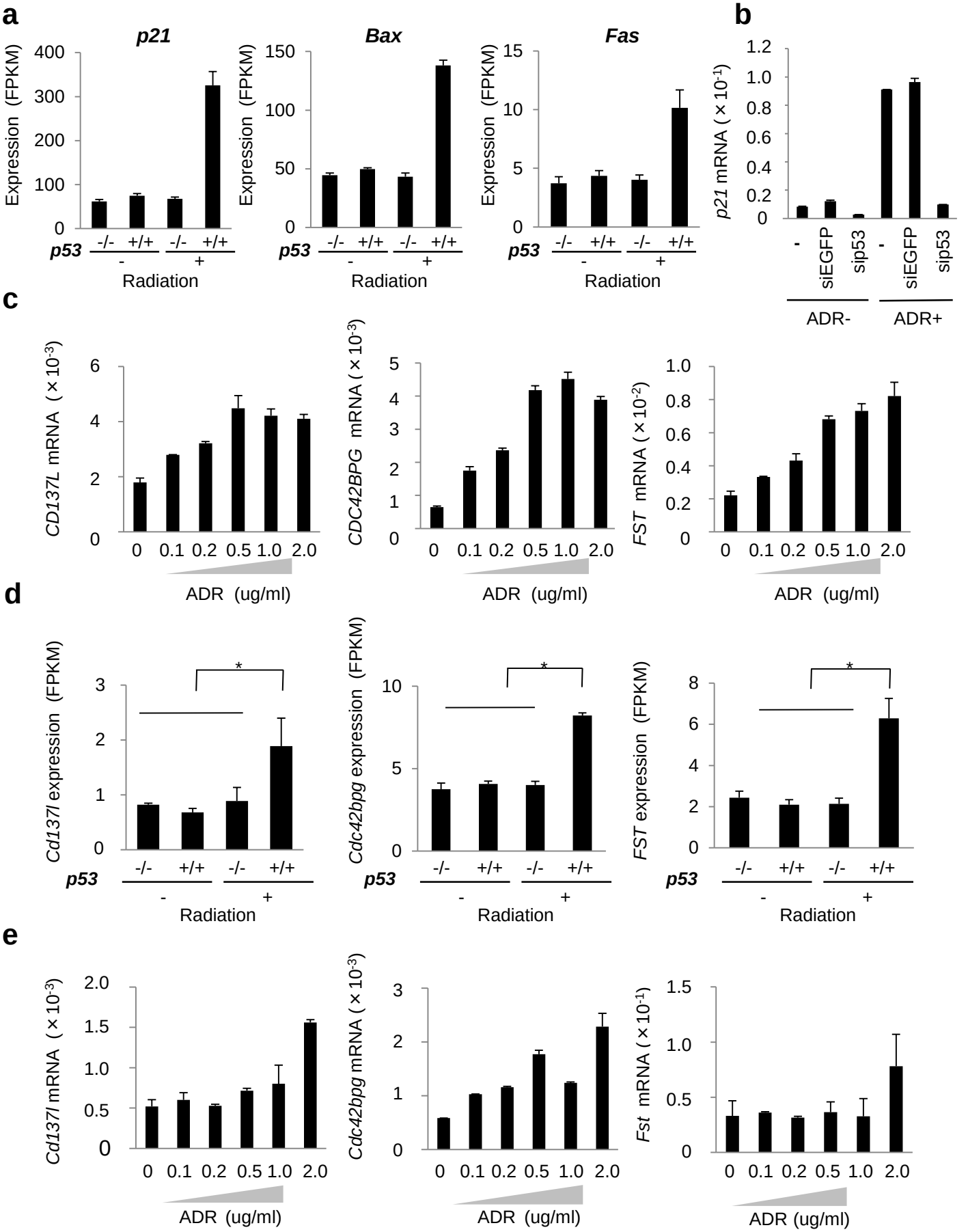
**Identification of a p53 target, *CD137L*, that mediates growth suppression and immune response of osteosarcoma cells**

Yusuke Tsuda, Chizu Tanikawa, Takafumi Miyamoto, Makoto Hirata, Varalee Yodsurang, Yao-zhong Zhang, Seiya Imoto, Rui Yamaguchi, Satoru Miyano, Hiroshi Takayanagi, Hirotaka Kawano, Hidewaki Nakagawa, Sakae Tanaka, Koichi Matsuda

**Supplementary Figure 1.**




**Supplementary Figure 1.** Regulation of *CD137L*, *CDC42BPG* and *FST* by p53

(a) Expression of representative p53 target genes *p21*, *Bax* and *Fas* based on RNA sequencing data. Error bars represent SD (n = 3). (b) At 24 h after transfection with each siRNA, U2OS cells were treated with ADR (2 μg/ml for 2 h). Then, 36 h after treatment, qPCR was performed. siRNA against *EGFP* was used as a control. β-actin was used for normalization of the expression levels. Error bars represent SD (n = 2). (c) qPCR in U2OS cells harvested 36 h after ADR treatment (0-2 μg/ml for 2 h). β-actin was used for normalization of the expression levels. Error bars represent SD (n = 2). (d) *Cd137l*, *CDC42BPG* or *FST* expression from RNA sequencing data. FPKM, fragments per kilobase of exon per million mapped fragments. Error bars represent SD (n = 3). *P < 0.05, Student's t-test. (e) qPCR in $p53^{+/+}$ calvarial osteoblasts harvested 36 h after ADR treatment (2 μg/ml for 2 h). β-actin was used for normalization of the expression levels. Error bars represent SD (n = 3).

# Supplementary Figure 2.

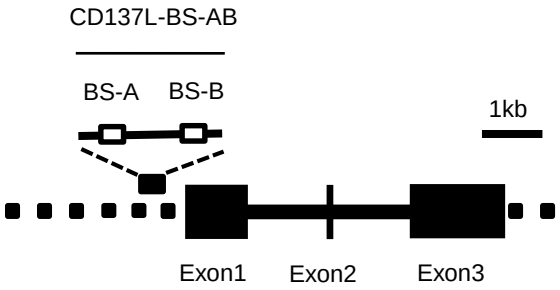
## a

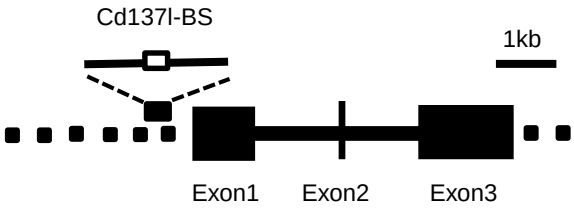
### Human

| | |
|---|---|
| Consensus | RRRCWWGYYYRRRCWWGYYY |
| CD137L-BS-A | AcACTAGCCagtAACATtaCT |
| CD137L-BS-B | GGGCAcGgTaAcGCATGaCT |

### Mouse

| | |
|---|---|
| Consensus | RRRCWWGYYYRRRCWWGYYY |
| Cd137l-BS | GtGCATGCaCAtACATGCag |



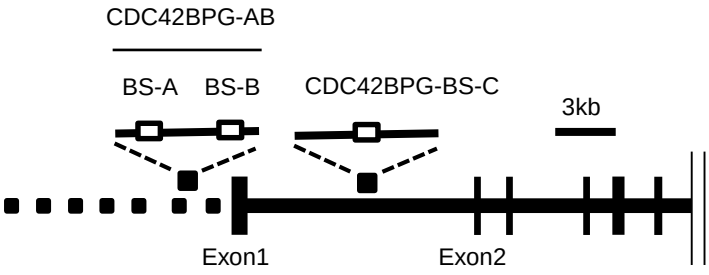

## b

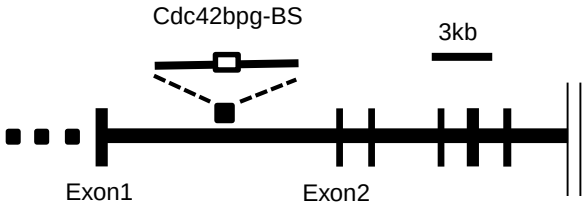
### Human

| | |
|---|---|
| Consensus | RRRCWWGYYYRRRCWWGYYY |
| CDC42BPG-BS-A | AGGCATGagCcAcCATGCCC |
| CDC42BPG-BS-B | AtGCcAGTCCcAGcCcTGCCC |
| CDC42BPG-BS-C | ctGCTTGTCTctACTTGTCC |

