

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

First image (1) below from 'Quick Learning Point'
<https://www.quicklearningpoint.com/chronic-obstructive-pulmonary-disease-copd/>

Second Image (2) below from 'Slide Cow'
powerpoint design <https://www.slidecow.com/powerpoint-tutorials/make-awesome-objectives-slide/>



Background:

- Emphysema:**

 - Tissue destruction
 - Loss of repair capacity
 - Loss of extra cellular matrix
 - Hypercompliance
- Chronic Bronchitis**

 - Fibrosis
 - Mucus Hypersecretion
 - Airway Narrowing (conducting airways)

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Primary objective: is to investigate the link between diabetes and COPD exacerbations.

Hypothesis: Hyperglycemia causes cellular senescence and inflammation in COPD airway fibroblasts, when compared to non-COPD

METHODS → 3 DAY EXPOSURE → TGF-β (2.5ng/mL) FOR 24 HR.

Cell Culture Conditions:

- Low Glucose (5.5mM)
- High Glucose (25mM).
- Mannitol Osmotic Control (25mM)
- TGF-β (2.5ng/mL)
- Transforming growth factor is a pro-fibrotic mediator in the airway

A Proliferation Assay

Cell culture in low Glucose (5.5mM) and high Glucose (25mM) (with osmotic control).

Cell count using Hoescht dye at various time points over a 72 hr. period.

B qPCR

Explored gene expression markers for:

- Senescence (p21)
 - P21 is a CDK inhibitor implicated in senescence mechanisms
- Inflammation (IL-8)
 - Interleukin-8 is an inflammatory neutrophil chemokine
- Fibrosis (COL1A1)
 - Collagen 1A1 is an extracellular matrix protein deposited in the lung.

HOW DO FIBROBLASTS FUNCTION IN COPD?

Fibroblasts are structural support cells of the lung.

ECM secretion

Play important roles in wound healing and fibrosis.

Altered function can contribute to lung disease.

Fibroblasts in COPD have altered phenotype.

Altered fibrotic capacity

Inflammatory

Senescence associated phenotype

RELEVANCE OF RESEARCH

COPD is the third leading cause of death worldwide.

- 1 in 10 COPD patients has comorbid diabetes
- 2 times greater risk of COPD- related deaths

★ Important implications for COPD pathogenesis.

★ Role in developmental origins of lung disease

Complication: Maternal diabetes.

