

Supplemental Table 1

	Age (w)	WT	cKO	p-value
Ct.Th	8	0.198 ± 0.016	0.198 ± 0.020	0.958
(mm)	18	0.256 ± 0.027	0.262 ± 0.021	0.475
Ct.TA	8	2.00 ± 0.20	1.88 ± 0.24	0.261
(mm²)	18	2.21 ± 0.24	2.20 ± 0.26	0.908
Ct.BA	8	0.892 ± 0.090	0.863 ± 0.114	0.526
(mm²)	18	1.14 ± 0.12	1.19 ± 0.14	0.288
Ct.MA	8	1.11 ± 0.14	1.02 ± 0.16	0.227
(mm²)	18	1.07 ± 0.17	1.01 ± 0.17	0.328
BV/TV	8	0.140 ± 0.047	0.118 ± 0.036	0.253
	18	0.116 ± 0.041	0.126 ± 0.041	0.509
vBMD	8	227 ± 42	211 ± 34	0.342
(mg/ccm)	18	207 ± 37.9	218 ± 38	0.412
Tb.N	8	4.76 ± 0.94	4.84 ± 0.57	0.805
(number/mm)	18	3.74 ± 0.71	3.72 ± 0.59	0.927
Tb.Th	8	0.046 ± 0.005	0.044 ± 0.005	0.297
(mm)	18	0.051 ± 0.008	0.054 ± 0.006	0.295
Tb.Sp	8	0.221 ± 0.057	0.214 ± 0.028	0.743
(mm)	18	0.280 ± 0.066	0.277 ± 0.049	0.871

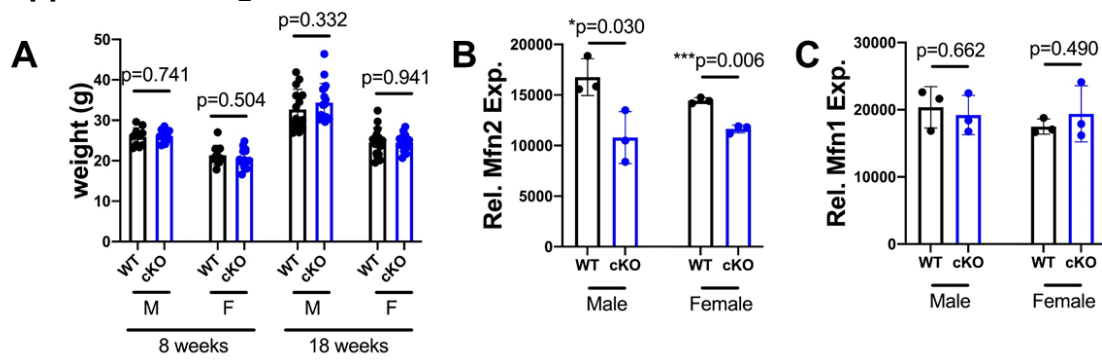
Supplemental Table 1. MicroCT parameters for male mice, showing mean ± SD. Group sizes: WT n=10 at 8 weeks and n=15 at 18 weeks; cKO n=11 at 8 weeks and n=17 at 18 weeks. Unpaired, two-tailed t-tests.

Supplemental Table 2

	Age (w)	WT	cKO	p-value
Ct.Th (mm)	8	0.167 ± 0.009	0.181 ± 0.019	0.035*
	18	0.229 ± 0.012	0.234 ± 0.014	0.005**
	30	0.239 ± 0.013	0.252 ± 0.012	0.012*
Ct.TA (mm²)	8	1.80 ± 0.16	1.74 ± 0.21	0.420
	18	1.71 ± 0.21	1.66 ± 0.10	0.416
	30	1.95 ± 0.16	1.91 ± 0.14	0.566
Ct.BA (mm²)	8	0.730 ± 0.063	0.762 ± 0.113	0.404
	18	0.875 ± 0.066	0.909 ± 0.064	0.182
	30	1.02 ± 0.06	1.05 ± 0.06	0.180
Ct.MA (mm²)	8	1.07 ± 0.11	0.976 ± 0.122	0.056
	18	0.840 ± 0.156	0.754 ± 0.068	0.070
	30	0.931 ± 0.123	0.859 ± 0.093	0.133
BV/TV	8	0.067 ± 0.024	0.082 ± 0.034	0.241
	18	0.068 ± 0.019	0.065 ± 0.015	0.620
	30	0.039 ± 0.010	0.035 ± 0.020	0.587
vBMD (mg/ccm)	8	163 ± 24	176 ± 39	0.359
	18	167 ± 19	164 ± 18	0.683
	30	136 ± 12	131 ± 22	0.503
Tb. N. (number/mm)	8	3.75 ± 0.54	4.04 ± 0.75	0.291
	18	2.99 ± 0.48	2.73 ± 0.13	0.174
	30	2.42 ± 0.35	2.16 ± 0.09	0.082
Tb. Th. (mm)	8	0.041 ± 0.003	0.043 ± 0.009	0.529
	18	0.044 ± 0.003	0.047 ± 0.003	0.044*
	30	0.047 ± 0.007	0.046 ± 0.004	0.543
Tb. Sp. (mm)	8	0.275 ± 0.042	0.260 ± 0.057	0.447
	18	0.359 ± 0.068	0.382 ± 0.060	0.227
	30	0.426 ± 0.064	0.480 ± 0.028	0.091