### Mouse

| | |
|---|---|
| Consensus | RRRCWWGYYYRRRCWWGYYY |
| Cdc42bpg-BS | cAACTTGTCCctGctCcTGCCC |



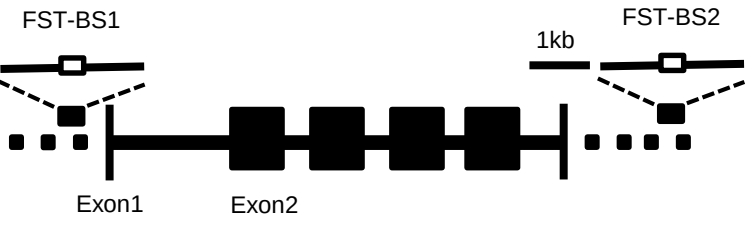

## c

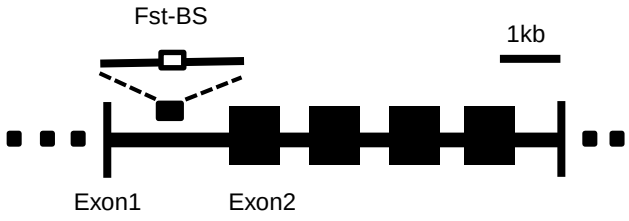
### Human

| | |
|---|---|
| Consensus | RRRCWWGYYYRRRCWWGYYY |
| FST-BS1 | GAACcAGTaTtGACcTGTgT |
| FST-BS2 | GGACcTGCCCAGACATGTCC |

### Mouse

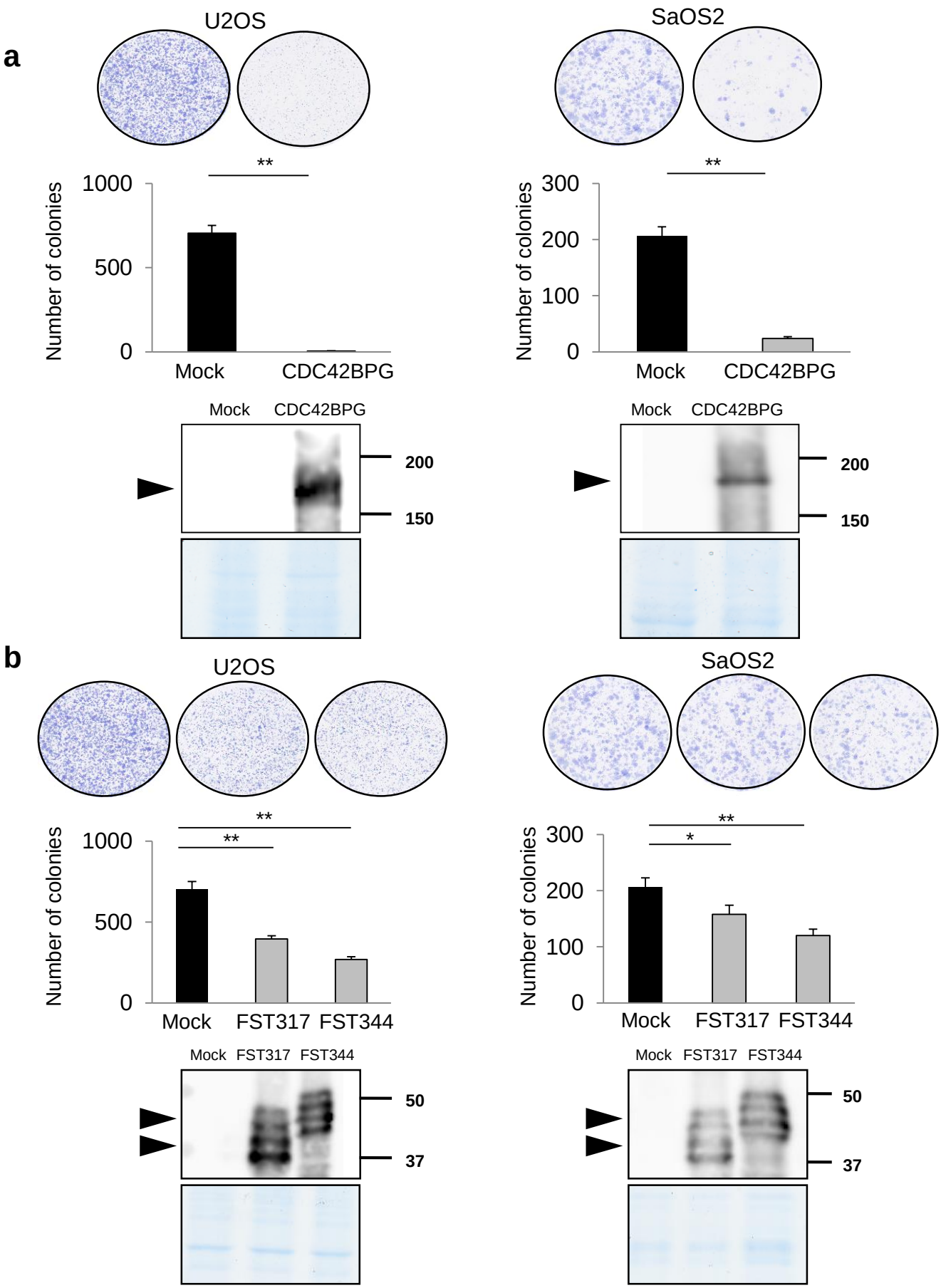
| | |
|---|---|
| Consensus | RRRCWWGYYYRRRCWWGYYY |
| Fst-BS | cGACATGTaaAAACATcCgT |



