Supplemental material

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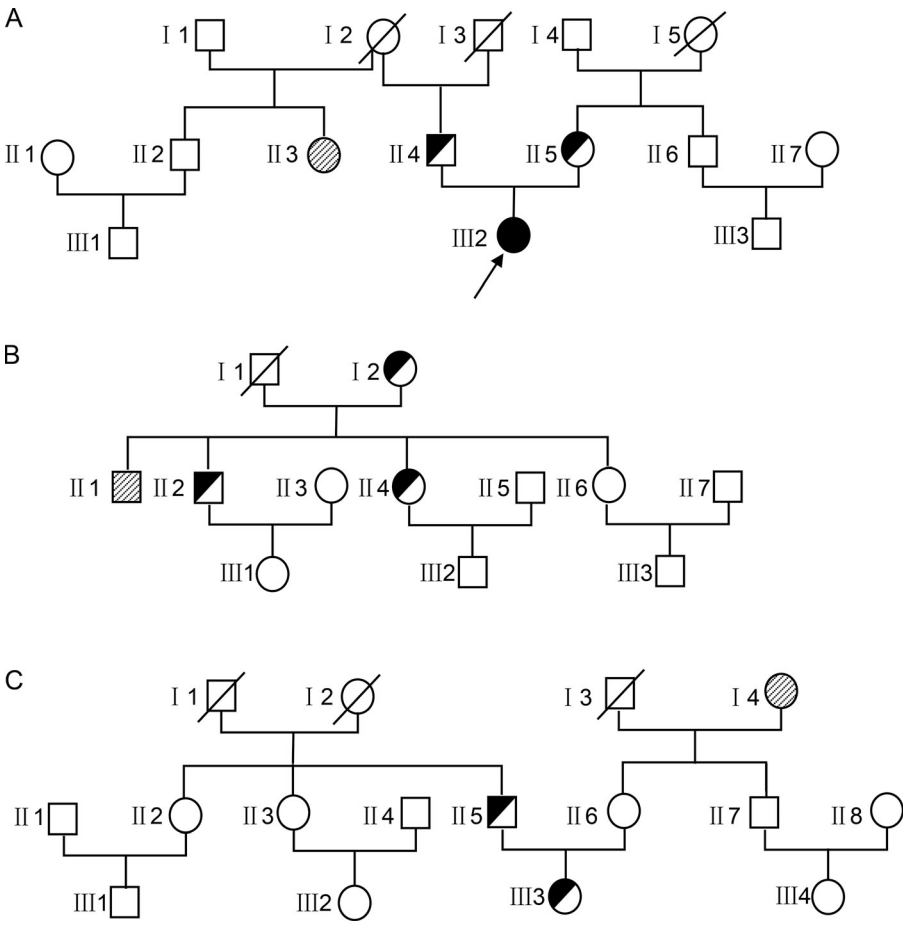

Figure S1. **The family trees of affected subjects.** Schematic representation of the *Reg1cp* genotypes of the three studied families. **(A)** The proband is indicated by an arrow. **(B and C)** Subject II2 in family (B) and subject III3 in family (C) belong to the 67 *Reg1cp*$^{+/mut}$ subjects identified on cohort study. Squares, male members; circles, female members; slashes, deceased members; shaded symbols, subjects who were not evaluated. *Reg1cp*$^{mut/mut}$ is indicated by closed symbols; *Reg1cp*$^{+/+}$ is indicated by open symbols; *Reg1cp*$^{+/mut}$ is indicated by half-shaded symbols.

