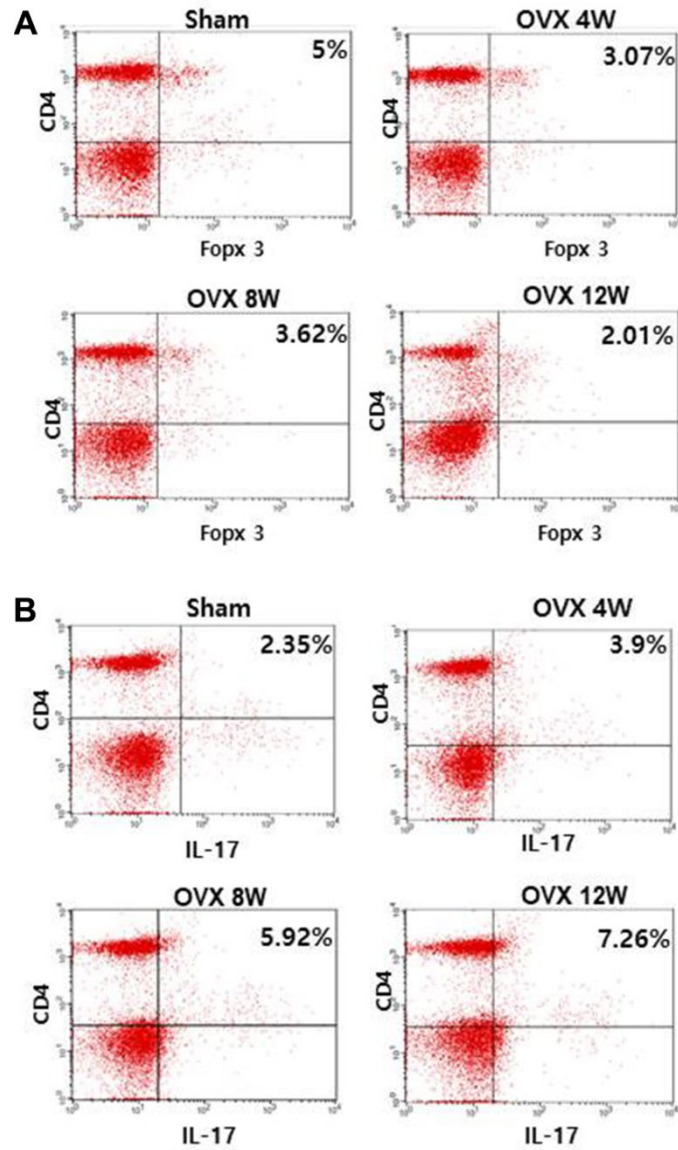
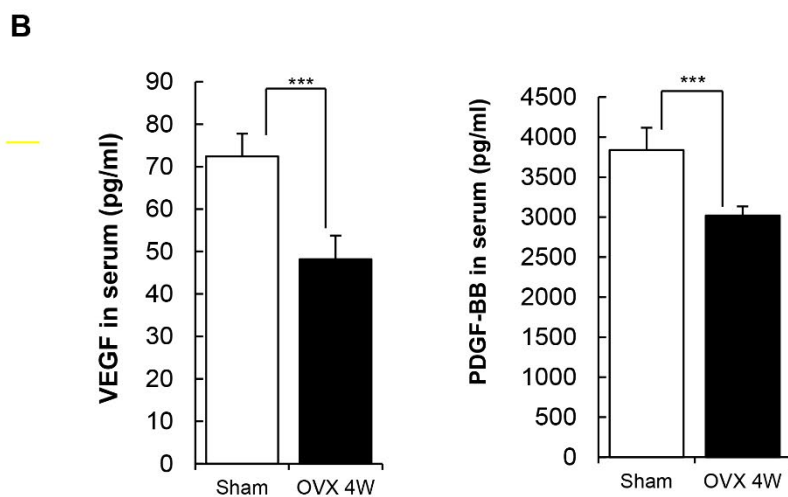
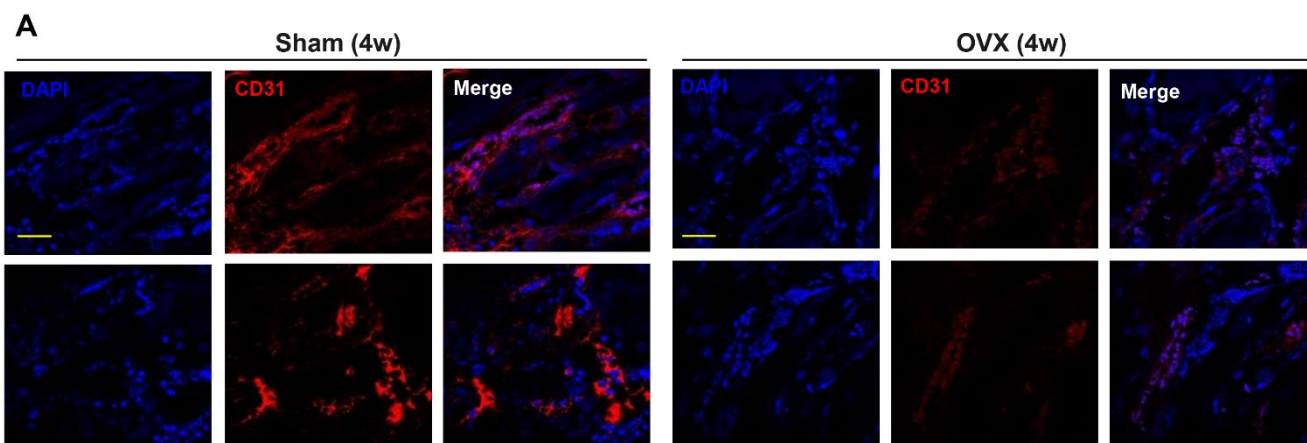


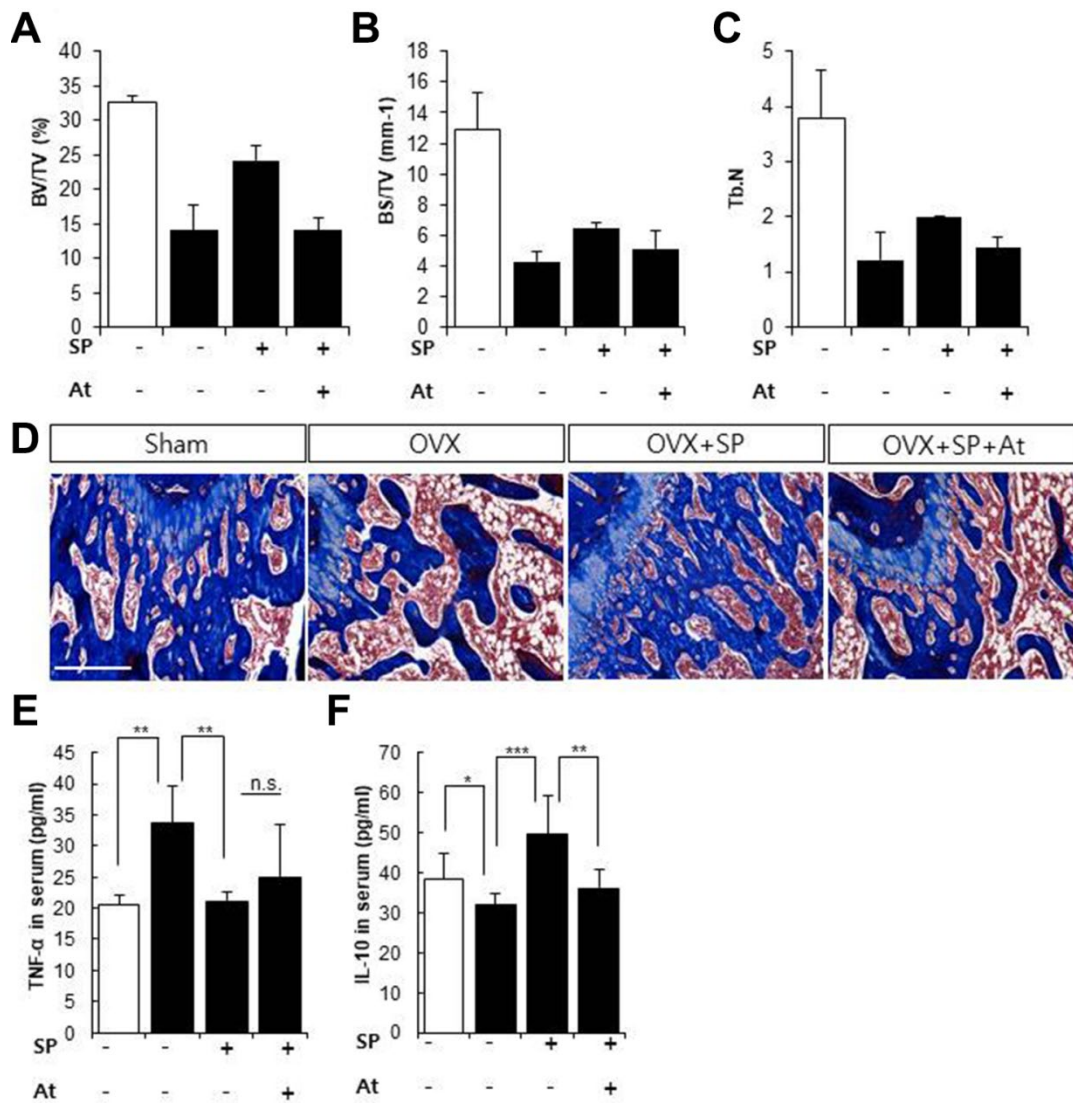
Supplementary Figure 3. OVX reduces Treg cell pools, enriching Th17 cell pools in the spleen. The ratios of (A) CD4⁺Foxp3⁺ cells and (B) CD4⁺IL17⁺ cells in splenocytes were measured by FACS analysis. The