

Maternal Diabetes and Smoking: The Impact on Asthma Development

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- Exposure of airway smooth muscle cells to hyperglycemia and nicotine induces pro-asthmatic phenotypic changes

Airway Remodeling Asthma

- Increased ASM mass
- Hypercontractility and hyperresponsiveness
- Inflammation

ASM phenotypes

- Synthetic phenotype
 - Proliferative
 - Secretory
 - Inflammation
- Contractile phenotype
 - Less proliferation
 - Less Secretion
- More concerned with contracting

Which phenotype will co-exposure to hyperglycemia and nicotine favor?

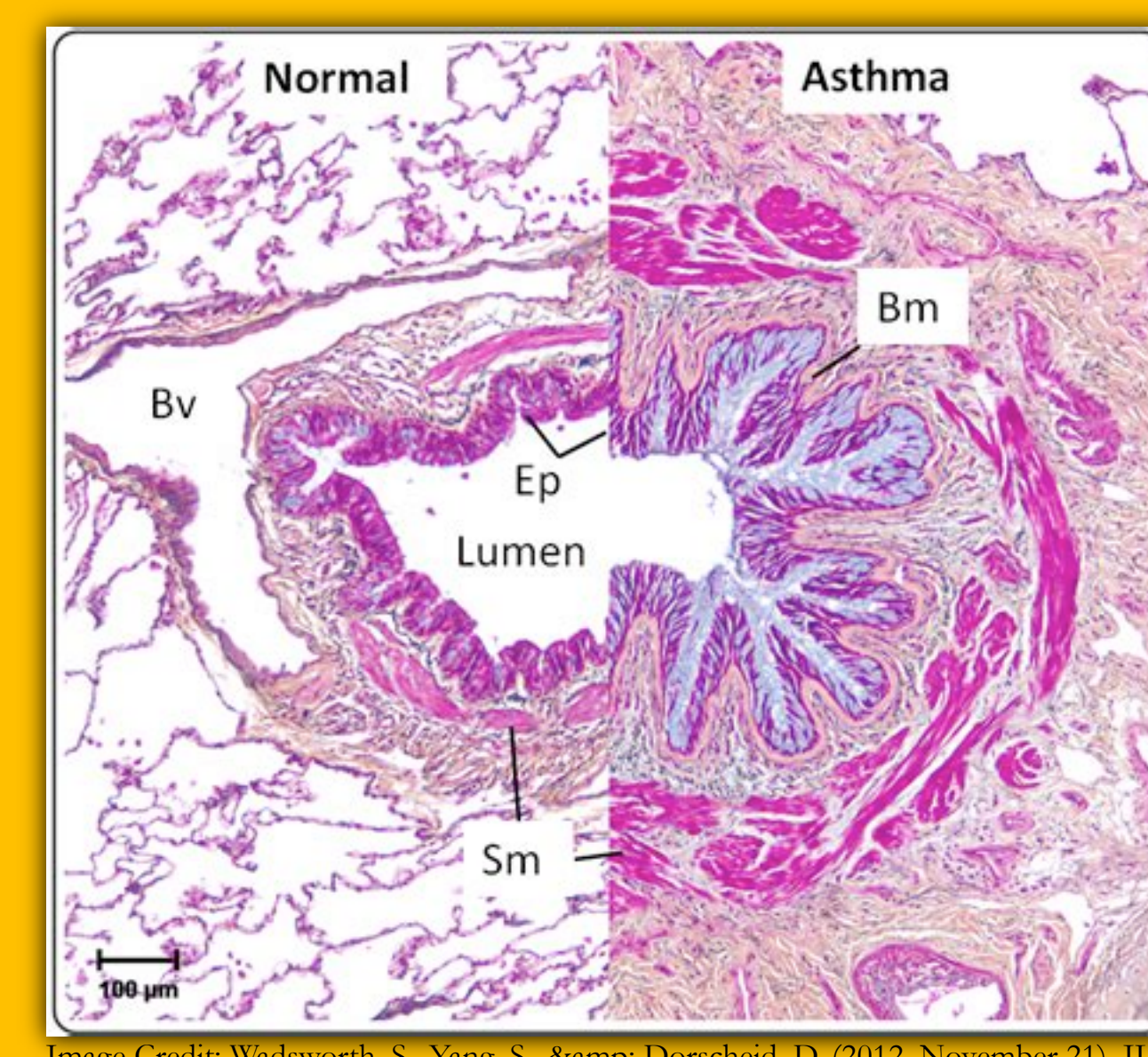


Image Credit: Wadsworth, S., Yang, S., Xiang, D. (2012, November 21). IL-13, Asthma and Glycosylation in Airway Epithelial Repair.

