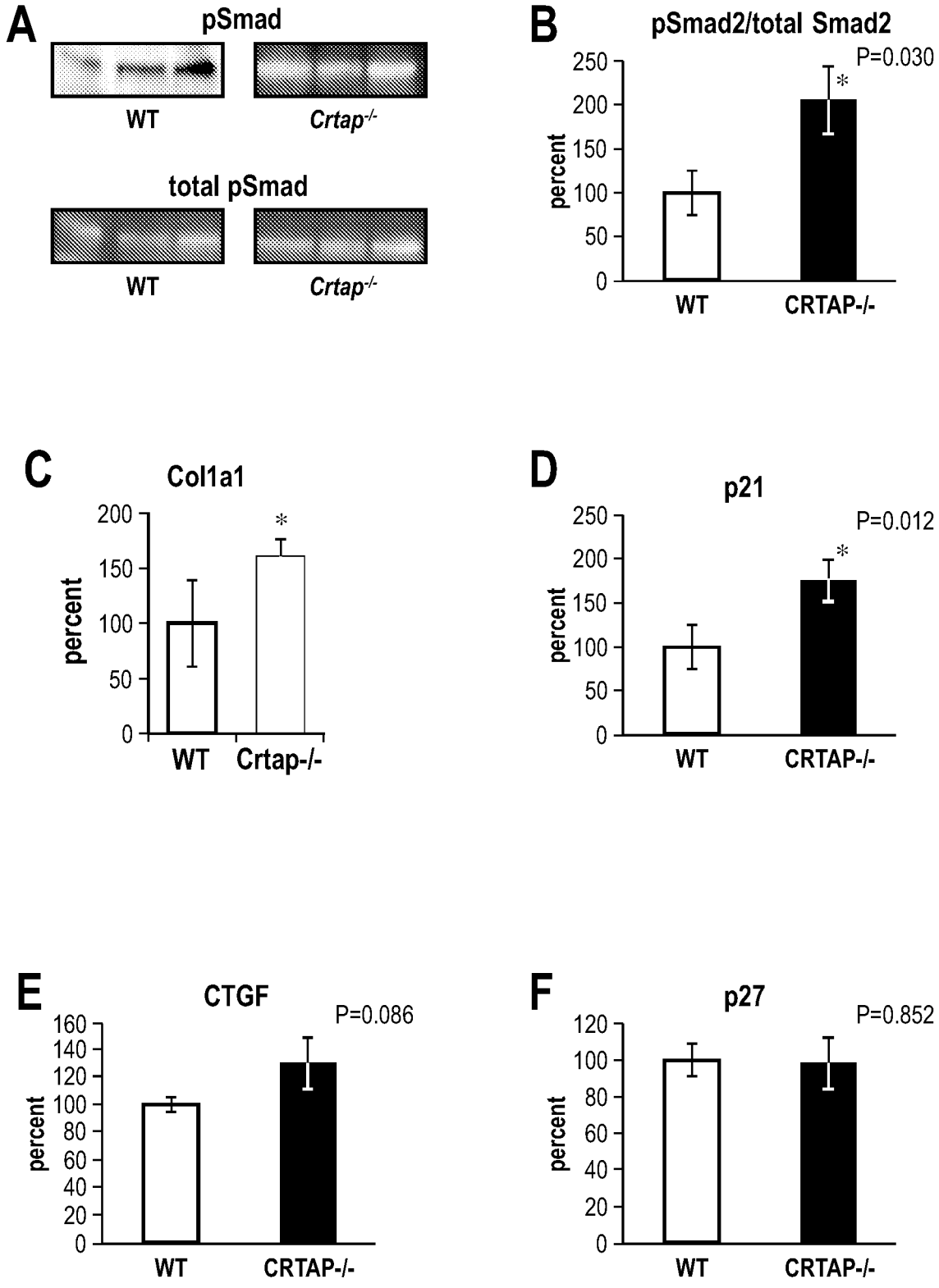

A
pSmad
WT
Crtap-/-
total pSmad
WT
Crtap-/-
B
pSmad2/total Smad2
P=0.030
percent
250
200
150
100
50
0
WT
CRTAP-/-
C
Col1a1
percent
200
150
100
50
0
WT
Crtap-/-
D
p21
P=0.012
percent
250
200
150
100
50
0
WT
CRTAP-/-
E
CTGF
P=0.086
percent
160
140
120
100
80
60
40
20
0
WT
CRTAP-/-
F
p27
P=0.852
percent
120
100
80
60
40
20
0
WT
CRTAP-/-

Fig. 1

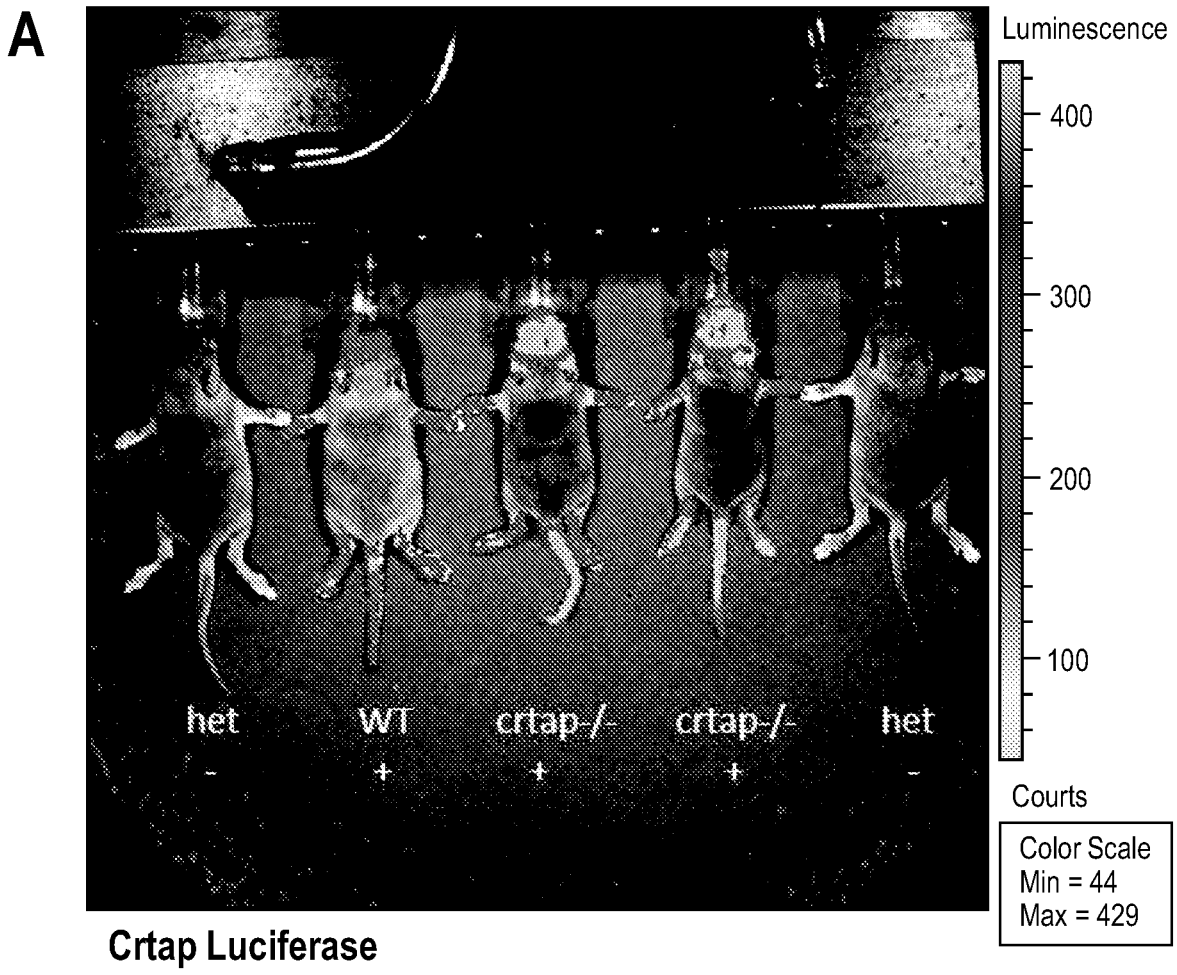

A
Luminescence
400
300
200
100
Courts
Color Scale
Min = 44
Max = 429
het
WT
crtap-/-
crtap-/-
het
-
+
+
+
-
Crtap Luciferase
B
TGFb reporter activity
Luciferase activity [total counts]
60000
50000
40000
30000
20000
10000
0
Luc neg
WT
Crtap-/-
Crtap-/-
Luc neg
C
TGFb reporter activity
Luciferase activity [total counts]
250
200
150
100
50
0
*
WT
Crtap-/-

