Supplemental Figure Legends

1. ***N. gonorrhoeae, N. flavascens, and N. cinerea*-induced IL-1β secretion by THP-1 cells is NLRP3 and ASC dependent:** THP-1-derived cell lines stably transduced with shRNA expressing retrovirus at $1x10^6$ cell/ml were incubated with N. gonorrhoeae (GC), *Neisseria flavescens* (N.f.), or *Neisseria cinerea* (N.c.) at an MOI of 10. After 4 hours, extracellular bacteria were killed by addition of gentamicin. Supernatants were collected and secreted IL-1β was measured by ELISA. The shRNA's are directed to knock down expression as follows: shCON - negative control (scrambled sequence with base content equal to shASC); shASC – shRNA directed against Apoptotic Speck Containing-protein; shNLRP3 – shRNA directed against NLRP3. Experiments were performed in triplicate and results from representative experiments are shown. Error bars represent the standard error of the mean for triplicate measurements of IL-1β.
2. **Treatment with Caspase inhibitors blocks caspase activity in THP-1 cell lysates.** THP-1 cells ($1x10^7$ cells) were incubated with vehicle (DMSO) or cell permeable caspase inhibitors: 20 μM pan-caspase inhibitor (AC-VAD-CHO), 20 μM caspase-3 inhibitor (AC-DVED-CHO), 20 μM caspase-1 inhibitor (AC-YVAD-CHO) for 30 min. The cells were collected and lysed in caspase assay buffer. Caspase assay buffer or the indicated THP-1 cell lysate was incubated for 15 minutes with 1 U of recombinant active caspase-1 (white bars) or caspase-3 (black bars). Caspase-1 activity was measured using fluorogenic caspase-1 substrate (AC-YVAD-AFC) and fluorogenic caspase-3 substrate (AC-DEVD-AFC) as described in the materials and methods. The Caspase activity is reported

as the percent of activity present when compared to recombinant caspase without cellular lysate added. The plot show mean values (bars) and standard deviation (error bars) of measurements done in triplicate. Representative experiments (of two) are shown.

3. **Cathepsin B inhibition attenuates GC-induced TNFα secretion**. THP-1 cells were treated with indicated concentration of inhibitors of Cathepsin B (CA-074-ME), Cathepsin L, or DMSO vehicle for 15 min prior to infection with GC at MOI of 2.0 (as described in Figure 5). TNFα secretion was measured in cell free culture supernatants using ELISA. Error bars represent standard error of the mean from measurements performed in triplicate.