Unexposed Airway smooth muscle cell

Image Credit: Vesels

Hyperglycemia and Nicotine

Pro-Asthmatic Phenotype Changes

Cell Culture

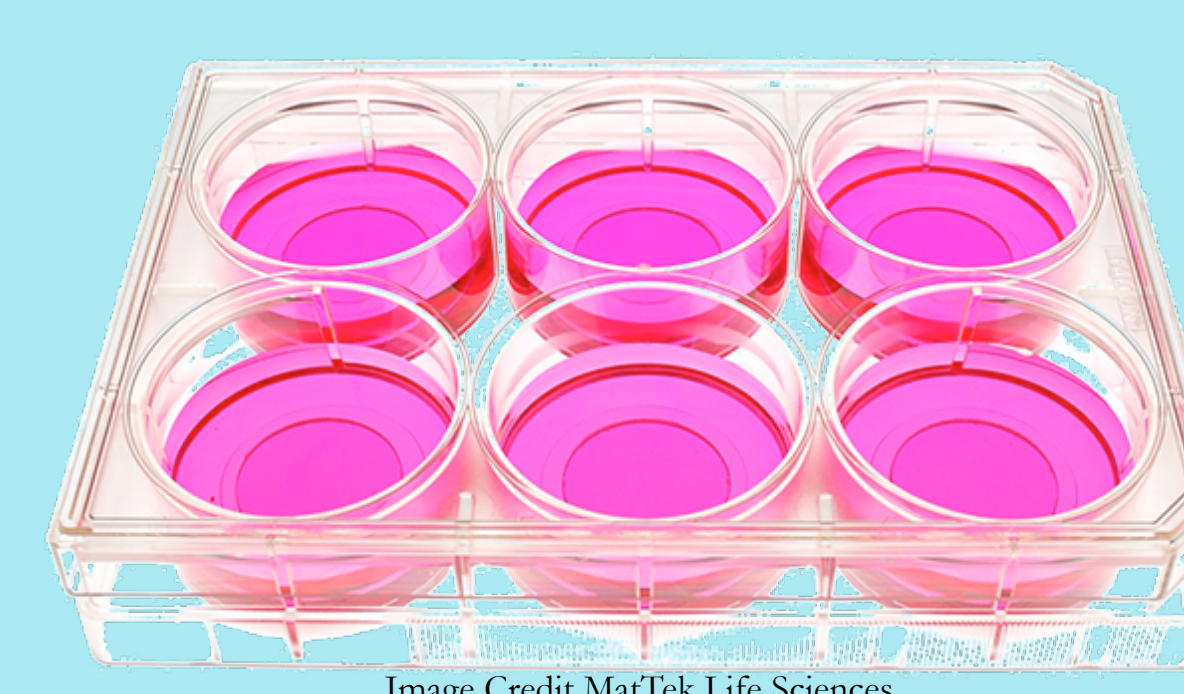


Image Credit: MatTek Life Sciences

Methods

Proliferation Assay and qPCR

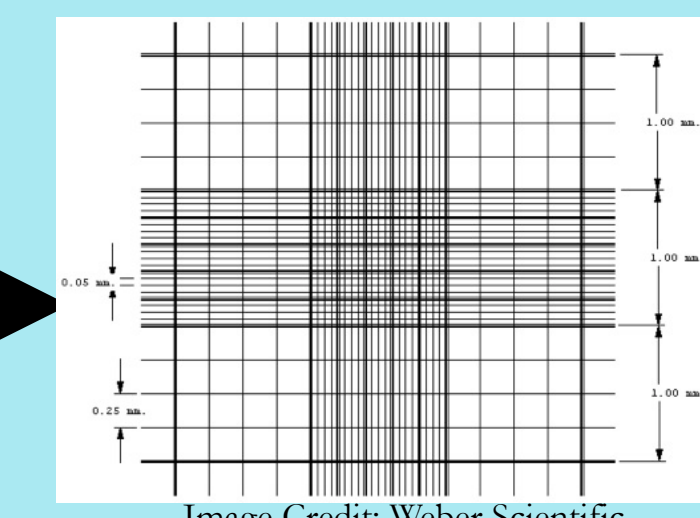


Image Credit: Weber Scientific

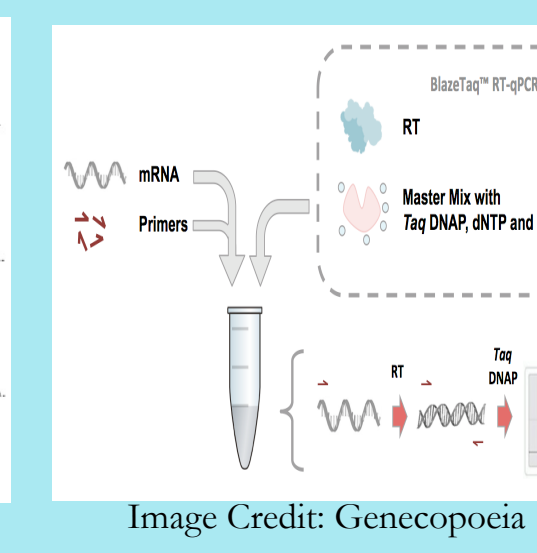


Image Credit: Genecopoeia

- Primary non-asthmatic airway smooth muscle cells
- Cell Culture Exposures
 - 5.5mM glucose (LG)
 - 25mM glucose (HG)
 - LG + 1uM nicotine (LG+N)
 - HG + 1uM nicotine (HG+N)

- Proliferation Assay
 - Baseline manual count
 - 3 day manual count
 - 5 day manual count

- qPCR markers for
 - Contractile (SM22)
 - Synthetic (COL1A1, IL8)

Background:

Asthma is a chronic obstructive lung disease with both environmental and genetic components

Maternal diabetes and environmental tobacco smoke are two major risk factors

Airway smooth muscle (ASM) plays a major role in asthma development

Objective: Explore phenotypic changes in airway smooth muscle in response to hyperglycemia and nicotine

Hypothesis Co-exposure of airway smooth muscle cells to hyperglycemia and nicotine causes a greater alteration in phenotype than either exposure alone.