Fig. 2

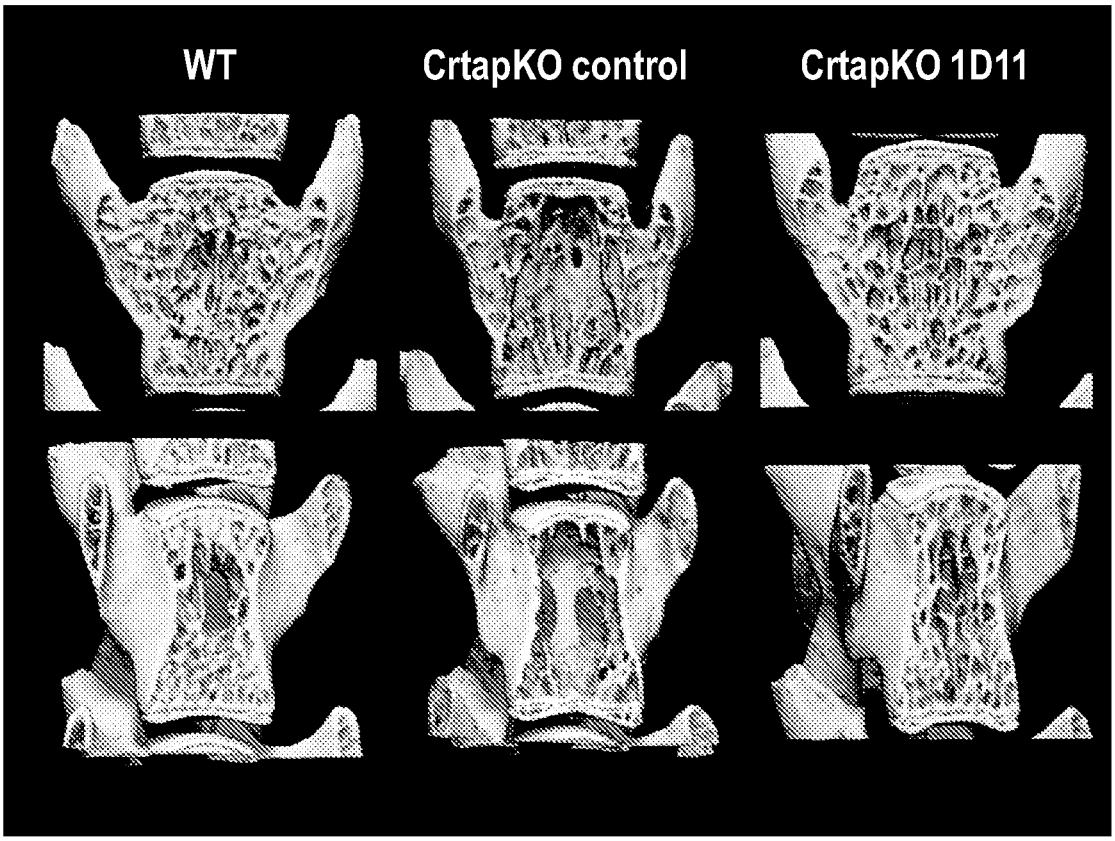


Fig. 3

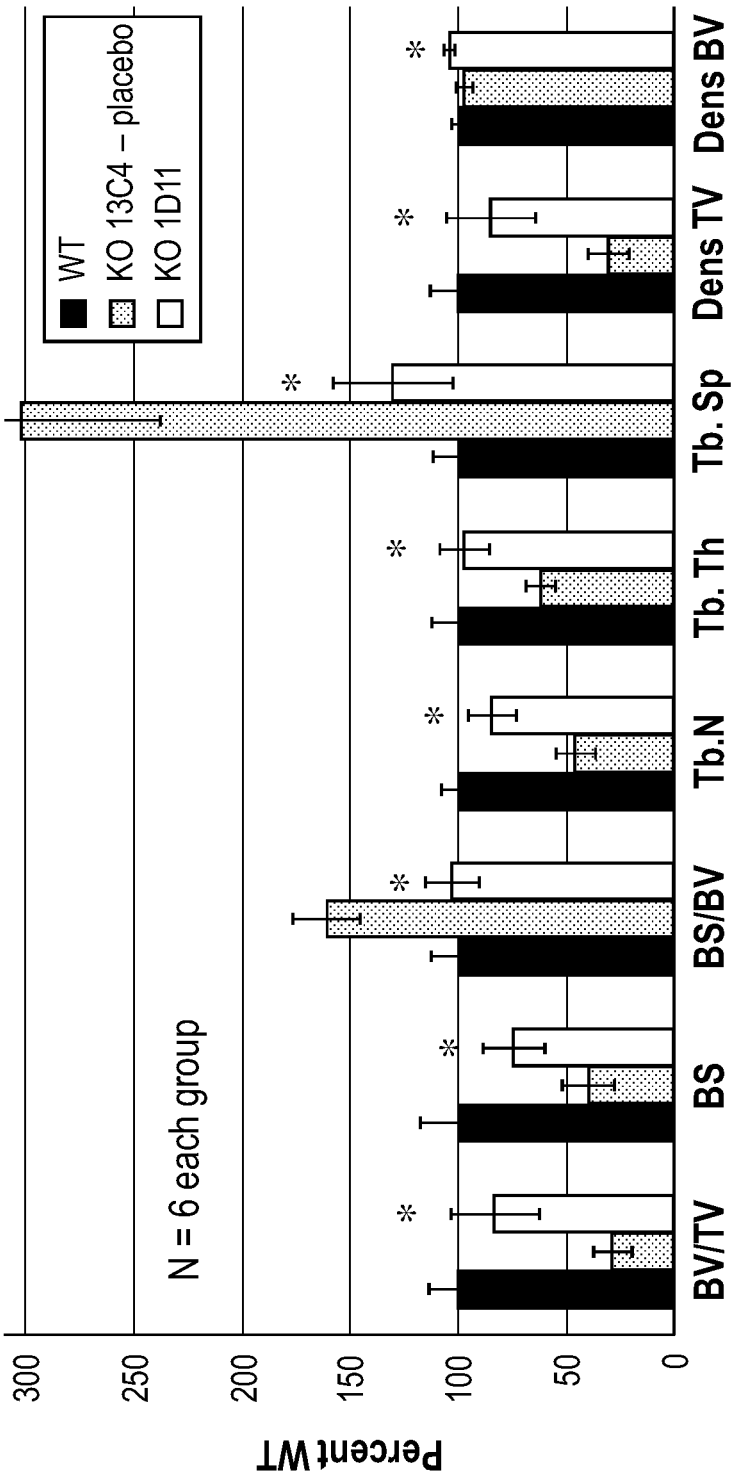

WT
KO 13C4 – placebo
KO 1D11
N = 6 each group
Percent WT
300
250
200
150
100
50
0
BV/TV
BS
BS/BV
Tb.N
Tb. Th
Tb. Sp
Dens TV
Dens BV
week 16 (treated wks 8 -16)

Fig. 4

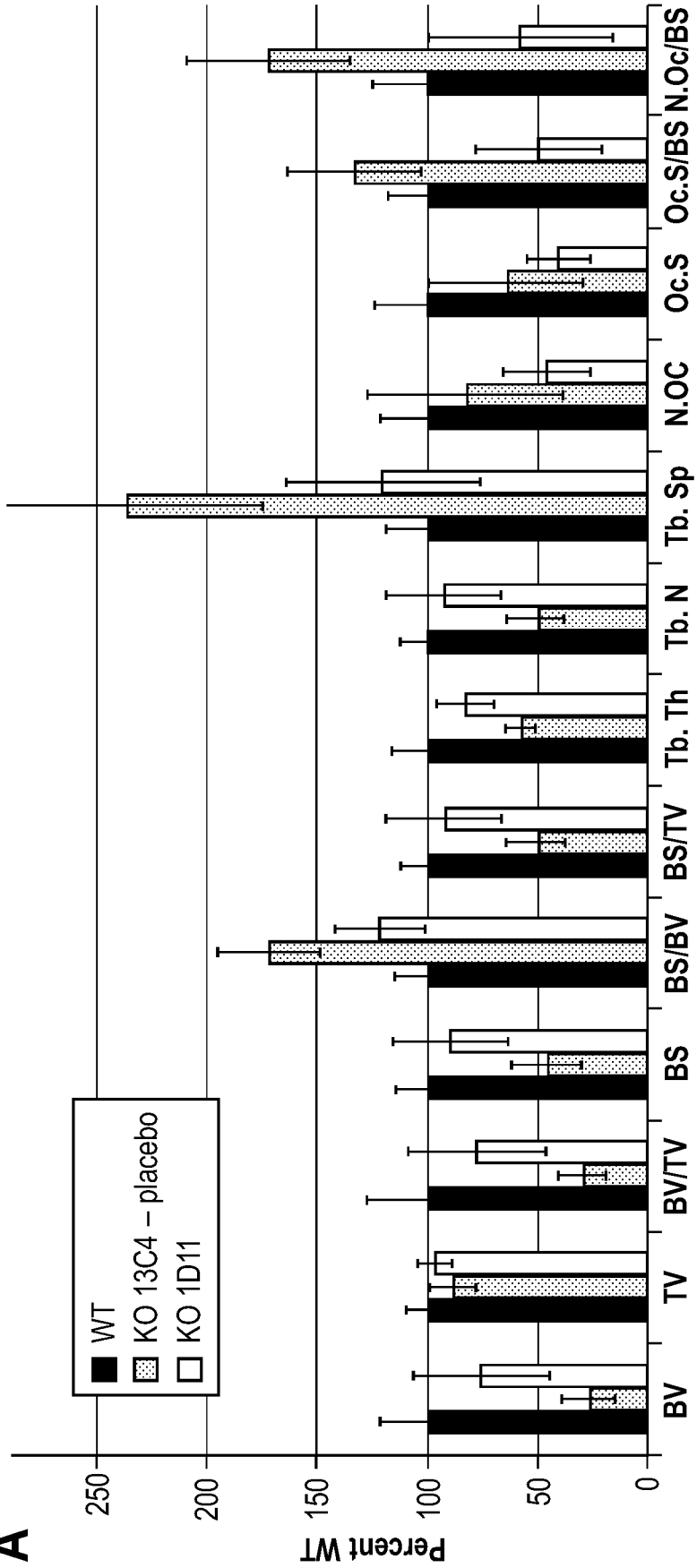

A
Percent WT
250
200
150
100
50
0
WT
KO 13C4 – placebo
KO 1D11
BV
TV
BV/TV
BS
BS/BV
BS/TV
Tb. Th
Tb. N
Tb. Sp
N.OC
Oc.S
Oc.S/BS
N.Oc/BS

Fig. 5

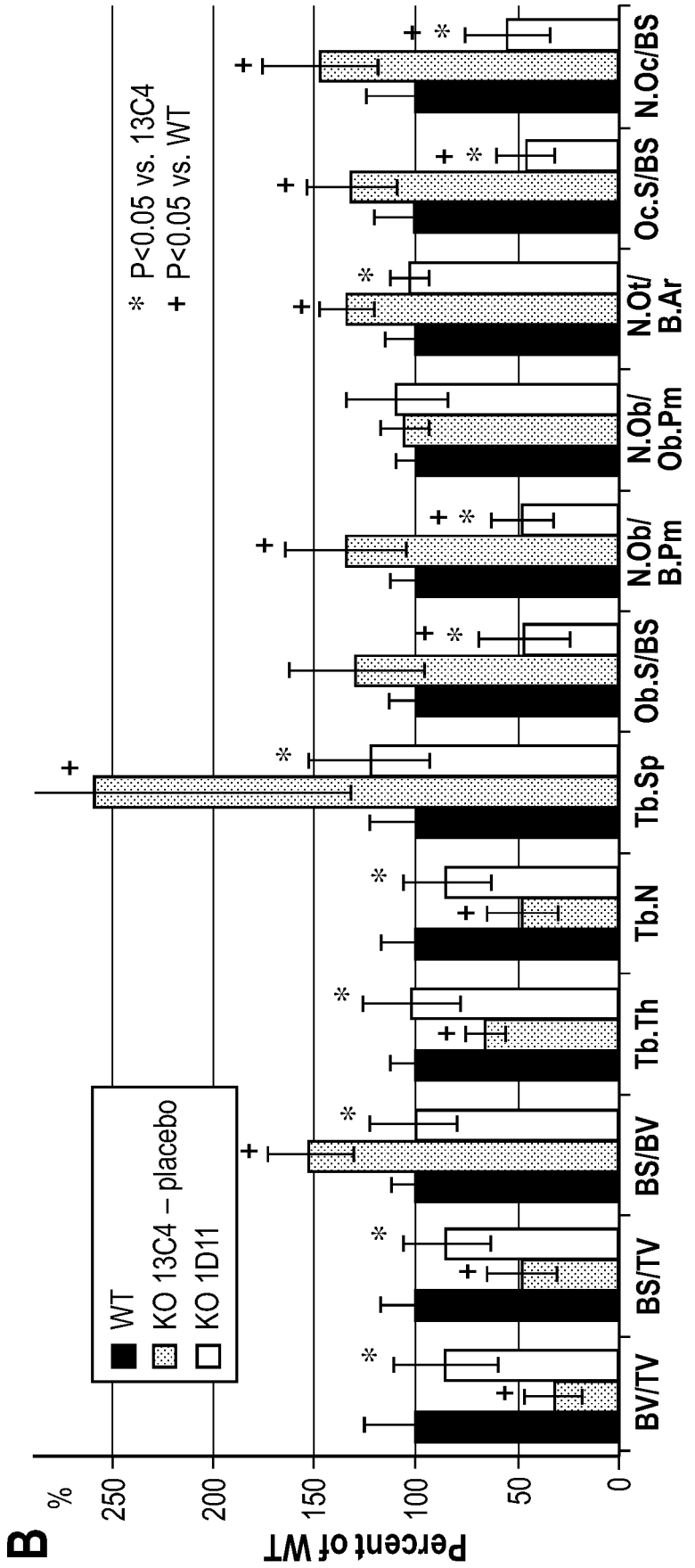

B
Percent of WT
250
200
150
100
50
0
WT
KO 13C4 – placebo
KO 1D11
* P<0.05 vs. 13C4
+ P<0.05 vs. WT
BV/TV
BS/TV
BS/BV
Tb.Th
Tb.N
Tb.Sp
Ob.S/BS
N.Ob/ B.Pm
N.Ob/ Ob.Pm
N.Ot/ B.Ar
Oc.S/BS
N.Oc/BS