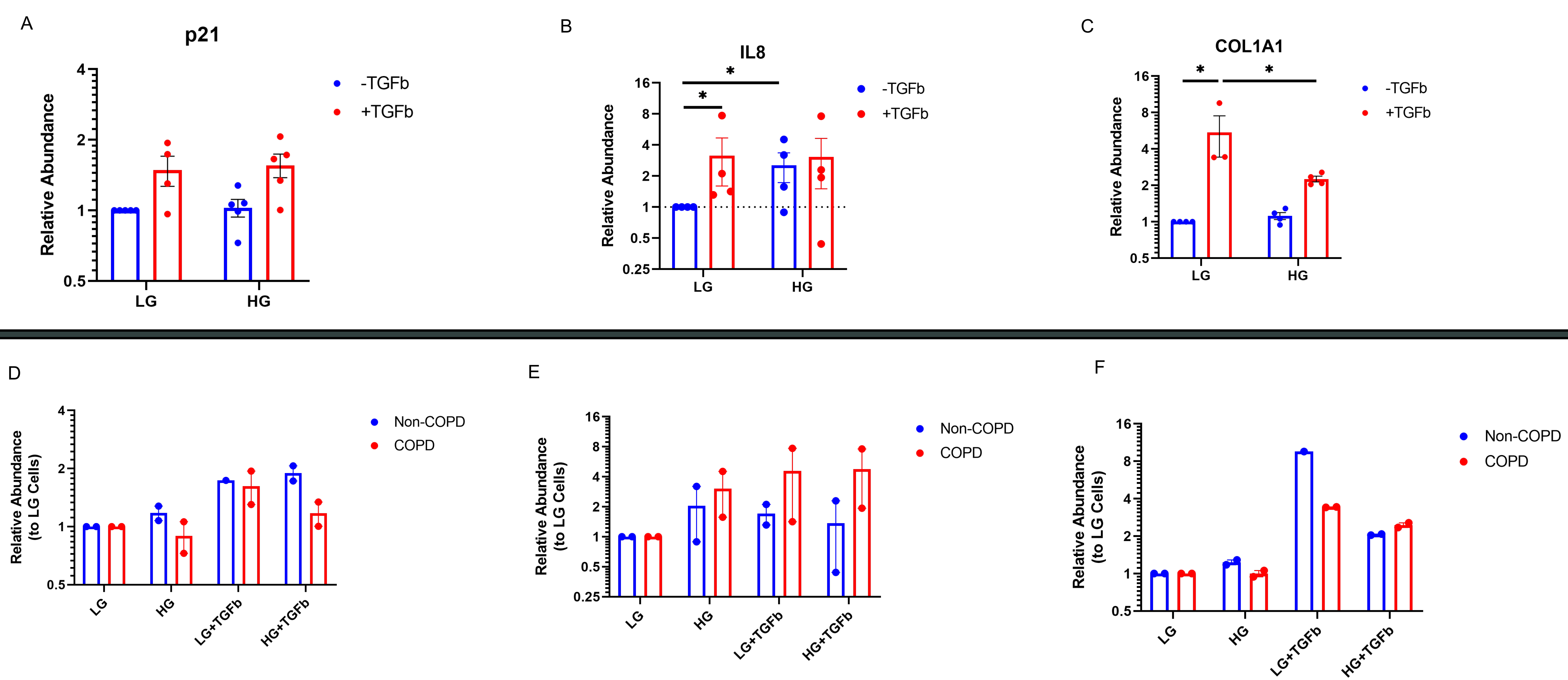
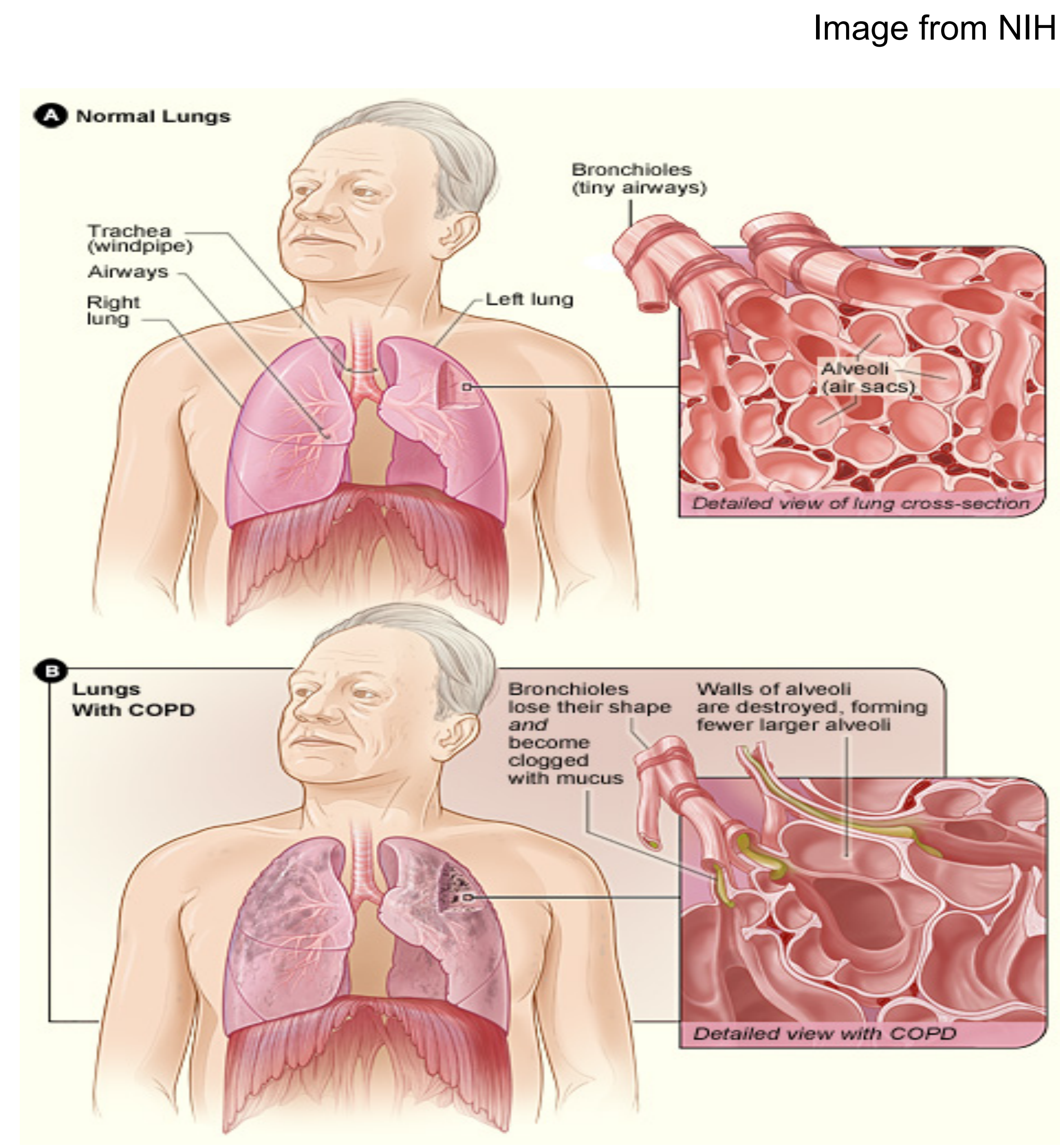


