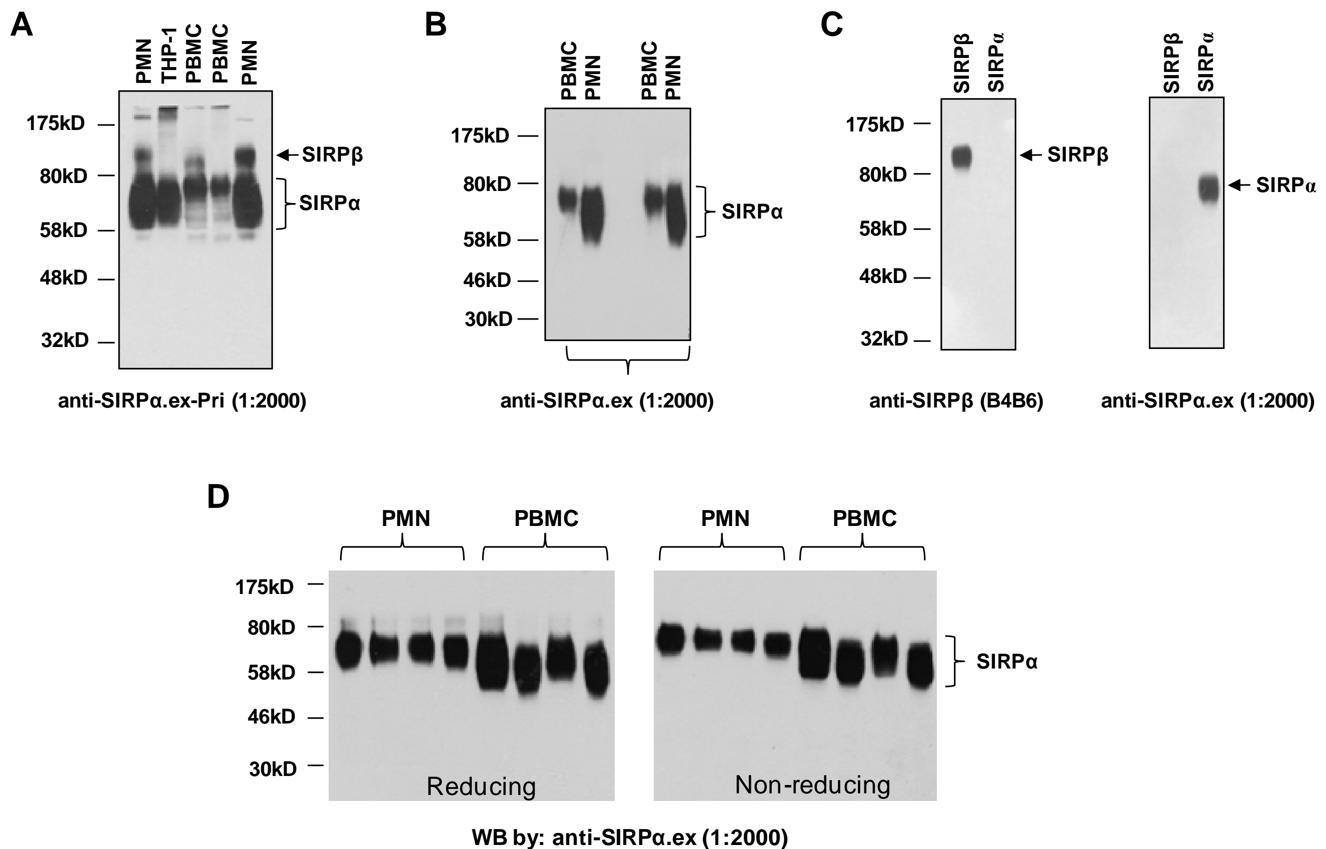
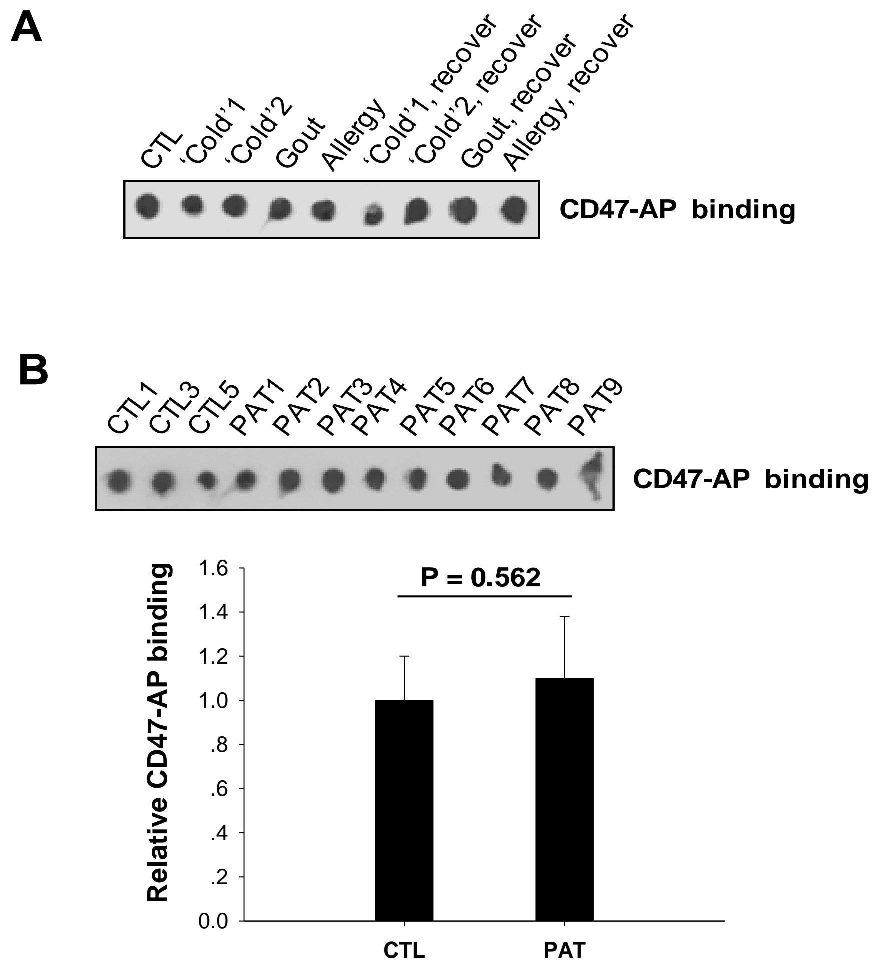