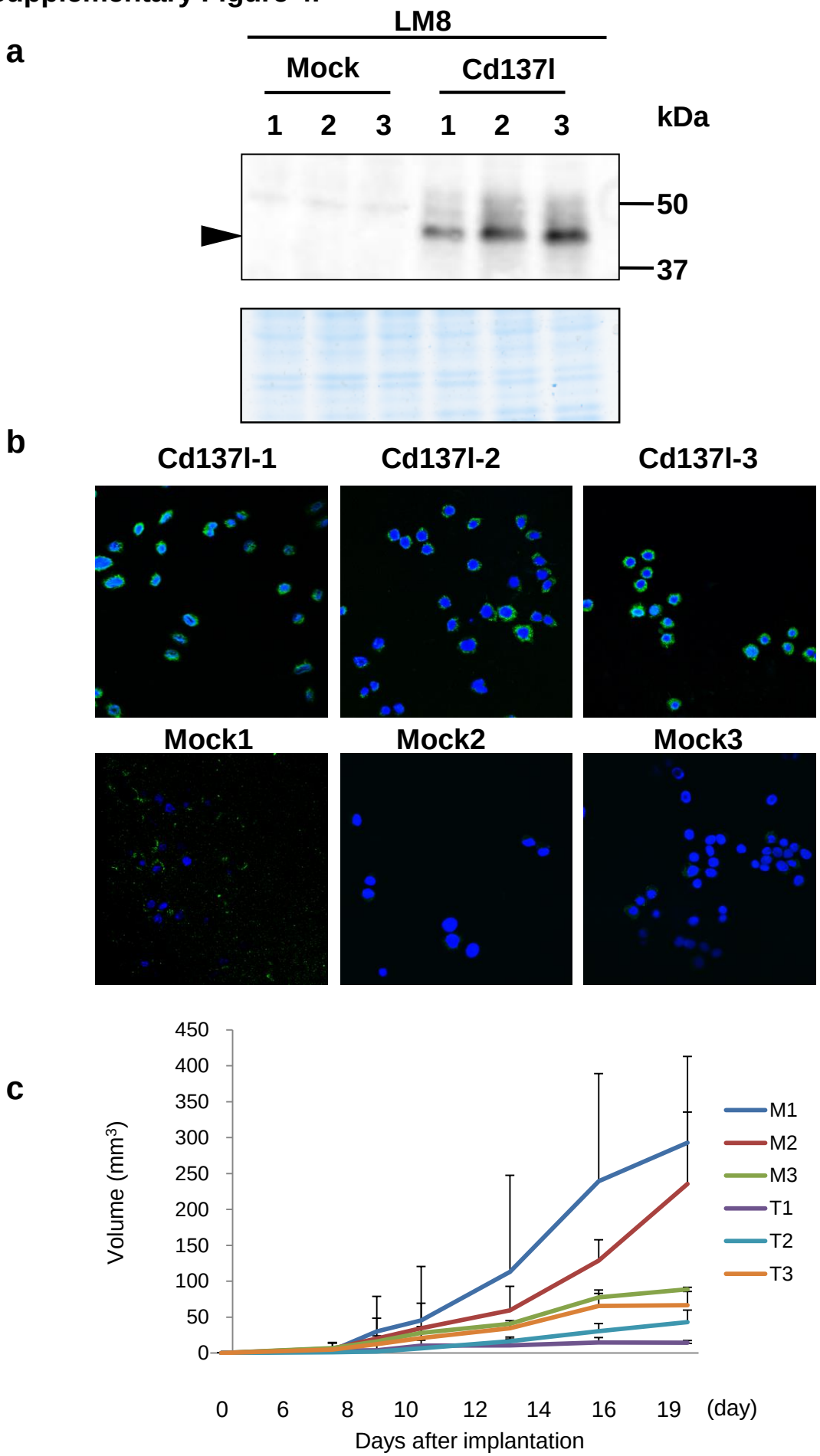

**Supplementary Figure 2.** Genomic structures
(a)(b)(c) The genomic structures of the human (left) and mouse (mouse) *CD137L* (a), *CDC42BPG* (b) and *FST* (c) genes. White boxes represent the location of potential p53-binding sequences (p53BSs). R, purine; W, A or T; Y, pyrimidine. Nucleotides identical to the consensus sequence are written in capital letters.

## Supplementary Figure 3.



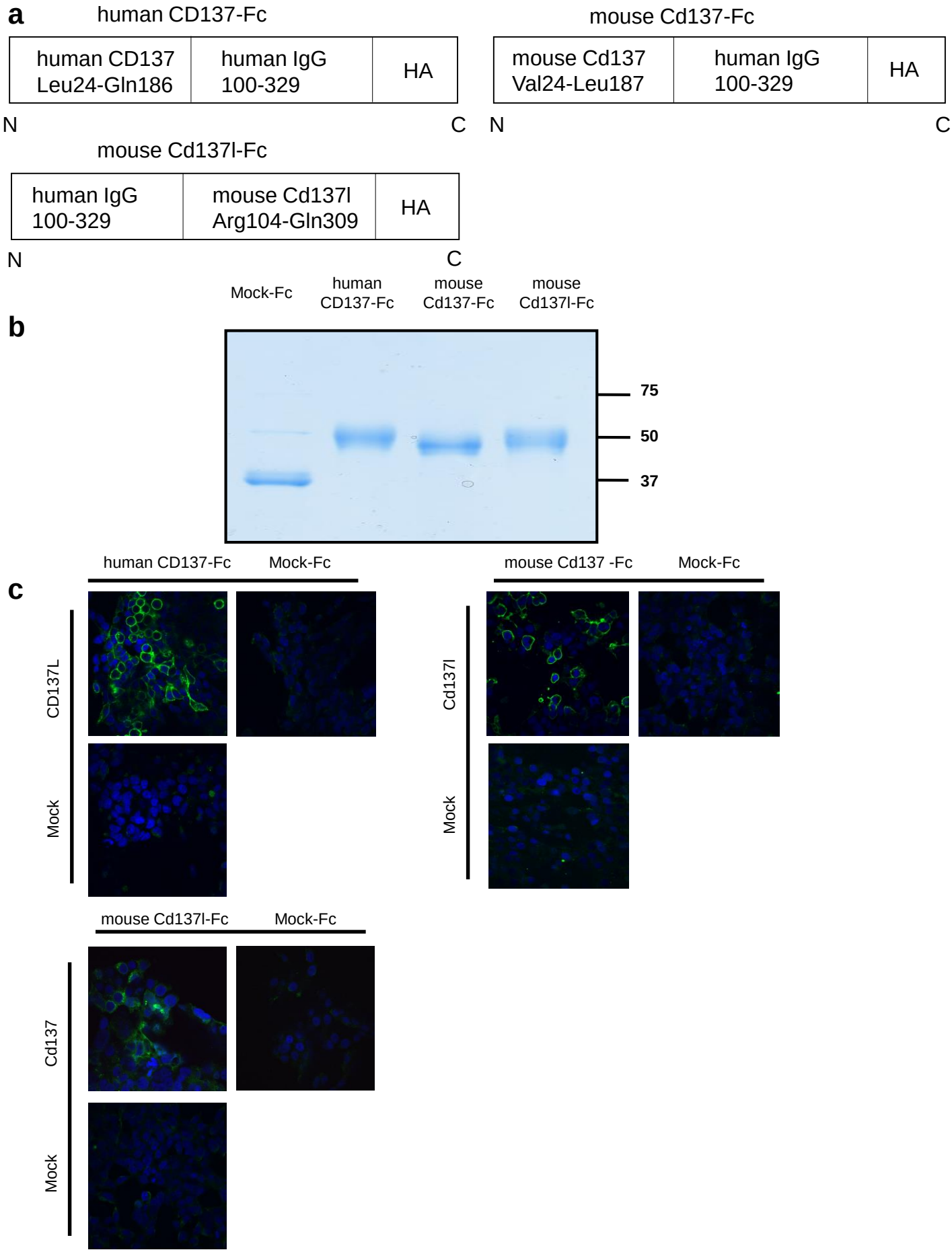

**Supplementary Figure 3.** Colony formation assay
(a)(b) A colony formation assay was performed. After ectopic expression of *CDC42BPG* (a), *FST* (b) or mock, the number of U2OS (left) or SaOS2 (right) colonies was determined. FST317 and FST344 are isoforms of FST. Whole cell extracts were subjected to western blotting with an anti-HA antibody. Coomassie Brilliant Blue staining was used as loading control.