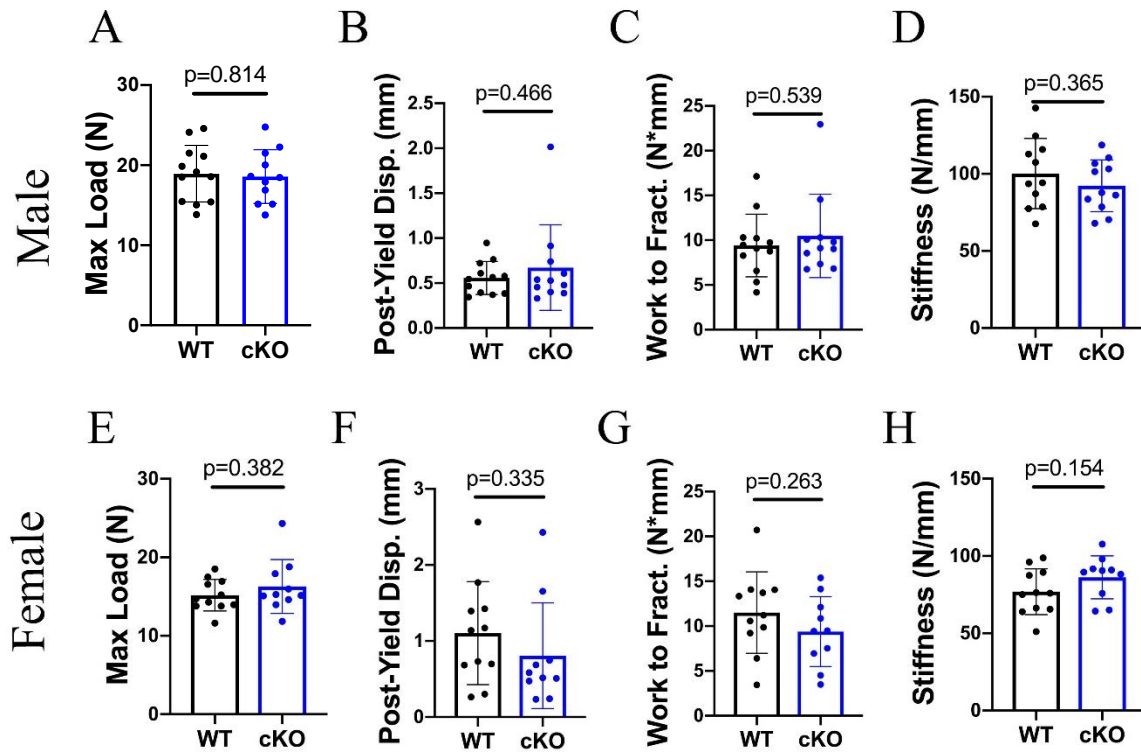
Supplemental Table 2. MicroCT parameters for female mice, showing mean ± SD. Group sizes: WT n=12 at 8 weeks, n=15 at 18 weeks, n=10 at 30 weeks; cKO n=12 at 8 and 18 weeks, n=16 at 30 weeks. Unpaired, two-tailed t-tests.

