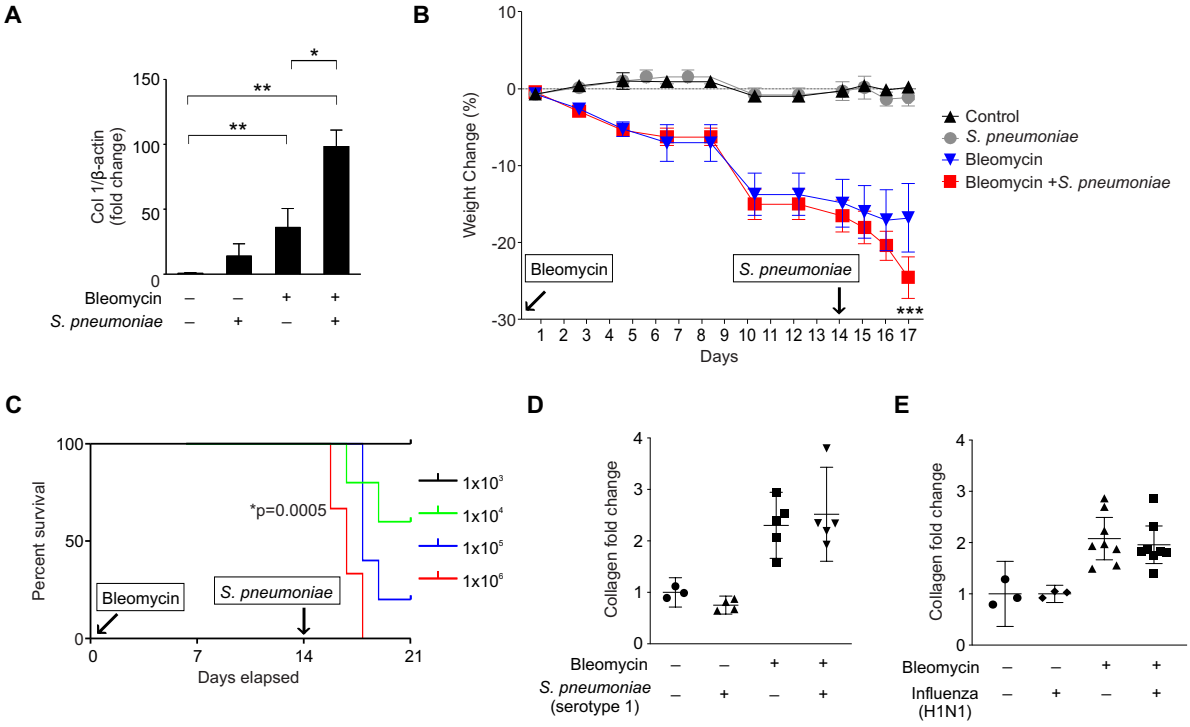
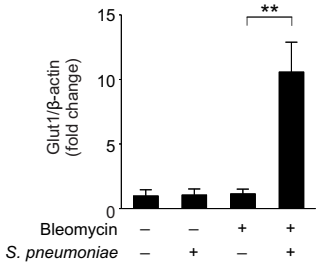
Supplementary Figure 1.