**Supplementary Figure 4.**



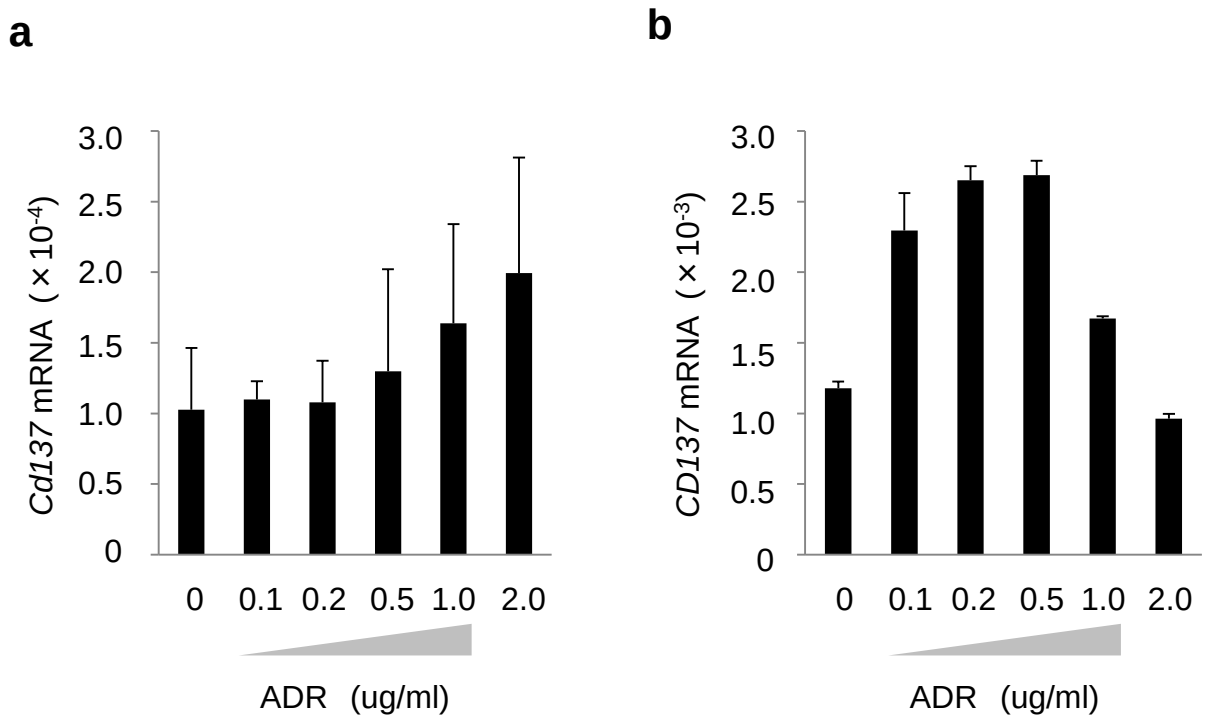

**Supplementary Figure 4.** Construction of stable cell lines and in vivo studies
(a) At 24 h after seeding, whole cell extracts were subjected to western blotting with an anti-Cd137l antibody. Coomassie Brilliant Blue staining was used as loading control. (b) Immunohistochemical staining for HA protein in Cd137l-expressing cells. (c) Cd137l (n = 3) or mock (n = 3) stable expression cell lines were inoculated into the left and right flanks of C3H mice; each group contains 2 mice. Tumor volume was calculated every 2 or 3 days.

**Supplementary Figure 5.**



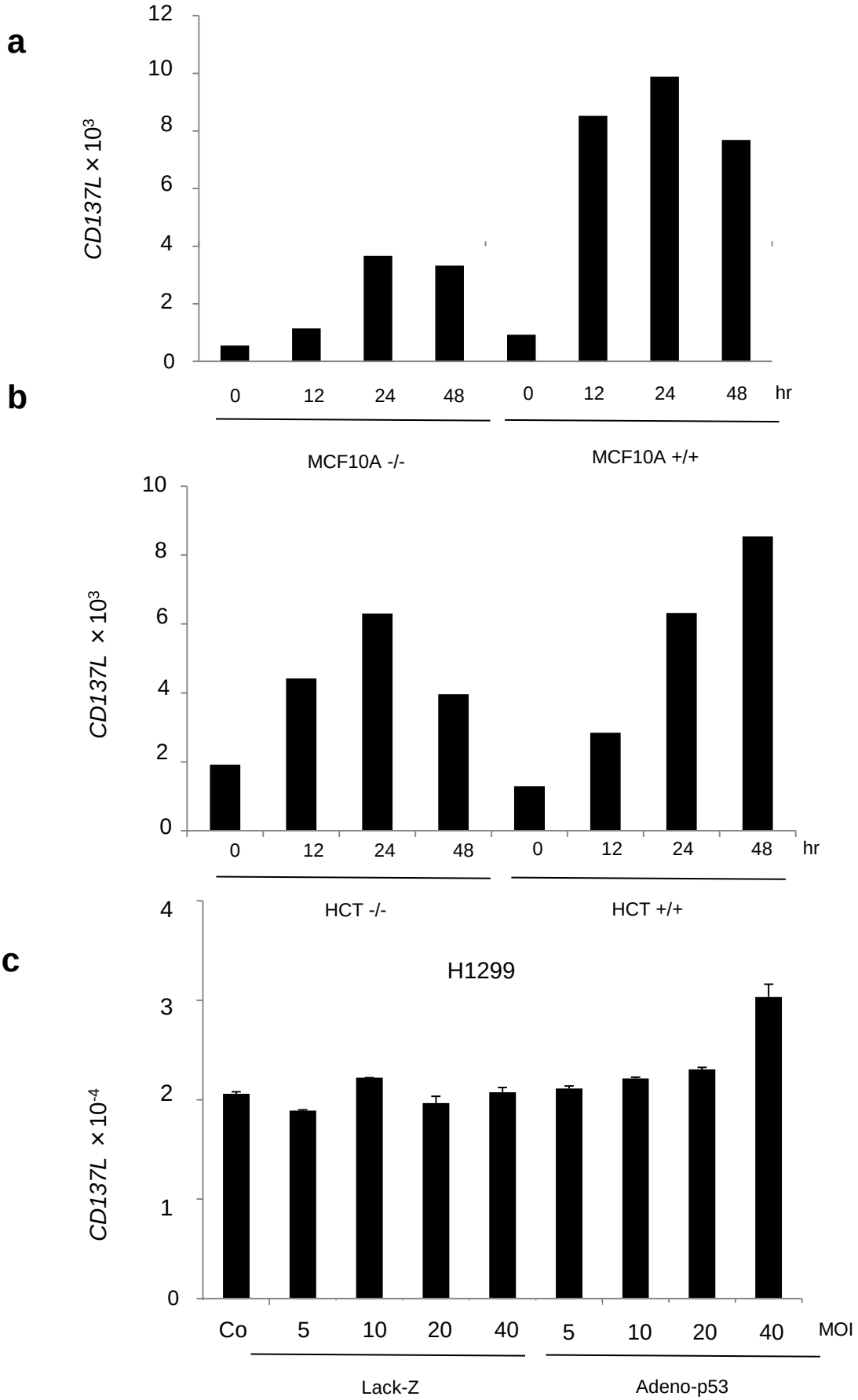

**Supplementary Figure 5.** Construction of recombinant proteins and in vivo studies
(a) The structures of recombinant proteins fused with the Fc fragment of IgG. Leu, Leucine; Gln, Glutamine; Val, Valine; Arg, Arginine. (b) Coomassie Brilliant Blue staining of recombinant proteins after purification. (c) After transfection with plasmid expressing CD137L or mock, the HEK293 cells were incubated with CD137-Fc (2 μg/ml) or mock-Fc (2 μg/ml) for 2 h. Immunohistochemical staining was performed using human IgG antibody to confirm binding ability in each recombinant protein. We also confirmed the interaction between Cd137 and Cd137l-Fc.

## Supplementary Figure 6.




**Supplementary Figure 6.** Expression of CD137
(a) qPCR of $p53^{+/+}$ osteoblasts harvested 36 h after ADR treatment (0-2 μg/ml for 2 h). β-actin was used for normalization of the expression levels. Error bars represent SD (n = 2). (b) qPCR of U2OS cells harvested 36 h after ADR treatment (0-2 μg/ml for 2 h). β-actin was used for normalization of the expression levels. Error bars represent SD (n = 2).

