

Expanded View Figures

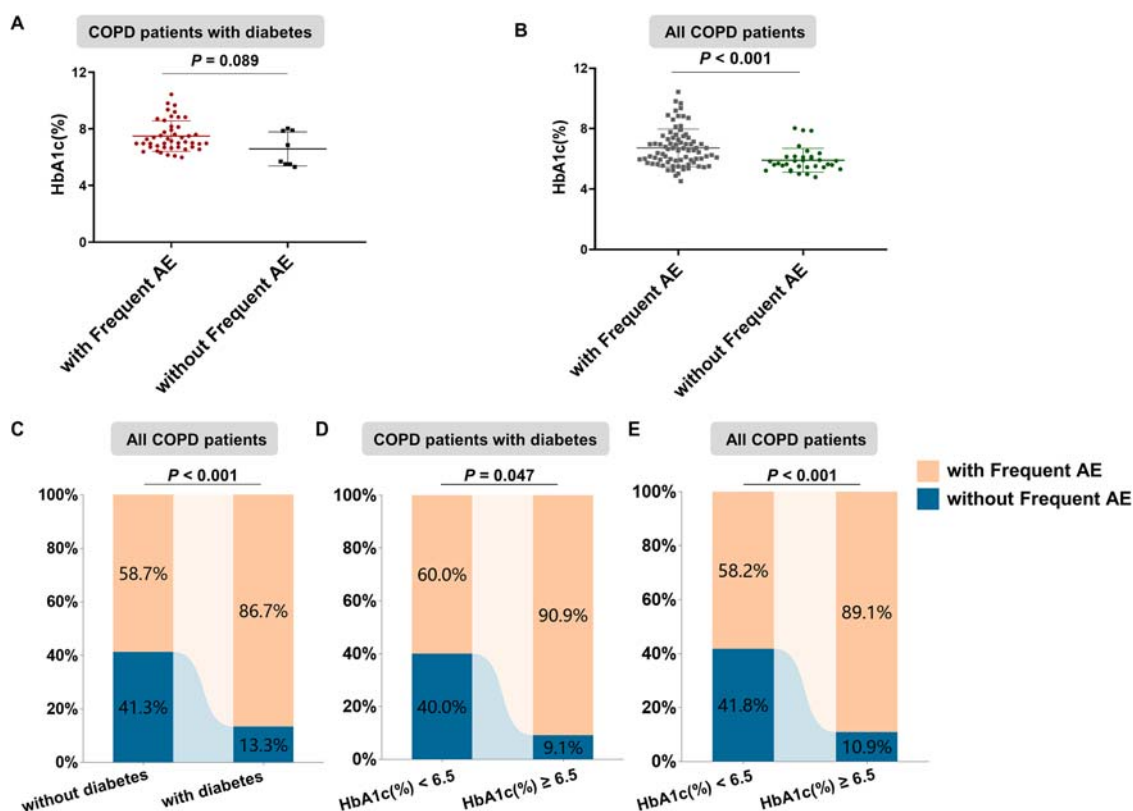


Figure EV1. HbA1c level correlates with frequent acute exacerbation (AE) in COPD Cohorts.

(A, B) HbA1c (%) level in the COPD patients with diabetes subgroup ($n = 60$) (A) and in the overall COPD cohort ($n = 123$, including non-diabetic subjects) (B), stratified by the presence or absence of frequent AE. (C) Proportion of patients with or without frequent AE in the overall COPD cohort stratified by those with or without diabetes. (D, E) Proportion of patients with or without frequent AE in the COPD patients with diabetes subgroup (D) and in the overall COPD cohort (E), stratified by HbA1c(%) < 6.5 vs. HbA1c(%) ≥ 6.5. Data are shown as Mean ± SD (A, B) or as percentage within each group (C-E). Statistical analyses were performed using the Mann-Whitney test (A, B), Chi-square with Yates' correction (D) or Chi-square (C, E). n indicates biological replicates.

