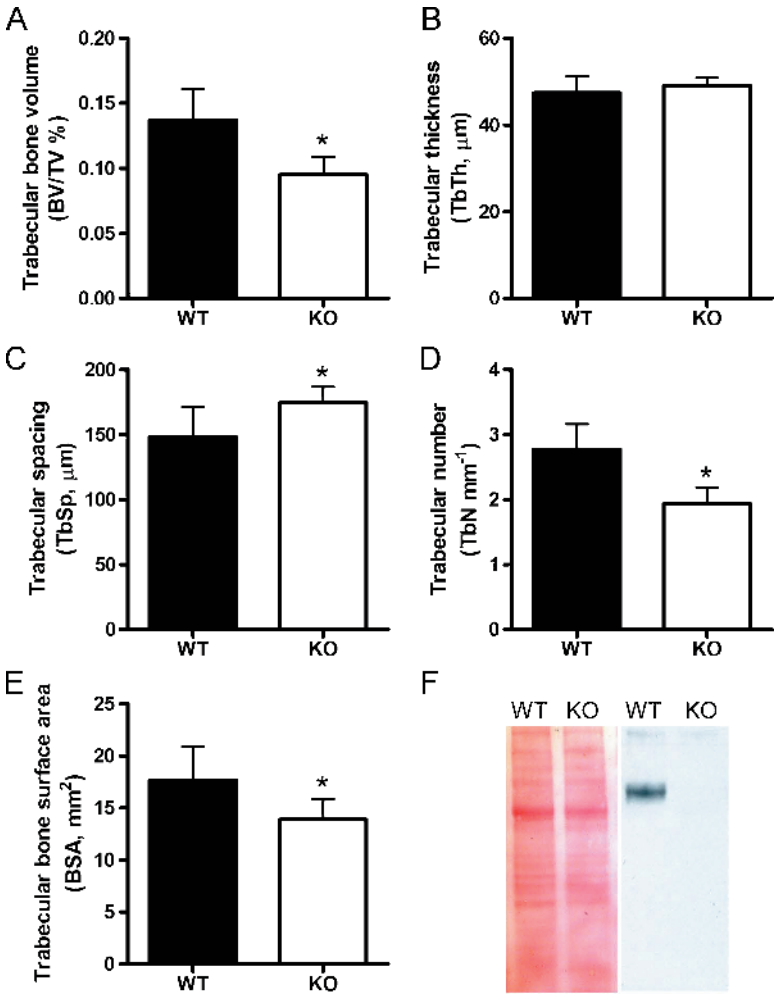

Figure W1. SPARC KO tibia display decreased trabecular morphometric parameters. (A–E) MicroCT was used to determine the bone morphometric parameters of SPARC WT (black columns) and KO (white columns) mice: (A) BV/TV, (B) Tb.Th, (C) Tb.Sp, (D) Tb.N, and (E) BSA. Values were represented as mean ± SD measured for nine mice. *$P < .05$ by Student's t test. (F) Whole bone extracts from femurs of SPARC WT and KO mice lysed with RIPA buffer and separated by SDS-PAGE (4%-12%). (Left) Ponceau S (Sigma)–stained nitrocellulose and (right) immunoblot analysis for SPARC (R&D Systems).

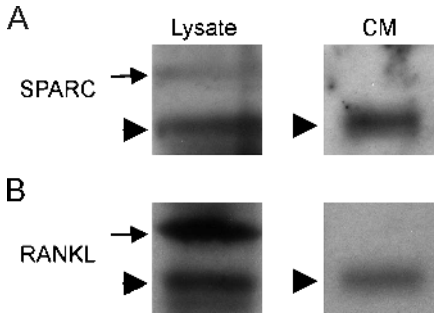

Figure W2. RM1 cells express and secrete SPARC and RANKL. RM1 culture lysates and conditioned medium (CM) were collected. Proteins were separated by SDS-PAGE (10%) followed by (A) SPARC and (B) RANKL (Santa Cruz Biotechnology) immunoblot analysis. Both total (SPARC) or transmembrane (RANKL) (arrow) and soluble (arrowhead) forms of the proteins were found.