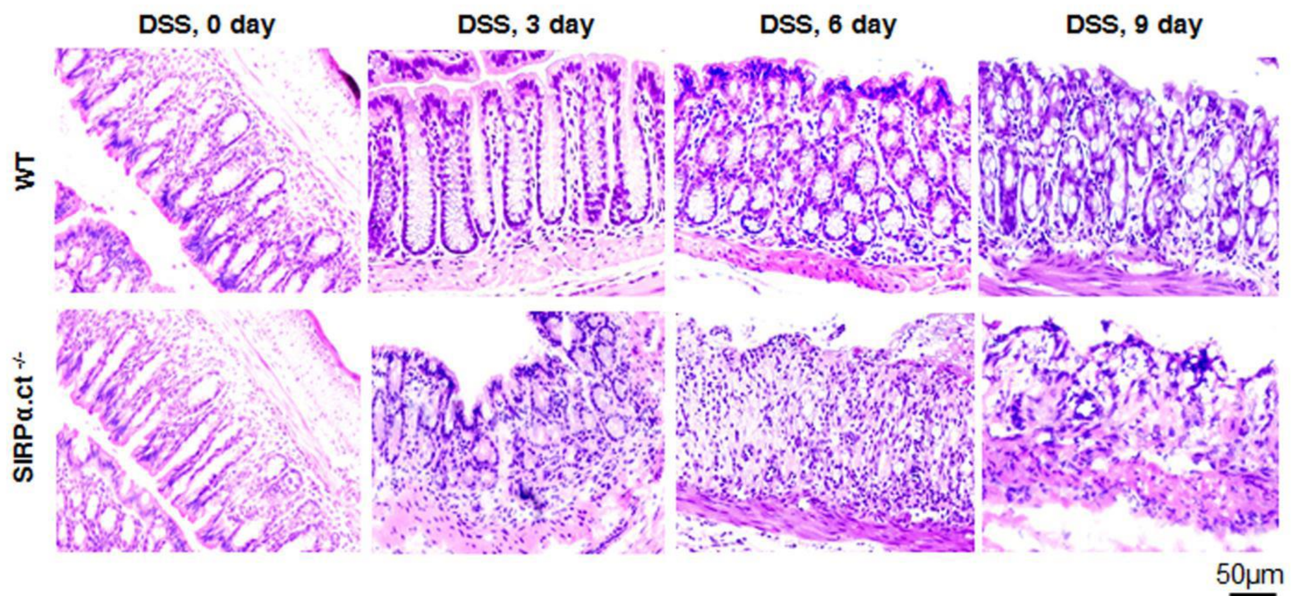