Fig. 5

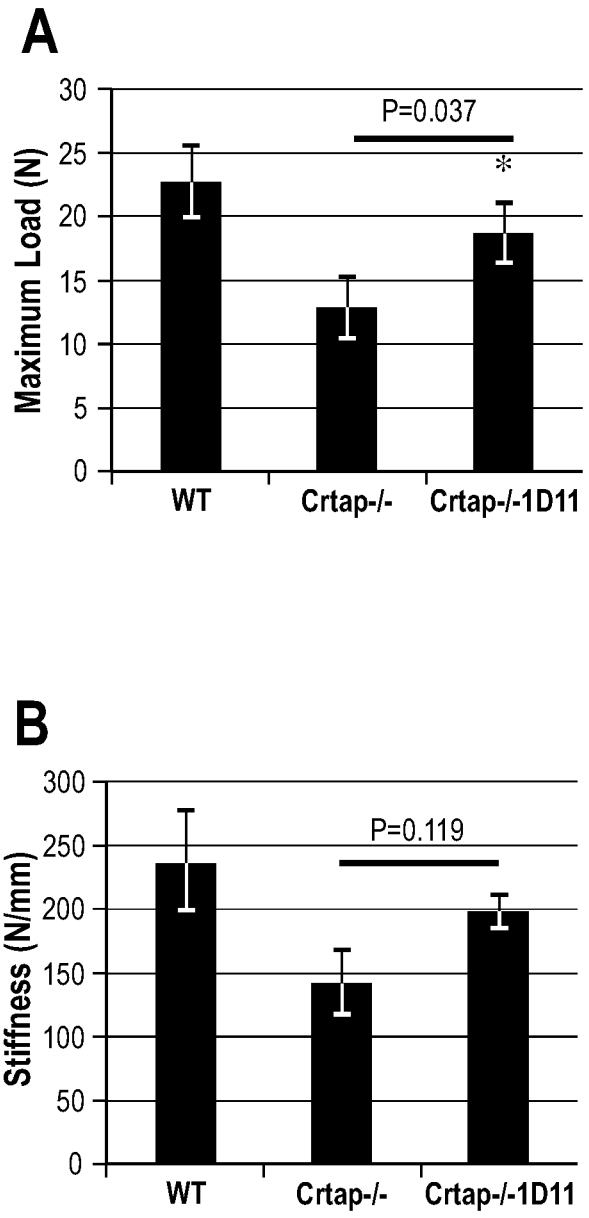

A
Maximum Load (N)
30
25
20
15
10
5
0
P=0.037
*
WT
Crtap-/-
Crtap-/-1D11
B
Stiffness (N/mm)
300
250
200
150
100
50
0
P=0.119
WT
Crtap-/-
Crtap-/-1D11

Fig. 6

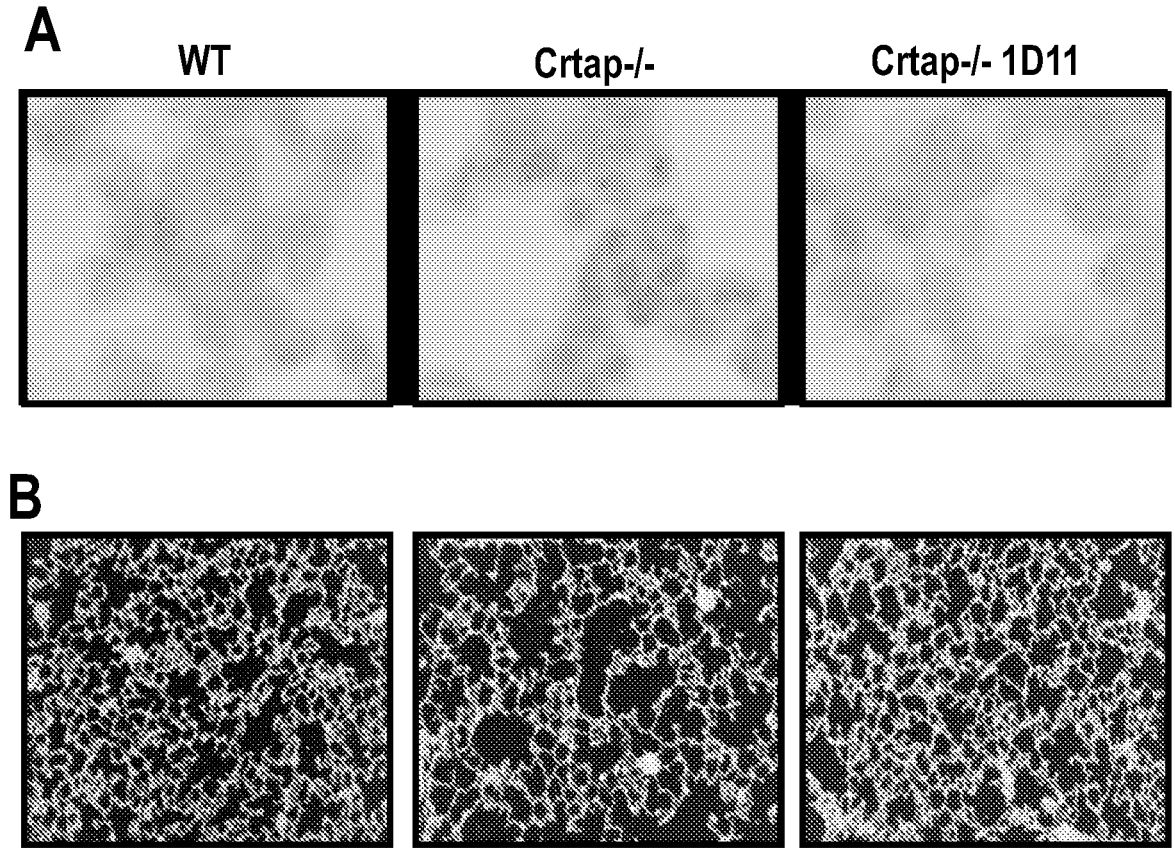

A
WT
Crtap-/-
Crtap-/- 1D11
B
C
Mean linear intercept
µm/intercept [± SD]
40
35
30
25
20
*
WT
Crtap-/- control
Crtap-/- 1D11

