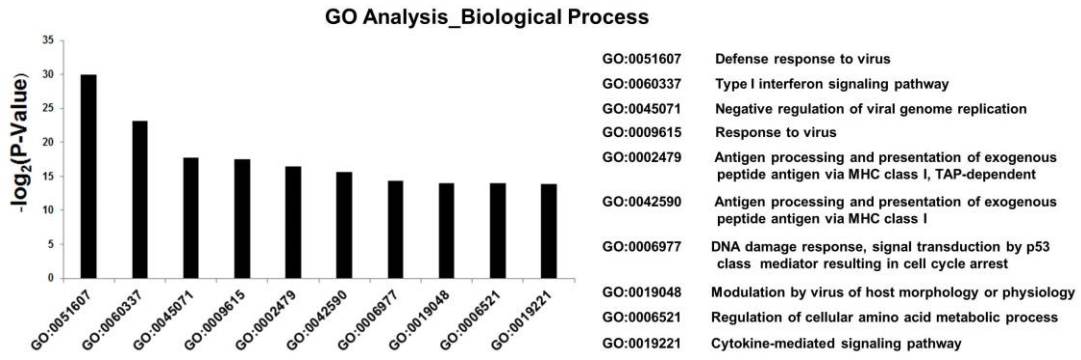
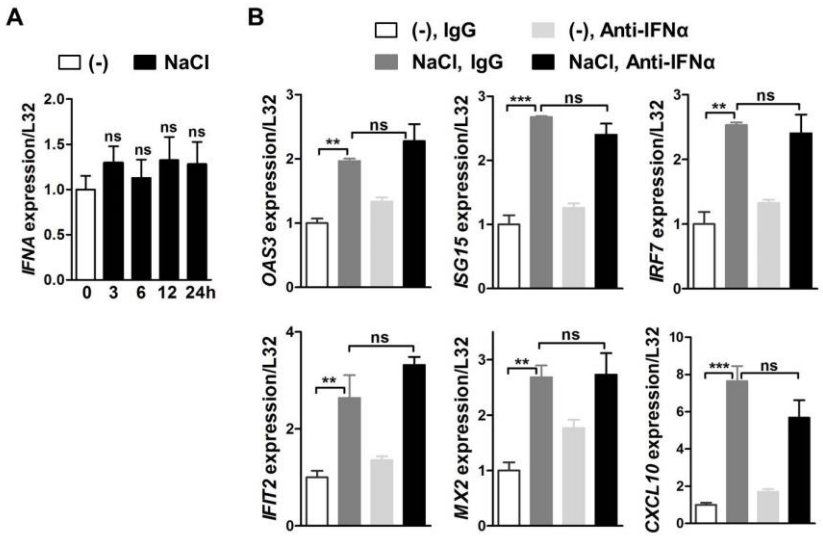
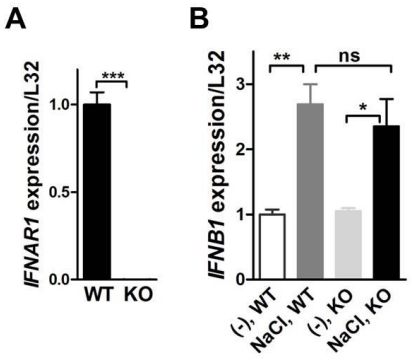


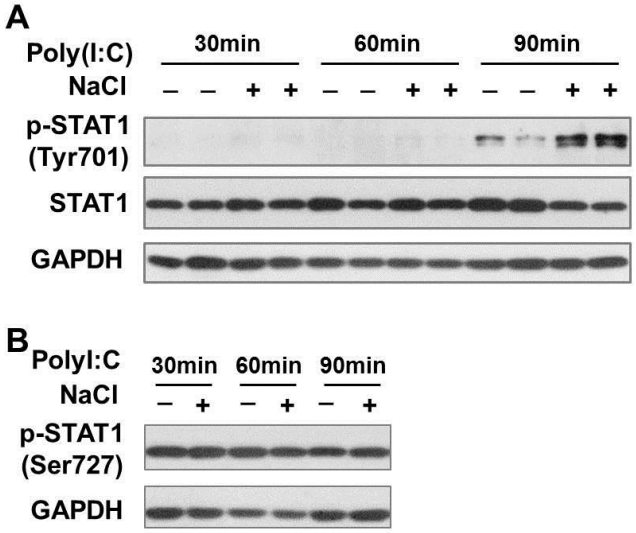
Supplementary figure 1. Top 10 biological processes promoted by high salt in human macrophages. Human monocyte-derived macrophages were treated with or without additional 50mM NaCl for 24 hours. Gene expression was measured using RNA-Seq. Fold changes of mRNA levels in high salt-treated macrophages relative to those in untreated macrophages were used for gene ontology (GO) analysis.



