC)#(mA)#(mU)#(fU)
	(mA)#(mA)#(mU)(fC)(mA)(fA)(mU)(fU)(mC)(fA)(mA)(mU)(mU)(fU)#(mG)#(mA)-TegChol
IL1B_NM_000576_729	P(mU)#(fU)#(mA)(fU)(fC)(fU)(mU)(fG)(mU)(fU)(mG)(fA)(mA)(fG)#(mA)#(fC)#(mA)#(mA)#(mA)#(mU)#(fU)

	(mG)#(mU)#(mC)(fU)(mU)(fC)(mA)(fA)(mC)(fA)(mA)(mG)(mA)(fU)#(mA)#(mA)-TegChol
IL1B_NM_000576_370	P(mU)#(fC)#(mU)(fU)(fC)(fU)(mU)(fC)(mA)(fA)(mA)(fG)(mA)(fU)#(mG)#(fA)#(mA)#(mG)#(mG)#(mU)#(fU)
	(mU)#(mC)#(mA)(fU)(mC)(fU)(mU)(fU)(mG)(fA)(mA)(mG)(mA)(fA)#(mG)#(mA)-TegChol
IL1B_NM_000576_868	P(mU)#(fC)#(mA)(fA)(fA)(fU)(mU)(fG)(mC)(fA)(mU)(fG)(mG)(fU)#(mG)#(fA)#(mA)#(mG)#(mU)#(mU)#(fU)
	(mU)#(mC)#(mA)(fC)(mC)(fA)(mU)(fG)(mC)(fA)(mA)(mU)(mU)(fU)#(mG)#(mA)-TegChol
IL1B_NM_000576_574	P(mU)#(fU)#(mA)(fC)(fU)(fU)(mU)(fC)(mU)(fU)(mC)(fU)(mC)(fC)#(mU)#(fU)#(mG)#(mU)#(mA)#(mU)#(fU)
	(mA)#(mA)#(mG)(fG)(mA)(fG)(mA)(fA)(mG)(fA)(mA)(mA)(mG)(fU)#(mA)#(mA)-TegChol
IL1B_NM_000576_746	P(mU)#(fA)#(mG)(fC)(fU)(fU)(mG)(fU)(mU)(fA)(mU)(fU)(mG)(fA)#(mU)#(fU)#(mU)#(mC)#(mU)#(mU)#(fU)
	(mA)#(mA)#(mU)(fC)(mA)(fA)(mU)(fA)(mA)(fC)(mA)(mA)(mG)(fC)#(mU)#(mA)-TegChol

Supplementary Table 5. Sequences of RT-PCR Primers

Mouse Genes	**Primer (5'-3')**
Id1 (Inhibitor of DNA binding 1)	F: ACATGAACGGCTGCTACTCAC R: GACTTCAGACTCCGAGTTCAGC
Tnalp (Tissue-nonspecific alkaline phosphatase)	F: CACAATATCAAGGATATCGACGTGA R: ACATCAGTTCTGTTCTTCGGGTACA
Ibsp (Integrin binding sialoprotein)	F: CAGGGAGGCAGTGACTCTTC R: AGTGTGGAAAGTGTGGCGTT
Osx (Osterix: SP7)	F: ATGGCGTCCTCTCTGCTTGA R: GAAGGGTGGGTAGTCATTTG
Bglap/Osteocalcin (Bone γ-carboxyglutamate protein)	F: GCAGCACAGGTCCTAAATAG R: GGGCAATAAGGTAGTGAACAG
Hprt (Hypoxanthine-guanine phosphoribosyl transferase)	F: CTGGTGAAAAGGACCTCTCGAAG R: CCAGTTTCACTAATGACACAAACG
Actb (Actin, Beta)	F: AGGGAAATCGTGCGTGACAT R:GGGCAATAAGGTAGTGAACAG
Gapdh (Glyceraldehyde-3-phosphate dehydrogenase)	F: ACAGTCCATGCCATCACTGCC R: GCCTGCTTCACCACCTTCTTG
Msx2 (Msh homeobox2)	F: GGAACTGGAAAAGCTGAAAATG R: CACAGGTCTATGGAAGGGGTAG
Sox9 (SRY-Box Transcription Factor 9)	F: CACACGTCAAGCGACCCATGAA R: TCTTCTCGCTCTCGTTCAGCAG
Inhba (Inhibin subunit beta A)	F: GGAGATAGAGGACGACATTGGC R: ACGCTCCACTACTGACAGGTCA
Acvr1 (activin A receptor, type 1)	F: CCATTGAAGGGCTCATCACCAC R: CCGTTCTCTGTACCAGGAAAGG
Human Gene	**Primer(5'-3')**
ACVR1^{R206H}	F: TGGTACAAAGAACAGTGGCTTA R: CCATACCTGCCTTTCCCGA
ACVR1^{WT}	F: GACGTGGAGTATGGCACTATCG R: CACTCCAACAGTGTAATCTGGCG
INHBA	F: GGATGACATTGGAAGGAGGGCA R: ACTGACAGGTCACTGCCTTCCT
ID1	F: GTTGGAGCTGAACTCGGAATCC R: ACACAAGATGCGATCGTCCGCA
GAPDH	F: GGTGTGATCTTAACTGCCG R: CAGATCAGCAGACTCTGGGT

Supplementary Table 6. A list of inflammatory cytokines and receptors (RT^2 profiler PCR array)

Chemokines & Chemokine receptors	*Ccl1, Ccl11, Ccl12, Ccl17, Ccl19, Ccl2, Ccl20, Ccl22, Ccl24, Ccl3, Ccl4, Ccl5, Ccl6, Ccl7, Ccl8, Ccl9, Cx3cl1, Cxcl1, Cxcl10, Cxcl11, Cxcl12, Cxcl13, Cxcl15, Cxcl5, Cxcl9, Ccr1, Ccr10, Ccr2, Ccr3, Ccr4, Ccr5, Ccr6, Ccr8, Cxcr2, Cxcr3, Cxcr5*
Interleukins	*Il11, Il13, Il15, Il16, Il17a, Il17b, Il17f, Il1a, Il1b, Il1rn, Il21, Il27, Il3, Il33, Il4, Il5, Il7, Il10ra, Il10rb, Il1r1, Il2rb, Il2rg, Il5ra, Il6ra, Il6st*
Others	*Aimp1, Bmp2, Cd40lg, Csf1, Csf2, Csf3, Fasl, Ifng, Lta, Ltb, Mif, Nampt, Osm, Pf4, Spp1, Tnf, Tnfsf10, Tnfsf11, Tnfsf13, Tnfsf13b, Tnfsf4, Vegfa, Tnfrsf11b*