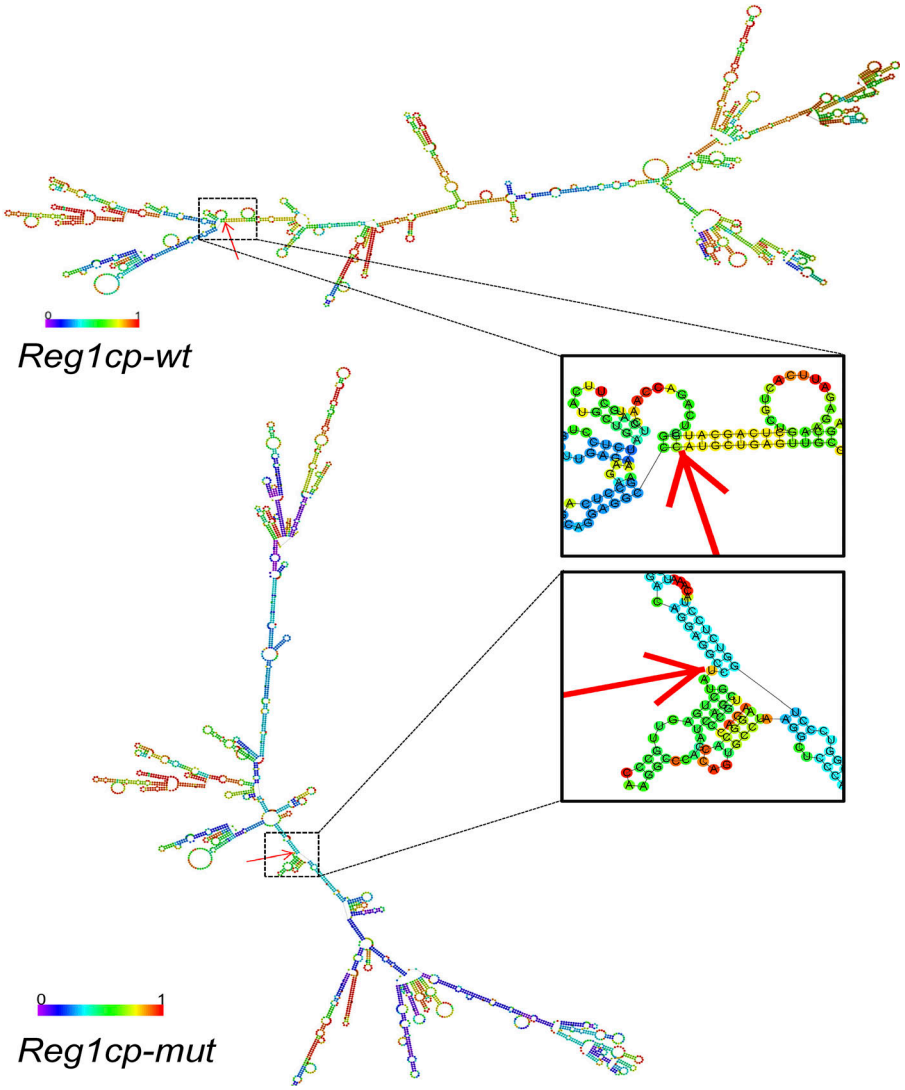

Figure S2. **Secondary structure prediction of *Reg1CP* and mutated*Reg1cp*.** Presenting the predicted secondary structure of *Reg1CP* (*Reg1cp-wt*) and mutated *Reg1cp* (*Reg1cp-mut*; RNAfold Webserver, http://rna.tbi.univie.ac.at/cgibin/RNAfold.cgi).

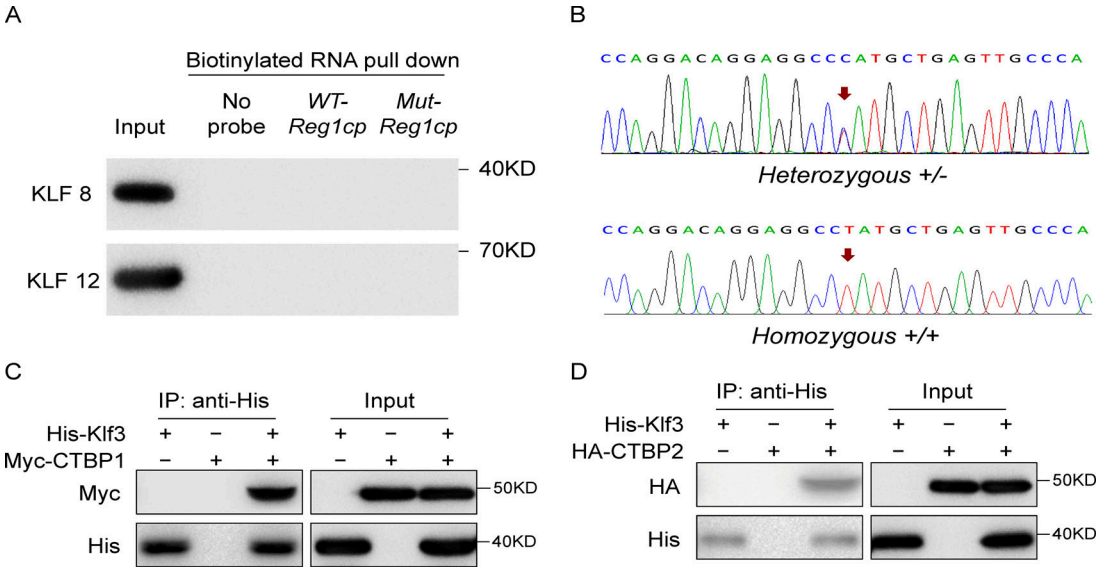

Figure S3. **Mutant Reg1cp does not retrieve KLF8 and KLF12 and does not affect the recruitment of corepressors CTBP1 and CTBP2 to Klf3. (A)** The immunoblotting results of mut-Reg1cp retrieve KLF8 and KLF12. **(B)** Sanger sequencing result of HMEC cell line with heterozygous or homozygous mutation in *Reg1cp* gene. **(C and D)** HMECs were transfected with *Reg1cp-mut* plasmid, His-Klf3, Myc-CTBP1, and HA-CTBP2. Co-immunoprecipitation (IP) of Klf3 and CTBP1 (C) and KLF3 and CTBP2 (D) was performed. Western blot analysis of cell extracts before IP served as input control. All the figures were representative of three independent experiments.