**Supplementary Figure 7.**

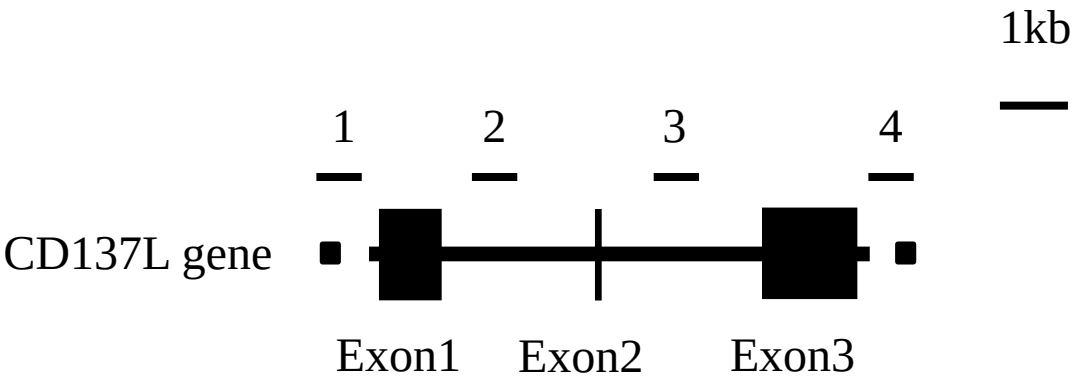



**Supplementary Figure 7.** Expression of CD137

(a) (b) Microarray analysis was performed after treatment with 2 μg/ml of adriamycin for 2. At 0 h, 12 h, 24 h and 48 h after ADR treatment, RNA was collected. (c) qPCR was performed after Lack-Z or Adeno-p53 infection (5-40MOI). β-actin was used for normalization of the expression levels. Error bars represent SD (n = 2).

**Supplementary Figure 8.**

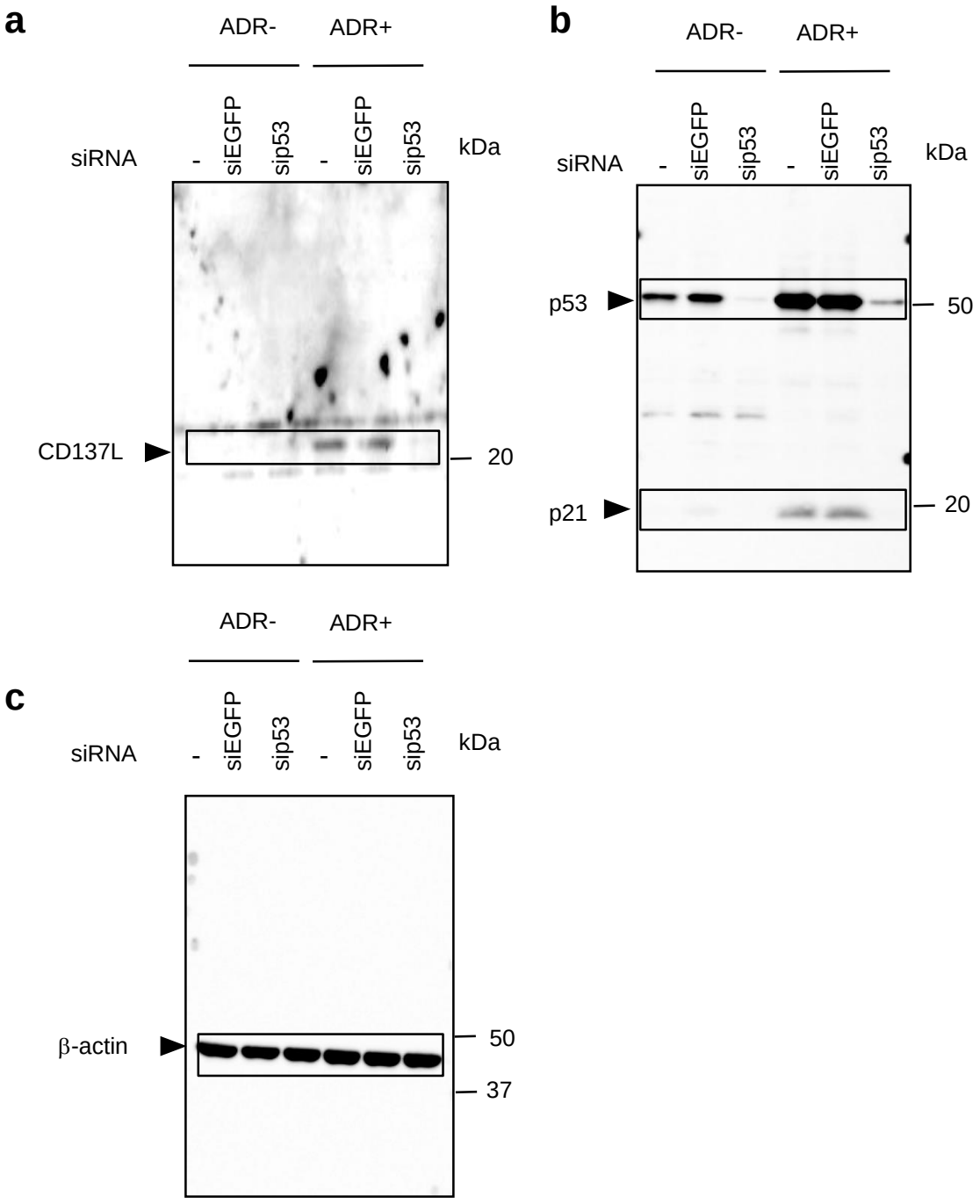
p53 binding regions in the *CD137L* gene (+/- 1kb)
Ch19: 6530010-6536939 (GRCh37/hg19)




| | | | | |
|---|---|---|---|---|
| 1 | chr19 | Promoter | 6530921 | 6531665 |
| 2 | chr19 | Intron1 | 6532281 | 6532324 |
| 3 | chr19 | Intron2 | 6534452 | 6534634 |
| 4 | chr19 | Downstream | 6536671 | 6536767 |