Fig. 7

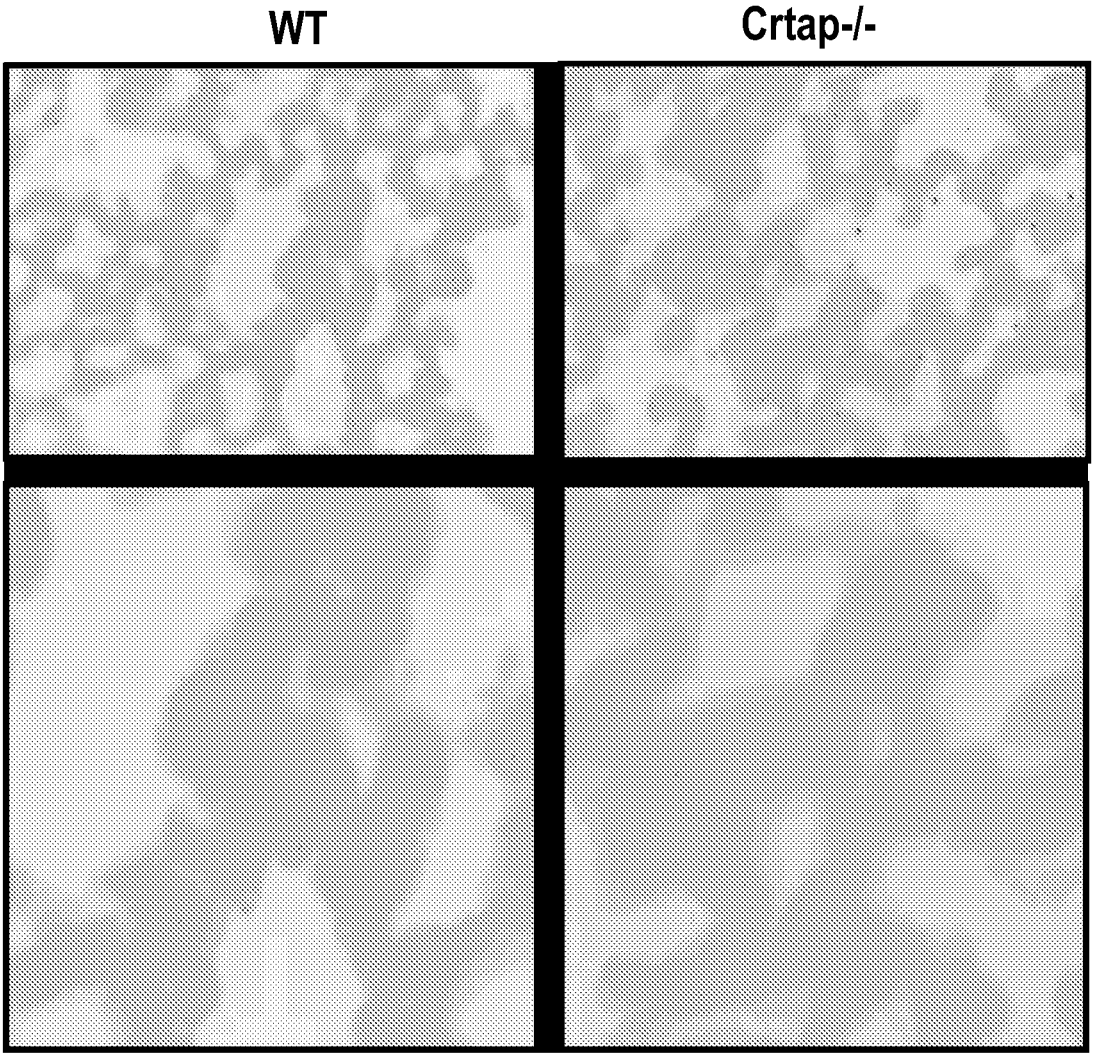


Fig. 8

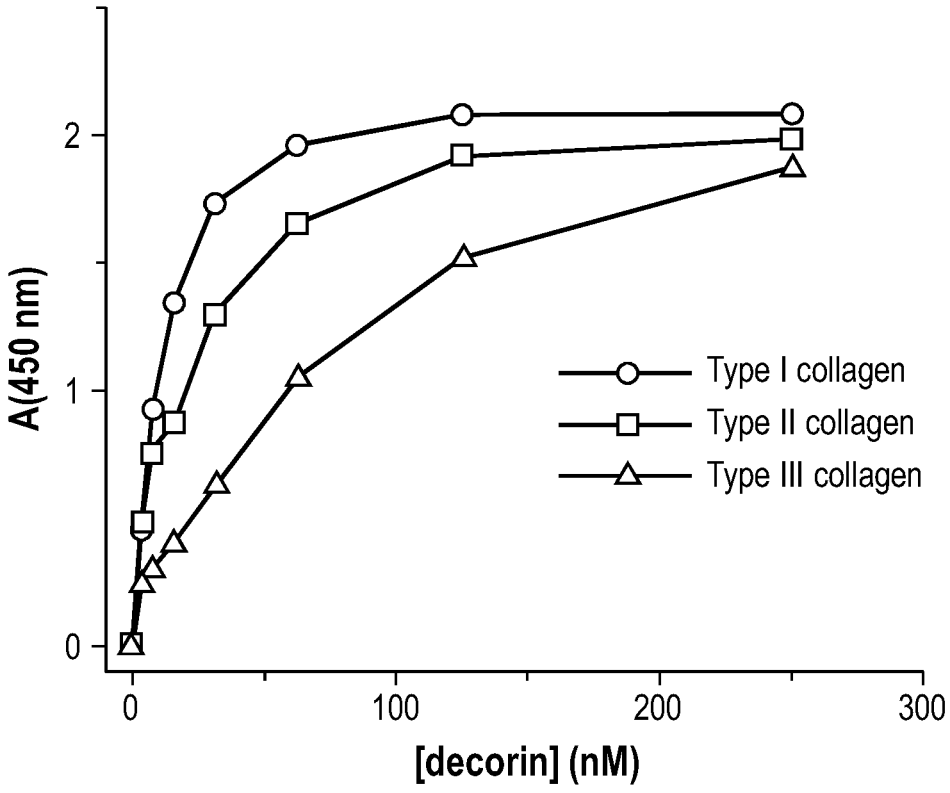

A(450 nm)
0
1
2
0
100
200
300
[decorin] (nM)
Type I collagen
Type II collagen
Type III collagen

Fig. 9

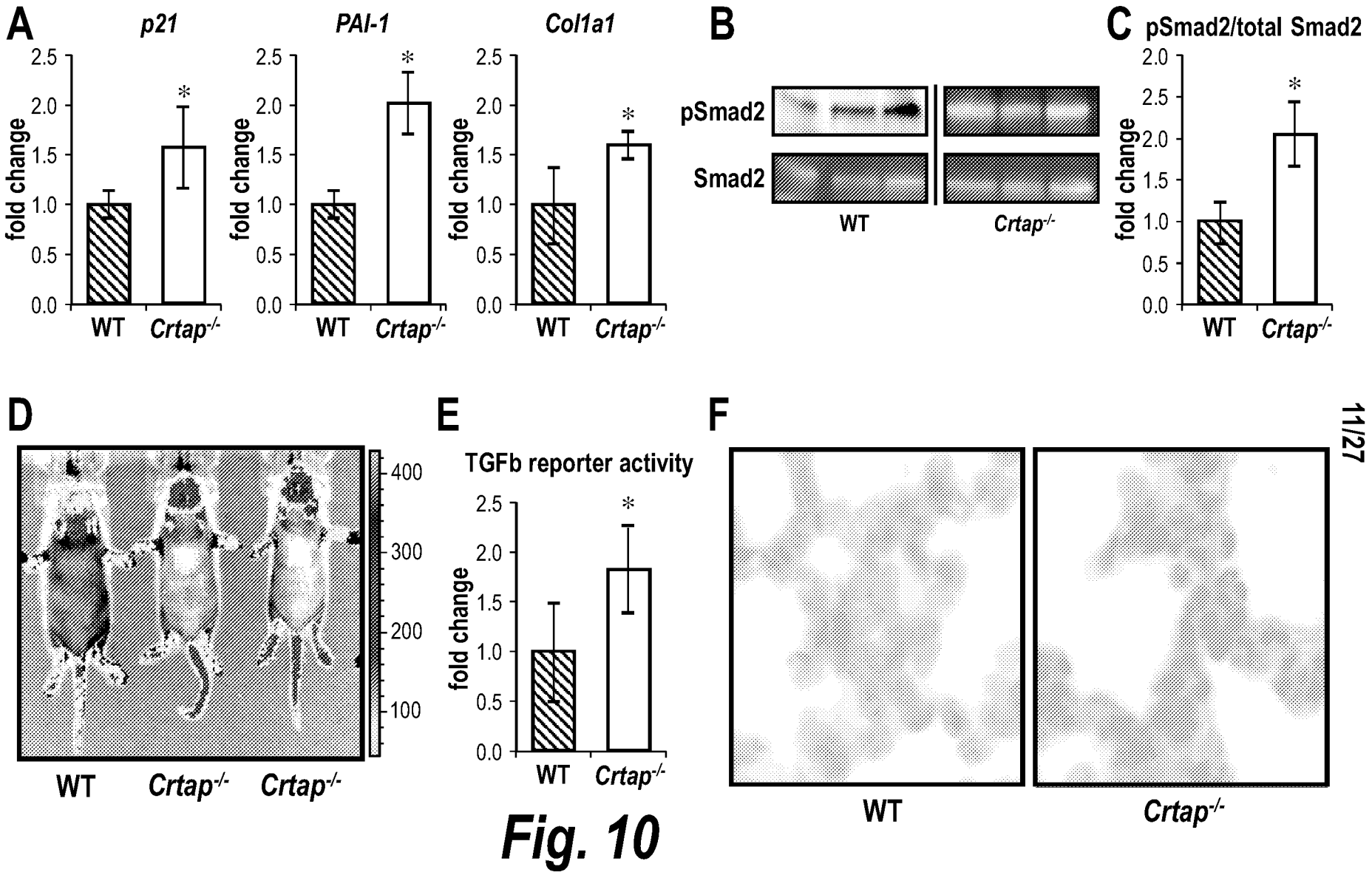

A
p21
PAI-1
Col1a1
fold change
2.5
2.0
1.5
1.0
0.5
0.0
*
WT
Crtap-/-
B
pSmad2
Smad2
WT
Crtap-/-
C
pSmad2/total Smad2
fold change
D
400
300
200
100
WT
Crtap-/-
Crtap-/-
E
TGFb reporter activity
fold change
F
WT
Crtap-/-

Fig. 10

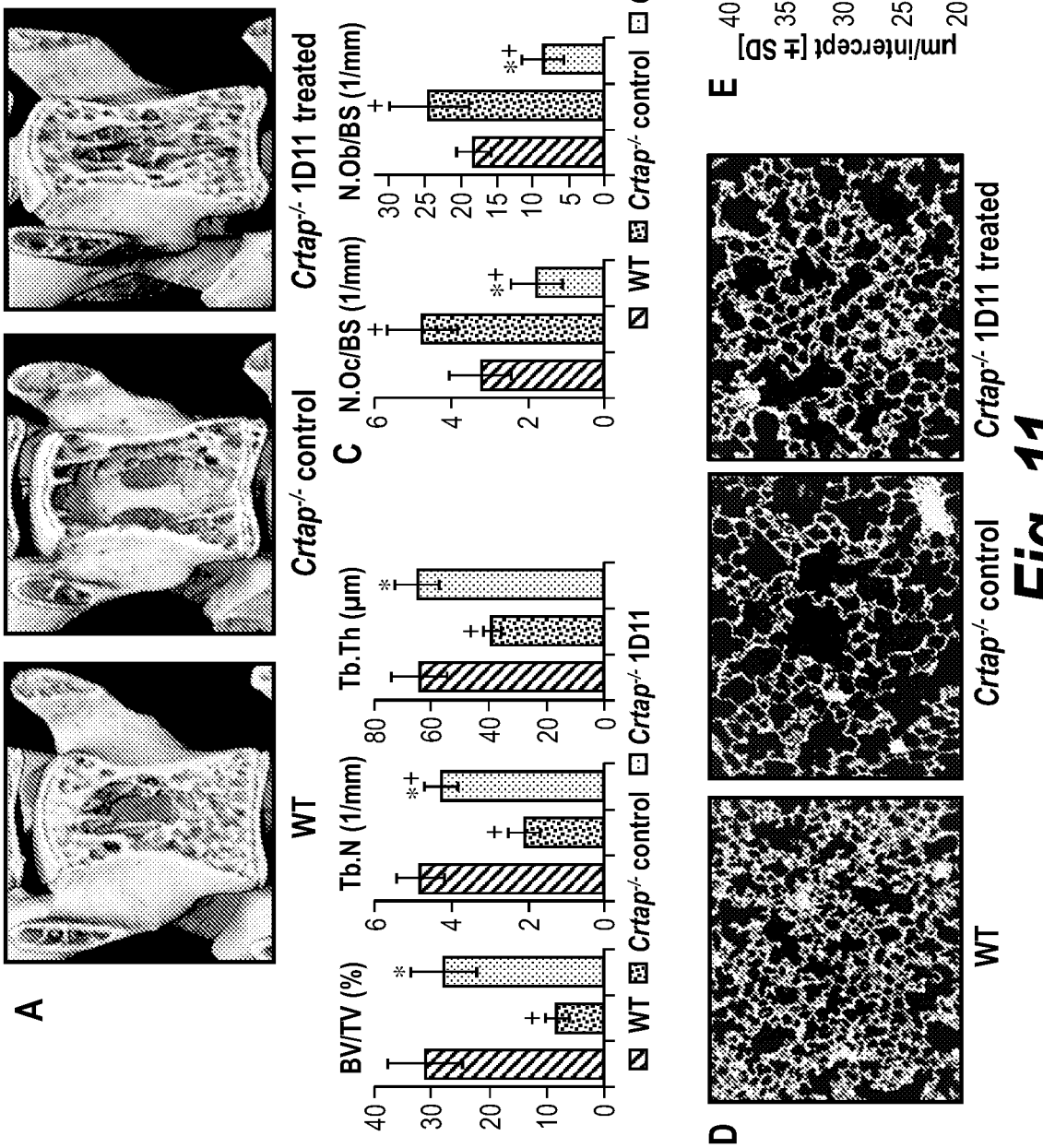

A
WT
Crtap-/- control
Crtap-/- 1D11 treated
B
BV/TV (%)
Tb.N (1/mm)
Tb.Th (µm)
WT
Crtap-/- control
Crtap-/- 1D11
C
N.Oc/BS (1/mm)
N.Ob/BS (1/mm)
N.Ot/B.Ar (1/mm2)
WT
Crtap-/- control
Crtap-/- 1D11
D
WT
Crtap-/- control
Crtap-/- 1D11 treated
E
Mean linear intercept
µm/intercept [± SD]
WT
Crtap-/-
Crtap-/-
control
1D11