data are expressed as the mean \pm standard deviation (SD) *p* values of less than 0.05 were considered statistically significant (* *p* < 0.05, ** *p* < 0.01, *** *p* < 0.001). The data are expressed as the mean \pm standard deviation (SD).



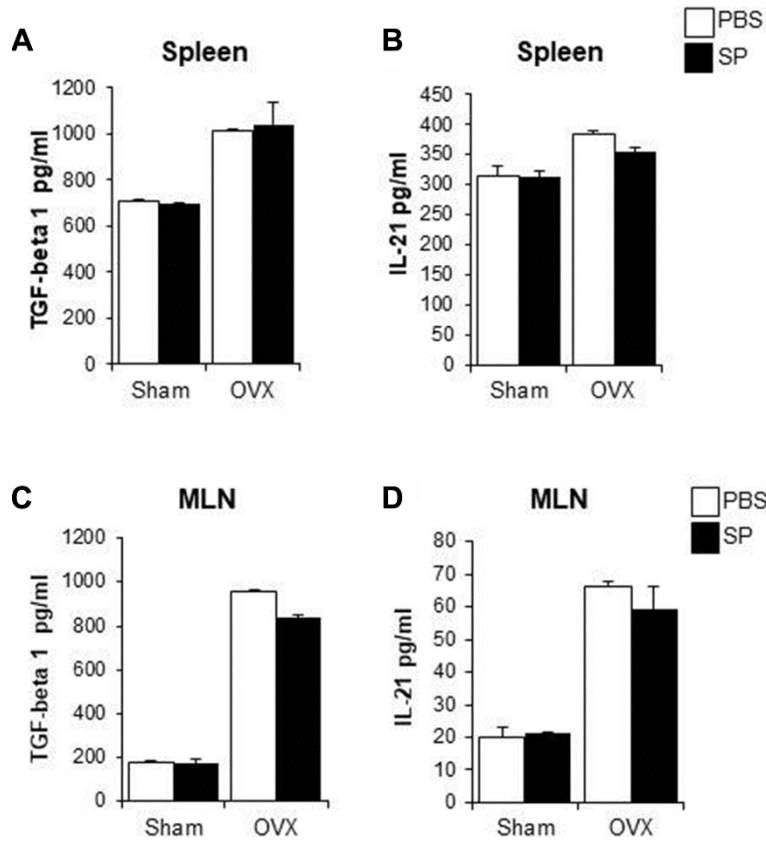
Supplementary Figure 4. OVX declines Treg cell pools but elevates Th17 cell pools in the mesenteric lymph node. The ratios of (A) CD4⁺Foxp3⁺ cells and (B) CD4⁺IL17⁺ cells in MLN cells were measured by FACS analysis. The data are expressed as the mean ± standard deviation (SD) *p* values of less than 0.05 were considered statistically significant (* *p* < 0.05, ** *p* < 0.01, *** *p* < 0.001). The data are expressed as the mean ± standard deviation (SD).