**Supplementary Figure 8.** Remap database indicates four p53 binding regions in CD137L gene (within ±1kb, GRCh37/hg19)

**Supplementary Figure 9.**




**Supplementary Figure 9.** Full-length gels and blots are shown in Figure 3b

## Supplementary Table 1a. p53-induced gene list

| gene | FPKM value | | | | | status |
|---|---|---|---|---|---|---|
| | WX | KX | W | K | WX/max | |
| Aen | 35.15 | 7.68 | 8.84 | 7.32 | 3.98 | R |
| AI414108 | 1.57 | 0.36 | 0.76 | 0.51 | 2.07 | M |
| Ak1 | 79.91 | 32.19 | 32.61 | 33.52 | 2.38 | R |
| Ano3 | 1.37 | 0.05 | 0.03 | 0.06 | 24.64 | N |
| Anxa8 | 36.83 | 16.46 | 15.49 | 14.13 | 2.24 | N |
| Ass1 | 11.15 | 3.46 | 2.28 | 2.63 | 3.22 | N |
| Atp1a2 | 13.71 | 6.47 | 3.39 | 4.68 | 2.12 | N |
| B230120H23Rik | 8.86 | 4.11 | 4.01 | 3.88 | 2.16 | M |
| Bax | 139.69 | 42.14 | 50.40 | 43.63 | 2.77 | R |
| Bbc3 | 16.85 | 4.86 | 5.52 | 4.87 | 3.05 | R |
| Cbln2 | 1.27 | 0.41 | 0.63 | 0.50 | 2.02 | N |
| Ccng1 | 75.24 | 14.88 | 17.13 | 15.05 | 4.39 | R |
| Cd80 | 2.00 | 0.64 | 0.51 | 0.41 | 3.14 | N |
| Cd137l | 1.76 | 0.81 | 0.72 | 0.81 | 2.17 | N |
| Cdc42bpg | 8.31 | 4.05 | 3.97 | 3.88 | 2.05 | N |
| Cdkn1a | 343.52 | 66.17 | 74.00 | 64.30 | 4.64 | R |
| Celf5 | 5.47 | 0.94 | 1.68 | 1.14 | 3.25 | N |
| Ces2e | 2.25 | 0.63 | 0.63 | 0.54 | 3.57 | M |
| Cox6b2 | 48.06 | 8.77 | 7.36 | 8.15 | 5.48 | N |
| Cpt1c | 27.30 | 9.44 | 11.19 | 10.20 | 2.44 | R |
| Dcxr | 41.06 | 6.28 | 6.28 | 5.57 | 6.54 | N |
| Dynlrb2 | 1.31 | 0.17 | 0.09 | 0.62 | 2.13 | N |
| Eda2r | 5.71 | 0.13 | 0.25 | 0.22 | 22.60 | R |
| Ephx1 | 73.75 | 6.92 | 9.36 | 8.42 | 7.88 | N |
| Exoc4 | 17.97 | 4.26 | 5.22 | 4.05 | 3.44 | N |
| Fam212b | 8.10 | 0.53 | 1.46 | 1.22 | 5.56 | N |
| Fas | 9.32 | 4.00 | 4.37 | 3.99 | 2.13 | R |
| Foxj1 | 1.72 | 0.31 | 0.54 | 0.72 | 2.38 | N |
| Fst | 6.16 | 2.13 | 2.01 | 2.30 | 2.67 | N |
| Gas6 | 364.76 | 106.60 | 122.06 | 121.24 | 2.99 | N |
| Gdf15 | 3.07 | 0.27 | 0.25 | 0.49 | 6.31 | R |
| Gdf5 | 1.52 | 0.41 | 0.53 | 0.71 | 2.14 | N |
| Gfap | 13.30 | 1.35 | 3.26 | 2.14 | 4.08 | N |
| Gm11974 | 19.70 | 7.27 | 8.98 | 8.32 | 2.19 | M |
| Gria3 | 9.27 | 2.07 | 2.76 | 2.47 | 3.35 | N |
| Inhbb | 4.18 | 1.23 | 1.90 | 1.65 | 2.20 | N |
| Lyve1 | 11.05 | 3.20 | 3.49 | 4.15 | 2.67 | N |
| Mdm2 | 32.38 | 15.10 | 15.44 | 14.19 | 2.10 | R |
| Mgmt | 19.86 | 6.86 | 6.28 | 6.37 | 2.90 | R |
| Mrap | 4.22 | 0.83 | 0.87 | 1.25 | 3.38 | N |
| Perp | 8.48 | 2.65 | 3.54 | 3.91 | 2.17 | R |
| Phlda3 | 90.31 | 18.02 | 23.24 | 19.30 | 3.89 | R |
| Pmaip1 | 8.73 | 2.88 | 2.39 | 1.86 | 3.03 | R |
| Polk | 4.79 | 1.81 | 1.89 | 1.87 | 2.53 | R |
| Pqlc3 | 27.80 | 12.27 | 12.74 | 10.70 | 2.18 | N |
| Psrc1 | 29.63 | 7.09 | 5.53 | 4.77 | 4.18 | R |
| Ptprv | 16.15 | 7.26 | 7.25 | 7.43 | 2.17 | R |
| Pvt1 | 2.63 | 1.17 | 1.00 | 0.89 | 2.25 | R |
| Rnf169 | 6.01 | 2.72 | 2.85 | 2.91 | 2.07 | N |
| Rprm | 3.03 | 0.67 | 0.92 | 0.84 | 3.29 | R |
| Rps27l | 222.32 | 95.94 | 103.78 | 96.33 | 2.14 | R |
| Serpina3n | 2.53 | 0.94 | 0.83 | 0.94 | 2.69 | M |
| Sesn2 | 17.52 | 3.66 | 4.21 | 3.62 | 4.16 | R |
| Slc19a2 | 7.75 | 1.19 | 1.73 | 1.35 | 4.49 | R |
| Slc2a9 | 2.73 | 0.64 | 0.61 | 0.65 | 4.23 | R |
| Slco1c1 | 3.56 | 0.46 | 0.77 | 0.84 | 4.25 | N |
| Svop | 1.44 | 0.01 | 0.39 | 0.23 | 3.67 | N |
| Syna | 1.24 | 0.48 | 0.31 | 0.33 | 2.61 | M |
| Tnfrsf10b | 9.93 | 2.95 | 3.04 | 2.91 | 3.27 | R |
| Trim7 | 7.52 | 1.62 | 1.27 | 1.74 | 4.33 | N |
| Trp53inp1 | 25.23 | 5.36 | 5.87 | 4.88 | 4.30 | R |
| Upk1b | 2.42 | 0.27 | 0.19 | 0.38 | 6.43 | N |
| Vnn1 | 1.67 | 0.44 | 0.38 | 0.55 | 3.04 | N |
| Zfp365 | 5.47 | 1.72 | 1.91 | 1.55 | 2.87 | R |
| Zmat3 | 15.04 | 3.06 | 3.82 | 3.15 | 3.94 | R |
| 1700003M07Rik | 1.32 | 0.37 | 0.59 | 0.51 | 2.25 | M |
| 1700007K13Rik | 3.76 | 0.05 | 0.29 | 0.23 | 13.01 | M |
| 2010001M06Rik | 10.09 | 1.03 | 2.00 | 1.84 | 5.06 | M |
| 9030617O03Rik | 11.29 | 2.76 | 3.29 | 2.68 | 3.43 | M |

FPKM, fragments per kilobase of exon per million mapped fragments

WX: irradiated $p53^{+/+}$ group, KX: irradiated $p53^{-/-}$ mice group, W: non-irradiated $p53^{+/+}$ group, K: non-irradiated $p53^{-/-}$ group.

WX/max is median of WX / maximum value in median K, median KX or median W.

R, reported gene as p53 target , N, non-reported gene as p53 target, M, mouse genes which don't have human homologu.