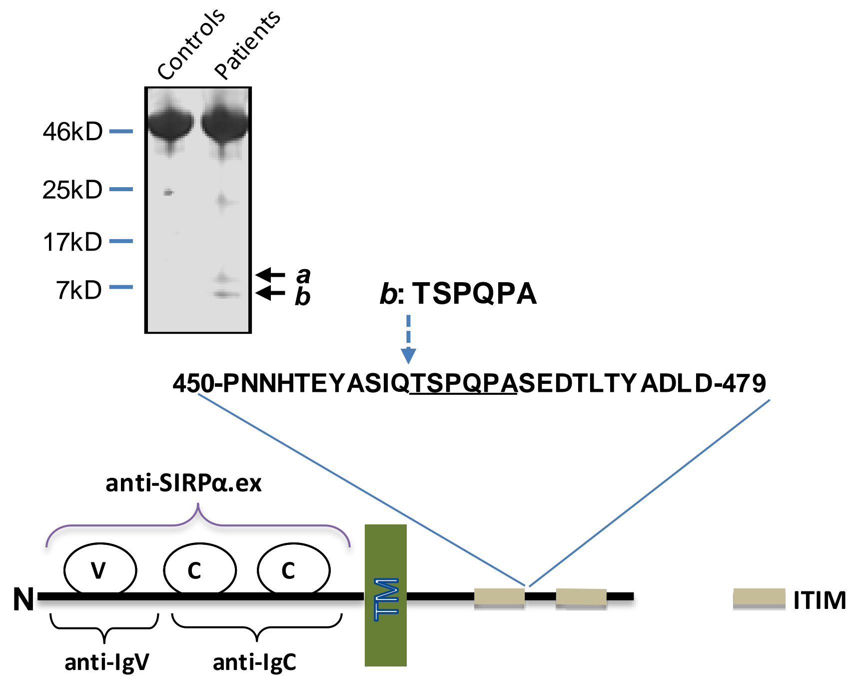

Supplementary Figure S1. **Characterization of anti-SIRPα.ex antibody.** The purified anti-SIRPα.ex antibody specifically recognizes SIRPα but not SIRPβ. Note that 100-110kD SIRPβ is still recognized by original anti-SIRPα.ex antisera (anti-SIRPα.ex-Pri) (A), however, after purification (absorption by immobilized SIRPβ recombinant), anti-SIRPα.ex antibody (IgG) does recognize SIRPα but not SIRPβ under both reducing (B) and non-reducing (D) condition. Importantly, the specificity of purified anti-SIRPα.ex antibody against SIRPα is verified via cross-WB using purified SIRPα and SIRPβ proteins (C). SIRPα and SIRPβ proteins were affinity isolated from human monocytes as previously described[1,6]. The recombinant GST fusion proteins containing SIRPβ extracellular domain (GST-SIRPβ) was prepared as previously described[2]. GST fusion proteins were produced in BL21 bacteria with 1 mM IPTG induction, followed by affinity purification using glutathione-Sepharose.