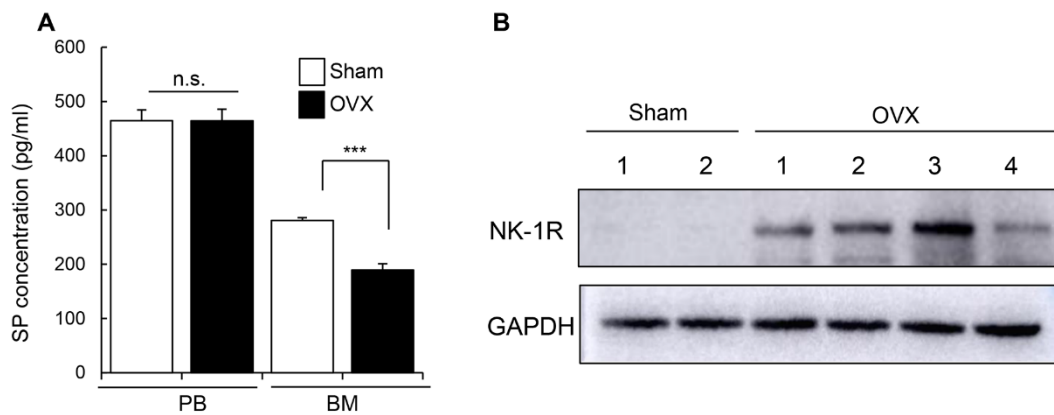
Supplementary Figure 5. OVX induce vessel damages in bone marrow within 4 weeks. (A) Representative images of immunofluorescence staining for CD31 (red) in distal femoral metaphysis from rat after sham-operation and OVX for 4 weeks. Scale bar: 200 μ m. (B) The concentrations of VEGF and PDGF-BB in serum were analyzed by ELISA after 4 weeks of OVX induction and compared with Sham group. p values of less than 0.05 were considered statistically significant (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$). The data are expressed as the mean \pm standard deviation (SD) of three independent experiments.



Supplementary Figure 6. SP ameliorates OVX-induced bone loss via binding NK-1R. (A–C) Quantitative analyses of the trabecular bone fraction of femur from rats. (D) Masson's Trichrome staining of distal femoral metaphysis sections from rats after sham-operation and OVX. Scale bar: 200 μ m. (E, F) TNF- α and IL-10 expression levels in serum were analyzed by ELISA. BV: trabecular bone volume. TV: total bone volume. BS: trabecular bone surface. Tb.N: the number of trabecular bone. *p* values of less than 0.05 were considered statistically significant (* *p* < 0.05, ** *p* < 0.01, *** *p* < 0.001). The data are expressed as the mean \pm standard deviation (SD) of three independent experiments.



Supplementary Figure 7. SP does not affect TGF-beta and IL-21 production from 2nd lymphoid organ. TGF-beta 1 (A) and IL-21 (B) expression levels in conditioned medium of splenocytes were analyzed by ELISA. The concentrations of TGF-beta 1 (C) and IL-21 (D) in conditioned medium of MLN cells were analyzed by ELISA. *p* values of less than 0.05 were considered statistically significant (* *p* <0.05, ** *p* <0.01, *** *p* <0.001). The data are expressed as the mean ± standard deviation (SD) of three independent experiments.



Supplementary Figure 8. OVX downregulates SP levels in the bone marrow but upregulates NK-1R expressions after 8 weeks. (A) The concentration of SP in bone marrow aspirates was analyzed by ELISA. (B) The level of NK-1R protein in bone marrow was elucidated by western blot analysis and quantified relatively. *p* values of less than 0.05 were considered statistically significant (* *p* <0.05, ** *p* <0.01, *** *p* <0.001). The data are expressed as the mean ± standard deviation (SD) of three independent experiments.