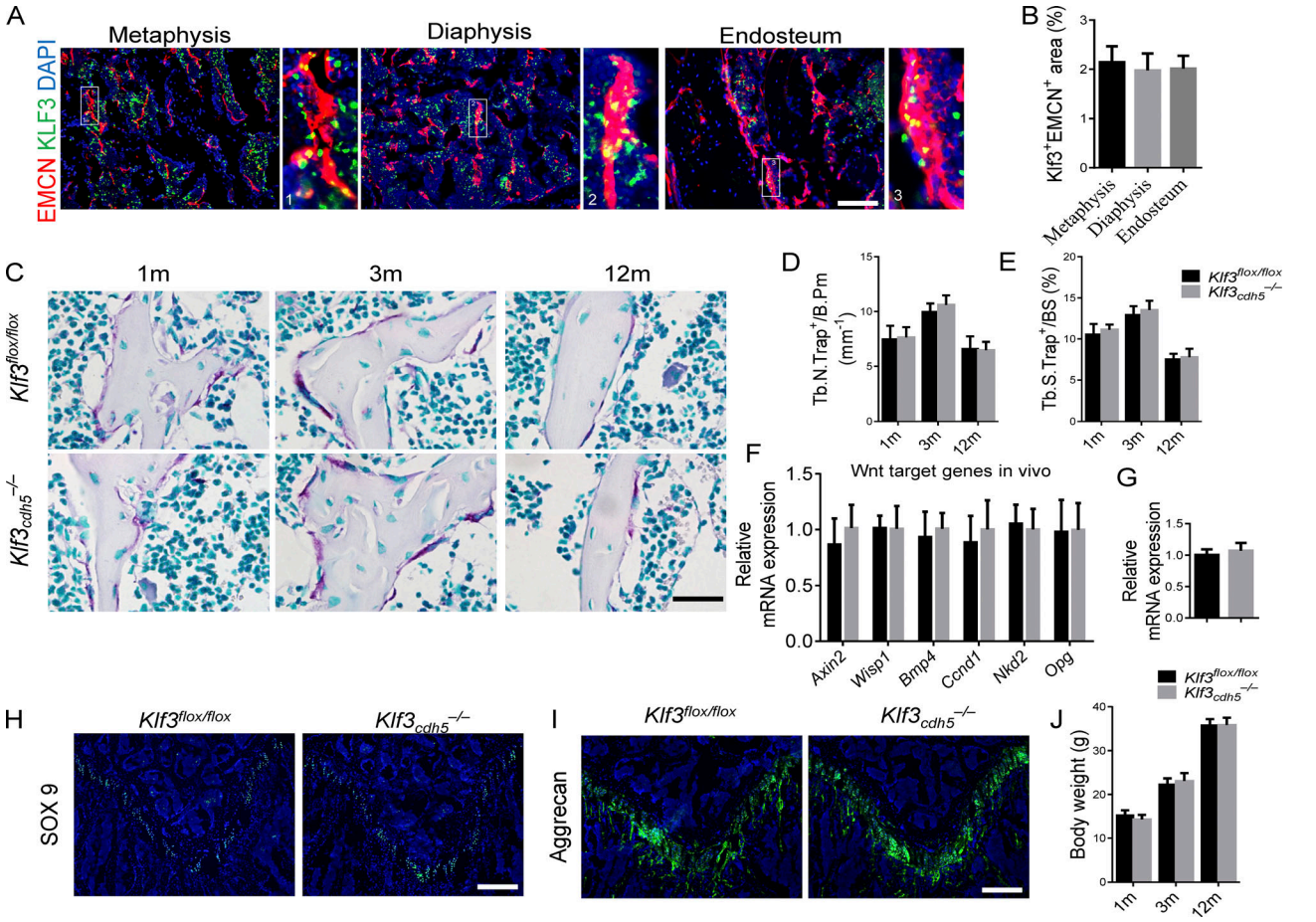

Figure S4. **Endothelial-specific *Klf3* knockout mice show no change in osteoclasts number, Wnt signaling, *Tph1* expression, and growth plate morphology. (A and B)** Representative images (A) and quantitation (B) of KLF3 (green) and EMCN (red) immunostaining in femora from C57/B6 mice. Scale bar, 100 µm. **(C)** Representative images of TRAP staining of femora from different time point of endothelial-specific *Klf3* knockout mice and their littermate controls. Scale bar, 50 µm. **(D and E)** Quantification data of TRAP$^+$ cells in trabecular bone surface. Number of TRAP$^+$ cells per bone perimeter (Tb.N.Trap$^+$/B.Pm), and TRAP$^+$ cells surface per bone surface (Tb.S.Trap$^+$/BS) were measured. **(F)** qRT-PCR analysis of Wnt target genes in the bones of endothelial-specific *Klf3* knockout mice and their littermate controls. **(G)** qRT-PCR analysis of Tph1 in the duodenum of endothelial-specific *Klf3* knockout mice and their littermate controls. **(H)** Representative images of SOX 9 staining of femora. Scale bar, 200 µm. **(I)** Representative images of Aggrecan staining of femora. Scale bar, 200 µm. **(J)** Body weight of endothelial-specific *Klf3* knockout mice and their littermate controls. $n = 6$ in each group from three independent experiments. Data shown as mean ± SD. Student's *t* test.