# Supplementary Table1b. p53-repressed gene list

| gene | FPKM value | | | | | status |
|---|---|---|---|---|---|---|
| | WX | KX | W | K | WX/max | |
| Ankle1 | 1.07 | 4.59 | 3.11 | 3.05 | 0.35 | N |
| Anln | 1.23 | 5.02 | 3.27 | 3.58 | 0.38 | N |
| Apitd1 | 1.37 | 3.08 | 3.67 | 3.01 | 0.45 | N |
| Asf1b | 1.95 | 10.43 | 7.53 | 7.02 | 0.28 | N |
| Atad2 | 1.34 | 3.99 | 3.02 | 3.06 | 0.44 | N |
| Aurkb | 2.27 | 14.10 | 7.80 | 9.87 | 0.29 | N |
| BC030867 | 0.43 | 2.41 | 1.23 | 1.47 | 0.35 | M |
| Birc5 | 6.25 | 35.08 | 20.28 | 22.11 | 0.31 | K |
| Bub1 | 0.75 | 3.99 | 2.14 | 2.42 | 0.35 | N |
| Bub1b | 2.22 | 8.43 | 5.06 | 5.47 | 0.44 | N |
| Ccna2 | 5.40 | 26.62 | 16.43 | 17.42 | 0.33 | N |
| Ccnb2 | 5.54 | 27.70 | 12.98 | 14.19 | 0.43 | N |
| Ccne2 | 0.65 | 1.92 | 1.87 | 1.74 | 0.38 | N |
| Ccr2 | 0.79 | 1.94 | 2.02 | 2.53 | 0.41 | N |
| Cd79b | 1.01 | 12.18 | 6.23 | 4.27 | 0.24 | N |
| Cdc45 | 1.91 | 7.22 | 4.69 | 5.22 | 0.41 | N |
| Cdc6 | 0.39 | 2.05 | 1.53 | 1.61 | 0.25 | N |
| Cdca2 | 0.94 | 4.08 | 2.23 | 2.27 | 0.42 | N |
| Cdca3 | 5.72 | 30.56 | 20.39 | 19.34 | 0.30 | N |
| Cdca5 | 0.92 | 5.25 | 2.75 | 3.56 | 0.34 | N |
| Cdca7 | 2.14 | 6.02 | 5.26 | 5.33 | 0.41 | N |
| Cdca7l | 0.67 | 2.43 | 1.99 | 2.03 | 0.33 | N |
| Cdca8 | 4.13 | 18.56 | 10.12 | 11.95 | 0.41 | N |
| Cdk1 | 4.57 | 19.31 | 9.90 | 10.90 | 0.46 | N |
| Cdkn3 | 2.15 | 9.79 | 5.10 | 4.55 | 0.47 | N |
| Cenpe | 0.75 | 2.77 | 1.54 | 1.70 | 0.49 | N |
| Cenpf | 0.44 | 2.37 | 1.40 | 1.41 | 0.31 | N |
| Cenph | 1.41 | 5.88 | 3.22 | 4.03 | 0.44 | N |
| Cenpi | 0.82 | 2.89 | 1.84 | 1.96 | 0.44 | N |
| Cenpk | 1.55 | 4.67 | 3.50 | 3.59 | 0.44 | N |
| Cenpm | 1.24 | 5.52 | 4.00 | 4.42 | 0.31 | N |
| Cenpn | 1.82 | 5.94 | 3.90 | 4.34 | 0.47 | N |
| Cenpp | 1.11 | 4.86 | 3.27 | 3.44 | 0.34 | N |
| Cep55 | 1.49 | 7.26 | 3.43 | 4.40 | 0.44 | N |
| Chad | 17.37 | 35.66 | 40.02 | 38.51 | 0.49 | N |
| Chek1 | 1.01 | 2.83 | 2.11 | 2.17 | 0.48 | R |
| Chtf18 | 1.12 | 3.31 | 2.29 | 2.76 | 0.49 | N |
| Ckap2l | 2.82 | 10.37 | 6.32 | 6.79 | 0.45 | N |
| Clspn | 0.50 | 2.81 | 1.90 | 2.01 | 0.27 | N |
| Cybb | 1.09 | 3.62 | 2.38 | 3.11 | 0.46 | N |
| Depdc1a | 0.95 | 4.97 | 2.82 | 3.26 | 0.34 | N |
| Dhfr | 0.96 | 2.72 | 2.08 | 2.21 | 0.46 | N |
| Dlgap5 | 1.62 | 7.76 | 3.63 | 3.91 | 0.45 | N |
| Dna2 | 0.59 | 1.54 | 1.21 | 1.38 | 0.49 | N |
| Dscc1 | 0.37 | 1.82 | 1.18 | 1.61 | 0.31 | N |
| E2f2 | 0.58 | 3.07 | 1.85 | 1.62 | 0.36 | N |
| E2f8 | 0.78 | 3.97 | 3.06 | 2.86 | 0.27 | N |
| Ect2 | 0.92 | 3.71 | 2.08 | 2.29 | 0.44 | N |
| Esco2 | 0.40 | 2.57 | 2.17 | 2.26 | 0.18 | N |
| Fam64a | 3.76 | 13.57 | 9.54 | 10.56 | 0.39 | N |
| Fbxo5 | 1.89 | 7.56 | 4.81 | 5.33 | 0.39 | N |
| Fignl1 | 1.17 | 4.28 | 3.18 | 3.46 | 0.37 | N |
| Foxm1 | 2.40 | 8.85 | 6.00 | 6.30 | 0.40 | N |
| Gins2 | 4.85 | 13.00 | 9.85 | 11.45 | 0.49 | N |
| Gpha2 | 10.17 | 26.16 | 25.66 | 20.35 | 0.50 | N |
| Gsg2 | 0.54 | 2.41 | 1.26 | 1.38 | 0.43 | N |
| Hells | 0.97 | 3.65 | 2.48 | 2.67 | 0.39 | N |
| Hmgb2 | 12.97 | 43.96 | 37.27 | 32.87 | 0.39 | N |
| Incenp | 5.67 | 18.42 | 11.53 | 11.94 | 0.49 | N |
| Iqgap3 | 0.56 | 3.02 | 2.28 | 2.48 | 0.25 | N |
| Kif11 | 1.35 | 7.05 | 4.40 | 4.81 | 0.31 | N |
| Kif15 | 0.46 | 2.98 | 1.97 | 2.06 | 0.23 | N |
| Kif18a | 0.65 | 2.05 | 1.60 | 1.37 | 0.47 | N |
| Kif20b | 0.52 | 2.16 | 1.24 | 1.39 | 0.42 | N |
| Kif22 | 3.84 | 14.39 | 9.36 | 9.80 | 0.41 | N |
| Kif23 | 1.72 | 7.99 | 4.79 | 5.09 | 0.36 | N |
| Kif2c | 1.86 | 8.10 | 3.95 | 4.83 | 0.47 | N |
| Kif4 | 0.88 | 3.80 | 2.14 | 2.54 | 0.41 | N |
| Lmnb1 | 7.19 | 23.94 | 17.09 | 18.85 | 0.42 | N |
| Map4k1 | 0.57 | 2.28 | 1.34 | 1.18 | 0.49 | N |
| Mcm10 | 0.79 | 3.44 | 1.94 | 2.11 | 0.41 | N |
| Mcm2 | 4.28 | 14.37 | 10.15 | 11.26 | 0.42 | N |
| Mcm3 | 5.06 | 18.28 | 12.70 | 13.30 | 0.40 | N |
| Mcm5 | 3.50 | 15.25 | 9.45 | 10.67 | 0.37 | N |
| Mcm6 | 8.75 | 24.29 | 19.22 | 20.86 | 0.46 | N |
| Melk | 0.80 | 5.19 | 3.27 | 3.90 | 0.24 | N |
| Mis18bp1 | 0.64 | 2.94 | 1.78 | 1.99 | 0.36 | N |
| Mki67 | 1.89 | 12.20 | 8.92 | 7.99 | 0.24 | R |
| Mns1 | 1.56 | 4.96 | 3.26 | 3.37 | 0.48 | N |
| Mxd3 | 1.12 | 7.81 | 6.11 | 6.10 | 0.18 | N |
| Mybl2 | 1.00 | 4.55 | 2.89 | 3.23 | 0.35 | N |
| Napsa | 0.77 | 5.17 | 2.14 | 2.62 | 0.36 | N |
| Ncapg | 0.63 | 3.25 | 2.06 | 2.46 | 0.31 | N |
| Ncapg2 | 0.88 | 2.60 | 1.89 | 2.16 | 0.47 | N |
| Ncaph | 3.19 | 9.88 | 6.55 | 6.85 | 0.49 | N |
| Ndc80 | 1.20 | 6.96 | 4.64 | 4.76 | 0.26 | N |
| Neil3 | 1.25 | 6.67 | 4.58 | 4.60 | 0.27 | N |
| Nek2 | 1.10 | 5.17 | 2.44 | 2.43 | 0.45 | N |
| Nsl1 | 0.84 | 2.93 | 1.94 | 1.91 | 0.44 | N |
| Nuf2 | 1.77 | 9.61 | 5.89 | 6.39 | 0.30 | N |
| Nusap1 | 2.54 | 13.80 | 7.75 | 7.80 | 0.33 | N |
| Oip5 | 0.59 | 2.71 | 1.68 | 1.78 | 0.35 | N |
| Pbk | 1.95 | 9.51 | 8.09 | 7.91 | 0.25 | N |
| Plk1 | 3.60 | 16.23 | 8.36 | 9.19 | 0.43 | R |
| Pole | 0.48 | 2.05 | 1.32 | 1.55 | 0.36 | N |
| Prc1 | 4.36 | 18.71 | 11.24 | 11.77 | 0.39 | N |
| Prim1 | 2.88 | 9.11 | 6.77 | 8.20 | 0.43 | N |
| Racgap1 | 4.82 | 19.10 | 11.62 | 13.16 | 0.41 | N |
| Rad51 | 1.71 | 5.20 | 3.51 | 3.68 | 0.49 | N |
| Rad51ap1 | 1.52 | 5.91 | 3.61 | 4.27 | 0.42 | N |
| Rrm2 | 4.84 | 22.29 | 17.55 | 16.90 | 0.29 | N |
| Sapcd2 | 0.39 | 1.77 | 1.09 | 1.22 | 0.36 | N |
| Sgol1 | 0.64 | 3.03 | 1.63 | 1.78 | 0.39 | N |
| Sgol2 | 0.70 | 2.88 | 1.54 | 1.65 | 0.45 | N |
| Shcbp1 | 1.29 | 6.91 | 4.83 | 4.28 | 0.30 | N |
| Ska1 | 0.33 | 1.77 | 1.25 | 1.29 | 0.27 | N |
| Ska3 | 0.83 | 3.67 | 2.02 | 2.22 | 0.41 | N |
| Smc2 | 1.52 | 5.15 | 3.93 | 3.67 | 0.42 | N |
| Snora81 | 0.00 | 1.87 | 1.82 | 1.86 | 0.03 | N |
| Spag5 | 1.45 | 5.84 | 3.05 | 3.51 | 0.48 | N |
| Spc24 | 1.83 | 9.19 | 5.56 | 6.14 | 0.33 | N |
| Spc25 | 3.04 | 10.43 | 7.02 | 7.86 | 0.43 | N |
| Spdl1 | 1.01 | 3.29 | 2.19 | 2.38 | 0.46 | N |
| Tcf19 | 5.84 | 17.81 | 15.21 | 17.29 | 0.38 | N |
| Tk1 | 3.44 | 19.77 | 14.98 | 17.65 | 0.23 | N |
| Top2a | 4.44 | 21.32 | 12.51 | 13.25 | 0.36 | N |
| Tpx2 | 3.14 | 13.18 | 7.40 | 7.94 | 0.42 | N |
| Trip13 | 1.35 | 4.02 | 3.00 | 3.03 | 0.45 | N |
| Ttk | 0.94 | 3.56 | 2.54 | 2.31 | 0.41 | N |
| Uhrf1 | 2.56 | 14.19 | 8.68 | 9.82 | 0.29 | N |
| Vpreb3 | 0.13 | 10.44 | 5.31 | 3.64 | 0.04 | N |
| Wdhd1 | 0.99 | 3.73 | 2.69 | 2.61 | 0.38 | N |
| Xpnpep2 | 0.71 | 1.63 | 1.74 | 1.60 | 0.44 | N |
| 1190002F15Rik | 3.01 | 9.45 | 6.67 | 7.00 | 0.45 | N |
| 2700099C18Rik | 1.47 | 5.75 | 3.68 | 3.59 | 0.41 | M |
| 2810417H13Rik | 2.42 | 17.16 | 10.64 | 11.48 | 0.23 | M |
| 4930579G24Rik | 1.88 | 4.55 | 3.92 | 4.04 | 0.48 | M |

