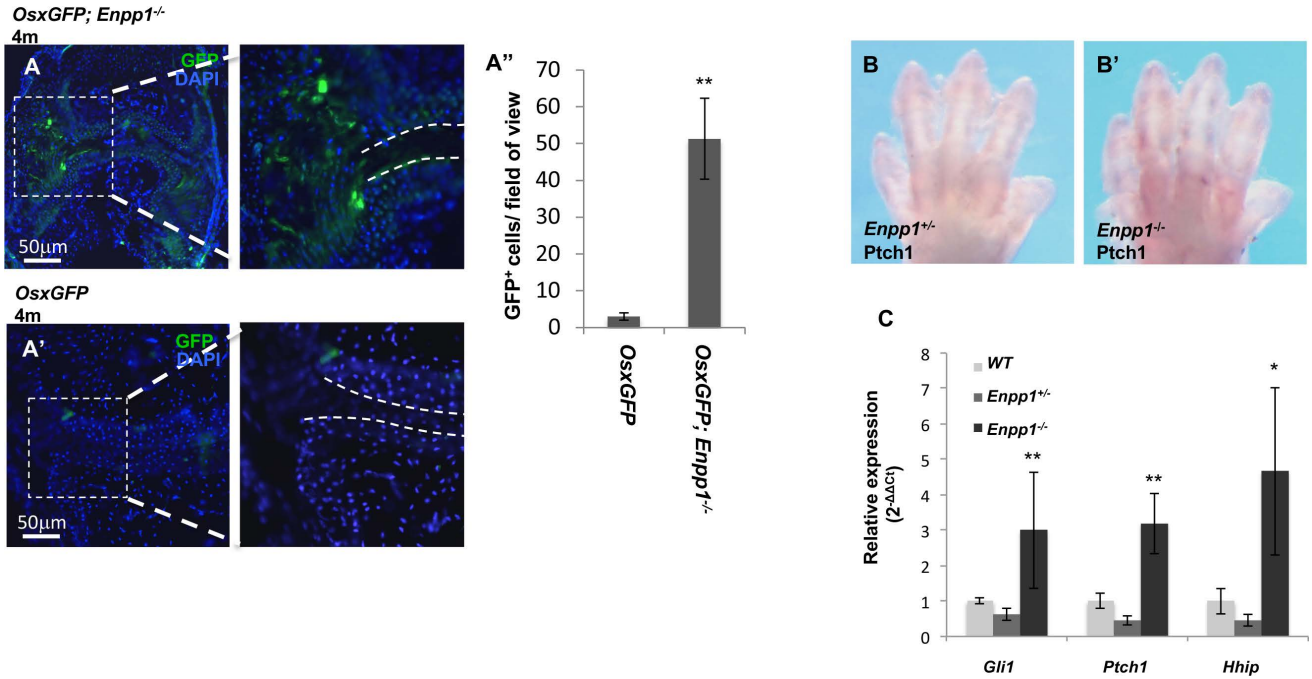
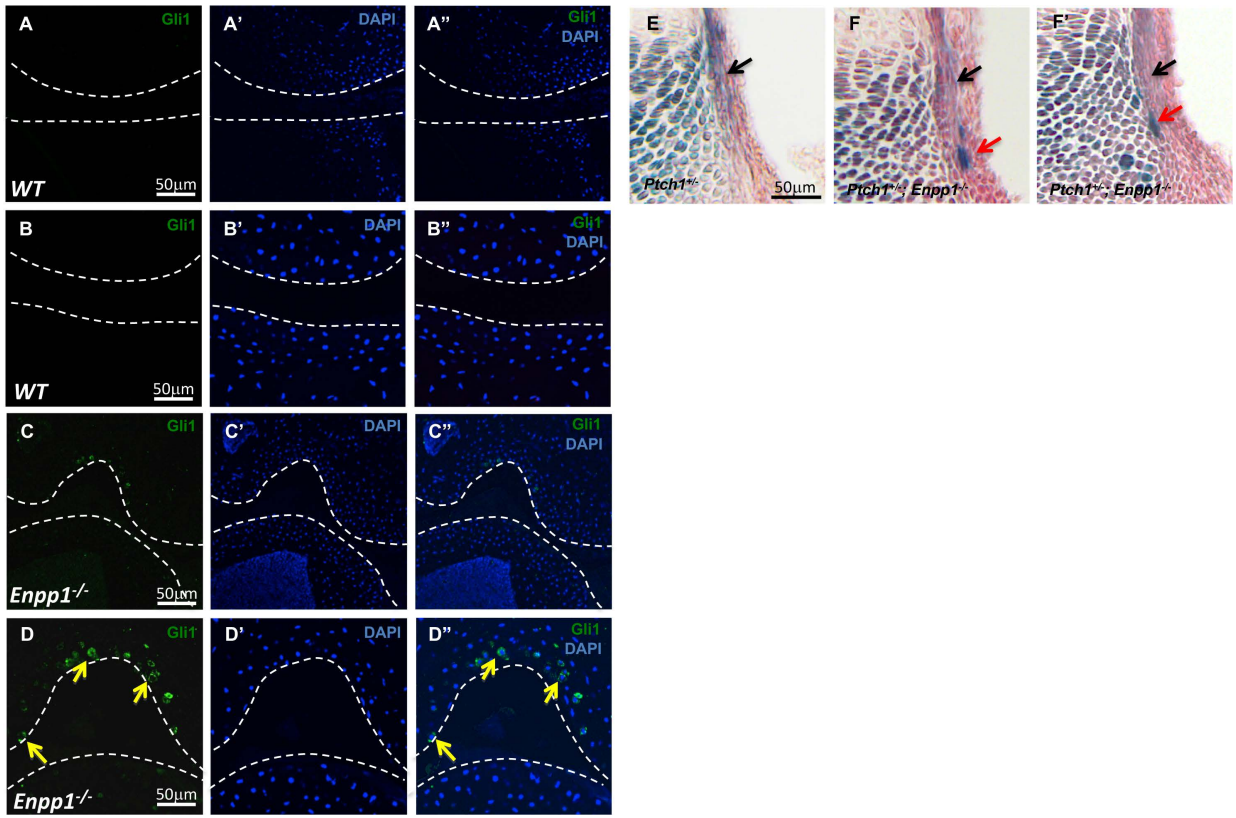