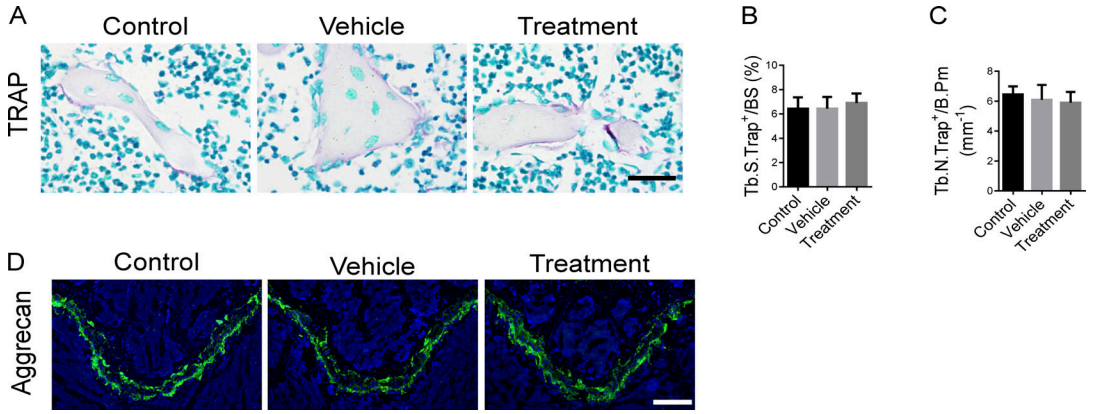

Figure S5. **Ophiopogonin D treatment does not affect osteoclast number and growth plate morphology in aged mice.** 12-mo-old C57/B6 mice were intraperitoneally treated with Ophiopogonin D at a dosage of 20 mg/kg every other day for 3 mo. **(A)** Representative images of TRAP staining of femora from Ophiopogonin D–treated mice and their controls. Bar, 50 µm. **(B and C)** Quantification data of TRAP$^+$ cells in trabecular bone surface. Number of TRAP$^+$ cells per bone perimeter (Tb.N. Trap$^+$/B.Pm), and TRAP$^+$ cells surface per bone surface (Tb.S.Trap$^+$/BS) were measured. **(D)** Representative images of Aggrecan staining of femora from Ophiopogonin D–treated mice and their controls. Scale bar, 200 µm. *n* = 6 in each group from three independent experiments. Data shown as mean ± SD. ANOVA.