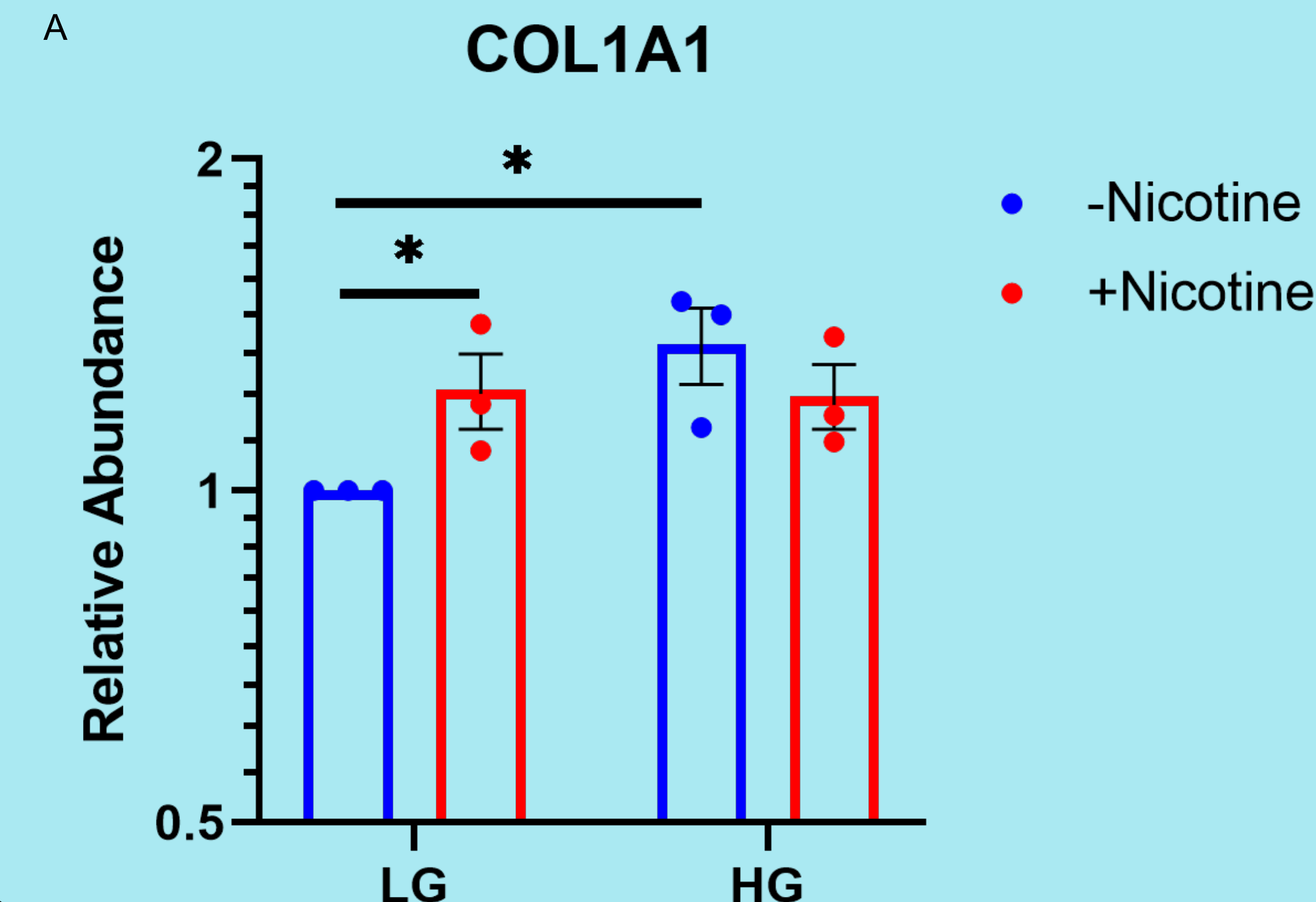


Figure 1: The effect of hyperglycemia and nicotine exposure on ASM synthetic phenotype marker COL1A1. Results normalized to LG condition. Data presented on log2 scale. n=3, different primary cells from one male and two female donors. Data presented as mean +/- SEM. Results analyzed using two way ANOVA with Fishers LSD post test. *p<0.05 based on post test analysis