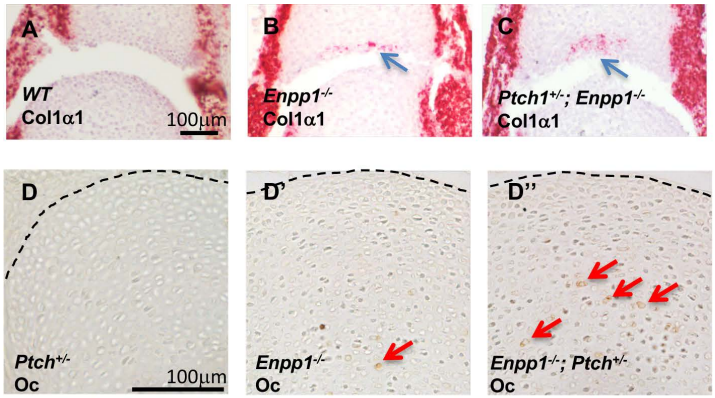
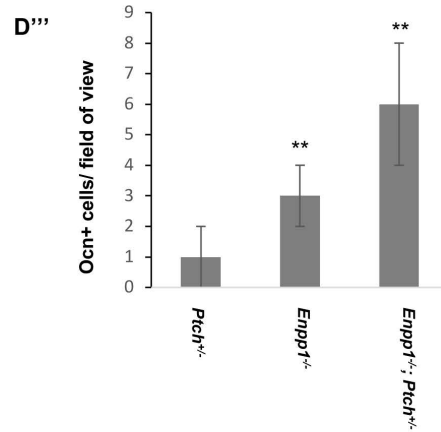