Supplemental Figure 1 -



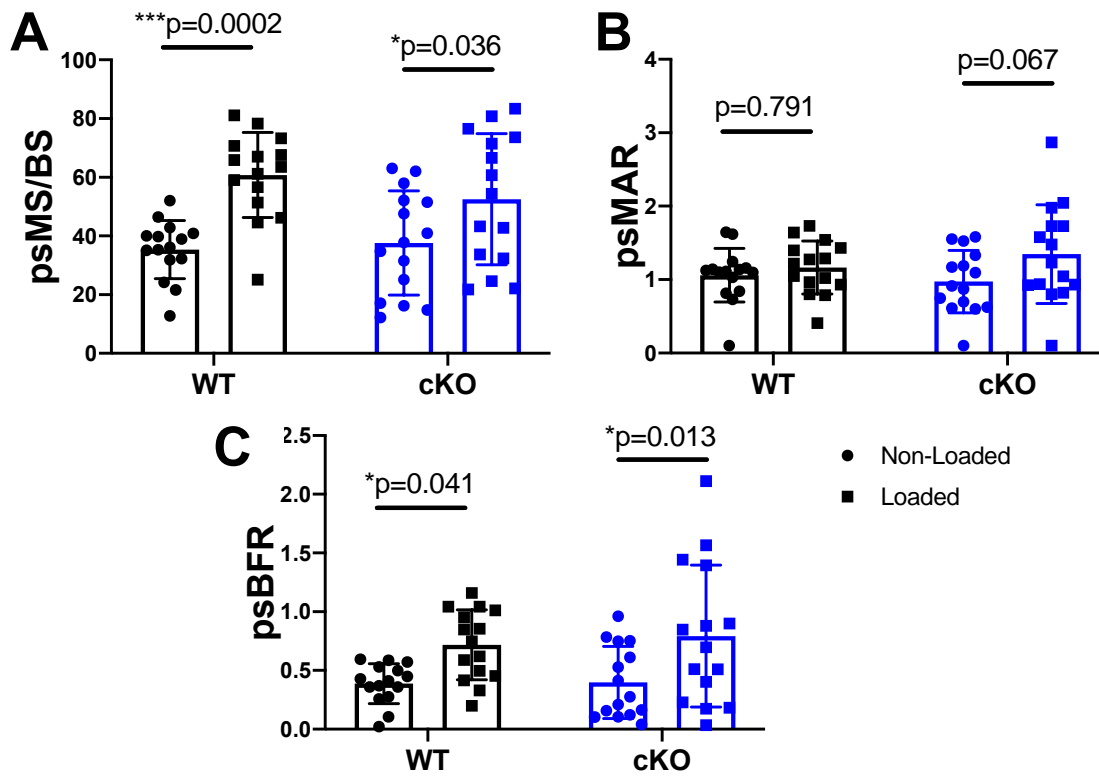
Supplemental Figure 1. A) No difference in weight in Mfn2 cKO mice at 8 or 18 weeks. B) Mfn2 mRNA is depleted in crushed cortical bone of both male and female cKO. C) Mfn1 mRNA is unchanged. Unpaired t-tests with Welch's correction.