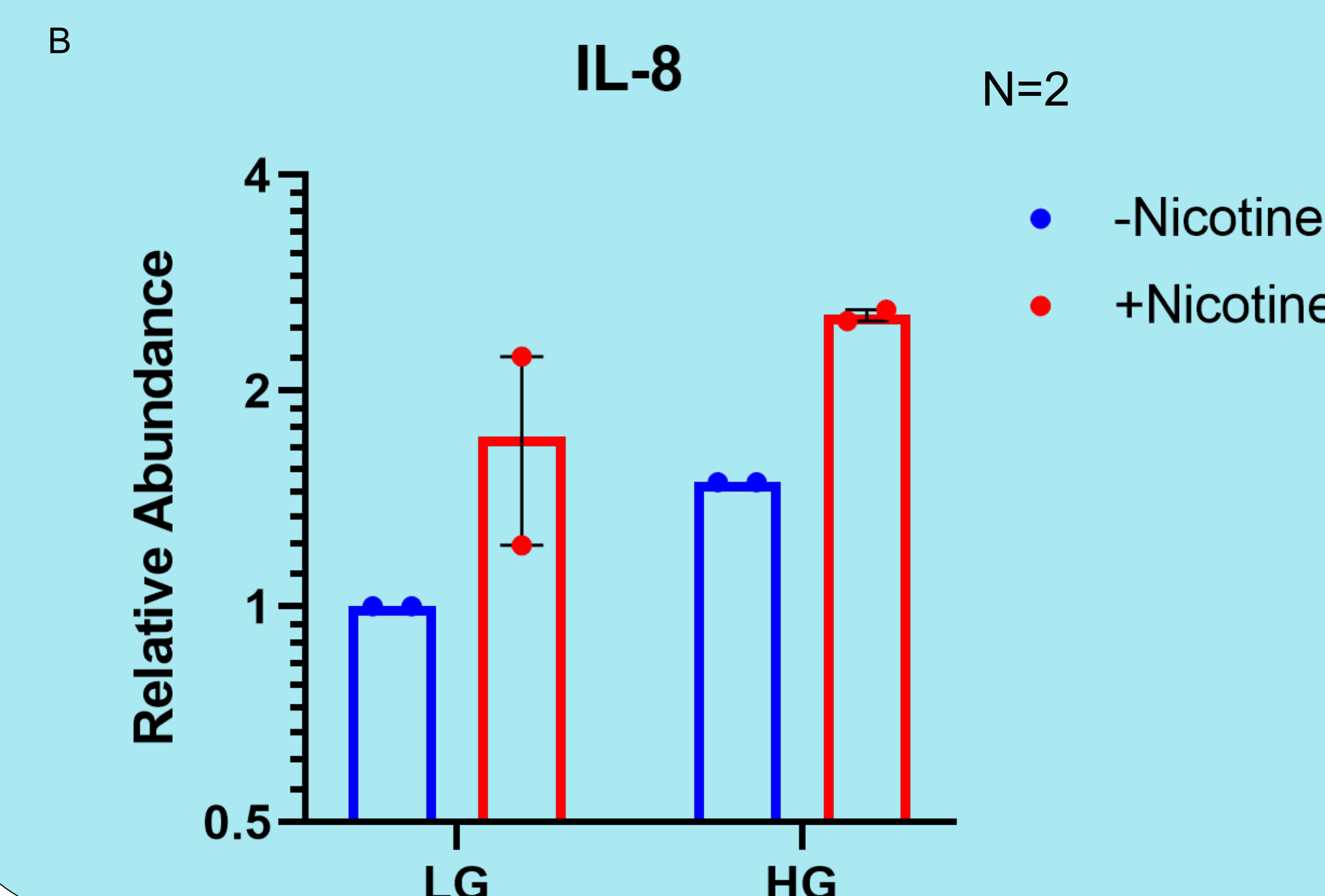


Figure 2: The effect of hyperglycemia and nicotine exposure on ASM synthetic phenotype marker IL8. Results normalized to LG condition. Data presented on log2 scale. n=2, different primary cells from one male and two female donors.