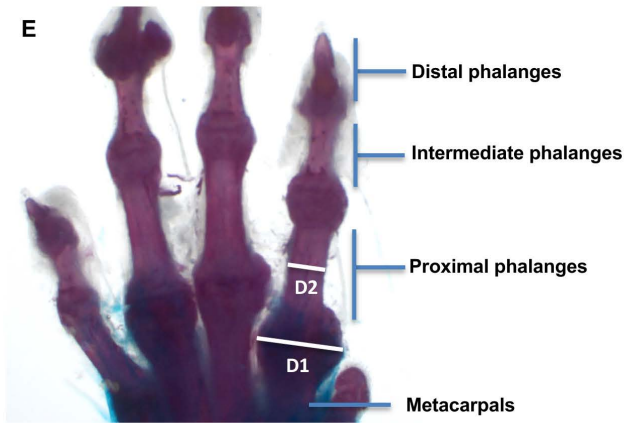
Supplementary Fig. 1. Increased Hh signaling activity in the joints of *Enpp1*$^{-/-}$ mice
(A-A") Direct fluorescence of OsxGFP with DAPI staining on the phalangeal joint sections from 4 months old *OsxGFPcre; Enpp1*$^{-/-}$ mice (A) or *OsxGFPCre* mice (A'). The number of GFP positive cells in the articular cartilage of the metacarpophalangeal joints was quantified as the number of GFP^{+}/ field of view under 40x objective magnification (n=4) (A").
(B-B') The E12.5 *Enpp1*$^{+/-}$ and *Enpp1*$^{-/-}$ embryos were collected for whole mount *in situ* hybridization with the Ptch1 riboprobe. (C) qRT-PCR analysis of Hh target genes and osteoblast genes expressed in the front paws of the 3 months old mice (n=3). *P < 0.05, **P < 0.01, ***P < 0.001 by student t test.