Table S1. **Clinical information of the 67 *Reg1cp*$^{+/mut}$ individuals**

Subject	Gender	Age (yr)	Menopause	BMI (kg/m²)	Total lumbar spine BMD (g/cm²)	Z-score for BMD at total lumbar spine	Femoral neck BMD (g/cm²)	Z-score for BMD at femoral neck	Total hip BMD (g/cm²)	Z-score for BMD at total hip	β-CTX (pg/ml)	PINP (ng/ml)
1	Female	22	No	20.57	1.185	2.8	0.949	1.6	1.083	2.2	69.51	431.81
2	Female	26	No	21.21	0.965	0.3	0.901	1.4	0.996	1.8	68.19	442.10
3	Female	30	No	22.64	1.079	1.1	0.923	1.1	0.946	0.8	63.20	364.48
4	Female	31	No	16.23	1.083	1.2	0.930	1.2	0.956	0.8	60.39	280.30
5	Female	32	No	23.19	1.077	1.1	0.945	1.3	1.064	1.8	60.20	296.87
6	Female	33	No	23.61	1.060	0.9	1.088	2.7	1.162	2.7	66.54	249.42
7	Female	33	No	21.93	1.013	0.5	0.976	1.6	1.014	1.4	55.96	385.53
8	Female	35	No	21.71	1.249	2.7	0.993	1.9	1.094	2.1	63.20	292.71
9	Female	36	No	24.02	0.885	−1.0	0.849	0.1	0.970	0.2	62.59	243.55
10	Female	37	No	25.00	1.435	4.0	1.032	2.0	1.188	2.3	64.30	307.09
11	Female	38	No	24.10	0.978	0.1	1.034	2.3	1.116	2.3	51.17	384.11
12	Female	40	No	21.34	1.019	0.6	0.673	−1.1	0.833	−0.3	28.97	237.16
13	Female	41	No	23.65	1.098	1.3	0.828	0.3	0.927	0.5	48.74	361.79
14	Female	41	No	23.81	1.073	1.1	0.942	1.4	0.976	1.1	56.13	268.50
15	Female	43	No	23.10	0.990	0.5	0.605	−1.6	0.758	−0.8	37.15	357.74
16	Female	44	No	23.50	1.118	1.7	0.739	−0.4	0.883	0.3	34.91	317.31
17	Female	44	No	28.84	0.986	0.3	0.910	1.1	0.890	0.3	45.44	279.61
18	Female	45	No	21.36	1.097	1.4	0.885	1.1	0.825	−0.2	41.51	355.72
19	Female	45	No	30.04	1.014	0.7	0.936	1.6	1.001	1.5	53.19	276.61
20	Female	47	No	23.24	0.946	0.2	0.889	1.1	0.974	1.2	58.43	269.04
21	Female	48	Yes	29.01	1.108	1.5	0.973	1.2	1.102	1.2	32.43	338.79
22	Female	46	Yes	25.64	1.228	2.5	0.888	1.1	0.954	1.0	47.86	201.04
23	Female	47	Yes	26.52	1.167	2.0	0.910	1.3	0.990	1.4	49.90	342.56
24	Female	47	Yes	27.60	0.924	0.0	0.918	1.4	0.901	0.5	52.24	380.48
25	Female	48	Yes	32.62	1.145	1.8	0.996	2.2	1.152	2.9	58.41	311.24
26	Female	49	Yes	29.71	0.907	−0.1	0.991	2.1	1.094	2.3	64.15	302.64
27	Female	49	Yes	23.94	1.089	1.3	0.910	1.3	1.042	1.8	57.86	352.86
28	Female	49	Yes	29.90	1.063	1.1	0.978	2.0	0.936	0.9	77.13	344.39
29	Female	50	Yes	25.56	1.119	2.1	0.872	1.4	0.938	1.3	46.43	403.06
30	Female	52	Yes	38.58	1.143	2.3	1.074	3.3	1.069	2.6	61.20	395.17
31	Female	52	Yes	21.94	1.049	1.6	0.853	1.2	0.935	1.3	49.21	429.10
32	Female	54	Yes	30.76	0.911	0.4	0.908	1.7	0.985	1.8	62.96	409.81
33	Female	55	Yes	28.31	1.247	3.4	0.852	1.7	0.917	0.3	48.91	415.45
34	Female	56	Yes	29.05	0.918	1.1	0.815	1.3	0.836	−0.3	52.52	382.10
35	Female	56	Yes	24.24	0.855	0.6	0.826	1.4	0.892	0.1	36.62	364.23
36	Female	56	Yes	29.30	0.934	1.2	0.790	1.1	0.881	0.0	52.52	349.38
37	Female	57	Yes	22.31	0.885	0.8	0.808	1.2	0.845	−0.2	37.12	374.73
38	Female	58	Yes	26.37	0.953	1.3	0.882	2.0	1.021	1.2	59.64	472.44
39	Female	64	Yes	24.36	0.976	2.2	0.640	0.1	0.794	0.9	53.90	414.21
40	Female	68	Yes	18.80	0.592	−1.0	0.534	−0.6	0.639	−0.2	40.81	407.22
41	Female	74	Yes	30.08	0.832	0.8	0.724	1.3	0.849	0.5	46.15	382.61
42	Male	23	-	21.36	1.166	1.8	1.042	1.3	1.243	2.4	85.38	593.50

Table S1. **Clinical information of the 67 *Reg1cp*$^{+/mut}$ individuals (*Continued*)**

Subject	Gender	Age (yr)	Menopause	BMI (kg/m²)	Total lumbar spine BMD (g/cm²)	Z-score for BMD at total lumbar spine	Femoral neck BMD (g/cm²)	Z-score for BMD at femoral neck	Total hip BMD (g/cm²)	Z-score for BMD at total hip	β-CTX (pg/ml)	PINP (ng/ml)
43	Male	27	-	24.57	1.139	1.5	1.106	2.0	1.092	1.3	89.75	604.56
44	Male	28	-	20.34	0.954	−0.1	0.920	0.7	1.011	0.7	64.07	386.06
45	Male	30	-	21.22	1.151	1.8	0.937	0.9	1.006	0.7	58.92	408.86
46	Male	30	-	22.23	1.034	0.7	1.103	2.5	1.145	2.0	64.20	377.23
47	Male	32	-	27.05	0.998	0.4	0.992	1.5	1.098	1.6	60.91	402.16
48	Male	35	-	28.03	1.254	2.5	1.070	2.6	1.194	2.8	79.75	469.07
49	Male	36	-	28.63	1.080	0.8	0.920	0.8	1.053	1.0	52.33	401.09
50	Male	44	-	23.51	1.001	0.2	0.783	−0.2	0.832	−0.8	44.56	396.11
51	Male	44	-	25.45	0.962	−0.2	0.981	1.7	1.042	1.1	53.04	368.65
52	Male	47	-	23.85	0.870	−0.9	0.789	0.0	0.831	−0.7	45.52	378.64
53	Male	50	-	29.59	1.129	1.4	0.949	1.8	1.184	2.5	63.08	395.45
54	Male	48	-	25.31	1.075	1.1	0.845	0.6	1.004	1.1	45.22	337.48
55	Male	50	-	22.49	0.982	0.2	1.074	3.1	1.193	2.8	65.60	382.93
56	Male	50	-	22.86	1.108	1.2	0.965	2.0	1.158	2.5	53.41	352.24
57	Male	54	-	24.73	1.210	2.1	0.884	1.1	1.071	1.7	51.77	363.79
58	Male	54	-	24.25	1.176	1.8	0.876	1.0	1.079	1.7	43.80	322.38
59	Male	54	-	28.55	1.099	1.2	0.901	1.3	1.079	1.7	52.38	282.98
60	Male	57	-	27.43	1.094	1.1	0.851	1.0	1.047	1.5	44.26	405.99
61	Male	59	-	24.09	1.281	2.5	0.904	1.6	1.072	1.7	48.98	378.67
62	Male	64	-	25.34	1.089	1.0	0.887	1.3	0.914	0.3	47.72	389.66
63	Male	65	-	23.45	1.206	1.7	0.751	0.2	1.015	1.2	47.63	304.95
64	Male	66	-	20.05	0.841	−0.6	0.651	−0.3	0.824	0.0	48.37	337.81
65	Male	69	-	24.97	1.082	1.4	0.903	2.2	0.951	1.2	55.15	322.40
66	Male	72	-	26.08	1.069	0.8	0.881	1.5	1.016	1.4	37.94	335.11
67	Male	74	-	23.29	1.114	1.1	0.894	1.6	0.986	1.2	50.86	299.53