Fig. 11

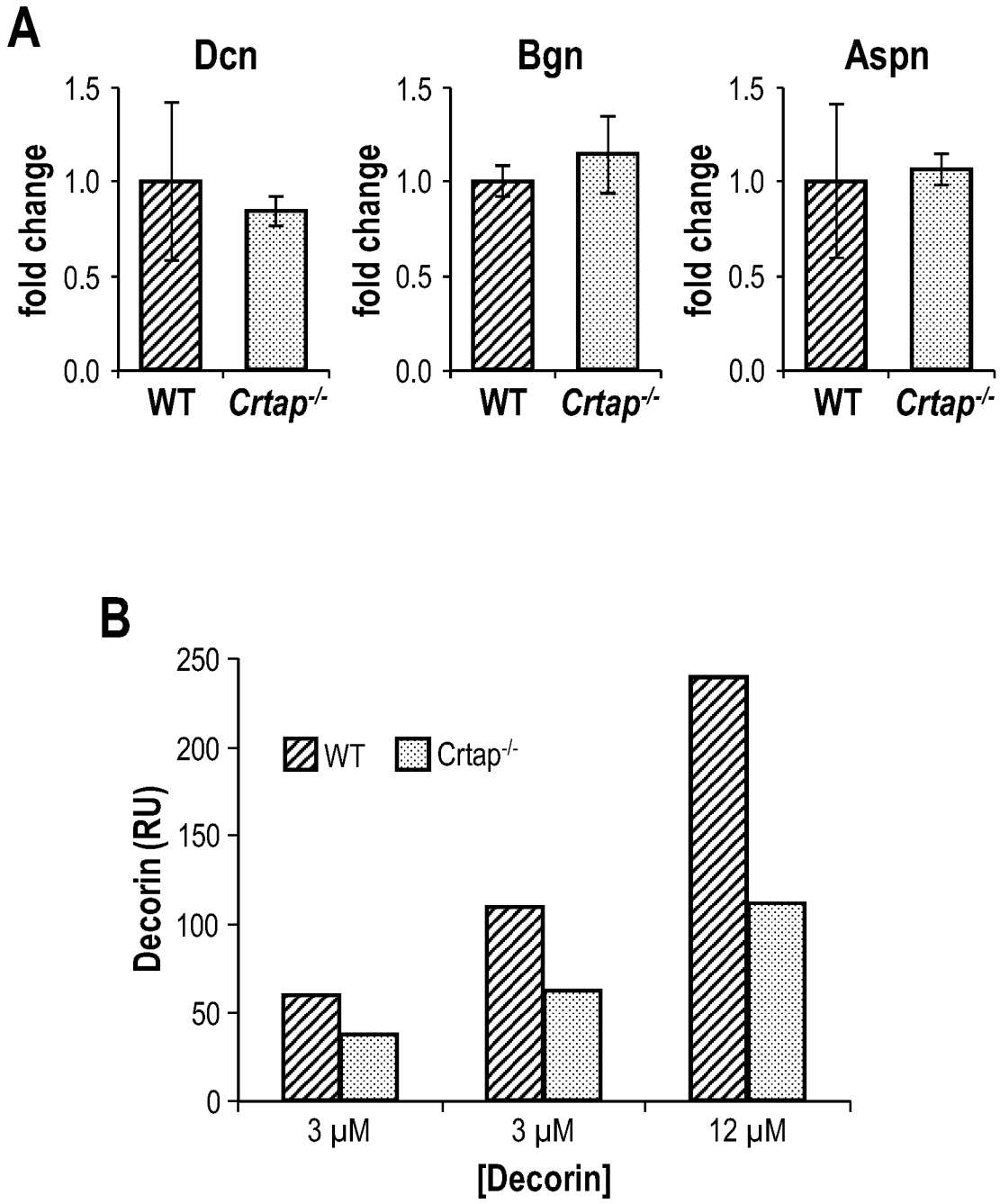

A
Dcn
Bgn
Aspn
fold change
1.5
1.0
0.5
0.0
WT
Crtap-/-
B
Decorin (RU)
250
200
150
100
50
0
WT
Crtap-/-
3 μM
3 μM
12 μM
[Decorin]

Fig. 12

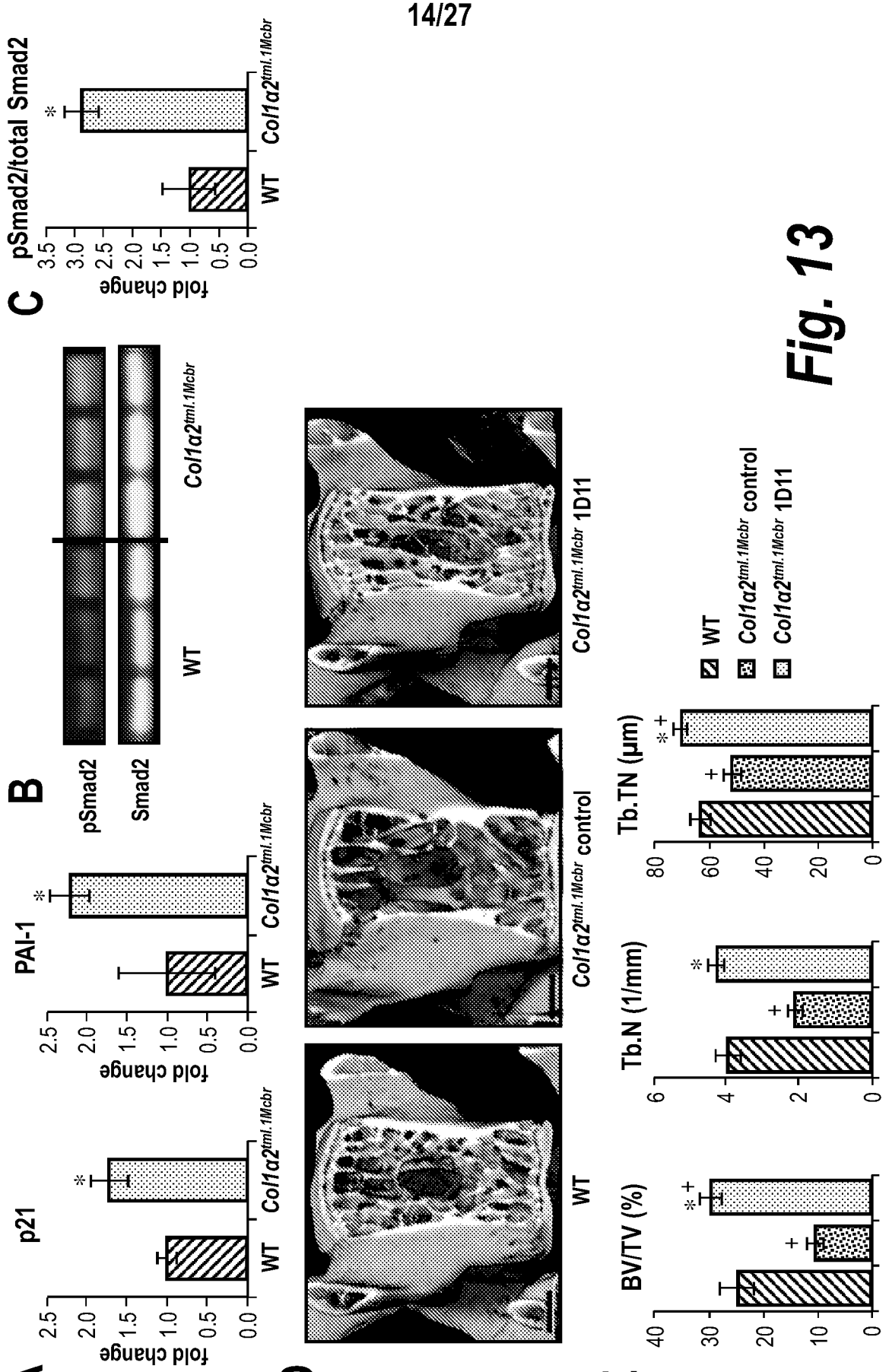

A
p21
fold change
WT
Col1a2tml.1Mcbr
PAI-1
B
pSmad2
Smad2
WT
Col1a2tml.1Mcbr
C
pSmad2/total Smad2
D
WT
Col1a2tml.1Mcbr control
Col1a2tml.1Mcbr 1D11
E
BV/TV (%)
Tb.N (1/mm)
Tb.TN (μm)
WT
Col1a2tml.1Mcbr control
Col1a2tml.1Mcbr 1D11

Fig. 13

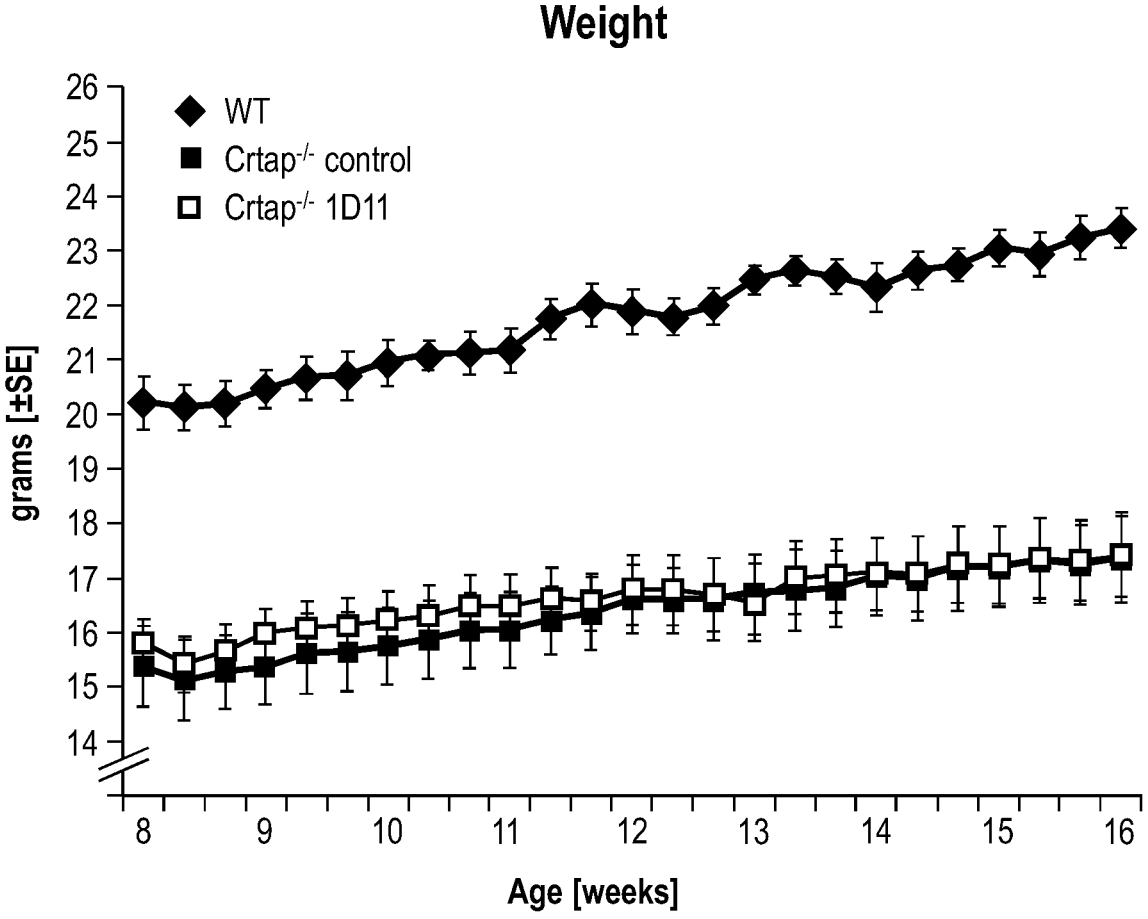

Weight
WT
Crtap-/- control
Crtap-/- 1D11
grams [±SE]
26
25
24
23
22
21
20
19
18
17
16
15
14
8
9
10
11
12
13
14
15
16
Age [weeks]

