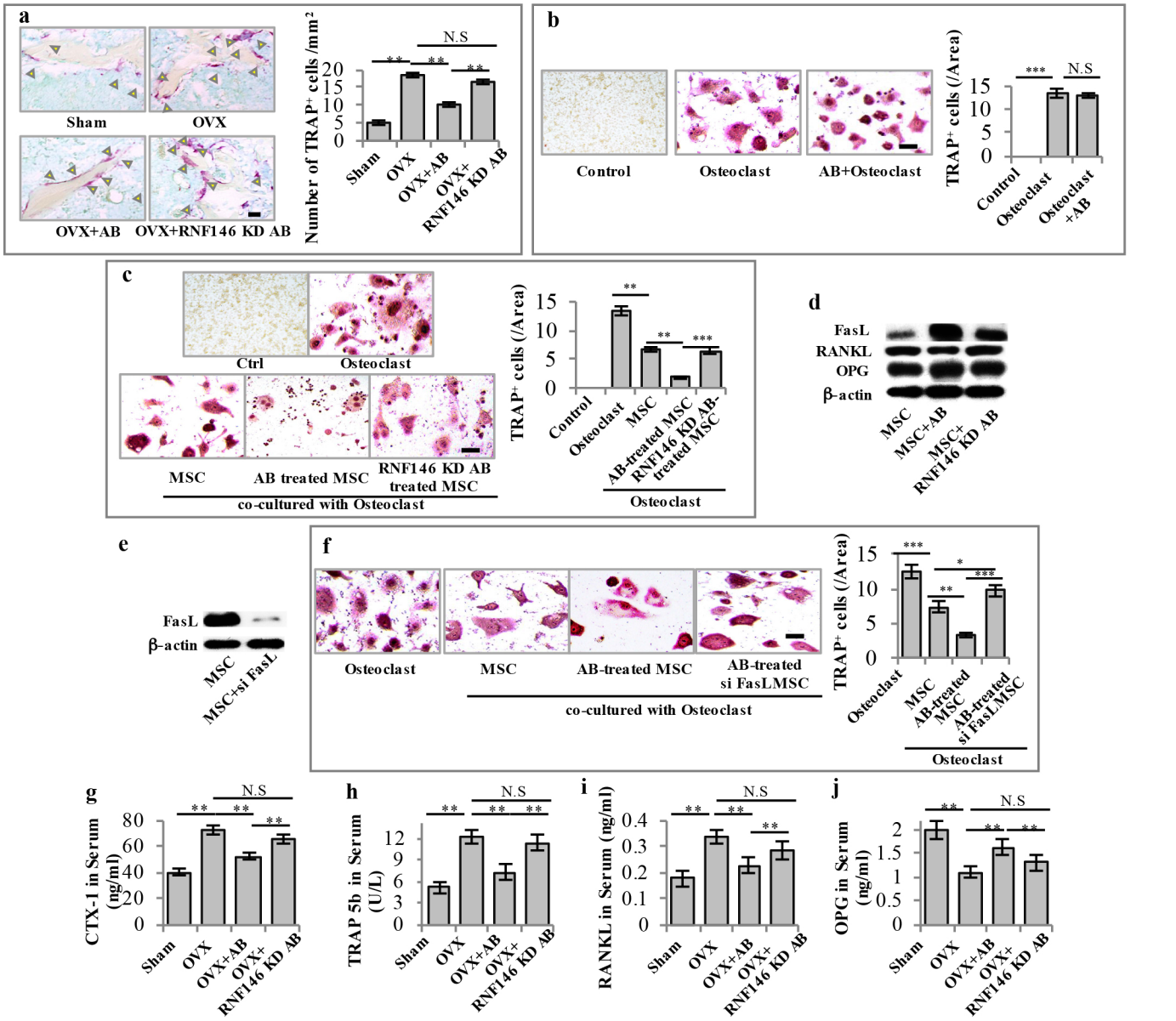

Supplementary Figure 6. Apoptotic body treatment ameliorated osteoporotic phenotype in OVX mice. a, TRAP staining showed that OVX resulted in increased TRAP+ cells (yellow arrows) in the femurs of OVX mice (n = 5). After 4 weeks of apoptotic body infusion, the increased number of TRAP+ cells in the femurs of OVX mice was reduced, but apoptotic bodies derived from RNF146 siRNA knockdown MSCs failed to reduce the increased number of TRAP+ cells. **b,** Osteoclast precursor cells were isolated from bone marrow and inducted with M-CSF and soluble RANKL. TRAP staining showed apoptotic body treatment failed to inhibit osteoclastogenesis in a co-culture system. **c,** TRAP staining showed that MSCs were able to reduce the numbers of osteoclasts when co-cultured with osteoclast precursor cells. The treatment of apoptotic body from wildtype MSCs, but not from RNF146 siRNA knockdown MSCs, improved MSC-mediated reduction of osteoclasts numbers. **d,** Western blot showed that apoptotic body treatment upregulated the FasL expression level in MSCs, however, there was no significant change in RANKL and OPG expression. Apoptotic bodies derived from RNF146 siRNA knockdown MSCs failed to upregulate the FasL expression level. **e,** Western blot showed that FasL siRNA effectively inhibited FasL expression in MSCs. **f,** When knockdown FasL expression by siRNA, AB treatment failed to improve MSC-mediated reduction osteoclast numbers, as assessed by TRAP staining. **g-j,** ELISA analysis showed that serum levels of CTX-1, TRAP 5b, RANKL were increased, along with reduced serum level of OPG in OVX mice when compared with sham group. After 4 weeks of apoptotic body infusion, the serum levels of CTX-1, TRAP 5b, RANKL were decreased along with elevated level of OPG, but apoptotic bodies derived from RNF146 siRNA knockdown MSCs failed to rescue the serum levels of CTX-1, TRAP 5b, RANKL, and OPG in OVX mice. 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, 50 μm (**a**), 25 μm (**b, c, f**). KD, knockdown.