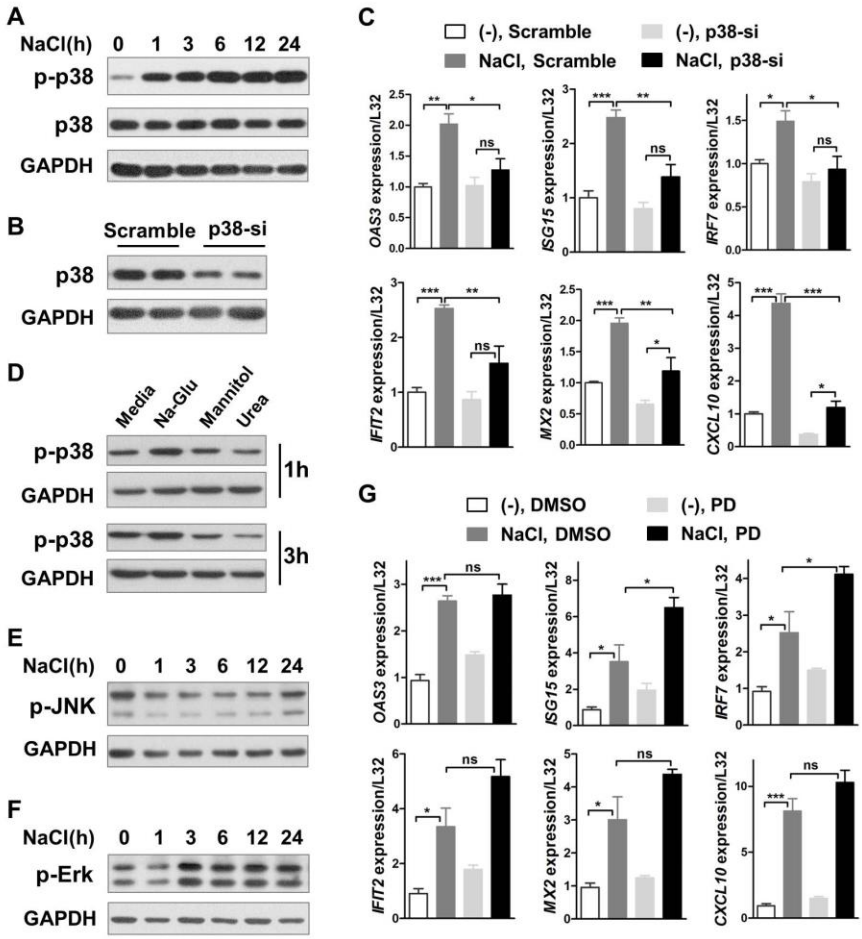
Supplementary figure 2. High salt upregulates expression of ISGs independently of IFNα in mouse BMDMs. (A) qRT-PCR analysis of *IFNA* in mouse BMDMs treated with additional 50mM NaCl for the indicated time periods. **(B)** qRT-PCR analysis of ISGs in mouse BMDMs treated with or without additional 50mM NaCl and in the presence of either immunoglobulin G (IgG) or IFNα neutralizing antibodies (Anti-IFNα). Representative results of three independent experiments are shown. One-way ANOVA followed by Turkey's multiple comparisons was used for statistical analysis. ns, not significant, ***P*<0.01, ****P*<0.001.



