Supplemental Figure Legends

Figure S1. CASP4/caspase-11 plays a role in cleavage of CASP1, IL1B, and CASP7 during *B. cenocepacia* infection. (**A**) Intracellular CFUs of *B. cenocepacia* (*B.c.*) MH1K in WT and *casp4*$^{-/-}$ macrophages at 6 h post infection. Values are fold changes relative to CFUs at 30 min post infection. Shown are mean ±SEM of 9 independent experiments (n=9). Statistical analysis was performed using paired t-test. (**B**) Immunoblot analysis of CASP4 in WT macrophages at 2 h post infection. (**C**) Densitometry analysis of CASP4 expression in WT macrophages at 2 h post infection. Shown are mean ±SEM of 4 independent experiments (n=4). Statistical analysis was performed using paired t-test. (**D**) Full immunoblot of pro-CASP1, cleaved CASP1 p20 and GAPDH (shown in Fig. 1F) from WT and *casp4*$^{-/-}$ macrophages infected with *B. cenocepacia* MH1K at 6 h post infection. (**E**) Immunoblot of pro-IL1B and cleaved IL1B p17 from WT, *casp4*$^{-/-}$, and *casp1*$^{-/-}$ macrophages infected with *B. cenocepacia* MH1K at 6 h post infection. Representative image of 3 independent experiments (n=3). (**F**) Immunoblot analysis of cleaved CASP7 in WT and *casp4*$^{-/-}$ macrophages infected with *B. cenocepacia* MH1K at 6 h post infection. (**G**) Densitometry analysis of *B. c.*-induced cleavage of CASP7. Shown are mean ±SEM of 5 independent experiments (n=5). Statistical analysis was performed using two-way ANOVA. *p≤0.05, ***p≤0.001. NT, no treatment.

Figure S2. CASP4/caspase-11 and MEFV/PYRIN contribute to *B. cenocepacia*-mediated activation of CASP1. (**A**) Immunoblot of CASP4 in wild-type (WT), *mefv*$^{-/-}$*/pyrin*$^{-/-}$, and *casp4*$^{-/-}$ macrophages infected with *B. cenocepacia* (*B.c.*) MH1K at 6 h post infection. Representative image of 3 independent experiments (n=3). (**B**) Immunoblot of CASP1 in WT, *mefv*$^{-/-}$, and *casp4*$^{-/-}$ macrophages infected with *B. cenocepacia* MH1K at 6 h post infection. Representative image of 3 independent experiments (n=3). NT, no treatment.

Figure S3. Histological scores and pulmonary CFUs of *B. cenocepacia*-infected mice. (**A**) Alveolitis and fibrin exudation scores of *B. cenocepacia* (*B.c.*)-infected WT and *casp4*$^{-/-}$ mice ($30x10^6$ CFU). (**B**) Recovered *B. cenocepacia* CFU at day 8 from lungs of surviving *casp4*$^{-/-}$ mice depicted in Fig 2C. Pooled data from 2 independent experiments are shown as mean ± SEM (n=6 surviving mice).

Figure S4. Intracellular survival and LC3-II conversion of *B. cenocepacia* ΔT6SS mutant and nonpathogenic *E. coli*. (**A**) Intracellular survival of *Escherichia* (*E.*) *coli* in wild-type (WT) and *casp4*$^{-/-}$ macrophages. Data are presented as mean ± SEM from 3 independent experiments (n=3). Statistical analysis was performed using two-way ANOVA. (**B**) Invasion of *B. cenocepacia* (*B.c.*) WT and ΔT6SS in WT macrophages. Data are presented as mean ± SEM from 3 independent experiments (n=3). Statistical

analysis was performed using Student's t-test. (**C**) Intracellular survival of *B. c.* WT and ΔT6SS in WT macrophages. Data are presented as mean ± SEM from 3 independent experiments (n=3). Statistical analysis was performed using two-way ANOVA. (**D**) Representative immunoblots of WT and *casp4*$^{-/-}$ macrophages infected with *B.c.* or *E. coli* at 6 h post infection. (**E**) Densitometry analysis of immunoblots shown in (D). Data are mean ±SEM of 3 independent experiments (n=3). Statistical analysis was performed using two-way ANOVA. (**F**) Representative immunoblots of WT and *casp4*$^{-/-}$ macrophages infected with *B. cenocepacia* WT or T6SS mutant at 6 h post infection. (**G**) Densitometry analysis of immunoblots shown in (F). Shown are mean ±SEM of 3 independent experiments (n=3). Statistical analysis was performed using two-way ANOVA. *p≤0.05, **p≤0.01, ***p≤0.001. NT, no treatment.