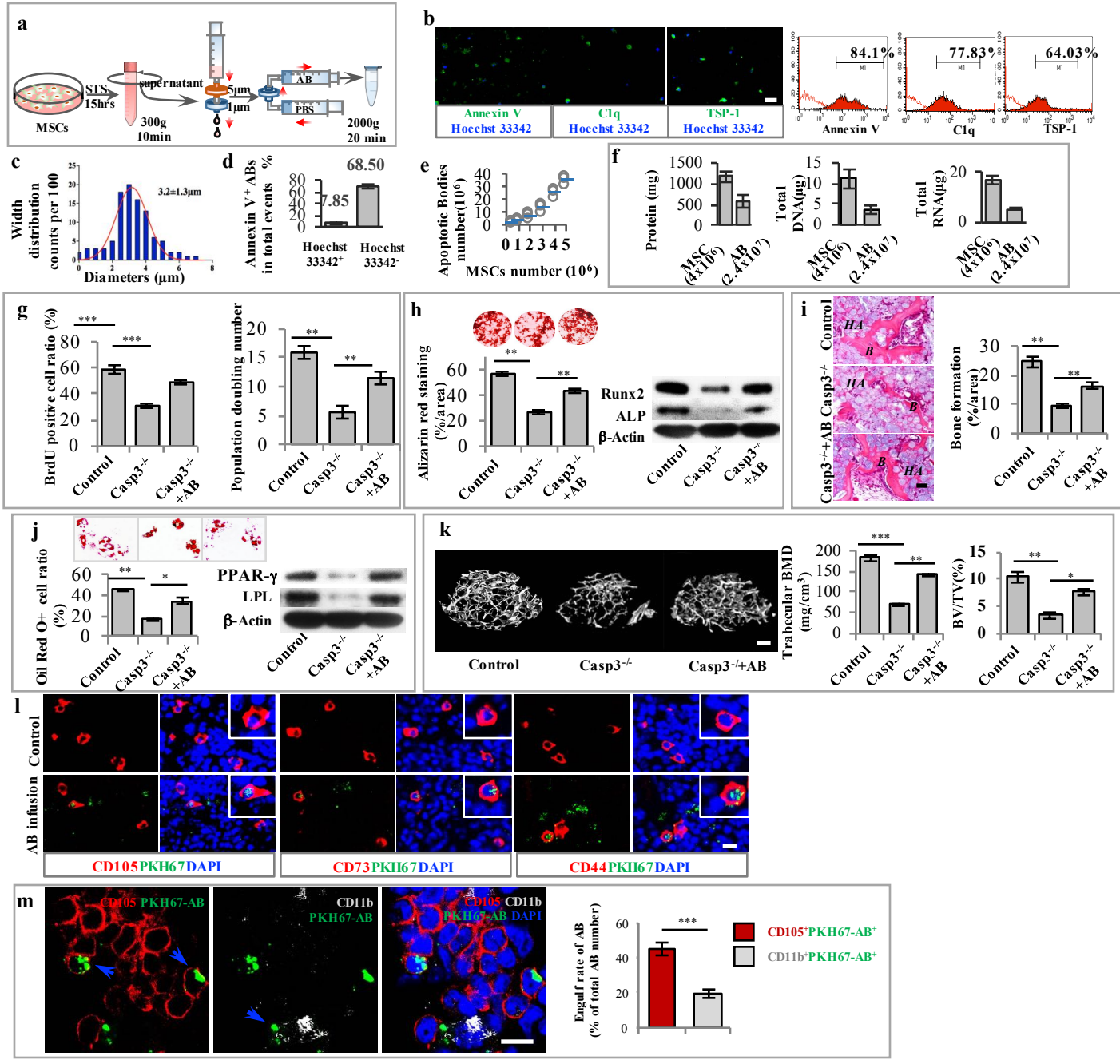


**Supplementary Figure 2. Systemic infusion of exogenous apoptotic bodies rescued impaired MSCs in *Casp3*$^{-/-}$ mice. a,** Scheme illustrating apoptotic body (AB) isolation from culture-expanded allogenic MSCs. Confluent MSCs were treated with 200nM staurosporine (STS) for 15 hours. After 300g *rcf* centrifugation to remove cell debris, the supernatant was subsequently filtered with 5 μm and 1 μm filters. After a 1 μm filter was used to collect apoptotic bodies, 2000g rcf centrifugation was used to isolate apoptotic bodies. **b,** Immunofluorescent staining and flow cytometry showed that apoptotic bodies expressed Annexin V, C1q and TSP-1. The light areas of flow cytometry indicated isotype, and the red areas indicated numbers of Annexin V, C1q and TSP-1 positive apoptotic bodies numbers analyzed by flow cytometric analysis. **c,** Histogram showing the width distribution of apoptotic bodies. Apoptotic bodies were observed under microscopy, and the diameter of AB were measured using MicroSuite Analytical Suite software (Olympus). The width distribution of apoptotic bodies was calculated after counting in ten random fields. Data are presented as the percentage of different sizes of apoptotic bodies out of the total numbers of apoptotic bodies. **d,** Flow cytometric assay showed 7.85% of the apoptotic bodies were Hoechst 33342 positive and 68.5% of the apoptotic bodies were Hoechst 33342 negative in the Annexin V positive population. **e,** Yield rate of apoptotic bodies from culture-expanded MSCs. **f,** Culture-expanded MSCs and apoptotic bodies contained protein (mg), DNA (mg) and RNA (mg). **g,** After 4 weeks of apoptotic body infusion, BrdU labeling and continued passage assay showed a rescue of the decreased proliferation and population doubling rates in *Casp3*$^{-/-}$ MSCs. **h,** After 4 weeks of apoptotic body infusion, MSCs from *Casp3*$^{-/-}$ mice showed significantly increased capacities to form mineralized nodules, as assessed by alizarin red staining (n = 5), and upregulated expression of osteogenic markers Runx2 and ALP, as assessed by Western blot. **i,** MSCs from apoptotic body-treated *Casp3*$^{-/-}$ mice showed increased capacities to generate new bone when implanted into immunocompromised mice subcutaneously using HA/TCP as a carrier (n = 5). H&E staining showed newly formed bone (*B*) and HA/TCP (*HA*) carrier. **j,** After 4 weeks of apoptotic body infusion, MSCs from *Casp3*$^{-/-}$ mice showed significantly increased capacities to differentiate into adipocytes under the adipogenic inductive culture conditions, as assessed by Oil red O staining (n = 5), and upregulated expression of adipogenic markers PPAR-γ and LPL, as assessed by Western blot. **k,** After 4 weeks of apoptotic body infusion, the femurs of *Casp3*$^{-/-}$ mice showed significantly increased bone mineral density (BMD) and bone volume/total volume (BV/TV), as assessed by MicroQCT (n = 5). **l,** After intravenous infusion of PKH67-labeled apoptotic bodies for 24 hours, immunofluorescent staining showed PKH67 co-localized with CD105, CD73 and CD44 positive cells in the femurs of *Casp3*$^{-/-}$ mice. **m,** Co-staining of MSCs marker CD105 and monocyte marker CD11b with PKH67-labeled systemically infused apoptotic body. Arrow indicate the apoptotic bodies engulfed by CD105 or CD11b positive cells. 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, 20 μm (**b**), 50 μm (**i**), 200 μm (**k**), 10 μm (**l, m**).