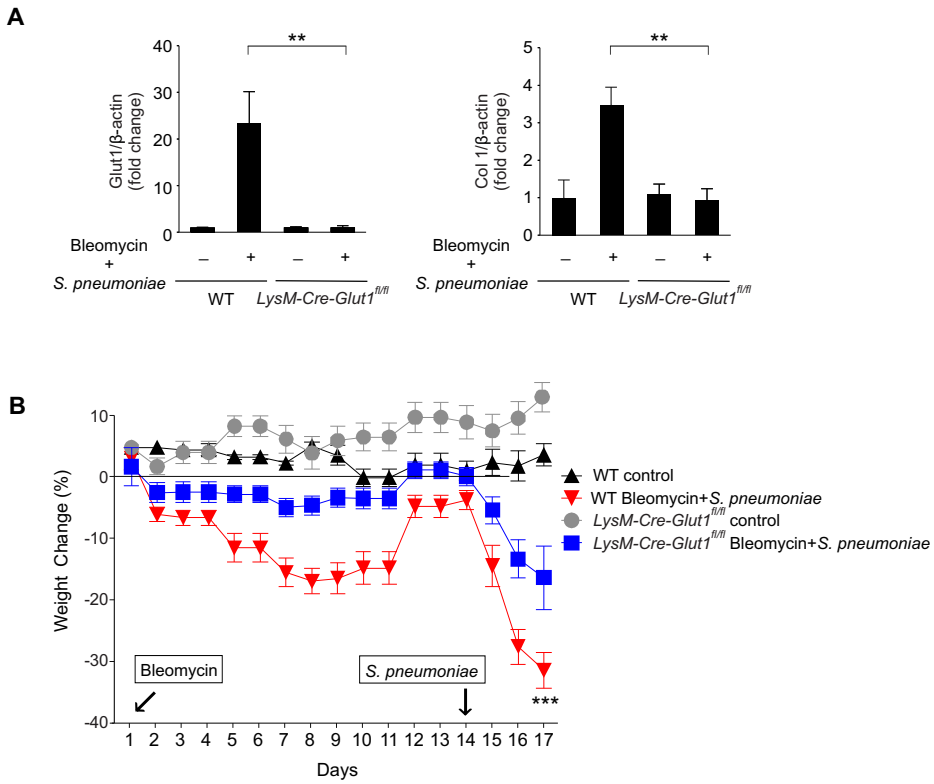
Supplementary Figure 1. *S. pneumoniae* infection in the setting of pulmonary fibrosis increases morbidity and mortality in murine fibrosis exacerbation model. Related to Figure 1.
(A) Densitometry of immunoblot assay for Collagen type 1(Col 1) in bleomycin treated mice in response to serotype 3 *S. pneumoniae* infection ($1x10^5$ CFU). Data are mean ± 95% CI (n ⩾ 5 mice/group). One-way ANOVA, *p < 0.05, **p < 0.01. (B) Weight change in bleomycin treated mice in response to serotype 3 *S. pneumoniae* infection. Data are mean ± 95% CI (n ⩾ 5 mice/group). One-way ANOVA, ***p < 0.001. (C) Survival curve of bleomycin mice after different doses of serotype 3 *S. pneumoniae* infection (n = 5-6 mice per group). p = 0.0005 by log-rank test. (D) Total lung collagen was quantified by Sircol assay after serotype 1 *S. pneumoniae* infection ($1x10^5$ CFU) (PBS/PBS, n = 3; PBS/serotype 1 *S. pneumoniae*, n = 4; bleomycin/PBS, n = 5, bleomycin/serotype 1 *S. pneumoniae*, n = 5). Data are mean ± SEM. (E) Total lung collagen was quantified by Sircol assay after influenza infection (PR8, $1x10^3$ PFU) (PBS/PBS, n = 3; PBS/Influenza, n = 3; bleomycin/PBS, n = 8, bleomycin/Influenza, n = 8). Data are mean ± 95% CI.

Supplementary Figure 2.



