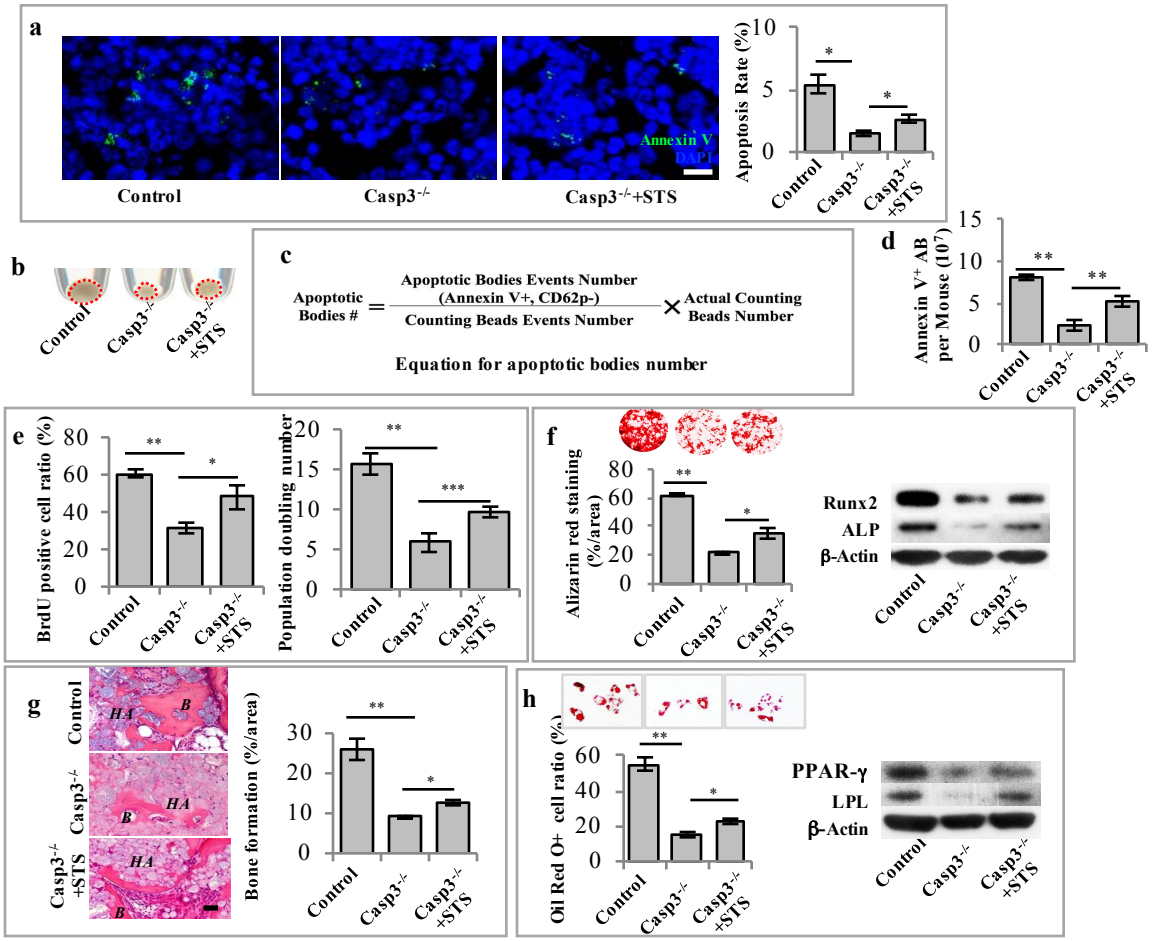


**Supplementary Figure 1. Staurosporine-induced apoptosis rescued impaired MSCs in *Casp3*$^{-/-}$ mice. a,** 3 ng Staurosporine (STS) was intraperitoneally administered to *Casp3*$^{-/-}$ mice twice a week for 4 weeks (a total of 8 injections). Annexin V was injected *via* the tail vein 2 hours prior to the sample collection to trace the apoptotic rate in the bone marrow. Immunostaining showed that STS injection rescued the reduced number of apoptotic cells in the bone marrow of *Casp3*$^{-/-}$ mice (n=5). **b,** The amount of apoptotic body-sized extracellular vesicles in pellets derived from *Casp3*$^{-/-}$ mice (n=5) was much less than in littermate control mice. After 4 weeks of STS infusion, the amount of apoptotic body-sized extracellular vesicles was increased in *Casp3*$^{-/-}$ mice. **c,** The equation for calculating the number of apoptotic bodies using flow cytometric analysis. **d,** The flow cytometric calculation showed the number of apoptotic bodies from the bone marrow of *Casp3*$^{-/-}$ mice (n=5) was reduced compared to littermate control mice. After 4 weeks of STS infusion, the number of apoptotic bodies from the bone marrow of *Casp3*$^{-/-}$ mice (n=5) was increased. **e,** BrdU labeling and continued passage assay showed that *Casp3*$^{-/-}$ MSCs (n=5) had reduced proliferation and population doubling rates when compared to the littermate control group. After 4 weeks of STS treatment, proliferation and population doubling rates were increased in *Casp3*$^{-/-}$ MSCs (n=5). **f,** Compared to littermate control MSCs, *Casp3*$^{-/-}$ MSCs showed reduced capacities to form mineralized nodules when cultured under osteogenic inductive conditions, assessed by alizarin red staining (n = 5), and reduced expression of osteogenic markers Runx2 and ALP, assessed by Western blot. After 4 weeks of STS treatment, reduced mineralized nodule formation and expression of Runx2 and ALP were rescued in *Casp3*$^{-/-}$ MSCs (n=5). **g,** Casp3$^{-/-}$ MSCs showed reduced capacities to form new bone when implanted into immunocompromised mice subcutaneously using HA/TCP as a carrier. After 4 weeks of STS infusion, reduced bone formation capacity was rescued in *Casp3*$^{-/-}$ MSCs (n=5). H&E staining showed new bone (*B*) and HA/TCP (*HA*) carrier. **h,** Compared to littermate control MSCs, *Casp3*$^{-/-}$ MSCs showed reduced capacity to differentiate into adipocytes when cultured under the adipogenic inductive conditions, as assessed by Oil red O staining (n = 5), along with reduced expression of adipogenic markers PPAR-γ and LPL, as assessed by Western blot. After 4 weeks of STS administration, reduced adipocyte formation and expression of PPAR-γ and LPL in *Casp3*$^{-/-}$ MSCs (n=5) were rescued. All results are representative of data generated in three independent experiments. Error bars represent the S.D. from the mean values. ***$P < 0.001$; **$P < 0.01$; *$P < 0.05$. Scale bar, 5 μm (**a**), 50 μm (**g**).