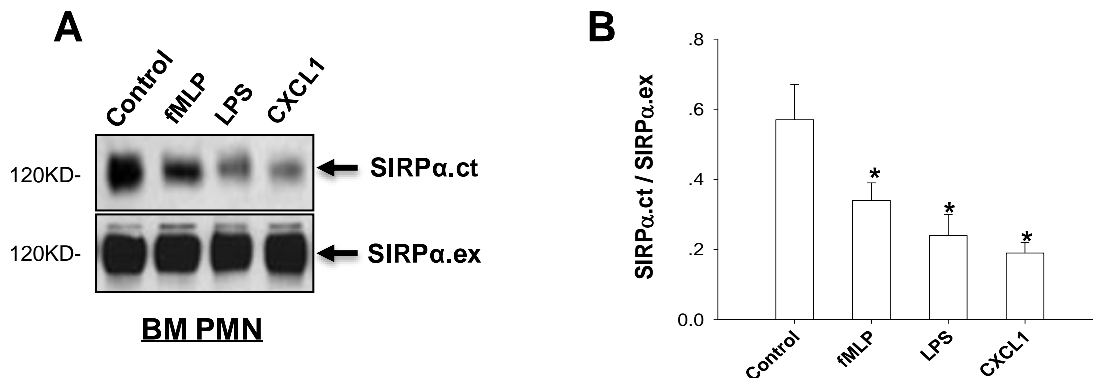

Supplementary Figure S2. **Assay of SIRPα in different PMNs binding to CD47.** The lysates of PMNs from different donors were immobilized on nitrocellulose by vacuum. The membrane was then incubated with CD47-AP (5 μg/ml) followed by washing and color development using Luminol-based ECL chemiluminescent substrate for alkaline phosphatase. As seen, AP-CD47 equally binds to immobilized cell lysate from PMN of healthy donors and patients with inflammatory conditions. The results are the means ± SE of three independent experiments. Statistical significance was tested by Student's *t* test