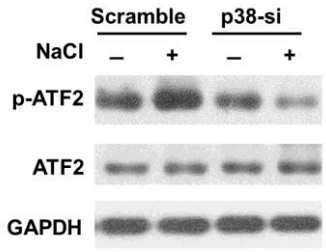
Supplementary figure 3. *IFNAR1* deficiency does not affect high salt-induced increase of *IFNB1* expression in mouse BMDMs. (A) qRT-PCR analysis of *IFNAR1* in BMDMs isolated from wild type (WT) and *IFNAR1* knockout (KO) mice. **(B)** qRT-PCR analysis of *IFNB1* in BMDMs isolated from either WT or KO mice and treated with or without additional 50mM NaCl for 6 hours. Representative results of three independent experiments are shown. Student's *t* test and One-way ANOVA followed by Turkey's multiple comparisons were respectively used in (A) and (B) for statistical analysis. ns, not significant, **P*<0.05, ***P*<0.01, ****P*<0.001.



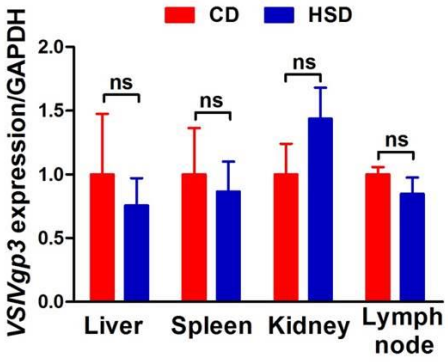
Supplementary figure 4, Effects of high salt pretreatment on levels of p-STAT1 and total STAT1 in Poly(I:C)-treated mouse BMDMs. (A) Western blotting analysis of p-STAT1 (Tyr701) and total STAT1 in mouse BMDMs. **(B)** Western blotting analysis of p-STAT1 (ser727) in mouse BMDMs. Cells were pretreated with or without additional 50mM NaCl for 16 hours, washed twice with PBS, and then treated with 100ug/ml Poly(I:C) in the absence of additional NaCl for the indicated time periods.



Supplementary figure 5. p38, but not JNK or Erk, mediates high salt-induced expression of ISGs in mouse BMDMs. (A) Western blotting analysis of phosphorylated and total p38 in mouse BMDMs treated with additional 50mM NaCl for the indicated time periods. **(B)** Western blotting analysis of p38 in mouse BMDMs transfected with either scramble siRNA (scramble) or p38α siRNA/p38β siRNA mixture (p38-si) for 36 hours. **(C)** qRT-PCR analysis of ISGs in mouse BMDMs transfected with scramble or p38-si for 24 hours, and treated with or without additional 50mM NaCl for another 24 hours. **(D)** Western blotting analysis of p-p38 in mouse BMDMs treated with additional 50mM Na-Gluconate, 100mM Mannitol, or 100mM Urea for 1 hour or 3 hours. **(E)** Western blotting analysis of p-JNK in mouse BMDMs treated with additional 50mM NaCl for the indicated time periods. **(F)** Western blotting analysis of p-Erk in mouse BMDMs treated with additional 50mM NaCl for the indicated time periods. **(G)** qRT-PCR analysis of ISGs in mouse BMDMs. BMDMs were pretreated with DMSO or 20uM PD98059 (PD) for 1 hour, and then treated with or without additional 50mM NaCl for 24 hours in the continued presence of DMSO or 10uM PD. Representative results of three independent experiments are shown. One-way ANOVA followed by Turkey's multiple comparisons was used for statistical analysis. ns, not significant, **P*<0.05, ***P*<0.01, ****P*<0.001.



Supplementary figure 6. p38 mediates high salt-induced phosphorylation of ATF2 in mouse BMDMs. Western blotting analysis of p-ATF2 and total ATF2 in mouse BMDMs. BMDMs were transfected with scramble siRNA (scramble) or p38α siRNA/p38β siRNA mixture (p38-si) for 36 hours, and then treated with or without additional 50mM NaCl for 1 hour.



Supplementary figure 7. High salt diet does not affect viral load of VSV in mouse liver, spleen, kidneys, or lymph nodes. qRT-PCR analysis of *VSIVgp3* in tissues of mice fed with chow diet (CD) or high salt diel (HSD) for 5 weeks and infected with VSV ($1.5x10^7$ pfu) intraperitoneally for 15 hours. n=9:9. Student's *t* test was used for statistical analysis. ns, not significant.