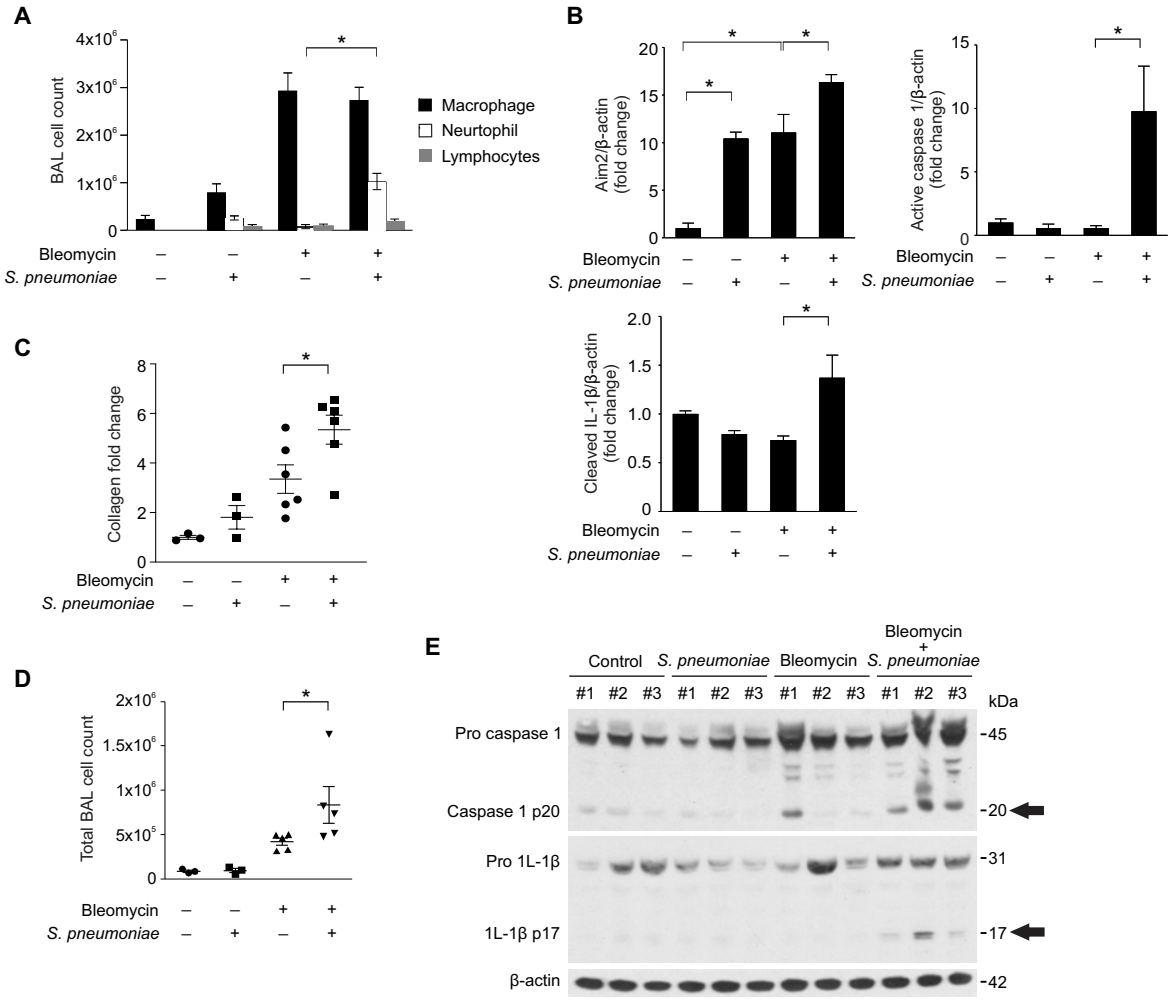
Supplementary Figure 2. GLUT1-depent glycolysis is increased in bleomycin treated mice after *S. pneumoniae* infection. Related to Figure 2.
Densitometry of immunoblot assay for GLUT1 in bleomycin treated mice in response to serotype 3 *S. pneumoniae* infection Data are mean ± SEM ($n \geqslant 5$ mice/group). One-way ANOVA, $^{**}p < 0.01$.

Supplementary Figure 3.



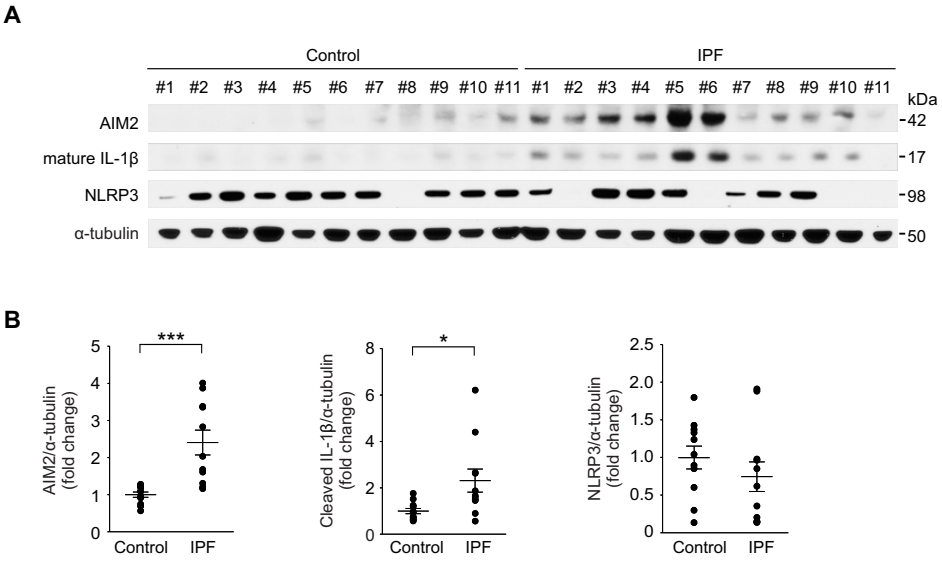
Supplementary Figure 3. GLUT1-depent glycolysis regulates exacerbation of lung fibrosis after *S. pneumoniae* infection. Related to Figure 3.
(A) Densitometry of immunoblot assay for GLUT1 and Collagen 1 in bleomycin treated mice in response to serotype 3 *S. pneumoniae* infection Data are mean ± SEM (n ⩾ 5 mice/group). One-way ANOVA, **p < 0.01.(B) Weight change in bleomycin treated WT and *LysM-Cre-Glut1*$^{fl/fl}$ mice in response to *S. pneumoniae* infection. Data are mean ± SEM (n ⩾5 mice/group). ***p< 0.001.