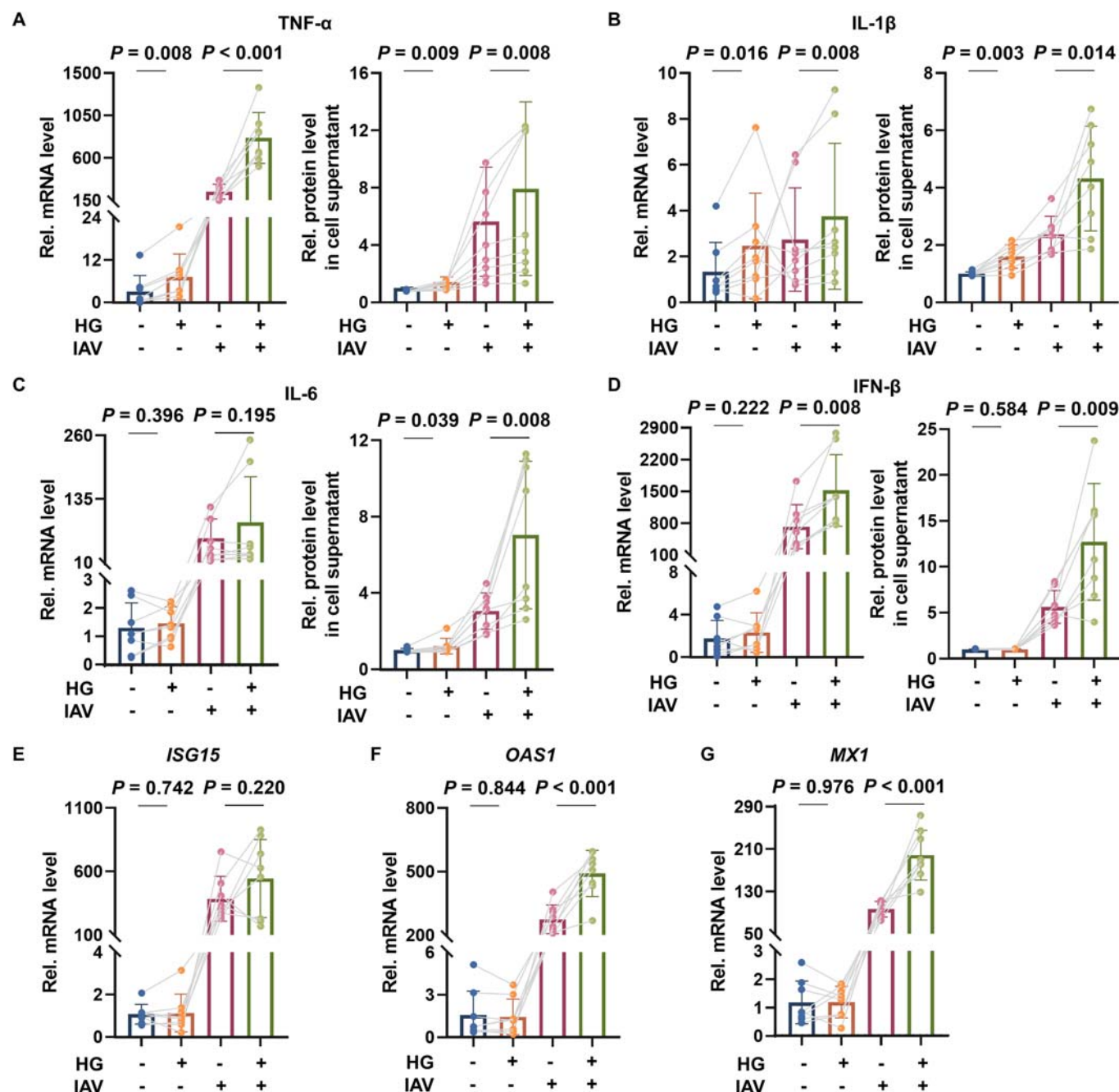


Figure EV2. High glucose (HG) potentiates IAV-mediated pro-inflammatory responses in airway epithelium derived from COPD.