Fig. 14

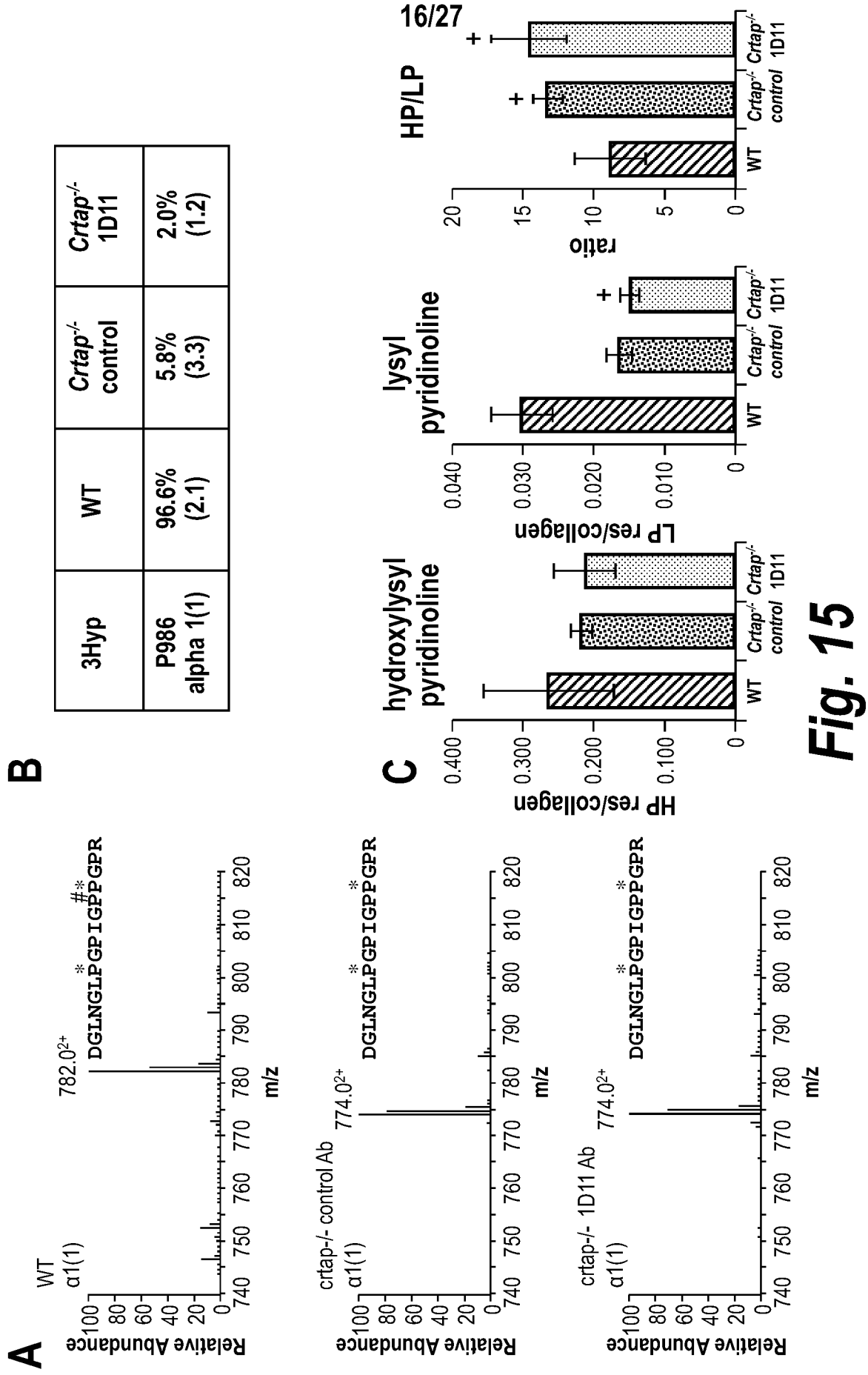

A
WT
α1(1)
782.0²⁺
DGLNGLPGPIGPPGPR
crtap-/- control Ab
774.0²⁺
crtap-/- 1D11 Ab
Relative Abundance
m/z
B
3Hyp
P986 alpha 1(1)
WT
96.6% (2.1)
Crtap-/- control
5.8% (3.3)
Crtap-/- 1D11
2.0% (1.2)
C
hydroxylysyl pyridinoline
HP res/collagen
lysyl pyridinoline
LP res/collagen
HP/LP
ratio
WT
Crtap-/- control
Crtap-/- 1D11

Fig. 15

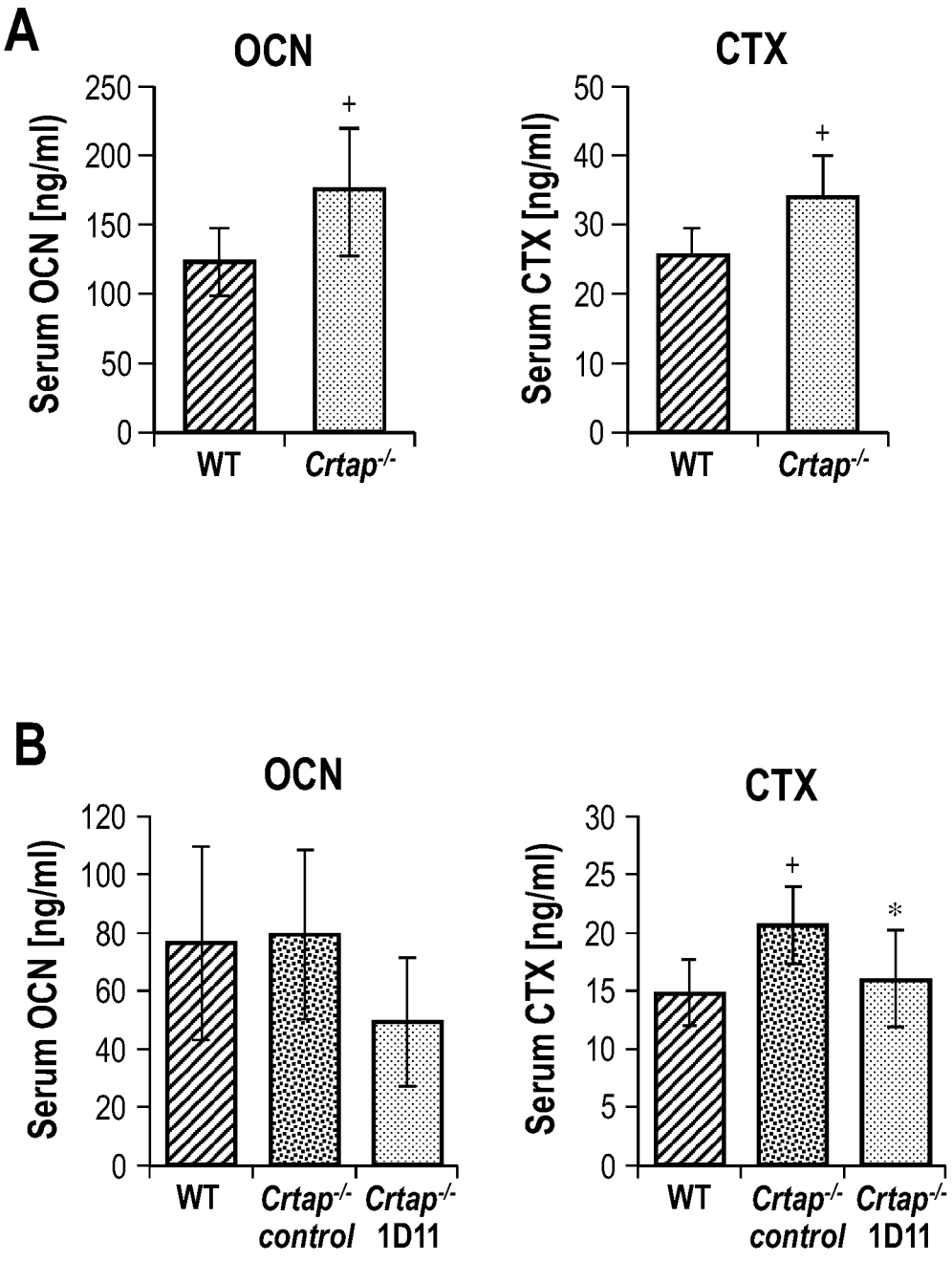

A
OCN
Serum OCN [ng/ml]
250
200
150
100
50
0
+
WT
Crtap-/-
CTX
Serum CTX [ng/ml]
50
40
30
20
10
0
+
WT
Crtap-/-
B
OCN
Serum OCN [ng/ml]
120
100
80
60
40
20
0
WT
Crtap-/- control
Crtap-/- 1D11
CTX
Serum CTX [ng/ml]
30
25
20
15
10
5
0
+
*
WT
Crtap-/- control
Crtap-/- 1D11

Fig. 16

	BV/TV	Tb.N	Tb.Th	Tb.Sp	BMD BV
	(%)	(1/mm)	(μm)	(mm)	(mg HA/ccm)
Wild type	**0.312**	**4.845**	**63.988**	**0.145**	**703.189**
SD	0.065	0.583	9.482	0.034	19.014
***Crtap*$^{-/-}$ control**	**0.084**	**2.130**	**38.888**	**0.450**	**677.416**
SD	0.020	0.409	2.931	0.118	16.138
***Crtap*$^{-/-}$ 1D11**	**0.280**	**4.290**	**64.650**	**0.171**	**746.862**
SD	0.056	0.435	7.407	0.030	26.564
ANOVA *P* value	**<0.001**	**<0.001**	**<0.001^{+}**	**<0.001^{+}**	**<0.001**
Pairwise *P* values					
Wild type vs. *Crtap*$^{-/-}$ control	<0.001	<0.001	<0.05	<0.05	0.023
Wild type vs. *Crtap*$^{-/-}$ 1D11	n.s.	0.031	n.s.	n.s.	<0.001
Crtap$^{-/-}$ control vs. *Crtap*$^{-/-}$ 1D11	<0.001	<0.001	<0.05	<0.05	<0.001