Supplementary Figure 4.



Supplementary Figure 4. AIM2 inflammasome expression and activation is augmented in bleomycin treated lung after *S. pneumoniae* infection. Related to Figure 4.
(A) Differential cell count of inflammatory cells in the BAL in bleomycin treated WT mice 3 days after *S. pneumoniae* infection (n ⩾ 5 mice/group). Data are mean ± SEM. **p < 0.01 by ANOVA. (B) Densitometry of immunoblot assay for AIM2, cleaved caspase 1 and mature IL-1β and Collagen 1 in bleomycin treated mice in response to serotype 3 *S. pneumoniae* infection Data are mean ± SEM (n ⩾ 5 mice/group). One-way ANOVA, **p < 0.01. (C) Total lung collagen was quantified in *Nlrp3*$^{-/-}$ mice by Sircol assay (PBS/PBS, n = 3; PBS/*S. pneumoniae*, n = 3; bleomycin/PBS, n = 7, bleomycin/*S. pneumoniae*, n = 7). (D) Total cell count in bronchoalveolar lavage (BAL) in bleomycin treated *Nlrp3*$^{-/-}$ mice 3 days after *S. pneumoniae* infection. (E) Immunoblot analysis for AIM2, activated caspase-1, cleaved IL-1β (black arrows) in bleomycin treated *Nlrp3*$^{-/-}$ mice lung after *S. pneumoniae* infection. β-actin served as the standard. Throughout, data are mean ± SEM. *p < 0.05 by ANOVA.

