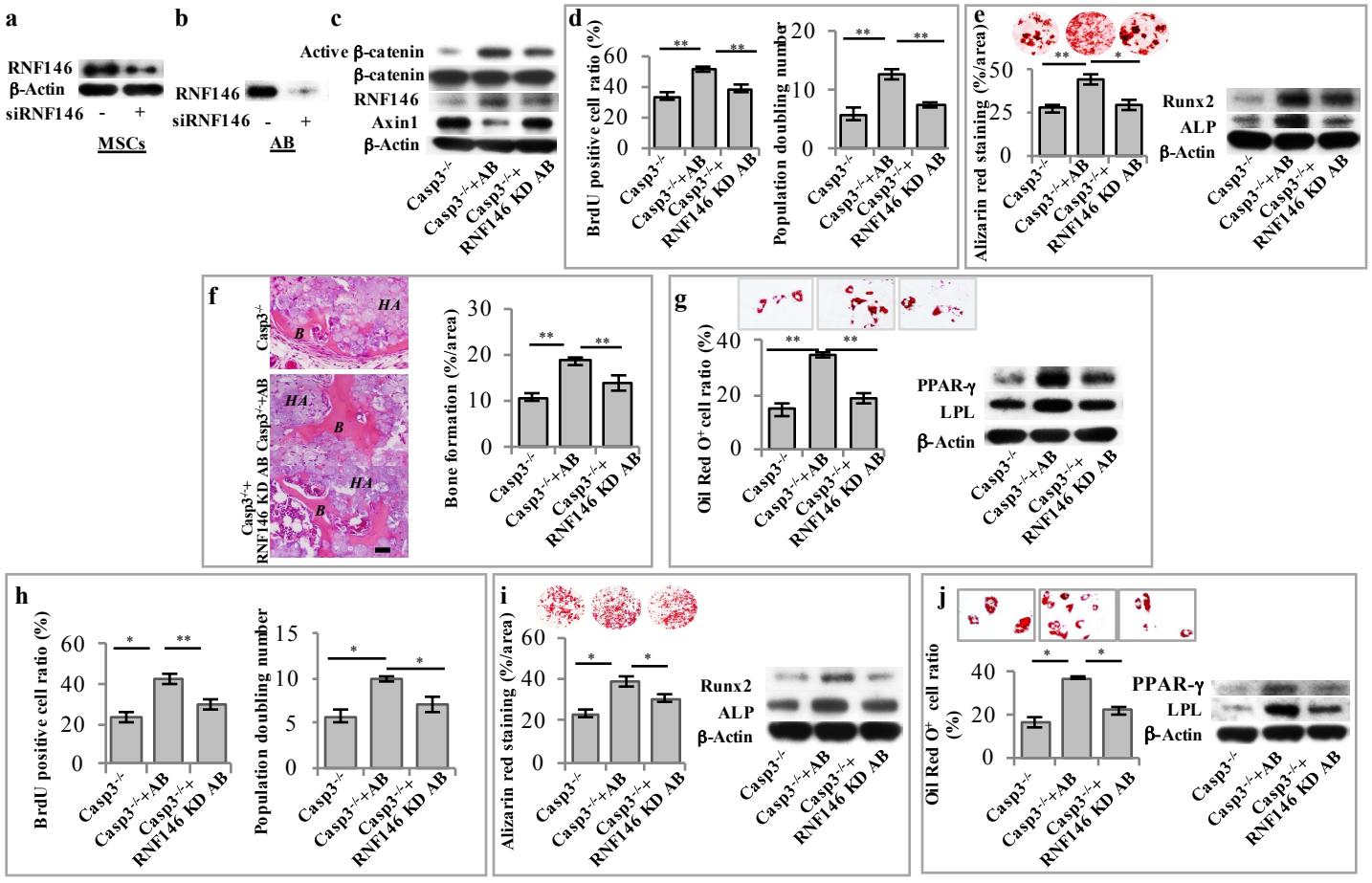

Supplementary Figure 5. RNF146 played an essential role in apoptotic body-mediated rescue of impaired *Casp3*$^{-/-}$ MSCs. a, Western blot showed that RNF146 siRNA effectively inhibited RNF146 expression in MSCs. **b,** Western blot showed that the level of RNF146 in apoptotic bodies derived from RNF146 siRNA-treated MSCs was significantly reduced when compared to the control group. **c,** Western blot showed that systemic infusion of apoptotic bodies from RNF146 siRNA knockdown MSCs failed to upregulate active β-catenin expression and downregulate Axin1 expression in *Casp3*$^{-/-}$ MSCs when compared to the control group at 4 weeks post-infusion. β-Actin was used as a protein loading control. **d,** BrdU labeling and continued passage assay showed that apoptotic bodies derived from RNF146 siRNA knockdown MSCs failed to rescue reduced proliferation and population doubling rates in *Casp3*$^{-/-}$ MSCs when compared to the control group. **e,** Apoptotic bodies derived from RNA146 siRNA knockdown MSCs also failed to rescue reduced capacities to form mineralized nodules in *Casp3*$^{-/-}$ MSCs at 4 weeks post-infusion when cultured under the osteogenic inductive conditions, as assessed by alizarin red staining (n = 5), and expression levels of Runx2 and ALP, as assessed by Western blot. **f,** Apoptotic bodies derived from RNF146 siRNA knockdown MSCs failed to rescue the reduced capacity to generate new bone in *Casp3*$^{-/-}$ MSCs at 4 weeks post-infusion 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. **g,** Apoptotic bodies derived from RNF146 siRNA knockdown MSCs failed to rescue the reduced capacity to differentiate into adipocytes under the adipogenesis inductive conditions, as assessed by Oil red O staining (n = 5), and expression levels of PPAR-γ and LPL, as assessed by Western blot, at 4 weeks post-infusion. **h,** BrdU labeling and continued passage assay confirmed that apoptotic bodies derived from RNF146 siRNA knockdown MSCs failed to rescue the reduced proliferation and population doubling rates of culture-expanded *Casp3*$^{-/-}$ MSCs. **i,** Apoptotic bodies derived from RNF146 siRNA knockdown MSCs failed to rescue the reduced capacity to form mineralized nodules under the osteogenic inductive conditions, as assessed by alizarin red staining (n = 5), and expression of Runx2 and ALP, as assessed by Western blot, in culture-expanded *Casp3*$^{-/-}$ MSCs. **j,** Apoptotic bodies derived from RNF146 siRNA knockdown MSCs failed to rescue the reduced capacity to differentiate into adipocytes under the adipogenic inductive conditions, assessed by Oil red O staining (n = 5), and expression of PPAR-γ and LPL, assessed by Western blot, in culture-expanded *Casp3*$^{-/-}$ MSCs. All results are representative of data generated in three independent experiments. Error bars represent the S.D. from the mean values. $^{**}P < 0.01$; $^{*}P < 0.05$. Scale bar, 50 μm (**f**). KD, knockdown.