Fig. 17

	BV/TV	Tb.N	Tb.Th	Tb.Sp	BMD BV
	(%)	(1/mm)	(μm)	(mm)	(mg HA/ccm)
Wild type	**0.107**	**2.808**	**37.413**	**0.341**	**733.864**
SD	0.036	0.684	5.071	0.108	25.997
***Crtap*$^{-/-}$ control**	**0.029**	**0.861**	**32.863**	**1.209**	**727.151**
SD	0.011	0.237	3.428	0.345	28.765
***Crtap*$^{-/-}$ 1D11**	**0.123**	**2.953**	**40.663**	**0.323**	**756.539**
SD	0.045	0.767	5.842	0.121	36.913
ANOVA *P* value	**<0.001^{+}**	**<0.001^{+}**	**0.015**	**<0.001**	**0.162**
Pairwise *P* values					
Wild type vs. *Crtap*$^{-/-}$ control	<0.05	<0.05	n.s.	<0.001	
Wild type vs. *Crtap*$^{-/-}$ 1D11	n.s.	n.s.	n.s.	n.s.	
Crtap$^{-/-}$ control vs. *Crtap*$^{-/-}$ 1D11	<0.05	<0.05	0.004	<0.001	

Fig. 18

	Cortical thickness	BMD BV	Diameter a.p.	CSA	CSMI m.l.	CSMI a.p.
	(mm)	(mg HA/ccm)	(mm)	(mm^2)	(mm^4)	(mm^4)
Wild type	**0.242**	**1084.726**	**1.239**	**0.905**	**0.134**	**0.221**
SD	0.014	28.375	0.063	0.079	0.023	0.042
***Crtap*$^{-/-}$ control**	**0.203**	**1084.885**	**1.142**	**0.731**	**0.101**	**0.162**
SD	0.020	34.256	0.065	0.082	0.021	0.034
***Crtap*$^{-/-}$ 1D11**	**0.221**	**1096.127**	**1.186**	**0.808**	**0.111**	**0.186**
SD	0.026	39.754	0.080	0.118	0.028	0.038
ANOVA *P* value	**0.003**	**0.753**	**0.039**	**0.005**	**0.032**	**0.021**
Pairwise *P* values						
Wild type vs. *Crtap*$^{-/-}$ control	<0.001		0.012	0.001	0.011	0.006
Wild type vs. *Crtap*$^{-/-}$ 1D11	n.s.		n.s.	n.s.	n.s.	n.s.
Crtap$^{-/-}$ control vs. *Crtap*$^{-/-}$ 1D11	n.s.		n.s.	n.s.	n.s.	n.s.

Fig. 19

	Maximum load	Stiff-ness	Energy to failure	Ultimate strength	Tough-ness to failure	Elastic modulus	Total displace-ment	Elastic displace-ment	Post-yield displace-ment
	(N)	(N/mm)	(N*mm)	(MPa)	(MPa)	(GPa)	(mm)	(mm)	(mm)
Wild type	**22.831**	**230.578**	**7.846**	**154.704**	**11.912**	**6.960**	**0.444**	**0.068**	**0.376**
SD	2.860	37.053	3.985	7.478	5.695	0.731	0.207	0.014	0.203
***Crtap*$^{-/-}$ control**	**12.943**	**151.689**	**1.228**	**114.496**	**2.208**	**6.663**	**0.127**	**0.079**	**0.048**
SD	2.402	27.384	0.913	18.240	1.677	1.154	0.057	0.006	0.058
***Crtap*$^{-/-}$ 1D11**	**18.818**	**200.804**	**1.991**	**145.633**	**3.408**	**7.248**	**0.156**	**0.073**	**0.083**
SD	2.337	15.644	0.834	19.074	1.851	0.271	0.055	0.013	0.055
ANOVA *P* value	**<0.001**	**0.009**	**0.009**	**0.004**	**0.009**	**0.658**	**0.015**	**0.360**	**0.012**
Pairwise *P* values									
Wild type vs. *Crtap*$^{-/-}$ control	<0.001	0.003	0.005	0.001	0.005		0.009		0.007
Wild type vs. *Crtap*$^{-/-}$ 1D11	n.s.	n.s.	0.017	n.s.	0.017		0.023		0.019
Crtap$^{-/-}$ control vs. *Crtap*$^{-/-}$ 1D11	0.015	n.s.	n.s.	0.016	n.s.		n.s.		n.s.

Fig. 20

	BV/TV	Tb.N	Tb.Th	Tb.Sp	N.Oc/BS	Oc.S/BS	N.Ob/BS	Ob.S/BS	N.Ot/B.Ar
	(%)	(1/mm)	(µm)	(µm)	(1/mm)	(%)	(1/mm)	(%)	(1/mm2)
Wild type	**11.956**	**4.003**	**29.554**	**226.736**	**3.226**	**15.051**	**18.142**	**20.827**	**549.002**
SD	3.067	0.656	3.536	50.077	0.812	3.089	2.368	2.754	83.665
***Crtap*$^{-/-}$ control**	**3.817**	**1.909**	**19.502**	**587.008**	**4.768**	**19.885**	**24.487**	**26.888**	**735.561**
SD	1.656	0.692	2.560	289.835	0.914	3.407	5.421	6.983	72.617
***Crtap*$^{-/-}$ 1D11**	**10.203**	**3.411**	**30.182**	**277.886**	**1.772**	**6.829**	**8.638**	**9.748**	**565.044**
SD	3.097	0.878	6.982	69.118	0.673	2.235	2.855	4.718	51.014
ANOVA *P* value	**<0.001**	**<0.001**	**0.002**	**0.003^{+}**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Pairwise *P* values									
Wild type vs. *Crtap*$^{-/-}$ control	<0.001	<0.001	0.002	<0.05	0.005	0.012	0.011	n.s.	<0.001
Wild type vs. *Crtap*$^{-/-}$ 1D11	n.s.	n.s.	n.s.	n.s.	0.007	<0.001	<0.001	0.002	n.s.
Crtap$^{-/-}$ control vs. *Crtap*$^{-/-}$ 1D11	<0.001	0.003	0.001	<0.05	<0.001	<0.001	<0.001	<0.001	<0.001

Fig. 21

	BV/TV	Tb.N	Tb.Th	Tb.Sp	BMD BV
	(%)	(1/mm)	(μm)	(mm)	(mg HA/ccm)
Wild type	**0.247**	**3.939**	**62.533**	**0.193**	**716.669**
SD	0.033	0.330	3.497	0.025	7.626
***Col1α2*$^{tm1.1Mcbr}$ control**	**0.106**	**2.071**	**51.067**	**0.435**	**731.436**
SD	0.015	0.195	2.999	0.047	11.792
***Col1α2*$^{tm1.1Mcbr}$ 1D11**	**0.297**	**4.244**	**69.983**	**0.166**	**754.115**
SD	0.020	0.199	2.329	0.013	7.844
ANOVA *P* value	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Pairwise *P* values					
Wild type vs. *Col1α2*$^{tm1.1Mcbr}$ control	<0.001	<0.001	<0.001	<0.001	0.015
Wild type vs. *Col1α2*$^{tm1.1Mcbr}$ 1D11	0.002	n.s.	<0.001	n.s.	<0.001
Col1α2$^{tm1.1Mcbr}$ control vs. *Col1α2*$^{tm1.1Mcbr}$ 1D11	<0.001	<0.001	<0.001	<0.001	<0.001

Fig. 22

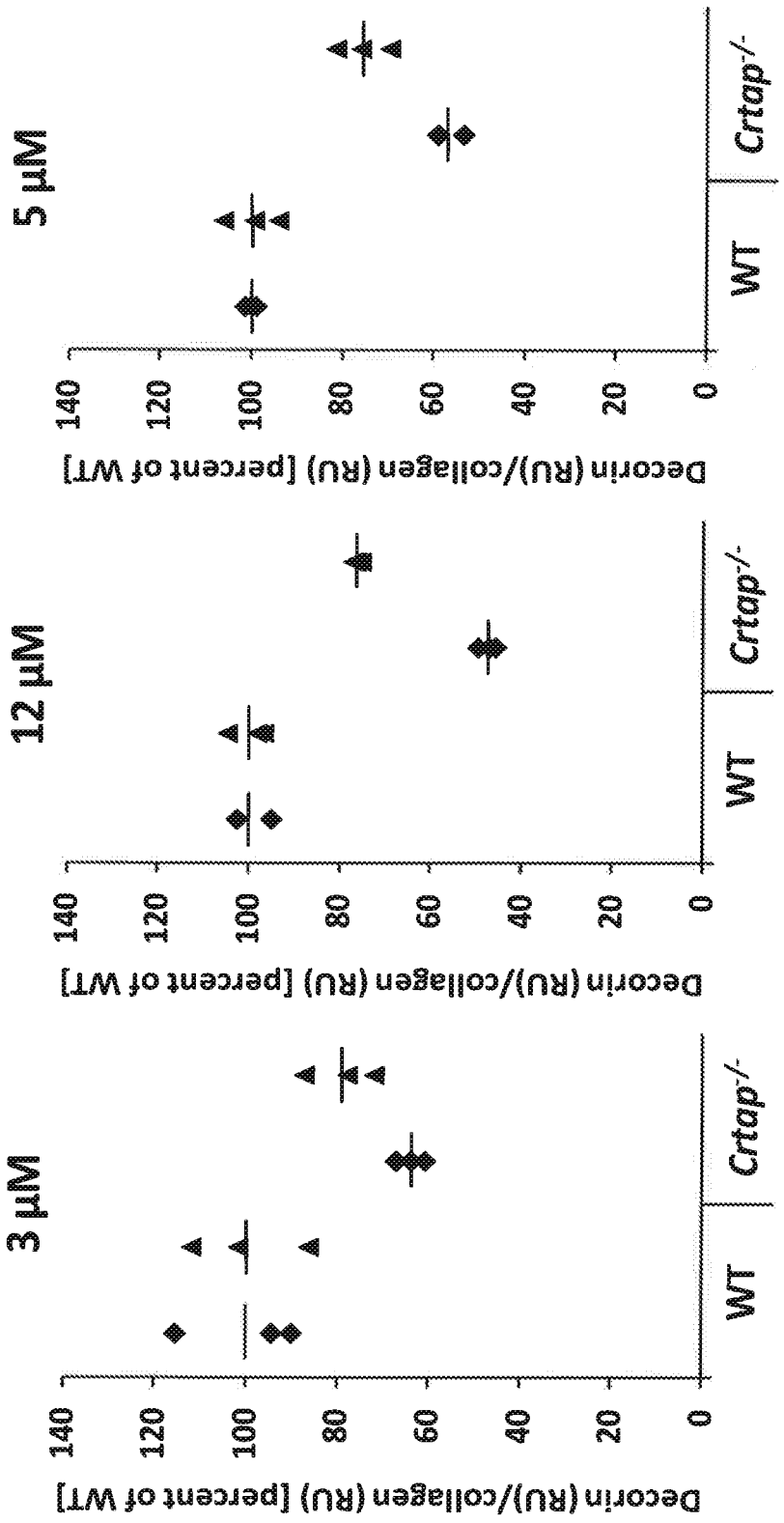

3 µM
12 µM
5 µM
Decorin (RU)/collagen (RU) [percent of WT]
0
20
40
60
80
100
120
140
WT
Crtap-/-