FPKM, fragments per kilobase of exon per million mapped fragments
WX, irradiated *p53*$^{+/+}$ group, KX, irradiated *p53*$^{-/-}$ mice group, W, non-irradiated *p53*$^{+/+}$ group, K, non-irradiated *p53*$^{-/-}$ group.
WX/min is median WX / minimum value of median K, median KX or median W.
R, reported gene as p53 target , N, non-reported gene as p53 target, M, mouse gene which don't have human homologue.

Supplementary Table 2. Primer sequence

| | | Forward | Reverse |
|---|---|---|---|
| Quantitative real-time PCR | human CD137L | TCAGGCTCCGTTTCACTTG | CAGGTCCACGGTCAAAGC |
| | human CD137 | CCTGAAGACCAAGGAGTGGA | GCAAAGCTGATTCCAAGAGAA |
| | human CDC42BPG | AGATGCTGAAGAGGGCTGAG | CCCCTTTCACGAGCACAT |
| | human FST | TCTGCCAGTTCATGGAGGA | TCCTTGCTCAGTTCGGTCTT |
| | mouse Cd137l | CGCCAAGCTACTGGCTAAAA | CGTACCTCAGACCTTGAGATAGGT |
| | mouse Cd137 | TGAGCTTCTCTCCCAGTACCA | AGCAGCAAAGCCGATGTC |
| | mouse Cdc42bpg | GCCATTTGTTGGCTTCACTT | GGGCAGCCATTAGCTCTG |
| | mouse Fst | AAGCATTCTGGATCTTGCAACT | GATAGGAAAGCTGTAGTCCTGGTC |
| p53 binding site | human CD137L-BS-AB | AAAGGTACCTCCTTCAACACTAGCCAGTAACA | AAAAAGCTTTGGAACTACAGGCACATACCA |
| | mouse Cd137l-BS | AAAGGTACCTCAGTGGCTGAGAGCATTTG | AAAAAGCTTTGCTCTTAACTGCTGAACCA |
| | human CDC42BPG-BS-AB | AAAGGTACCCACCCAGGCTGATCTTGAAC | AAAAAGCTTTGTGTGACCTCAGGCAAGTC |
| | human CDC42BPG-BS-C | AAAGGTACCTGCCTGTGTTGTTGTCACC | AAAAAGCTTGGACAGGCTGCCTAATCCT |
| | mouse Cdc42bpg-BS | AAAGGTACCTTCTCCCTGCCTGCCTCT | AAAAAGCTTCCTGCAGAAATATCAGAGGTGA |
| | human FST-BS | AAACTCGAGAACAAAAATGAAAGGCGACA | AAAAGATCTGCAGCTTGGTGTTTGTTTAGTG |
| | mouse Fst-BS | AAAGGTACCCCTGCAGATTCATATTCATTCTC | AAAAAGCTTTTGCATTGACTTTTACTAGACTGTTT |
| Expression vector | human CD137L | AAAGAATTCTCTCGTCATGGAATACGCC | AAACTCGAGTTCCGACCTCGGTGAAGG |
| | mouse Cd137l | AAAGAATTCACCGTGGTAATGGACCAGCAC | AAACTCGAGTTCCCATGGGTTGTCGGGTTT |
| | human CDC42BPG | AAAGGTACCATGGAGCGGCGGCTGCGCGCG | AAAAGATCTAGGAGAGCTCTCCAATTC |
| | human FST317 | AAAGGTACCCCCAGGATGGTCCGC | AAACTCGAGGTTGCAAGATCCGGA |
| | human FST344 | AAAGGTACCCCCAGGATGGTCCGC | AAACTCGAGCCACTCTAGAATAGA |
| Reconbinant protein | human CD137 | AAAGGTACCCAGGATCCTTGTAGTAACTGC | AAAGAGCTCGATCTGCGGAGAGTGTCCTGG |
| | mouse Cd137 | AAAGGTACCCAGAACTCCTGTGATAACTGT | AAAGAGCTCAGCTGCTCCAGTGGTCTTCTT |
| | mouse Cd137l | AAAGAATTCACCGAGCCTCGGCCAGCGCTC | AAACTCGAGTCATTCCCATGGGTTGTCGGG |
| Genotyping | mouse p53 | GTTATGCATCCATACAGTACA | CCGCAGGATTTACAGACACC |
| CHIP assay | CD137L | TCCTTCAACACTAGCCAG | TCTCAGCACTGTGATGCC |
| | CDC42BPG | GGCCCTCTGTTGACAATCTC | ACAGGCTGCCTAATCCTCTG |
| | FST | GATGCCCACAGAAAGCCTAT | TGTCTGCTCCAAATCAGCAC |
| siRNA | | Sence | Antisense |
| | siP53 | GACUCCAGUGGUAAUCUACTT | AGUAGAUUACCACUGGAGUCTT |
| | siEGFP | GCAGCACGACUUCUUCAAGT | CUUGAAGAAGUCGUGCUGC |