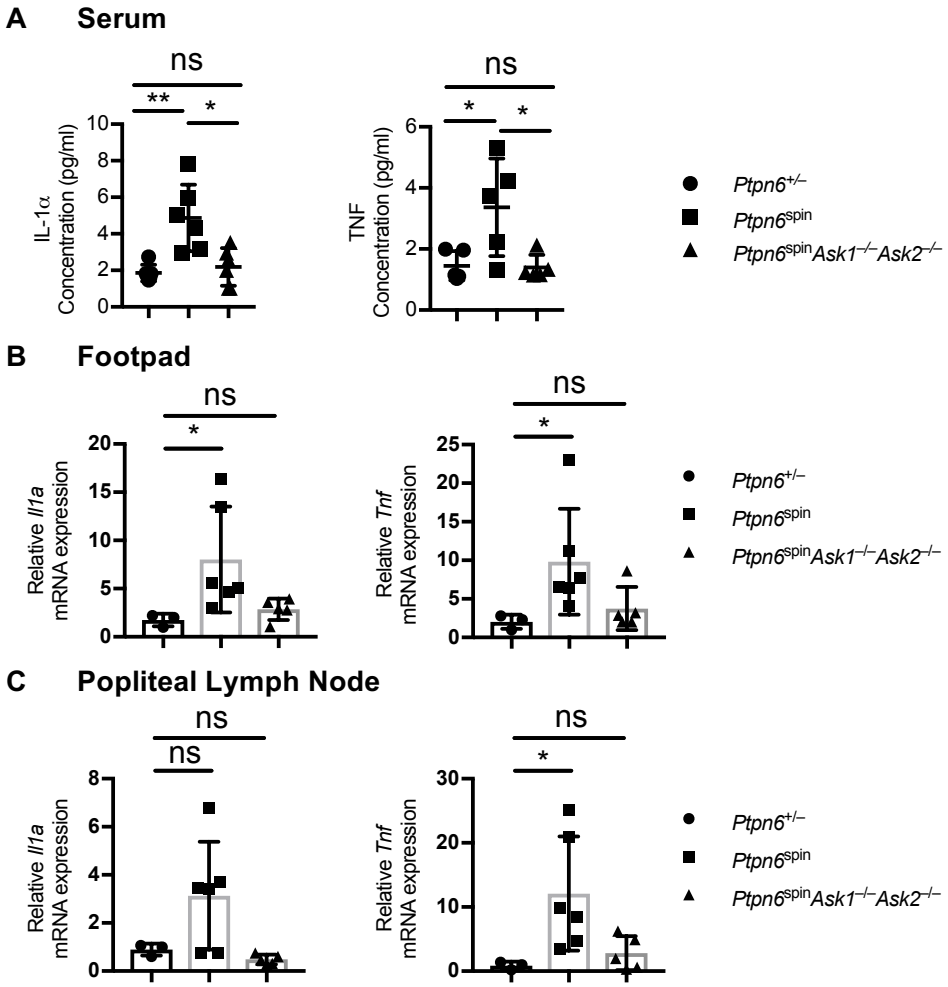
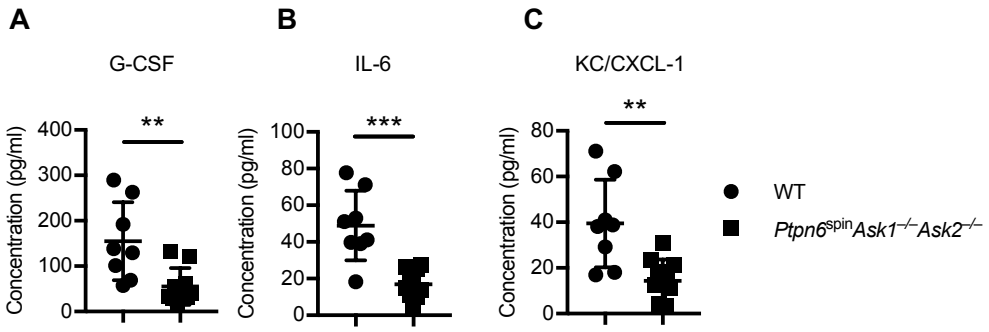


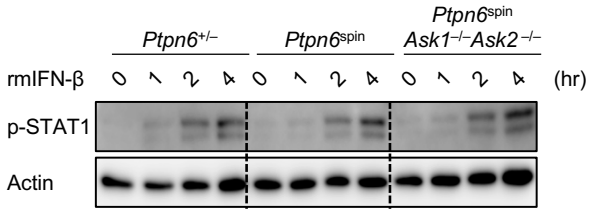
Supplemental Figure 1. ASK1 and ASK2 signaling regulates *Ptpn6*^{spin}-mediated disease through the control of pro-inflammatory signaling.

(A) Serum were harvested from *Ptpn6*$^{+/-}$ (n = 6), *Ptpn6*^{spin} (n = 6), and *Ptpn6*^{spin}*Ask1*$^{-/-}$ *Ask2*$^{-/-}$ (n = 6) mice. **(B)** Footpads, and **(C)** popliteal Lymph nodes were harvested from *Ptpn6*$^{+/-}$ (n = 3), *Ptpn6*^{spin} (n = 6), and *Ptpn6*^{spin}*Ask1*$^{-/-}$*Ask2*$^{-/-}$ (n = 5) mice. **(A)** Serum concentration of IL-1α and TNF were measured by ELISA. RNA was isolated from **(B)** Footpads and **(C)** Popliteal Lymph nodes and the expression of *Il1a* and *Tnf* mRNAs were measured by qPCR. Two-way ANOVA **(A)** and two-tailed Student's *t*-test **(B and C)** were used to determine the significance between the two groups analyzed. ns not significant, *P < 0.05 and **P < 0.01.



