Supplementary Materials and Methods

Osteoblast mineralization assay with primary cells

Primary calvarial osteoblasts were isolated from 2-day-old to 5-day-old C57BL/6N mice. Cells were plated in 96-well plates at 1.5×10^4 cells per well or in 24-well plates at 0.8×10^5 cells per well, and cultured to confluence. Subsequently, the cells were cultured in the presence of 100 ng/ml BMP2 to induce differentiation. Cells were exposed to different concentrations of ERI (0, 10, or 25 nM) during incubation. Calcium deposition was evaluated by Alizarin Red S staining on day 14. For gene expression analysis, total RNA was extracted on day 7.

Supplementary Figure Legends

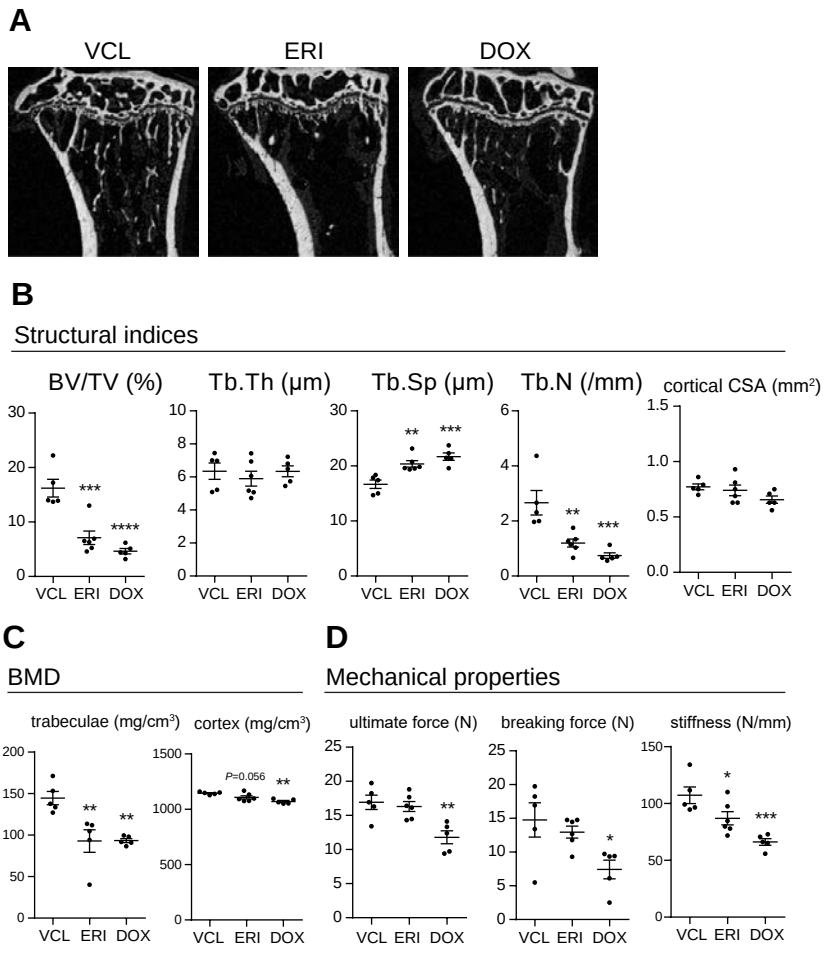
Supplementary Figure S1. A. Representative reconstructed μCT images of the proximal tibia of each treatment group. Because of the termination of the experiment due to severe weight loss, mice treated with TBD were not included in the analysis. B, C, and D. Structural indices (B), BMD (C), and mechanical properties (D) of mice in each treatment group. Five mice per treatment group were analyzed. *, $P < 0.05$; **, $P< 0.01$; ***; $P < 0.001$; ****, $P < 0.0001$ (compared with those in the VCL-treated group).

Supplementary Figure S2. ERI does not affect osteoblast differentiation or the expression of *Tnfs11* and *Tnrsf11b* transcripts *in vitro*. Mouse primary calvarial osteoblasts were incubated with 100 ng/ml recombinant human BMP2 for 2 weeks (A) or 1 week (B) in the presence of ERI (1, 10, or 25 nM) or VCL. A. Representative photomicrographs of primary osteoblasts stained with Alizarin Red staining. Bar, 500 μm. B. Expression levels of *Tnfsf11* and *Tnfrsf11b* transcripts and the *Tnfsf11/Tnfrsf11b* ratio in the primary osteoblasts cultured in the presence or absence of ERI. Three independent experiments were performed. ns, not significant.

Supplementary Table S1. The nucleotide sequences of the oligos used in this study.

Gene	Forward	Reverse
Gapdh	AACAGCAACTCCCACT	CCTGTTGCTGTAGCCG
Tnfsf11	TCTGCAGCATCGCTCTGTTC	AGCAGTGAGTGCTGTCTTCTGATATT
Tnfrsf11b	TCCCGAGGACCACAATGAAC	TGGGTTGTCCATTCAATGATGT
Nfatc1	CCAAGTCTCTTTCCCCGACATC	AAGCTCGTATGGACCAGAATGTG
Ctsk	TATGACCACTGCCTTCCAATAC	GCCGTGGCGTTATACATACA
Acp5	GCAACATCCCCTGGTATGTG	GCAAACGGTAGTAAGGGCTG

Supplementary Figure S1



Supplementary Figure S2