BMI, body mass index.

Table S2. **Index of bone mass in 26 male *Reg1cp*$^{+/mut}$ individuals and 590 male *Reg1cp*$^{+/+}$ individuals**

Age (yr)	Index	Lumbar		Femoral neck		Hip		Subjects (*n*)	
		Reg1cp$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$
20–50	BMD (g/cm²)	0.930 ± 0.111	1.063 ± 0.106[a]	0.801 ± 0.125	0.957 ± 0.108[a]	0.904 ± 0.123	1.057 ± 0.126[a]	237	13
	Z-score	−0.271 ± 1.025	0.851 ± 0.970[a]	−0.314 ± 1.102	1.255 ± 0.885[a]	−0.217 ± 1.114	1.213 ± 1.107[a]		
≥50	BMD(g/cm²)	0.932 ± 0.135	1.104 ± 0.110[a]	0.737 ± 0.105	0.879 ± 0.099[a]	0.877 ± 0.112	1.031 ± 0.098[a]	353	13
	Z-score	−0.069 ± 0.966	1.188 ± 0.783[a]	−0.063 ± 0.999	1.346 ± 0.854[a]	0.096 ± 0.962	1.461 ± 0.754[a]		

[a]$P < 0.05$, compared with the *Reg1cp*$^{+/+}$ control.

Table S3. **Index of bone mass in 41 female *Reg1cp*$^{+/mut}$ individuals and 808 female *Reg1cp*$^{+/+}$ individuals**

Period	Index	Lumbar		Femoral neck		Hip		Subjects (*n*)	
		Reg1cp$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$
Premenopausal	BMD (g/cm^2)	0.955 ± 0.104	1.068 ± 0.120[a]	0.773 ± 0.100	0.901 ± 0.118[a]	0.854 ± 0.104	0.983 ± 0.113[a]	357	20
	Z-score	0.156 ± 0.959	1.084 ± 1.103[a]	−0.105 ± 0.976	1.040 ± 1.083[a]	0.031 ± 0.996	1.095 ± 0.991[a]		
Postmenopausal	BMD (g/cm^2)	0.801 ± 0.129	1.002 ± 0.156[a]	0.661 ± 0.100	0.864 ± 0.123[a]	0.743 ± 0.113	0.942 ± 0.119[a]	451	21
	Z-score	0.166 ± 0.965	1.290 ± 0.998[a]	−0.051 ± 0.881	1.423 ± 0.766[a]	−0.535 ± 1.015	1.022 ± 0.916[a]		

[a]P < 0.05, compared with the *Reg1cp*$^{+/+}$ control.

Table S4. **Biochemical survey for bone remodeling parameters in 26 male *Reg1cp*$^{+/mut}$ individuals and 226 male *Reg1cp*$^{+/+}$ individuals**

Age (yr)	Index	PINP (ng/ml)		β-CTX (pg/ml)		Subjects (*n*)	
		Reg1cp$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$
20–29	Mean ± SD	65.85 ± 9.84	79.74 ± 13.74[a]	516.05 ± 32.65	528.04 ± 123.08	45	3
	Range	44.53~87.80	64.07~89.75	432.73~578.84	386.06~604.56		
30–39	Mean ± SD	53.32 ± 7.92	63.22 ± 10.20[a]	395.49 ± 32.93	411.68 ± 34.25	40	5
	Range	40.06~70.61	52.33~79.75	315.86~453.57	377.22~469.07		
40–49	Mean ± SD	42.46 ± 7.61	50.28 ± 7.94[a]	360.25 ± 31.01	375.27 ± 24.11	40	5
	Range	25.48~61.33	44.56~63.08	307.23~413.25	337.48~396.11		
50–59	Mean ± SD	36.97 ± 8.10	51.46 ± 7.32[a]	351.47 ± 40.50	355.57 ± 41.38	42	7
	Range	22.02~60.35	43.80~65.60	268.61~448.58	282.98~405.99		
60–69	Mean ± SD	35.53 ± 8.37	49.72 ± 3.64[a]	314.28 ± 34.47	338.71 ± 36.52	35	4
	Range	21.36~54.08	47.63~55.15	260.59~386.03	304.95~389.66		
70–79	Mean ± SD	26.96 ± 5.91	44.40 ± 9.14	285.58 ± 37.19	317.32 ± 25.16	24	2
	Range	18.11~39.51	37.94~50.86	232.13~344.26	299.53~335.11		

[a]P < 0.05, compared with the *Reg1cp*$^{+/+}$ control.

