and the formation of enchondroma-like lesions in the bone marrow.

Supplemental Figure 1 **ERK1/2 inactivation using the Osx-Cre transgene delays bone growth.** (A) X-rays of the hindlimbs of 3-week-old WT-like, Control, and cKO_{osx} mice. (B) Skeletal preparations of the hindlimbs of 3-week-old WT-like, Control, and cKO_{osx} mice. (C) Safranin O staining of enchondroma-like lesions in the bone marrow at P14, indicating the presence of cartilaginous matrix. (D) The body weight of cKO_{osx} mice was significantly decreased compared with WT-like and Control mice at 3 weeks. Data represent mean ± standard error, n=5 per group. (E) Alcian blue and HE staining of the tibia of cKO_{osx} mice at P3 showed abundant cartilage remnants resembling cartilage islands in the bone marrow, indicating defective cartilage resorption. At this stage, these cartilaginous remnants are still connected to the growth plate, suggesting that the cartilage islands develop from the unresorbed cartilage. Boxed areas (1-2) are magnified in the corresponding panels. Scale bars at the right bottom of each panel indicate 100μm.

Supplemental Figure 2. **Chondrocyte proliferation, apoptosis, and matrix mineralization in cKO_{osx} mice.** (A) Matrix mineralization was assessed by von Kossa's staining in the tibiae at E15.5, E17.5, and P0. There was no obvious difference in matrix mineralization between cKO_{osx} and control mice. (B) BrdU-labeled cells were identified by immunohistochemistry in cKO_{osx} and control tibiae at E15.5 and E18.5. There was no significant difference in the proportion of BrdU-labeled cells in the resting and proliferating zones between cKO_{osx} and control mice. Data represent mean ± standard error, n=3 per group. (C) Apoptotic cells were

identified by TUNEL staining in cKO_{osx} and control tibiae at E18.5. cKO_{osx} mice show an increase in the number of apoptotic cells in the zone of hypertrophic chondrocytes. Scale bars at the right bottom of each panel indicate 100μm.

Supplemental Figure 3. **cKO_{osx} mice exhibit delayed endochondral ossification, while angiogenesis and osteoclast recruitment at the chondro-osseous junction remain unaffected.**

(A) Alcian blue staining and immunostaining for von Willebrand factor (vWF) of cKO_{osx} and control tibiae at E16.5. CON, control mice; cKO, cKO_{osx} mice. (B) vWF immunostaining of cKO_{osx} and control tibiae at E18.5. (B) vWF immunostaining of cKO_{osx} and control tibiae at E18.5. (C) Mmp9 immunostaining of cKO_{osx} and control tibiae at E18.5. (D, E) TRAP staining of cKO_{osx} and control tibiae at E18.5 and P7. No differences were noted in the number of TRAP-positive cells adjacent to chondro-osseous junction at both stages (right panels). Data represent mean ± standard error, n=5 per group. NS, not significant; COJ, chondro-osseous junction. Scale bars at the right bottom of each panel indicate 100μm.

Supplemental Figure 4. ***Vegf* and *Runx2* expression in the tibiae at E18.5.** In situ hybridization indicated similar levels of *Vegf* (A) and *Runx2* (B) expression in cKO_{osx} and control mice. Scale bars at the right bottom of each panel indicate 100μm.

Supplemental Table 1. **Methods for RNA in situ hybridization.**