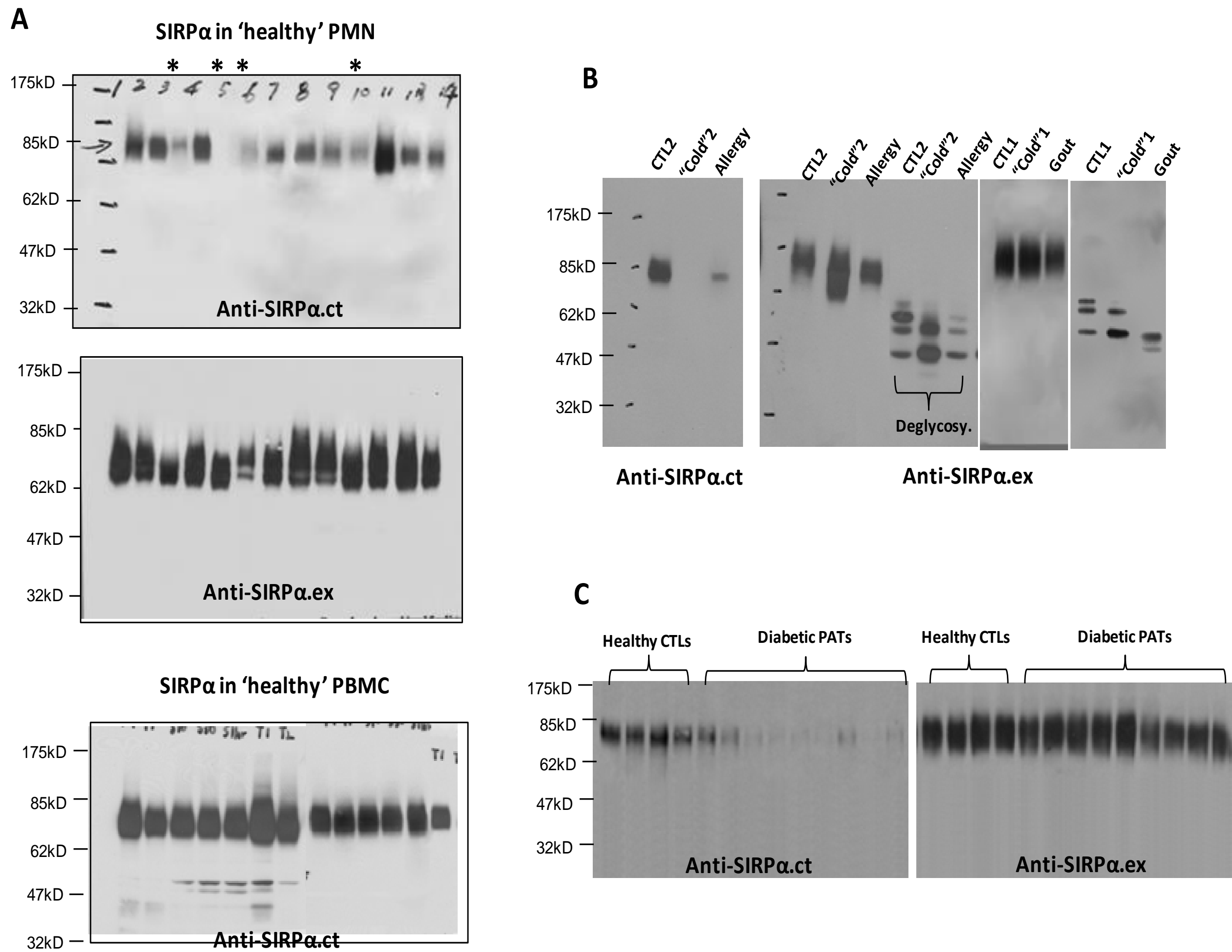

Supplementary Figure S3. **Inducing colitis in WT and SIRPα.ct$^{-/-}$ mice by 2% DSS.** The figure shows differential colon tissue damage in SIRPα.ct$^{-/-}$ mice and their WT littermates.