Table S5. **Biochemical survey for bone remodeling parameters in 41 female *Reg1cp*$^{+/mut}$ individuals and 213 female *Reg1cp*$^{+/+}$ individuals**

Age (yr)	Index	PINP (ng/ml)		β-CTX (pg/ml)		Subjects (*n*)	
		Reg1cp$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$	*Reg1cp*$^{+/+}$	*Reg1cp*$^{+/mut}$
20–29	Mean ± SD	56.61 ± 13.12	68.85 ± 0.93	388.44 ± 47.01	436.95 ± 7.27	42	2
	Range	40.77–81.63	68.19–69.51	300.48–578.15	431.81–442.10		
30–39	Mean ± SD	41.84 ± 7.99	60.84 ± 4.70[a]	291.80 ± 32.47	311.56 ± 54.30	42	9
	Range	30.14–59.40	51.17–66.54	222.20–341.78	243.55–385.53		
40–49	Mean ± SD	40.55 ± 10.51	49.67 ± 12.33[a]	292.54 ± 32.31	311.62 ± 49.75	39	17
	Range	27.00–81.73	28.97–77.13	234.81–366.37	201.04–380.48		
50–59	Mean ± SD	44.08 ± 6.86	50.71 ± 9.15[a]	381.61 ± 33.51	399.55 ± 35.37	40	10
	Range	28.02–60.34	36.62–62.96	317.20–442.08	349.38–472.44		
60–69	Mean ± SD	45.00 ± 6.65	47.35 ± 9.26	395.59 ± 43.58	410.71 ± 4.95	31	2
	Range	29.00–58.31	40.81–53.90	343.11–564.17	407.22–414.21		
70–79	Mean ± SD	43.03 ± 6.69	46.15	351.13 ± 31.22	382.61	19	1
	Range	32.19–55.93	-	302.00–403.67	-		

[a]P < 0.05, compared with the *Reg1cp*$^{+/+}$ control.

Table S6. **Top 21 selected small molecules**

ID	Grid score	Rank	Name	CAS	Molecule information
TMA0820	−72.72	1	Calenduloside E	26020-14-4	https://pubchem.ncbi.nlm.nih.gov/compound/176079
TMA0493	−63.08	2	Theaflavin 3′-O-gallate	28543-07-9	https://pubchem.ncbi.nlm.nih.gov/compound/71307578
TMA1113	−62.99	3	Ophiopogonin D	41753-55-3	https://pubchem.ncbi.nlm.nih.gov/compound/46173859
TMA0902	−61.43	4	Picfeltarraenin IB	97230-46-1	https://pubchem.ncbi.nlm.nih.gov/compound/102120501
TMA2594	−61.40	5	Tetracycline hydrochloride	64-75-5	https://pubchem.ncbi.nlm.nih.gov/compound/54704426
TMA1054	−60.65	6	Grosvenorine	156980-60-8	https://pubchem.ncbi.nlm.nih.gov/compound/101568804
TMA1923	−59.80	7	Narirutin	14259-46-2	https://pubchem.ncbi.nlm.nih.gov/compound/442431
TMA0997	−59.13	8	Ganoderic Acid G	98665-22-6	https://pubchem.ncbi.nlm.nih.gov/compound/20055988
TMA1641	−58.89	9	Isosaponarin	19416-87-6	https://pubchem.ncbi.nlm.nih.gov/compound/154105
TMA0922	−58.15	10	Corilagin	23094-69-1	https://pubchem.ncbi.nlm.nih.gov/substance/254771366
TMA1513	−57.54	11	Punicalagin	65995-63-3	https://pubchem.ncbi.nlm.nih.gov/substance/254782436
TMA1421	−55.81	12	Sanggenon C	80651-76-9	https://pubchem.ncbi.nlm.nih.gov/substance/254785279
TMA0545	−55.04	13	Polyporenic acid C	465-18-9	https://pubchem.ncbi.nlm.nih.gov/substance/366940831
TMA1553	−54.42	14	Silicristin	33889-69-9	https://pubchem.ncbi.nlm.nih.gov/substance/355202202
TMA1512	−53.73	15	Punicalin	65995-64-4	https://pubchem.ncbi.nlm.nih.gov/substance/312811563
TMA1085	−53.25	16	7-(deoxyadenosin-N(6)-yl)aristolactam I	127191-86-0	https://pubchem.ncbi.nlm.nih.gov/substance/366187468
TMA1207	−52.51	17	Procyanidin B1	20315-25-7	https://pubchem.ncbi.nlm.nih.gov/substance/347759397
TMI0945	−51.86	18	Enoxolone	471-53-4	https://pubchem.ncbi.nlm.nih.gov/substance/363901912
TMA1555	−50.79	19	Silydianin	29782-68-1	https://pubchem.ncbi.nlm.nih.gov/substance/348955837
TMA0416	−50.69	20	α-Viniferin	62218-13-7	https://pubchem.ncbi.nlm.nih.gov/substance/254761476
TMA0598	−50.44	21	Etoposide	33419-42-0	https://pubchem.ncbi.nlm.nih.gov/substance/374243615

CAS, Chemical Abstracts Service.