qPCR (A–D, left panel; E–G) and ELISA (A–D, right panel) measurement of several cytokines and antiviral-related genes in ALI culture treated with or without 9 g/L HG for 3 days, followed by IAV infection (MOI = 0.5, 24 h) or mock infection. $n = 8$. Data were shown as Mean $\pm$ SD. The Wilcoxon signed-rank test was used for the following panels: A left panel (first two groups), A right panel (last two groups), B left panel, C left panel (last two groups), C right panel, D left panel (last two groups), E left panel (first two groups), and F left panel (first two groups). The paired t -test was used for all other comparisons. n indicates biological replicates. Related to Fig. 1.

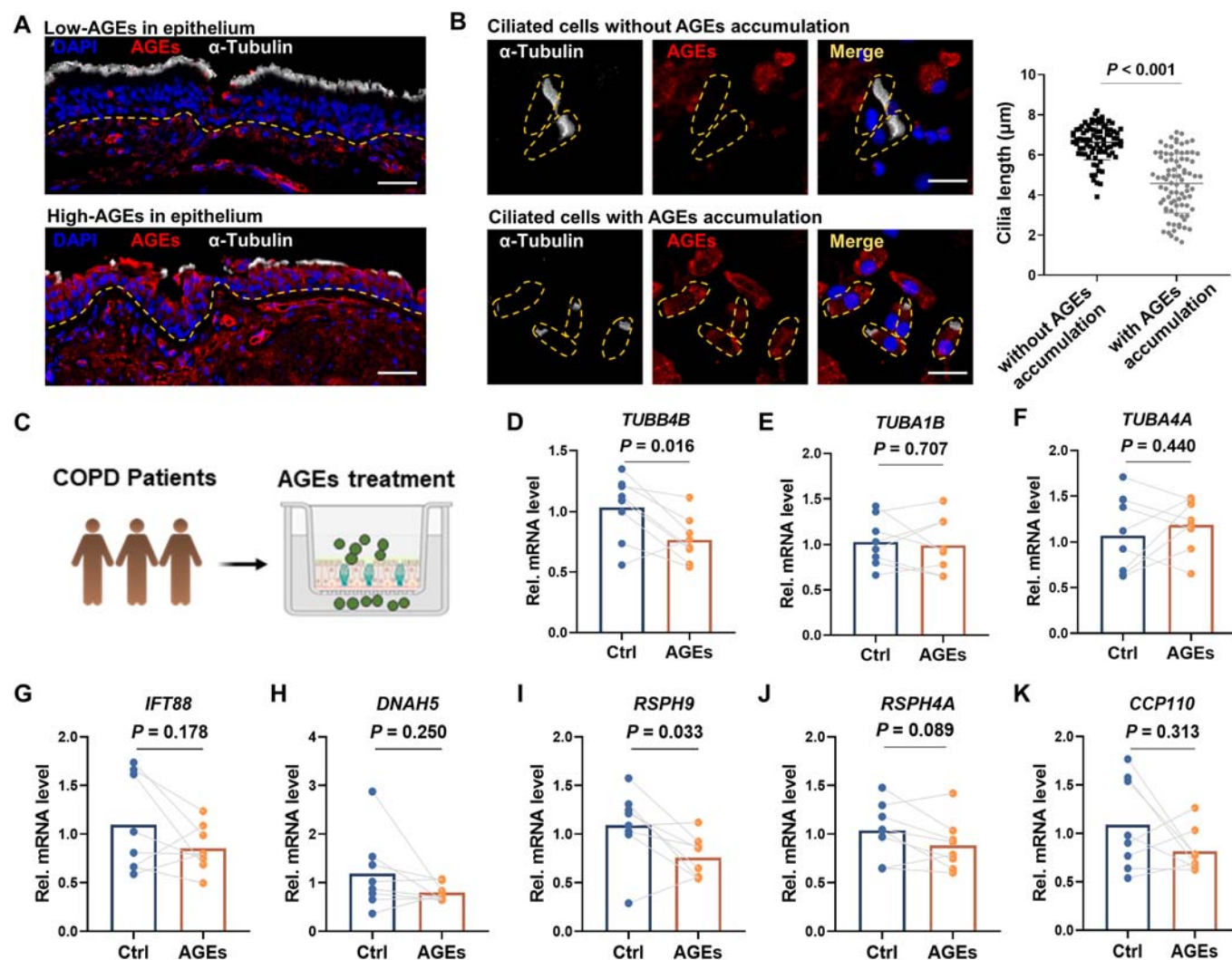


Figure EV3. AGEs exposure is associated with epithelial damage.

(A) Immunofluorescence staining image of airway cilia (α -Tubulin, white) in low-AGEs regions (upper panel, red) or high-AGEs areas (lower panel, red). Nuclei: DAPI (blue). The dashed line indicates the basal side of the airway mucosal epithelium. Representative images from three independent experiments are shown. Scale bar: 50 μ m. (B) Representative immunofluorescence staining image of cilia (α -Tubulin, white) in BALF-cytospin