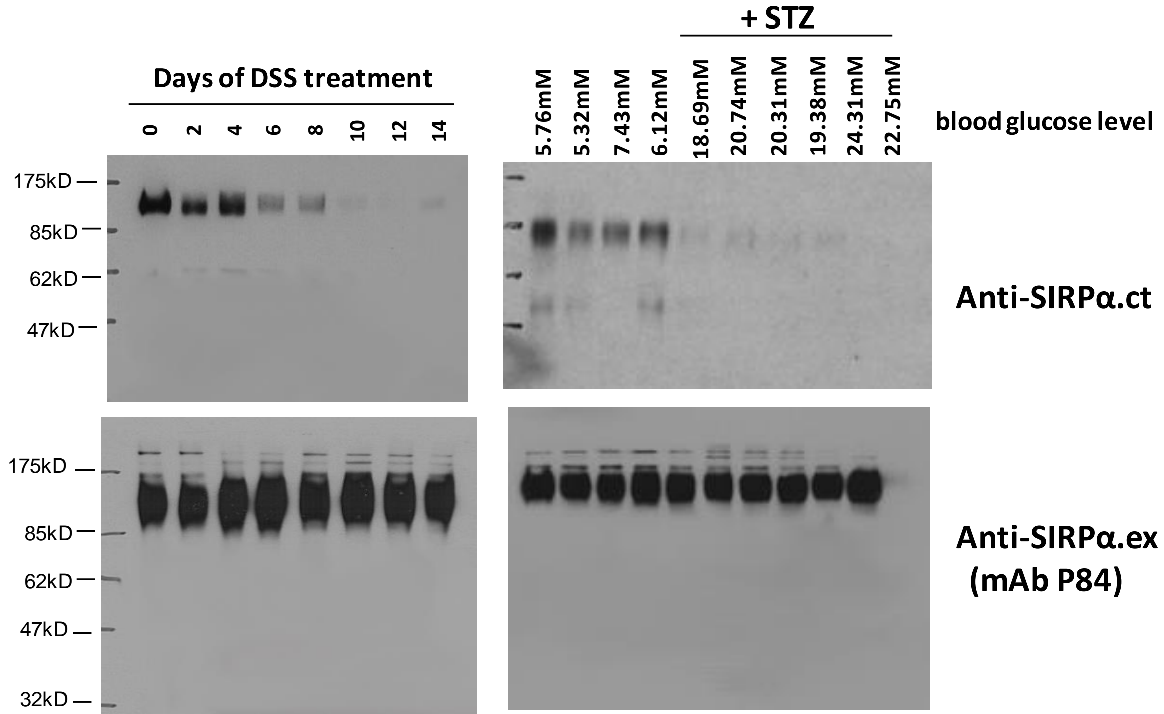

Supplementary Figure S4. **Identification of the potential cleavage site on SIRPα cytoplasmic domain.** Human PMN isolated from healthy donors and donors under inflammatory conditions were lysed in the absence of detergents followed by IP of the cleaved SIRPα cytoplasmic tail using anti-SIRPα.ct antibody. The resolved protein bands (*a* and *b*) by SDS-PAGE were subjected to N-terminal amino acid sequencing. The deduced sequence from band *b* was shown to match a position close to the proximal ITIM within the SIRPα cytoplasmic domain.



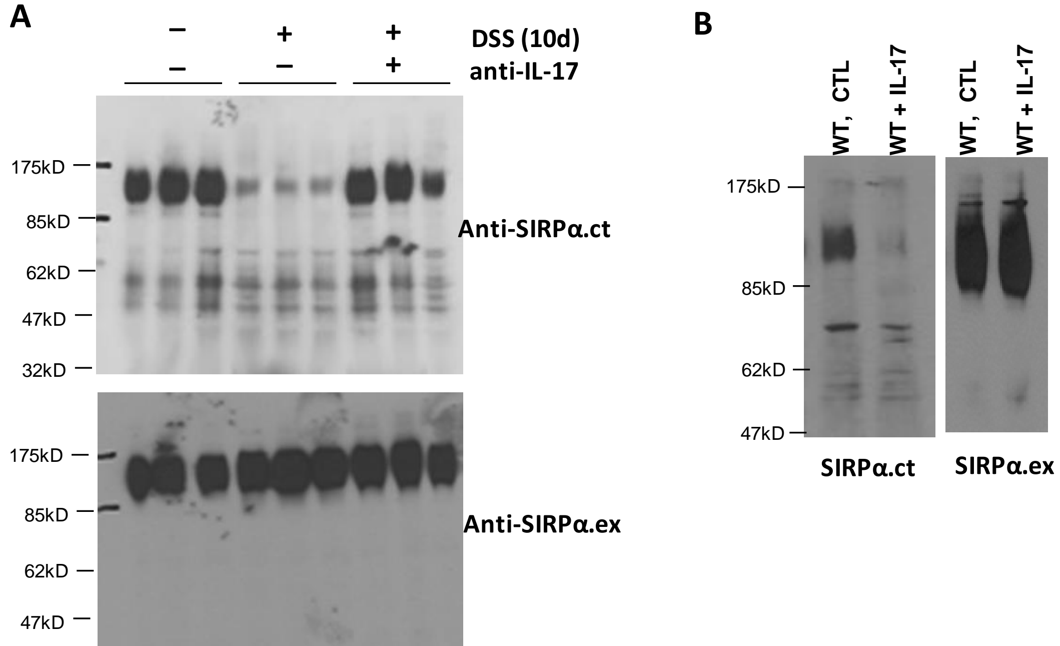

Supplementary Figure S5. **Expression pattern of SIRPα in mouse PMN after various treatments.** For lipopolysaccharide (LPS) treatment, LPS [*Escherichia coli* serotype 026:B6 (sigma), 0.3mg/kg body weight] was administered via nares every other day for 14 days to induce chronic bronchitis and lung inflammation. For CXCL1 and fMLP treatment, 300pg recombinant murine CXCL1 (R&D Systems) or $10^{-7}$M fMLP (Sigma), as well as control PBS, was intravenously injected into mice. In Western blot analysis, SIRPα in the same PMN sample was blotted by anti-SIRPα.ex and anti-SIRPα.ct antibodies, respectively. The results are the means of three different experiments. Statistical significance was tested by Student's *t* test *, $p<0.05$.