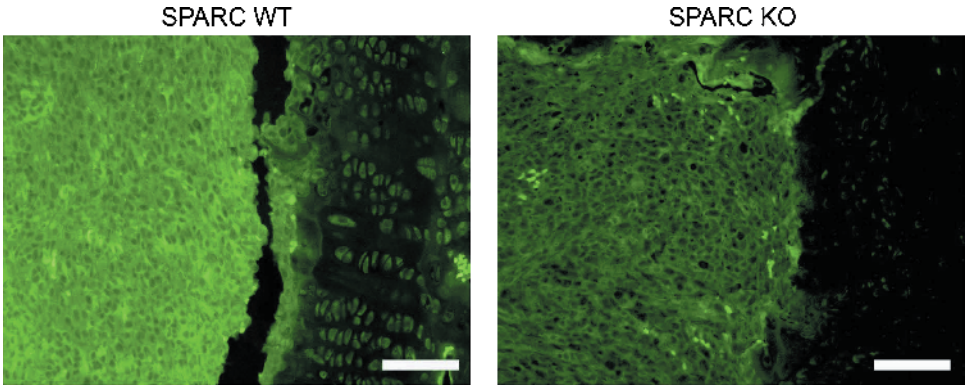

Figure W3. RM1 cells produce SPARC *in vivo*. RM1 cells (1×10^3) were injected into the tibia of SPARC WT or KO. Bones were isolated after 2 weeks of intraosseous tumor growth and paraffin-embedded bone sections were stained for SPARC (green) using a method modified from Trombetta and Bradshaw (*J Histochem Cytochem* 2010;58:871–879). In brief, sections were deparaffinized, rehydrated, and blocked in 2% donkey serum/0.2% Triton X-100/PBS. Slides were incubated for 1 hour with SPARC antibody (R&D Systems) followed by incubation with an antigoat secondary antibody conjugated to Alexa 488 (Molecular Probes). Coverslips were mounted with Vectashield (Vector Laboratories, Burlingame, CA). Images were taken with a Leica DM2500 light microscope. Scale bars, 50 μm. Representative images from nine mice are shown.

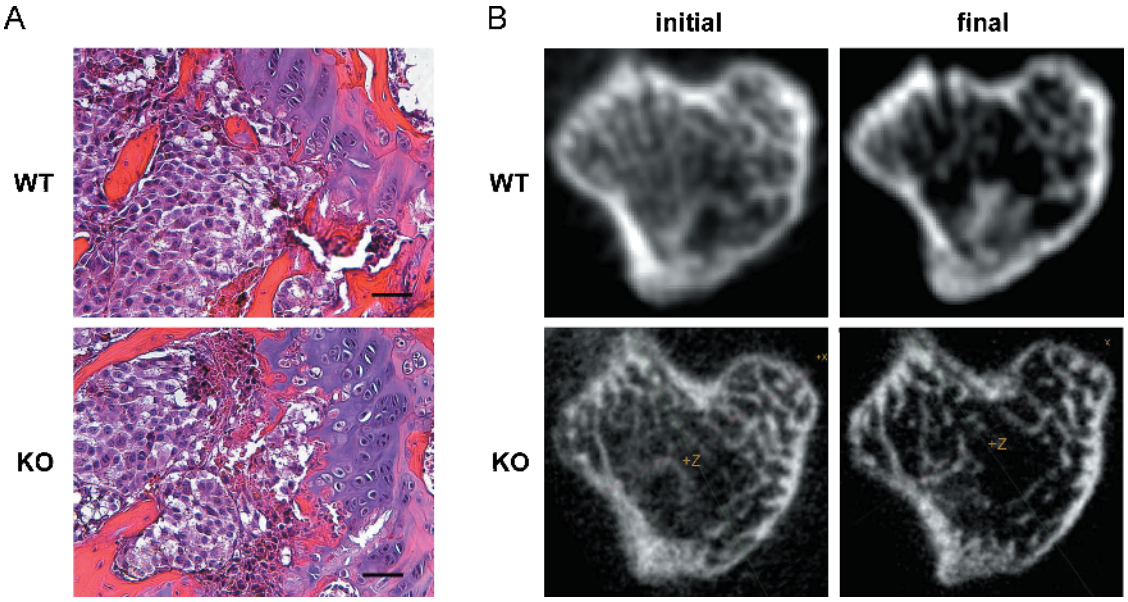

Figure W4. Melanoma implantation does not promote osteolysis. B16-F10 murine melanoma cells (1×10^4) were injected into the tibiae of SPARC WT and KO mice. (A) Bones were isolated after 2 weeks of intraosseous tumor growth, sectioned, and stained with H&E. B16-F10 cells can be seen growing within proximal metaphysis. Scale bars, 50 μm. (B) MicroCT-derived proximal metaphyseal transaxial slices of the tibiae both 1 day (initial) and 2 weeks (final) after B16-F10 cell implantation. Representative images from nine mice are shown.

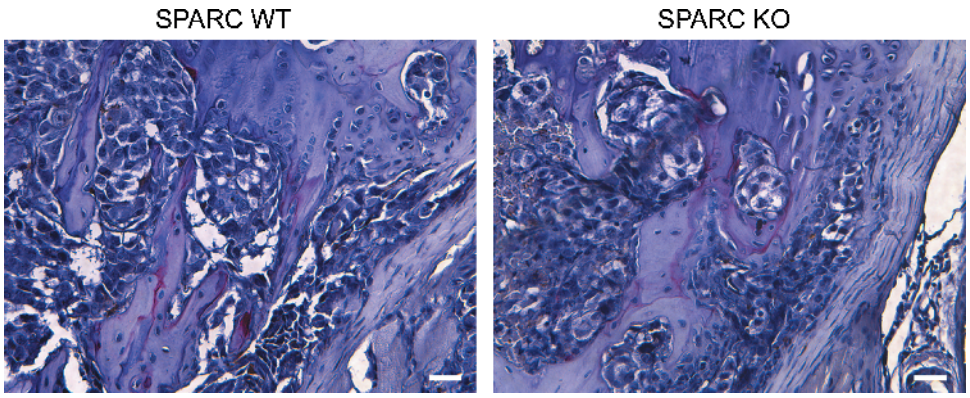

Figure W5. Melanoma implantation does not stimulate osteoclast differentiation. B16-F10 cells (1×10^4) were injected into the tibia of SPARC WT or KO mice. Bones were isolated after 2 weeks of intraosseous tumor growth and sectioned. Osteoclasts were visualized by TRAP staining (dark red) and counterstained with hematoxylin. Scale bars, 50 μm. Representative images from nine mice are shown.