Table S7. **Nucleotide sequences of primers used for quantitative RT-PCR detection**

Primer	Sequence (5′ to 3′)	Size
Reg1CP (human)	F: GGGAGCTTTGTGTGTAGAGAAACTG	25
	R: CTCCTCACTCACATCTGCATAAACC	25
CD31(human)	F: AACAGTGTTGACATGAAGAGCC	22
	R: TGTAAAACAGCACGTCATCCTT	22
EMCN (human)	F: AGCAACCAGCCGGTCTTATTC	21
	R: AGCACATTCGGTACAAACCCA	21
VEGFa (human)	F: AGGGCAGAATCATCACGAAGT	21
	R: AGGGTCTCGATTGGATGGCA	20
VEGFb (human)	F: GAGATGTCCCTGGAAGAACACA	22
	R: GAGTGGGATGGGTGATGTCAG	21
PDGFa (human)	F: GCAAGACCAGGACGGTCATTT	21
	R: GGCACTTGACACTGCTCGT	19
PDGFb (human)	F: CTAATGGTGGAAACCCACAACG	22
	R: TATCGCCAGGAATTGTTGCTG	21
FGF-1 (human)	F: ACAGCCCTGACCGAGAAGTT	20
	R: CCGTTGCTACAGTAGAGGAGT	21
TGFβ-1 (human)	F: GGCCAGATCCTGTCCAAGC	19
	R: GTGGGTTTCCACCATTAGCAC	21
JunB (human)	F: ACAAACTCCTGAAACCGAGCC	21
	R: CGAGCCCTGACCAGAAAAGTA	21
β-actin (human)	F: CGTGGACATCCGCAAAGAC	19
	R: TCGTCATACTCCTGCTTGCTG	21
Klf3 (mouse)	F: TACAGGAGAAAAGCCGTACAAATG	24
	R: TCATCAGACCGAGCGAACTTC	21
JunB (mouse)	F: CCAGATCTCGGATGTGCACGAAAATG	26
	R: GCAAGAATTCGGAGGCTCTCAGAAGG	26
VEGFa (mouse)	F: CTGCCGTCCGATTGAGACC	19
	R: CCCCTCCTTGTACCACTGTC	20
Axin2 (mouse)	F: TGACTCTCCTTCCAGATCCCA	21
	R: TGCCCACACTAGGCTGACA	19
Wisp1 (mouse)	F: CAGCACCACTAGAGGAAACGA	21
	R: CTGGGCACATATCTTACAGCATT	23
Bmp4 (mouse)	F: TTCCTGGTAACCGAATGCTGA	21
	R: CCTGAATCTCGGCGACTTTTT	21
Ccnd1 (mouse)	F: GCGTACCCTGACACCAATCTC	21
	R: CTCCTCTTCGCACTTCTGCTC	21
Nkd2 (mouse)	F: GAGCGGAAGAAACGGACCG	19
	R; CCTTAGGGTCTCCATTGAGCA	21
Opg (mouse)	F: ACCCAGAAACTGGTCATCAGC	21
	R: CTGCAATACACACACTCATCACT	23
Tph1 (mouse)	F: TTTCCATCCGTCCTGTGG	18
	R: TCATCTTCTCCTTTGCATCTTC	22

Table S7. **Nucleotide sequences of primers used for quantitative RT-PCR detection (*Continued*)**

Primer	Sequence (5′ to 3′)	Size
β-Actin (mouse)	F: CTGTCCCTGTATGCCTCTG	19
	R: TGATGTCACGCACGATTT	18

F, forward primer; R, reverse primer; Size, primer size.

Table S8. **Nucleotide sequences of primers used for ChIP-PCR**

Primer	Sequence (5′ to 3′)
JunB-1 (human)	F: GGGCTGTTGCCACACTTC
	R: CCTCCCCTATTGACCCTG
JunB-2 (human)	F: TTACAAGGACACGCGCTTCC
	R: GCCTGAGCCACACGCCTT

F, forward primer; R, reverse primer.

Table S9. **Information from the biotin-labeled probe used for EMSA**

Oligo name	Items	Bases	Purification	Working solution
JunB(G)-TP	5′biotin-TTGGGCGACCGCGCCCCAGCCGTCGGGC-3′	28	HAP	238 nM
JunB(G)-BM	5′biotin-GCCCGACGGCTGGGGCGCGGTCGCCCAA-3′	28	HAP	238 nM
JunB(A)-TP	5′biotin-CCGCCGAGCCACCCGGCCCGTGGCCGCT-3′	28	HAP	238 nM
JunB(A)-BM	5′biotin-AGCGGCCACGGGCCGGGTGGCTCGGCGG-3′	28	HAP	238 nM