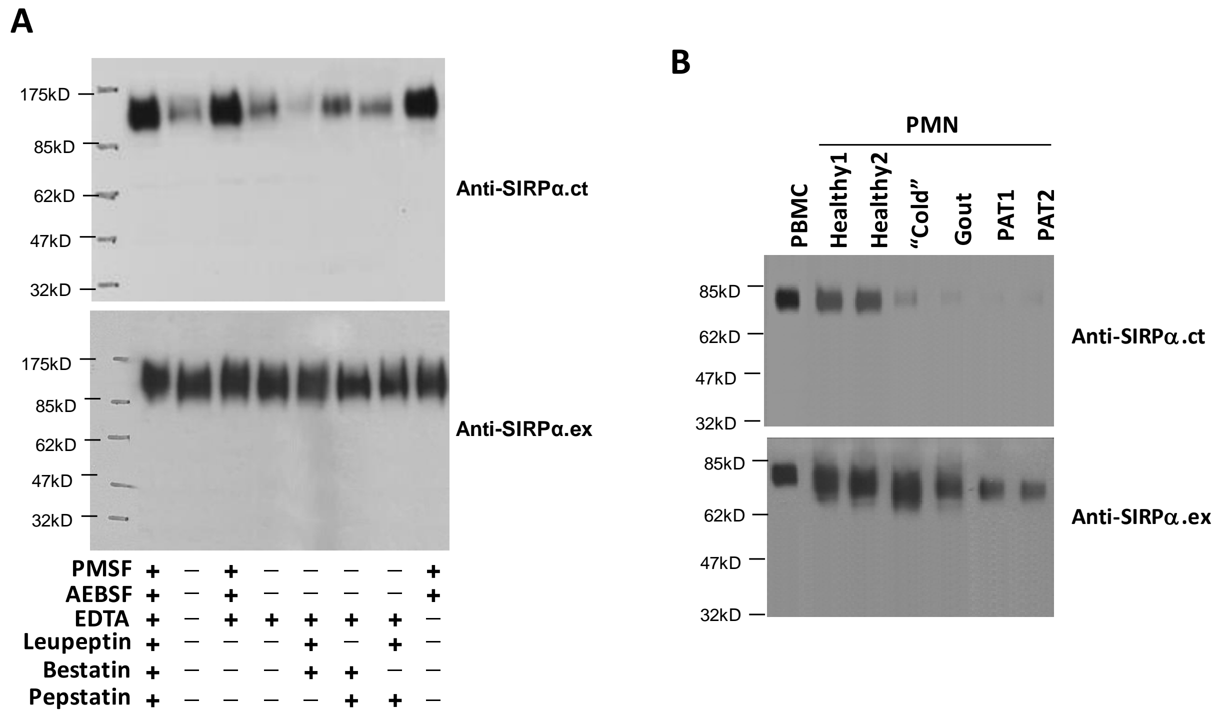

Supplementary Figure S6. **SIRPα in PMN under healthy and inflammatory conditions**. A) Detection of SIRPα in PMNs and monocytes (PBMCs) obtained from random selected healthy donors. B) Detection of SIRPα in PMNs obtained from inflammatory donors. C) Detection of SIRPα in PMNs obtained from healthy donors (CTL) and individuals with type 2 diabetes complicated with cardiovascular conditions (PAT).




Supplementary Figure S7. **SIRPα in PMNs from mice under 2% DSS treatment or STZ-induced diabetes.**




Supplementary Figure S8. **Effect of IL-17 on SIRPα cleavage in PMNs.** A) WT mice under DSS-induced colitis were administrated with, or without, a neutralization anti-IL-17 antibody. SIRPα in bone marrow PMNs was assessed by anti-SIRPα.ex and anti-SIRPα.ct antibodies. B) Inducing SIRPα cleavage in PMNs by IL-17A in healthy WT mice.




Supplementary Figure S9. **A) Cleavage of ITIM$^+$SIRPα by PMN protease(s). B) Purification of SIRPα from different PMNs and PBMCs.** The presence and absence of SIRPα ITIM-containing cytoplasmic tail was confirmed by WB using anti- SIRPα.ex and anti- SIRPα.ct antibodies.