Figure 1: Impact of various cell culture conditions (with or without a TGF-B stimulus) on gene expression in fibroblasts indicates an increase in inflammation and TGF-B insensitivity. Fig 1. A-C display a combination of non-COPD and COPD cells (n=4) while Fig 1.D-F displays a breakdown of results by 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 COPD vs non- COPD fibroblasts grown in LG, HG, LG+TGF- β, HG+TGF- β) Relative abundance of IL-8 in fibroblasts grown in LG, HG, LG+TGF- β, HG+TGF- β in non-COPD vs COPD F) Relative abundance of COL-1A1i n fibroblasts grown in LG, HG, LG+TGF- β, HG+TGF- β in non-COPD vs COPD. (LG= 25 mM, HG= 5 mM, TGF- β + 2.5 ng/mL)

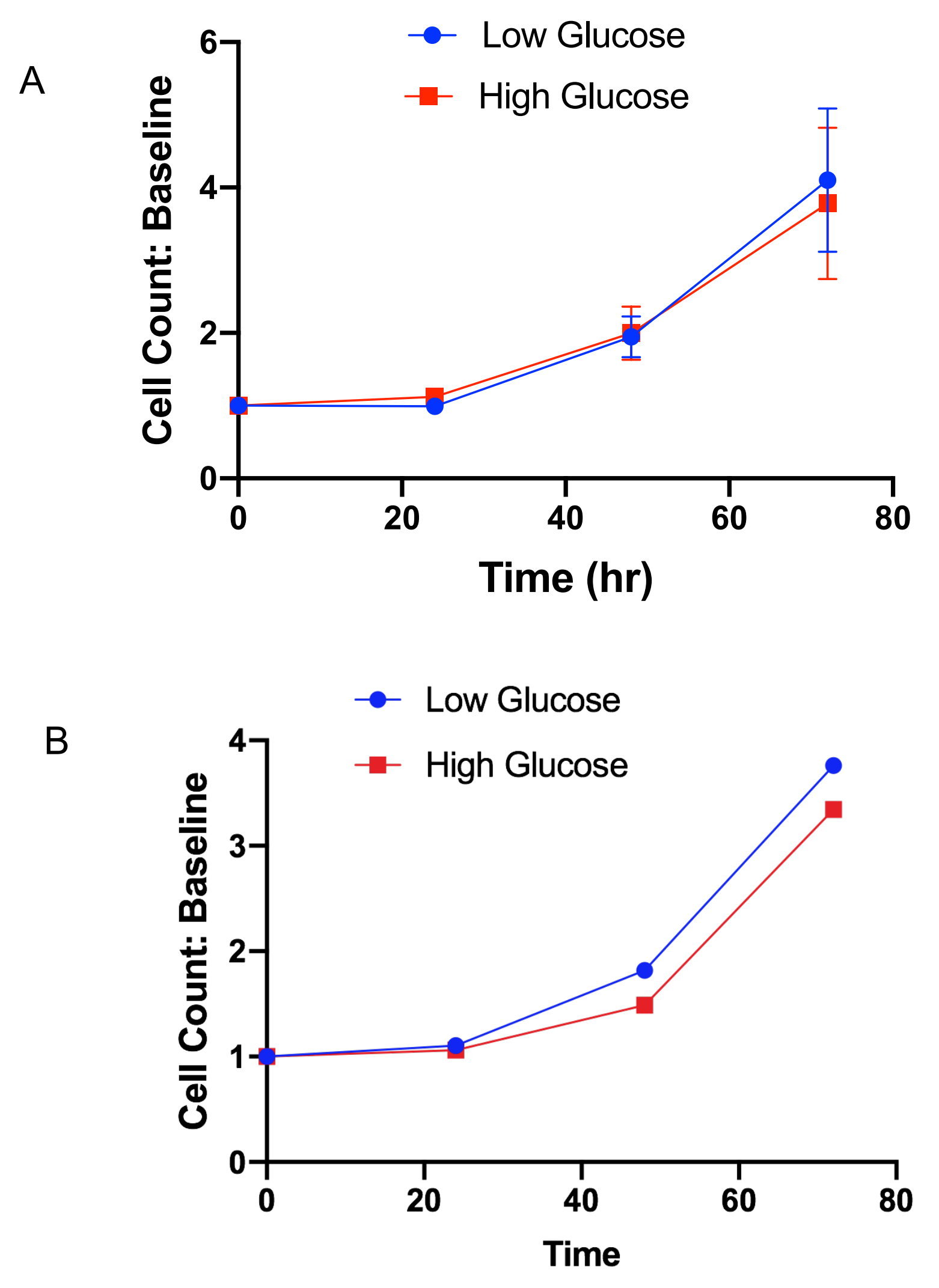


Figure 2: Hyperglycemia decreases the rate of proliferation in COPD cells. A) non-COPD fibroblast cell count (relative to baseline) over time (n=3) in high glucose (25 mM) vs. low glucose (5 mM). B) COPD fibroblast cell count (relative to baseline) over time (n=3) in high glucose (25 mM) vs. low glucose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