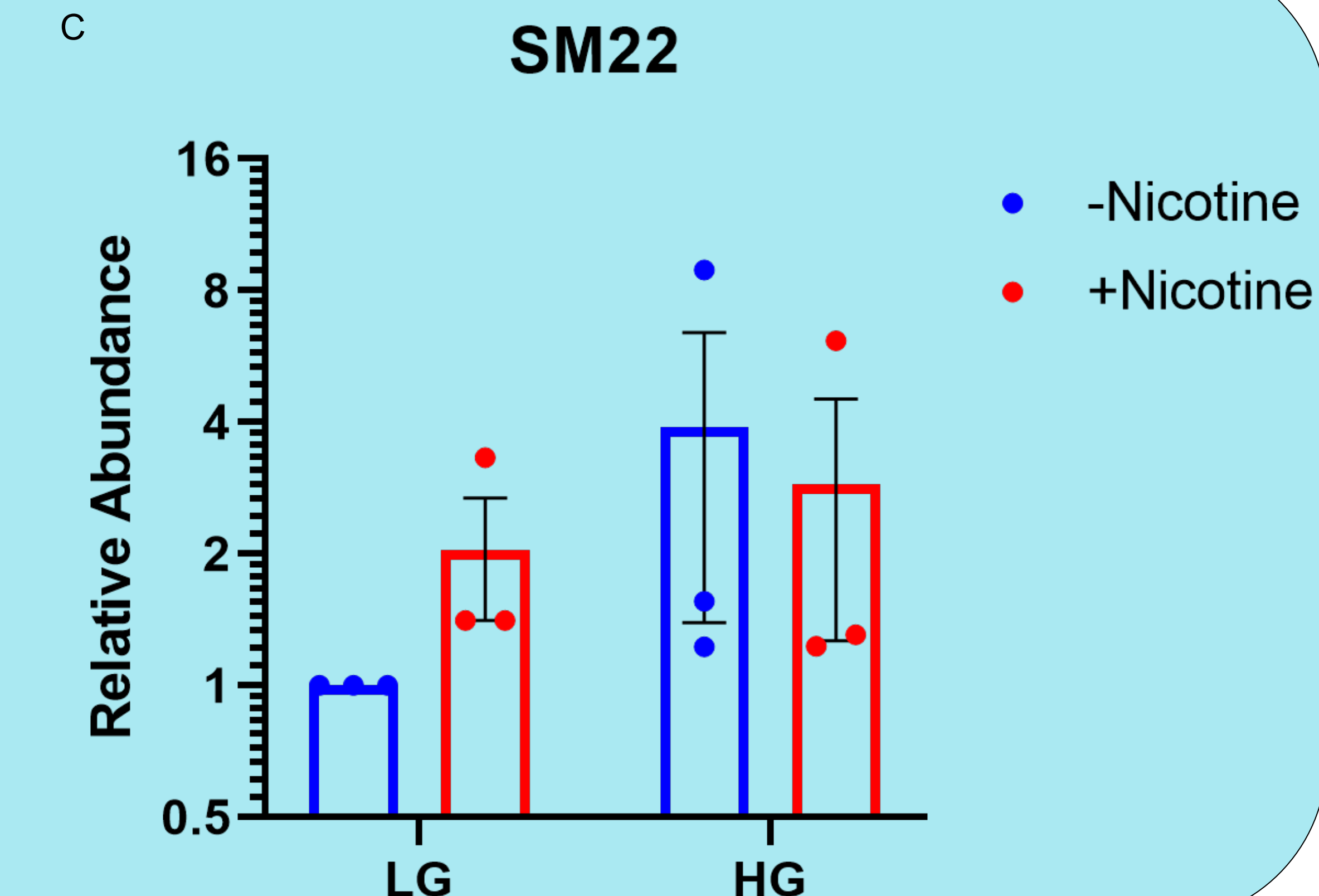


Figure 3: The effect of hyperglycemia and nicotine exposure on ASM contractile phenotype marker SM22. Results normalized to LG condition. Data presented on log2 scale. n=3, different primary cells from one male and two female donors. Data presented as mean +/- SEM. Results analyzed using two way ANOVA with fishers LSD post test.

