

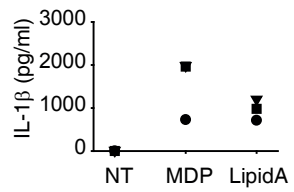
Supplementary Fig. 1. MDM from Leu1007insC homozygotes/compound heterozygotes fail to secrete IL-1 β following MDP stimulation. Human MDM from Nod2 WT healthy controls (*top*: solid symbols, n=3), Nod2 WT CD patients (*middle*: solid symbols, n=3), or Leu1007insC homozygotes/compound heterozygote CD patients (*bottom*: empty symbols, n=3) were stimulated with 100 μ g/ml MDP or 0.1 μ g/ml lipid A for 24h. Supernatants were assayed for IL-1 β .

Supplementary Fig. 2. The IL-1 autocrine loop has varying contributions to MDP-mediated IL-8 induction in human epithelial cell lines. (A) 5×10^5 Human HepG2 or CaCo-2 cells were stimulated with 100 μ g/ml MDP or 100 μ g/ml MDP with IL-1R signaling blockade (0.5 μ g/ml IL-1Ra and 1 μ g/ml anti-IL-1 β antibody) for 24 h. Supernatants were assayed for IL-8. (B) Summarized data from triplicates of two independent experiments are represented as the percent IL-8 secretion by cells upon IL-1R signaling blockade normalized to cells in the absence of the blockade (represented by the dotted line at 100%) + SEM. Significance compared to cells in the absence of the IL-1R blockade is shown. ***, $p < 0.001$.

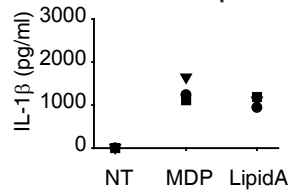
Supplementary Fig. 3. Selective activation of JNK and p38 by UV light rescues the decreased cytokine secretion observed during Nod2 signaling in the absence of the IL-1 autocrine loop. (A,B) Human MDM from healthy controls (n=4) were stimulated with 100 μ g/ml MDP or 100 μ g/ml MDP with 0.5 μ g/ml IL-1Ra and 1 μ g/ml anti-IL-1 β antibody in the presence or absence of UV light at 50-100 J/m². (A) Shown are representative flow cytometry plots with indicated MFI values. (B) Data are represented as the fold MAPK activation normalized to untreated cells + SEM. (C) Human MDM from healthy controls (n=8) were stimulated with the indicated MDP doses in the presence or absence of UV light. Data are represented as cytokine concentrations in supernatant normalized to the stimulation of cells without IL-1R block (represented by the dotted line at 100%) + SEM. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; †, $p < 1 \times 10^{-4}$; ††, $p < 1 \times 10^{-5}$.

Supplementary Figure 1

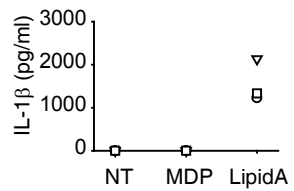
Nod2 WT healthy controls



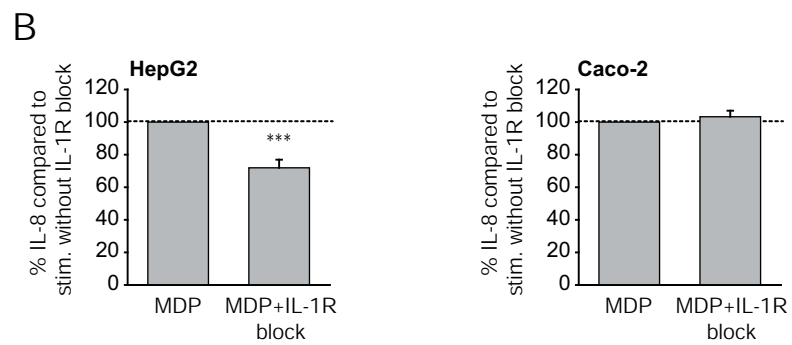
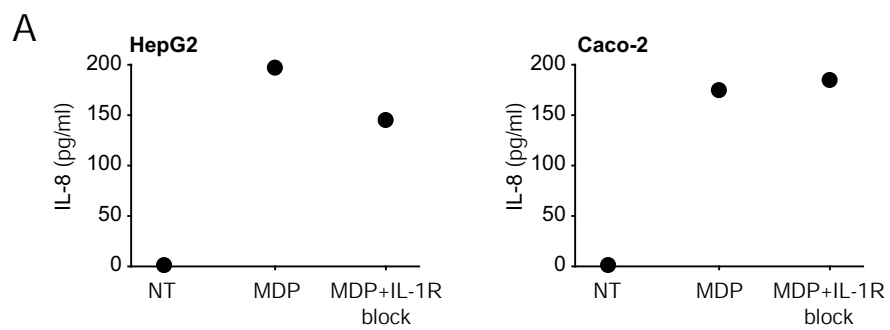
Nod2 WT CD patients



Nod2 Leu1007insC CD patients



Supplementary Figure 2



Supplementary Figure 3

