Exposure to high glucose promotes airway inflammation and wound repair in fibroblasts

Background:
- Emphysema: Promotes airway hypercompliance.
- Chronic Bronchitis (COPD): Conducting airways.
- COPD: Airway narrowing.
- Mucus hypersecretion.
- Fibrosis.
- Hypothesis: Hyperglycemia causes cellular senescence and inflammation in COPD airway fibroblasts, when compared to non-COPD fibroblasts.

Methods:
- Cell Culture Conditions:
  - Low Glucose (5.5mM)
  - High Glucose (25mM)
  - Mannitol Osmotic Control (25mM)
  - TGF-β (2.5ng/mL)
- A) Proliferation Assay
  Cell culture in low Glucose (5.5mM) and high Glucose (25mM) (with osmotic mannitol control).
- B) qPCR
  Exploratory gene expression markers for:
  - Senescence (p21)
  - Inflammation (IL-8)
  - Matrix Hypersorption
  - Airway Narrowing (conducting airways)

RELAVANCE OF RESEARCH
COPD is the third leading cause of death worldwide.
- 1 in 10 COPD patients has emphysema.
- 2 times greater risk of COPD-related death.

Important implications for COPD pathogenesis.
- Role in developmental origin of lung disease.

Figure 1: Impact of various cell culture conditions (with or without a TGF-β stimulus) on gene expression in fibroblasts indicates an increase in inflammation and TGF-B insensitivity. Fig 1-A-C display a combination of non-COPD and COPD cells (n=4) while Fig 1-D-F displays a breakdown of results by disease status (n=2, preliminary data).
- A) Relative abundance of p21 in fibroblasts grown in LG, HG, LG+TGF-β, HG+TGF-β.
- B) Relative abundance of IL-8 in fibroblasts grown in LG, HG, LG+TGF-β, HG+TGF-β.
- C) Relative abundance of COL1A1 in fibroblasts grown in LG, HG, LG+TGF-β, HG+TGF-β.
- D) Relative abundance of p21 in all fibroblasts grown in LG, HG, LG+TGF-β, HG+TGF-β.
- F) Relative abundance of COL1A1 in fibroblasts grown in LG, HG, LG+TGF-β, HG+TGF-β.

Figure 2: Hyperglycemia decreases the rate of proliferation in COPD cells. A) non-COPD fibroblast cell count (relative to baseline) over time (n=3) in high glucose (25 mM) vs. low glucose (5 mM). B) COPD fibroblast cell count (relative to baseline) over time (n=3) in high glucose (25 mM) vs. low glucose (5 mM).