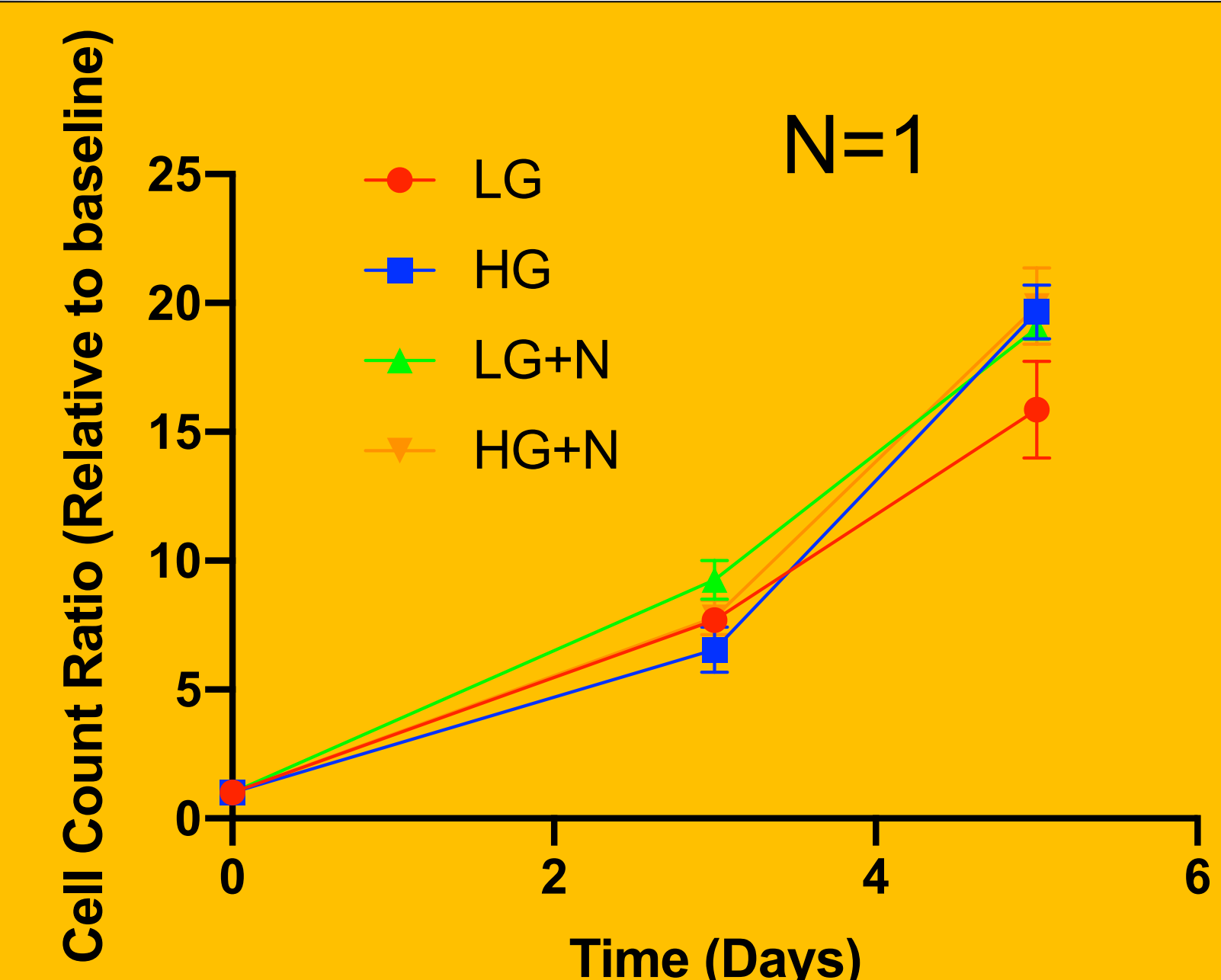


Figure 4: The effect of hyperglycemia and nicotine on ASM proliferation rates. Results are normalized to LG condition. Data is displayed as a ratio. n=1.

Closing Remarks

Unexposed Airway smooth muscle cell

Hyperglycemia and Nicotine

Inflammation->IL8
Fibrotic->COL1A1

Pro Asthmatic Changes!

- Inflammation, fibrosis and increased ASM mass play important roles in airway remodeling
- Through an understanding of how early life environment impacts ASM function, we may be able to develop therapeutic strategies that limit ASM dysfunction in asthma