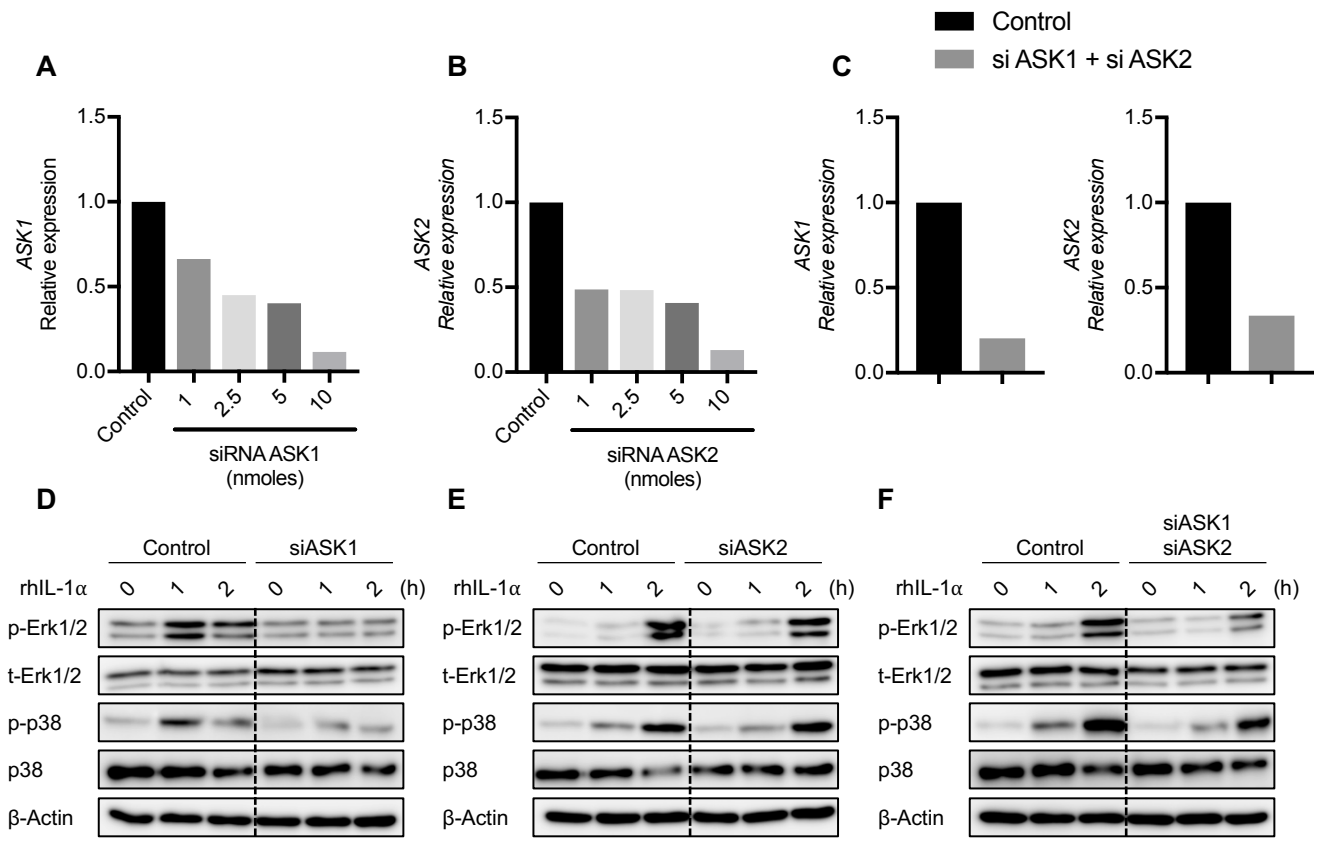
Supplemental Figure 2. Wound-healing response was completely rescued in *Ptpn6*^{spin} mice lacking Ask1 and Ask2.

(A–C) Footpads of WT (n = 8) and *Ptpn6*^{spin}*Ask1*$^{-/-}$*Ask2*$^{-/-}$ (n = 10) mice were microabrated, and the concentrations of **(A)** G-CSF, **(B)** IL-6 and **(C)** KC were measured in the footpads 5 hour post microabrasion. Each point represents an individual mouse, and the line represents the Mean ± SEM. Two-way ANOVA was used to determine the significance between the two groups analyzed. **P < 0.01 and ***P < 0.001.



Supplemental Figure 3. *Ptpn6*^{spin}-mediated disease is independent of interferon signaling.

Neutrophils were isolated from respective strains of mice and stimulated with recombinant mouse IFN-β for indicated time period. Neutrophil lysates were prepared and expression of p-STAT1 was determined by western blotting. β-Actin was used as an internal control. Results are representative of two independent experiments.



Supplemental Figure 4. ASK is important for IL-1α signaling in human cells.
(A-C) siRNA mediated knockdown was performed in HEK293T cells using different concentrations of stealth siRNA for **(A)** ASK1, **(B)** ASK2 and combination of both **(C)** ASK1 and ASK2. **(D-F)** Successful knockdown cells for **(D)** ASK1, **(E)** ASK2 and both **(F)** ASK1 and ASK2, were stimulated with the recombinant human IL-1α (10 ng/ml) for the indicated time period. Whole cell lysates were prepared and expression of p-ERK1/2, ERK1/2, p-p38, and p38 was determined by western blotting. β-Actin was used as an internal control. Results are representative of two independent experiments.