cells without or with AGEs (red) accumulation. Yellow dashed borders outline individual ciliated epithelial cells. Nuclei: DAPI (blue). Scale bar: 10 μ m. $n = 83$ –84. (C) Schematic of exogenous AGEs exposure in ALI culture. (D–K) qPCR measurement of several cilia-related genes in ALI culture treated with or without 200 μ g/mL AGEs for 1 day. $n = 8$. Data were shown as Mean $\pm$ SD and analyzed by unpaired t -test (B), paired t -test (D–G, I, J) or Wilcoxon signed-rank test (H, K). n indicates the number of cells (B) or biological replicates (D–K). Related to Fig. 2.

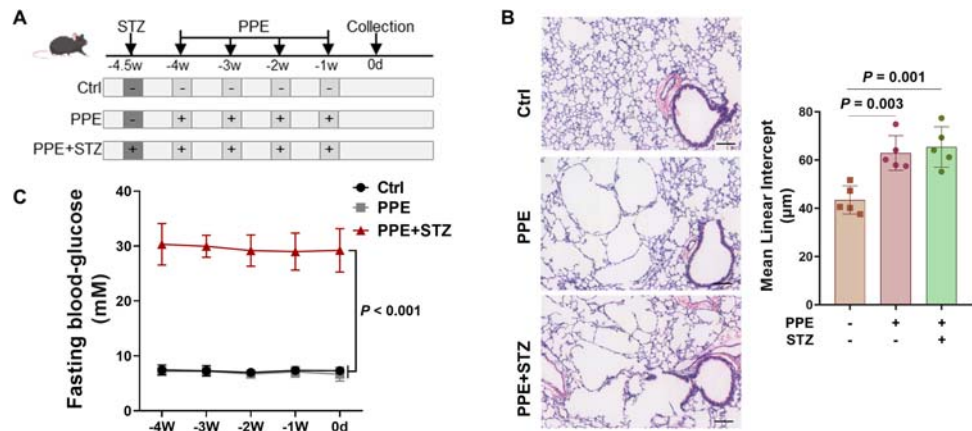


Figure EV4. Characterization of COPD-diabetes comorbid mouse model.

(A) Schematic showing C57BL/6 mice received PPE (porcine pancreatic elastase, intranasal, 1.2 U) + STZ (streptozotocin, intraperitoneal, 200 mg/kg) to establish a COPD-diabetes model. (B) Representative images of H&E-stained lung sections and the mean linear intercept (MLI) measurement. Scale bar: 100 μ m. $n = 5$. (C) Fasting blood glucose levels of the COPD-diabetes mouse model. $n = 5$. Data were shown as Mean $\pm$ SD and analyzed by one-way ANOVA with Fisher's LSD post hoc test. n indicates biological replicates. Related to Fig. 3.