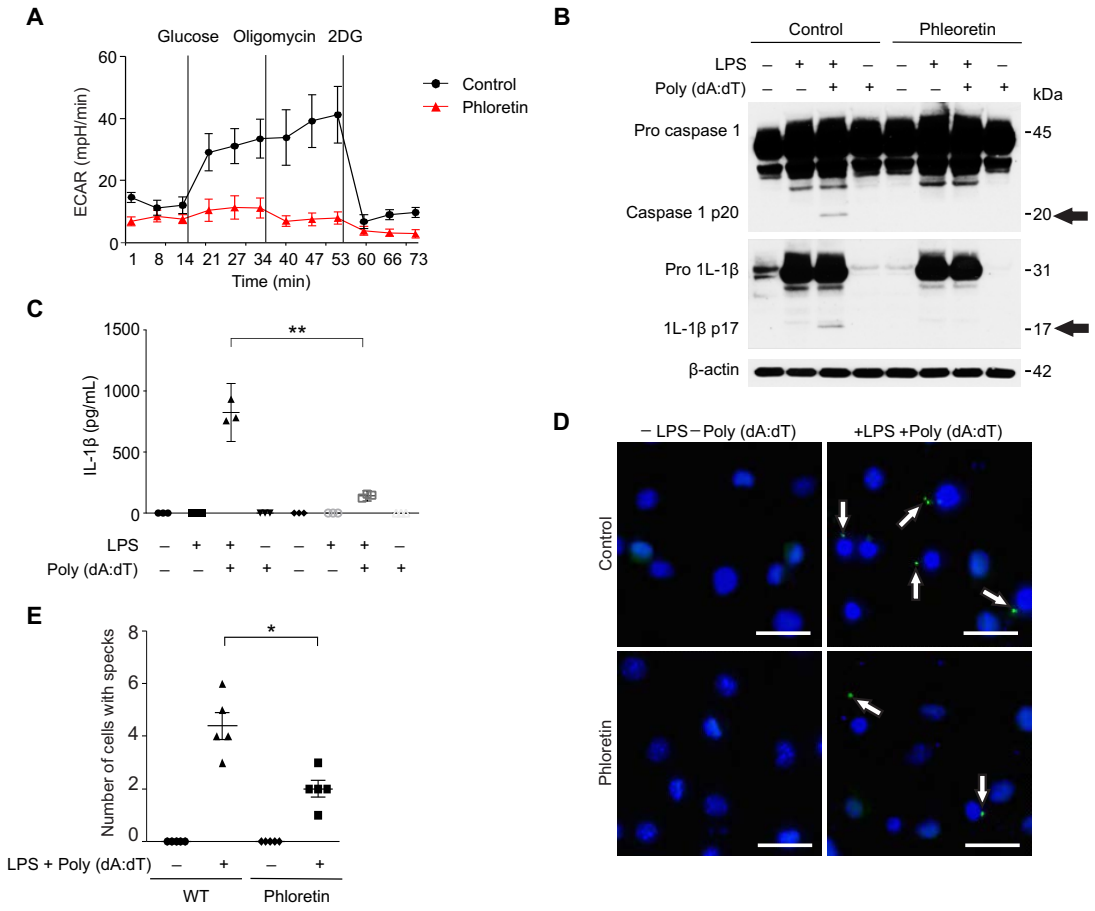
Supplementary Figure 5.



Supplementary Figure 5. AIM2 inflammasome expression is augmented in IPF patients lung

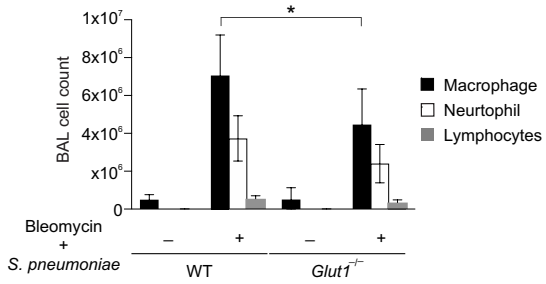
(A) Immunoblot analysis for AIM2, IL-1β and NLRP3 in lung lysates from IPF patients and control subjects. α-tubulin served as the standard. (B) Densitometry of immunoblot assay for AIM2, mature IL-1β and NLRP3 in IPF patients and control lungs. α-tubulin served as the standard.Data are mean ± SEM. *p < 0.05, ***p<0.001 by Student t-test.

Supplementary Figure 6.



