

Figure S1. IL-6 and BMDM enhance antimicrobial and anti-inflammatory ability of mice with pneumococcal pneumosepsis. (A-D) Pneumococcal load of BALF (n=4-6/group), lung (n=4-6/group), spleen (n=3-6/group) and liver (n=4-6/group) of mice when treated with WT BMDM during pneumococcal pneumosepsis. **(E-G)** H&E staining of lung tissues sections (n=5/group), histologic score (n=5/group) and total protein in BALF (n=4-5/group) of mice when treated with WT BMDM during pneumococcal pneumosepsis. Black arrow, inflammatory cell infiltration; blue arrow, epithelial cell shedding; red arrow, bleeding. **(H)** Pneumococcal load of lung (n=5/group) of mice when treated with *IL-6*^{-/-} BMDM during pneumococcal pneumosepsis.

Figure S2. BALF cells during pneumococcal pneumosepsis. Total numbers of inflammatory cells, macrophages and neutrophils in BALF from 1 to 3 dpi during pneumococcal pneumosepsis (n=6-11/group).

Figure S3. CXCL-2 and CXCL-5 levels in infected mice. (A) CXCL-2/MIP-2 and **(B)** CXCL-5 in lung homogenates of *S. pneumoniae* infected *IL-6*^{-/-} and WT mice 72 hpi as measured by ELISA (n=4-6/group).

Figure S4. IL-6 regulates *S. pneumoniae*-induced lung cell death. (A-B) PI⁺ cells (n=4-5/group) and early apoptotic cells (n=11/group) in BALF from mice during *S. pneumoniae* infection at the indicated times. **(C-D)** Lung cell death in mice during *S. pneumoniae* infection assessed by *in situ* cell death

detection kit and immunohistochemical staining (cleaved caspase-3) (n=3/group).

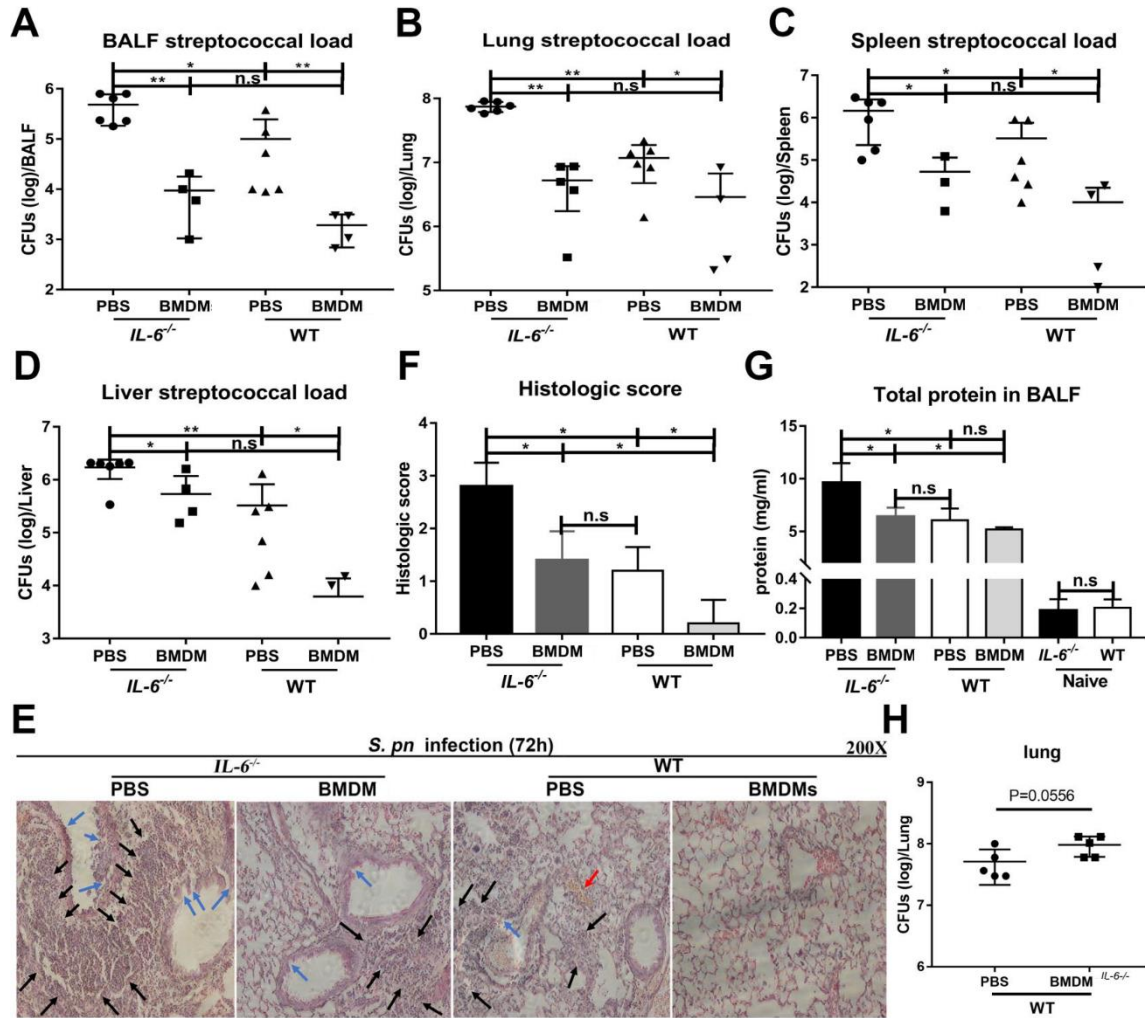
Figure S5. IL-6 only minimally affects mRNA levels of pyroptosis-related