Supplemental Figure 2



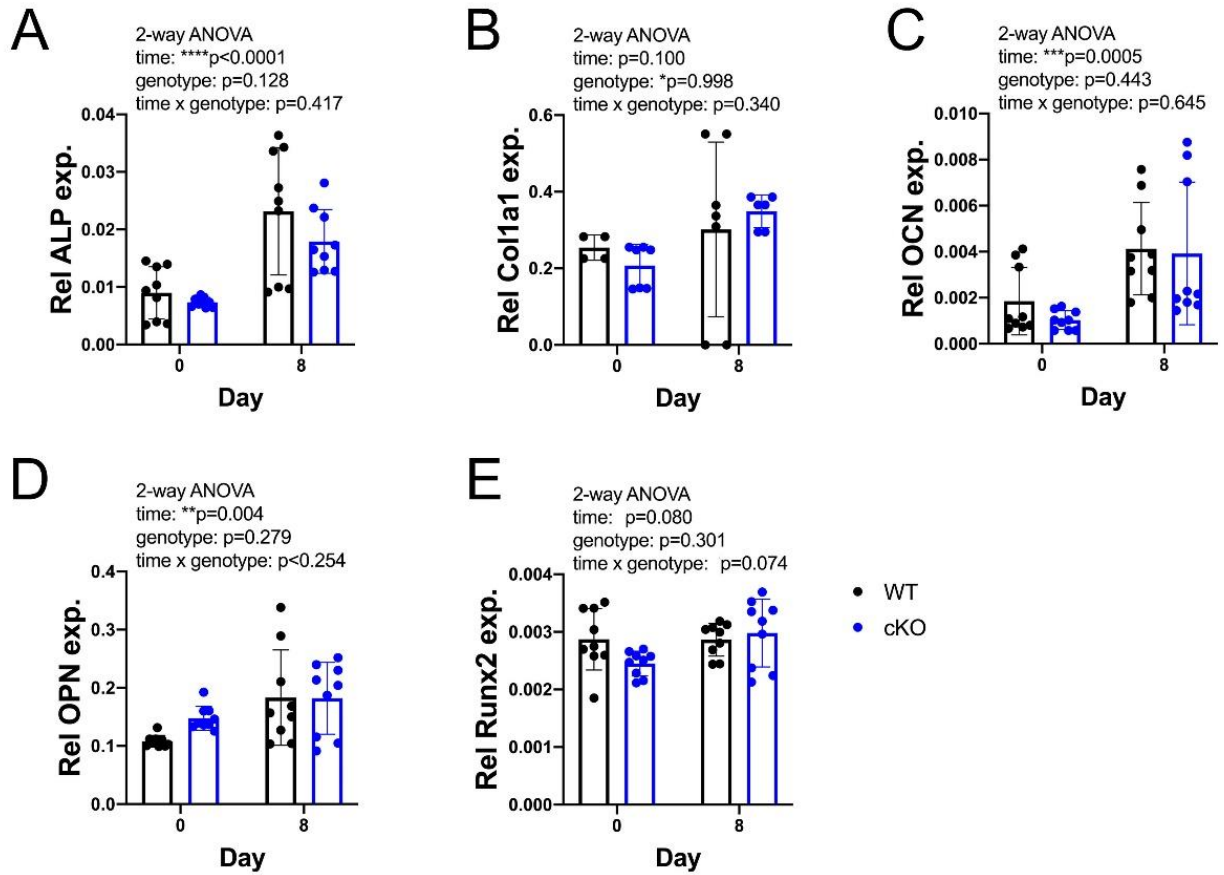
Supplemental Figure 2. No change in bone strength of femurs by mechanical testing at 8 weeks of age in either males (A-D) or females (E-H).

Supplemental Figure 3



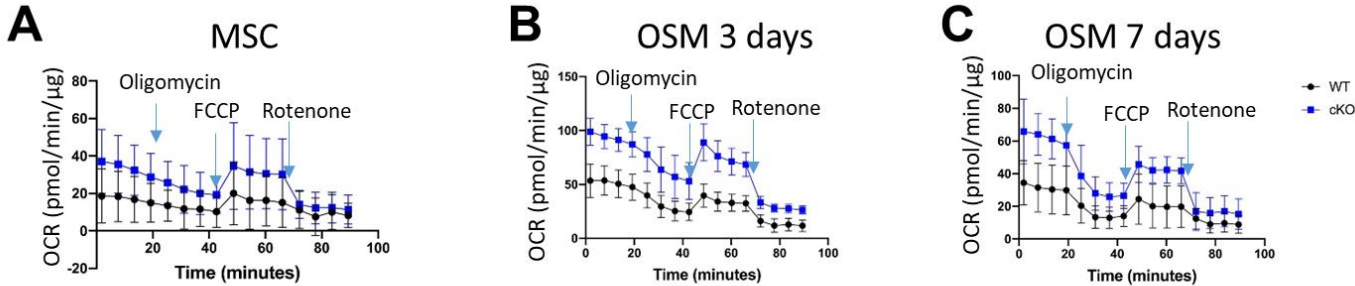
Supplemental Figure 3. Similar response to mechanical loading of the tibia in 18 week female mice. Dynamic histomorphometry was performed at peak strain site. 2-way ANOVA showed the indicated responses to 5 days of loading in each genotype, but no differences by genotype or interaction between loading and genotype.

Supplemental Figure 4



Supplemental Figure 4. Markers of osteogenesis in MSCs induced with high dose (10 mM) β -GP are similar in WT and cKO cultures. Data points represent biological replicates. 2-way ANOVA.

Supplemental Figure 5



Supplemental Figure 5. Tracings used for oxygen consumption rates in undifferentiated MSCs (A) or those differentiated in OSM for 3 days (B) or 7 days (C). Timing of addition of oligomycin, FCCP, and rotenone are indicated with arrows.