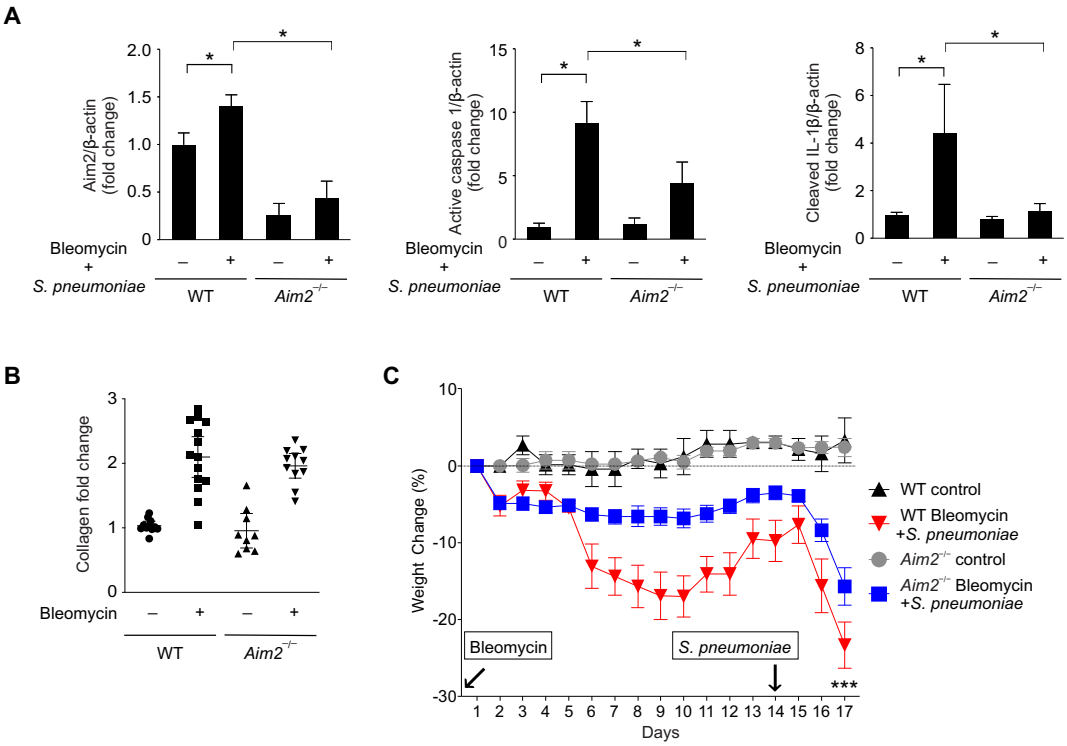
Supplementary Figure 6. GLUT1-dependent glycolysis regulates AIM2 inflammasome activation in vitro. Related to Figure 5.
(A) ECAR was measured in BMDMs from *Nlrp3*$^{-/-}$ mice (1x10^5 cells/well) treated with phloretin or vehicle 30 minutes prior to LPS and poly (dA:dT) stimulation. (B) Immunoblot analysis for activated caspase-1, cleaved IL-1β (black arrows) from LPS-primed *Nlrp3*$^{-/-}$ BMDMs treated with phloretin or vehicle 30 minutes prior to LPS and poly (dA:dT) stimulation. β actin served as the standard. (C) Quantification of IL-1β level from *Nlrp3*$^{-/-}$ BMDMs treated with phloretin or vehicle 30 minutes prior to LPS and poly (dA:dT) stimulation. Representative immunofluorescence images (n = 5 individual images per group) of ASC speck formation (white arrows) images (D) and quantification (E) in *Nlrp3*$^{-/-}$ BMDMs treated with phloretin or vehicle 30 minutes prior to LPS and poly (dA:dT) stimulation. Scale bars, 20 μm. Throughout, data are mean ± 95% CI. *p < 0.05, **p < 0.01 by ANOVA. Results are representative of three or more independent experiments.

Supplementary Figure 7.



Supplementary Figure 7. GLUT1-dependent glycolysis regulates AIM2 inflammasome activation in murine fibrosis exacerbation model. Related to Figure 6.
Differential cell count of inflammatory cells in the BAL in bleomycin treated WT mice and *LysM-Cre-Glut1*$^{fl/fl}$ mice 3 days after *S. pneumoniae* infection (n ⩾ 5 mice/group). Data are mean ± 95% CI. *p < 0.05 by ANOVA.

Supplementary Figure 8.



Supplementary Figure 8. Deficiency of AIM2 ameliorates fibrosis exacerbation in bleomycin treated lung after *S. pneumoniae* infection. Related to Figure 7.

(A) Densitometry of immunoblot assay for AIM2, cleaved caspase 1 and mature IL-1β and collagen 1 in WT and *Aim2*$^{-/-}$ mice after bleomycin treatment followed by *S. pneumoniae* infection. Data are mean ± SEM (n ⩾ 5 mice/group). One-way ANOVA, *p < 0.05. (B) Total lung collagen was quantified by Sircol assay. Data are mean ± 95% CI. (WT/PBS, n = 11; WT/Bleomycin, n = 14; *Aim2*$^{-/-}$/PBS, n = 9, *Aim2*$^{-/-}$/Bleomycin, n = 11). (C) Weight change in bleomycin treated WT and *Aim2*$^{-/-}$ mice in response to *S. pneumoniae* infection. Data are mean ± SEM (n ⩾ 5 mice/group). ***p < 0.0001 by one-way ANOVA and p=0.016 between WT/Bleomycin+*S. pneumoniae* and AIM2$^{-/-}$/Bleomycin+*S. pneumoniae* by post hoc analysis.