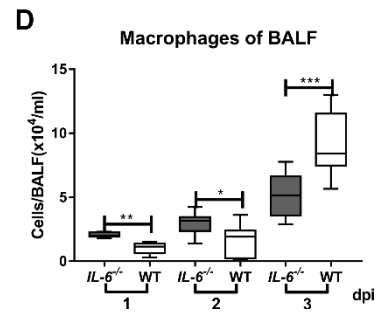
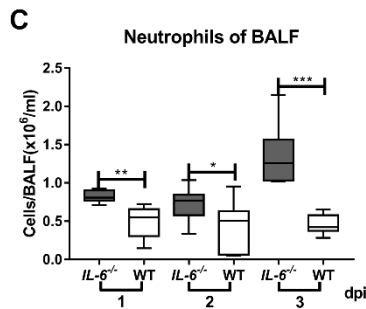
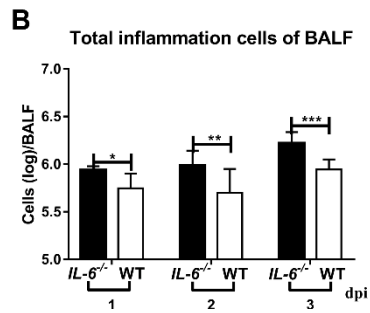
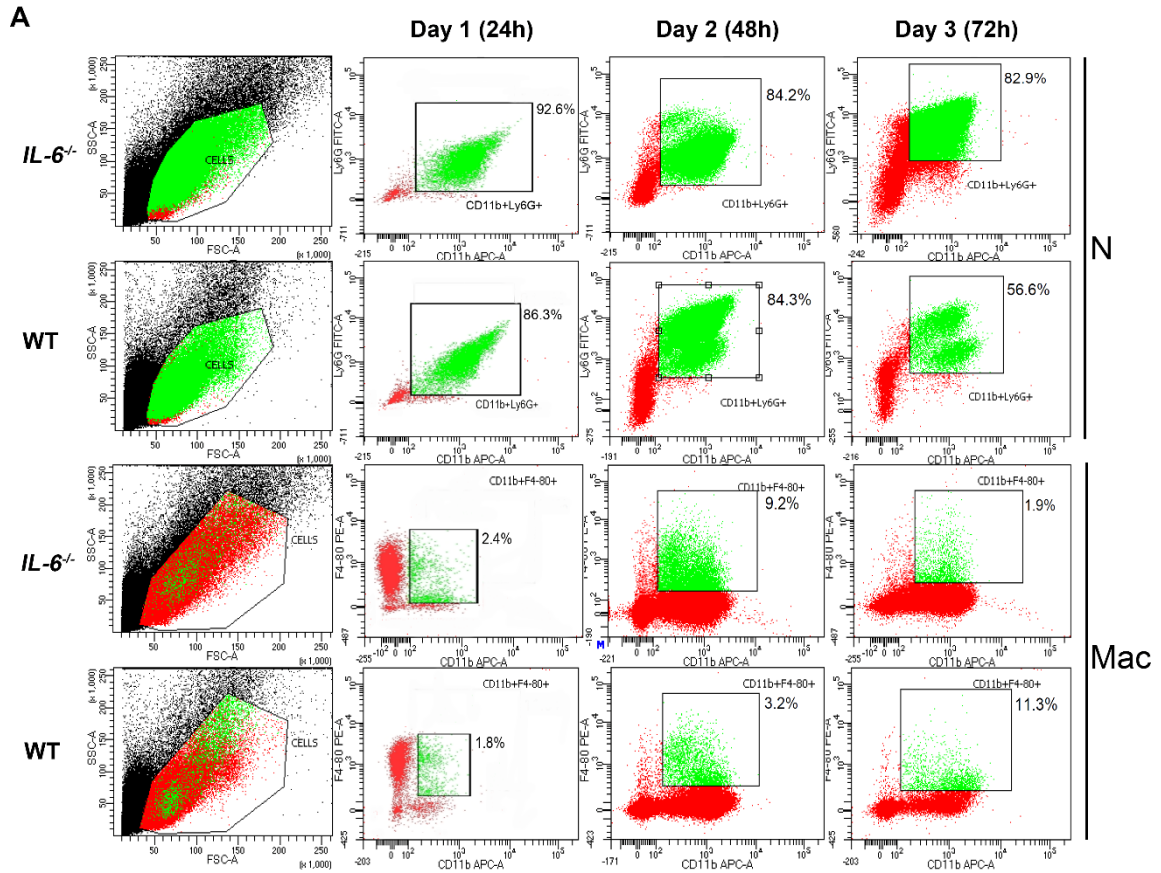
proteins. *In vivo* mRNA levels of the following proteins from lungs of *S.*

pneumoniae-infected *IL-6*^{-/-} and WT mice. **(A)** *Caspase-3* (n=3/group),

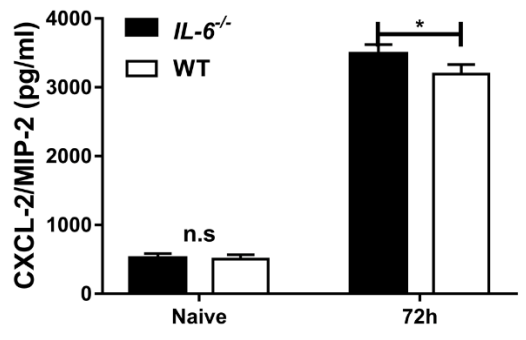
Gsdme (n=3/group) and *Il1β* (n=3-6/group) and **(B)** *Caspase-1* (n=3-5/group),

Gsdmd (n=3-5/group) and *Il18* (n=3/group) at the indicated times.





A CXCL-2/MIP-2 in lung homogenate



B CXCL-5 in lung homogenate