Supplementary Fig. 2. Ectopic expression of Gli1 in the articular cartilage of *Enpp1*$^{-/-}$ at 4 months of age
(A-D") Immunofluorescent Gli1 staining of phalangeal joint sections from 4 months old mice. Nucleus were shown by DAPI staining. (B-B", D-D") Enlarged images of (A-A") and (C-C") respectively. Gli1 expression was detected in the articular chondrocyte of *Enpp1*$^{-/-}$ mice (Yellow arrows), not in the wild type ones. (E-F') Hh signaling activity was detected by *Ptch1-LacZ* expression in the metacarpophalangeal joints from the P2 *Ptch1*$^{+/-}$, and *Ptch1*$^{+/-}$*; Enpp1*$^{-/-}$ mice. *Ptch1-LacZ* expression in the perichondrium is shown by back arrows and aberrant ectopic upregulation of *Ptch1-LacZ* is shown by red arrows.

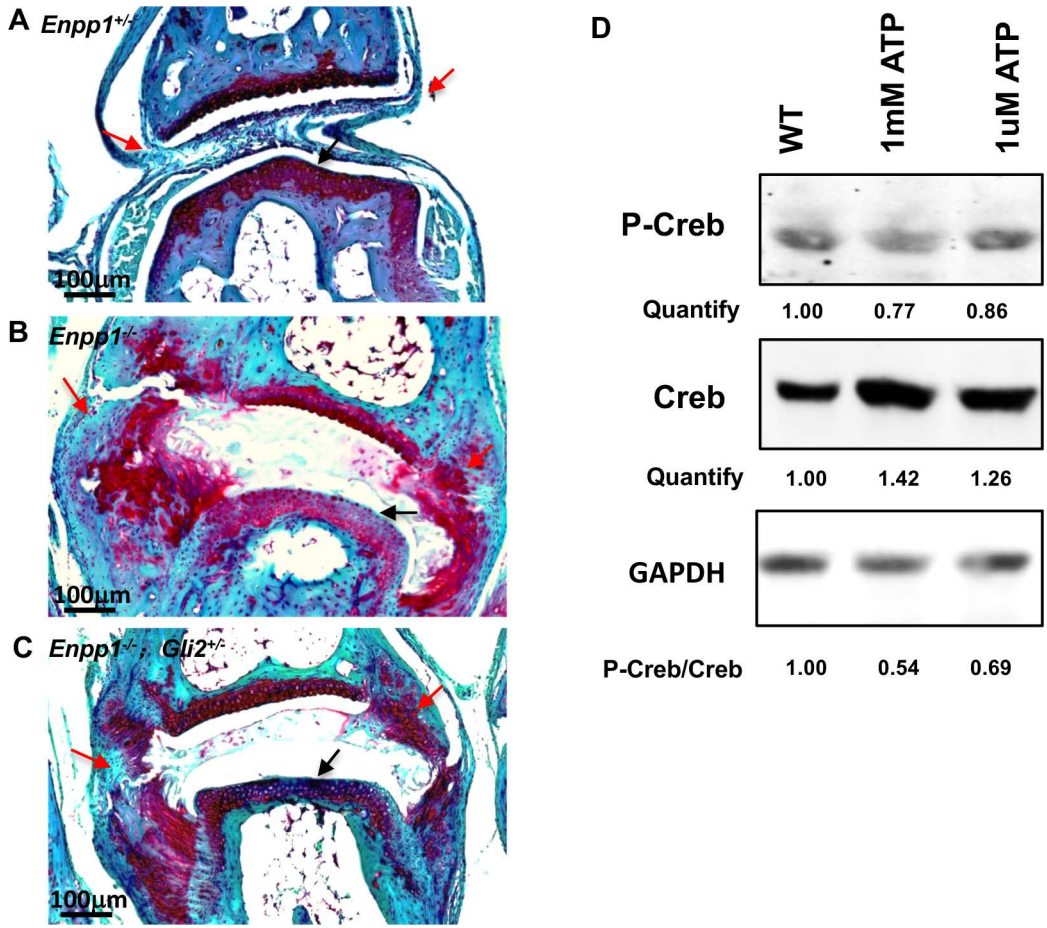






Supplementary Fig. 3. Enhanced osteoblastic differentiation in the *Ptch1*$^{+/-}$*; Enpp1*$^{-/-}$ joint and the measurement of forelimb phalangeal joint size

(A-C) Col1a1 expression in the phalangeal joint section of P2 mice was detected by *in situ* hybridization. (D-D''') Analysis of Oc expression in the articular cartilage (n=3). Oc positive cells number were counted and quantified under 40X magnification / field (D'''). **P < 0.01 by student t test. Forelimbs were used for quantification of the metacarpophalangeal joint size. The joint sizes were measured by image J. The metacarpophalangeal joint size (D1) and the diameters of the proximal phalanges (D2) were measured, then the ratios of D1/D2 of each digit were calculated as the relative joint size and used for the statistical analysis (E).



Supplementary Fig. 4. Reduced join phenotypes in the *Gli2*$^{+/-}$; *Enpp1*$^{-/-}$ mice and p-Creb regulation by ATP in synovial cells

(A-C) Safranin-O staining of metacarpophalangeal joint sections from forelimbs of 10 weeks old mice. Black arrows indicate articular cartilage and red arrows indicate joint capsule. (D) PKA activity measured by p-Creb/ Creb ratio in primary synovial cells from the wild type mice. Cells were treated for 10 min with indicated ATP concentrations. Protein bands in the Western blotting were quantified by densitometry and analyzed using Image J. The numbers indicate relative gray scale values of P-Creb and Creb in each lane and P-Creb/Creb ratio was calculated.