Fig. 23

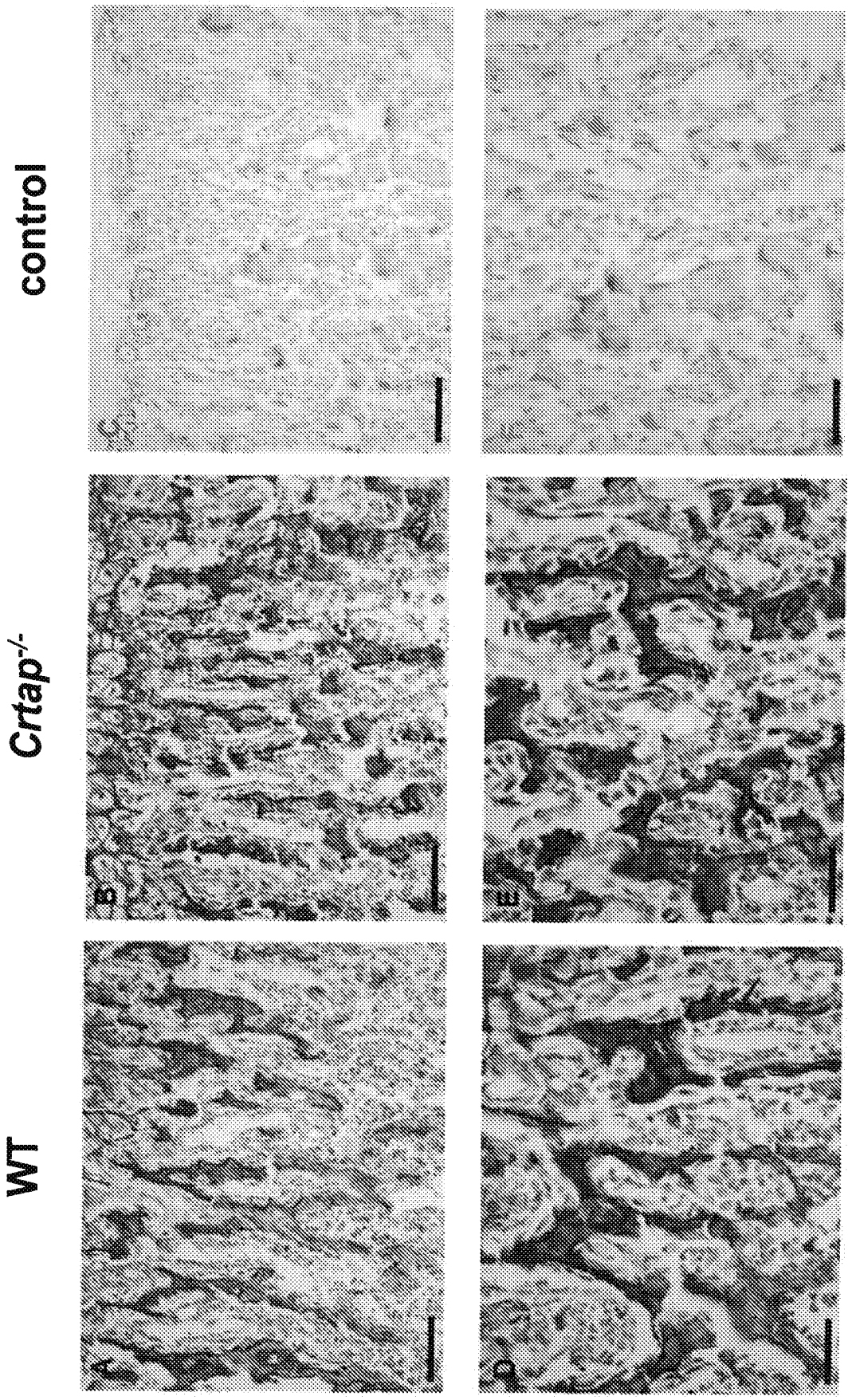


Fig. 24

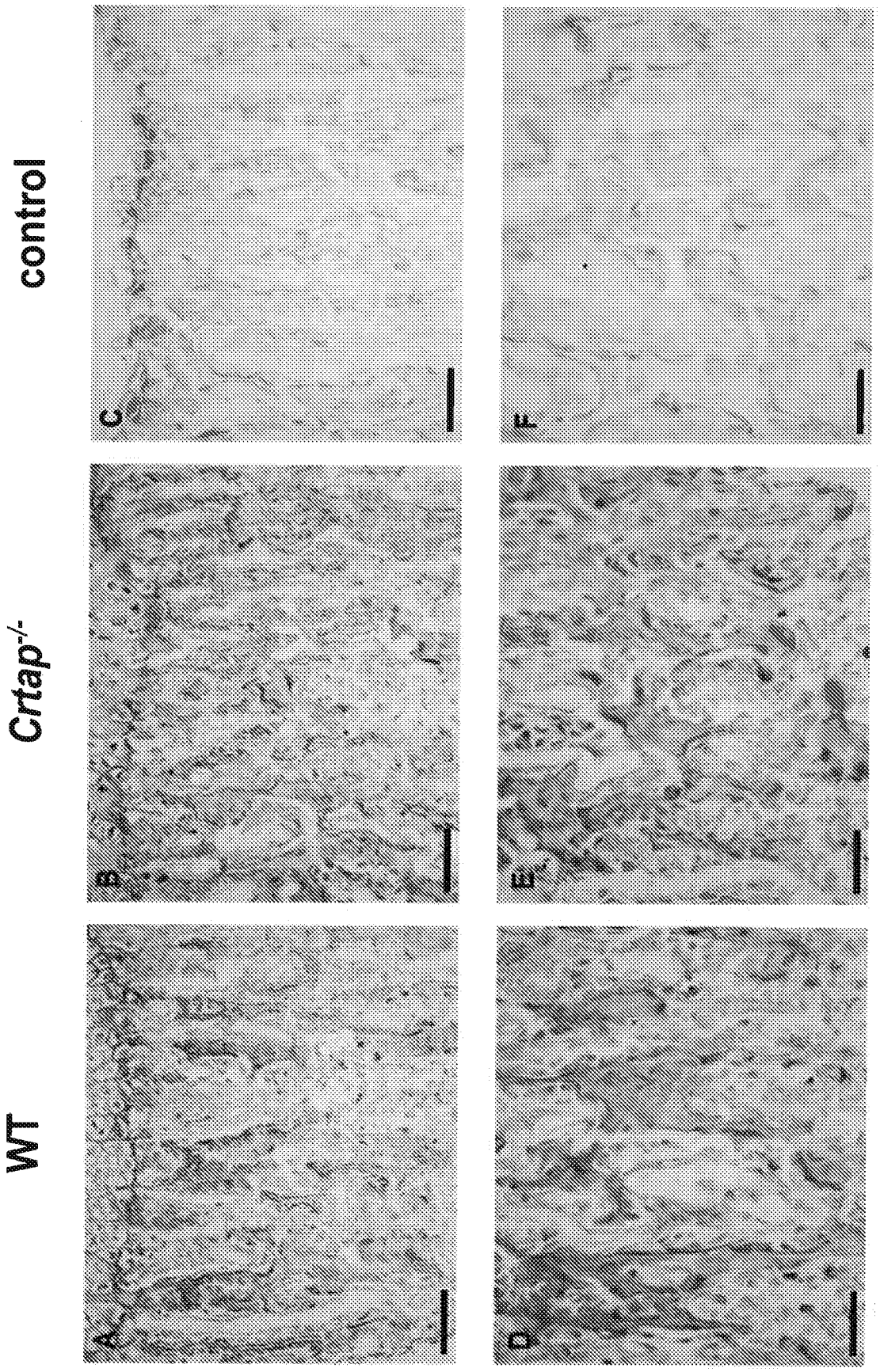


Fig. 25

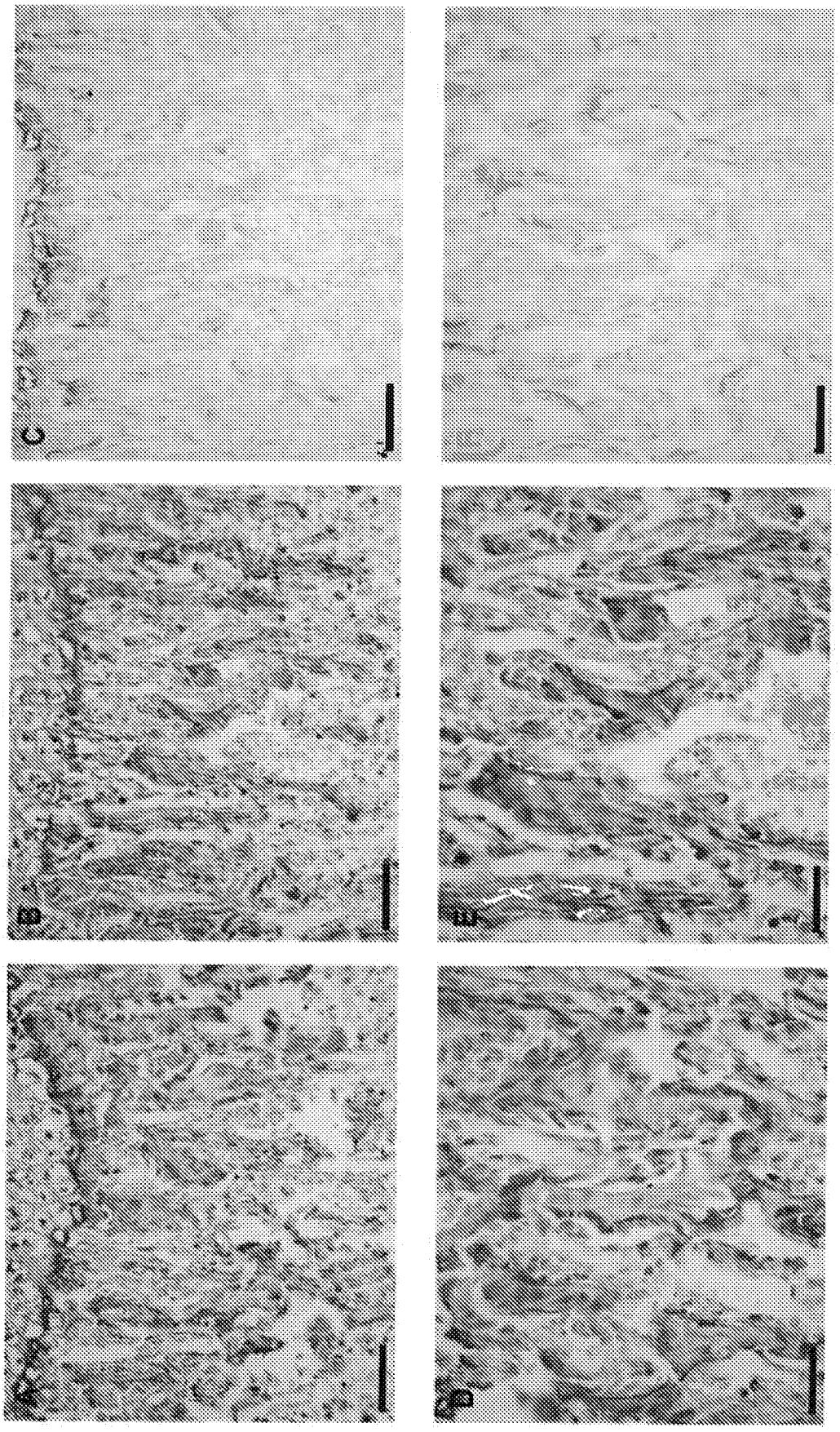


Fig. 26