Integrated high-throughput human airway model and AeroLung for studying asthma pathophysiology and inhaled therapeutic response

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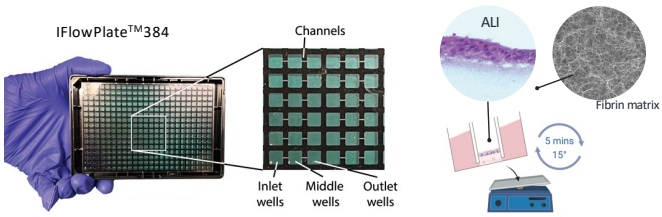
Introduction

The human airway is continually exposed to pollutants, allergens, and therapeutics, and individuals with chronic respiratory diseases like asthma exhibit heightened sensitivity to these exposures, yet most preclinical models lack cellular complexity of disease and scalable delivery of physiologically relevant aerosols. To bridge this gap, we integrate IFlowPlate384 with the AeroLung nebulizer to generate scalable primary airway tissues and deliver aerosols across the entire plate. This platform models healthy and IL-13–stimulated (asthma-like) epithelium and supports screening of inhaled corticosteroids with clinically relevant responses. We further explore sex-dependent differences in mucus secretion and response to corticosteroid therapy.

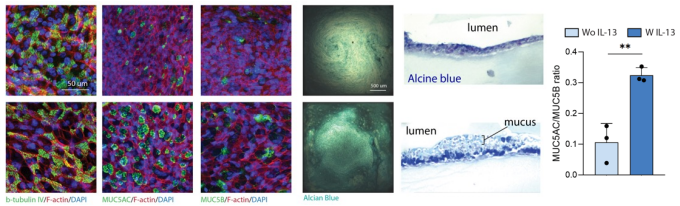
IFlowPlate™384 for airway barrier model

IFlowPlate384 is a customized multi-well plate with interconnected wells. Primary human airway cells were differentiated and matured on the IFlowPlate at air-liquid interface (ALI) over a period of four weeks. During this time, the cells were continuously perfused, receiving nutrients from the basolateral compartment.



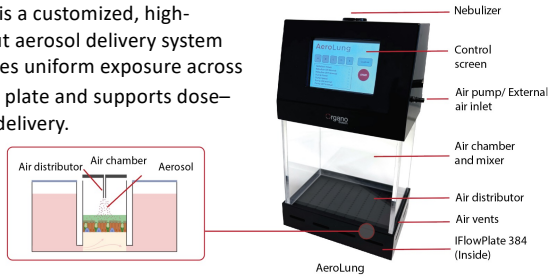
Asthmatic airway model

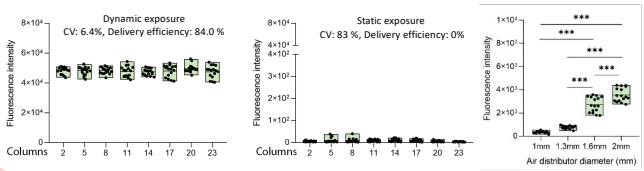
To simulate asthmatic conditions, airway barriers were stimulated with IL-13, which induced a significant increase in mucus secretion, particularly from MUC5AC (+) mucin-producing cells. A thick mucus layer was observed at the airway ALI interface compared to healthy controls. IL-13 exposure did not significantly alter the function of ciliated cells or the secretion of MUC5B mucin.



AeroLung for scalable aerosol delivery

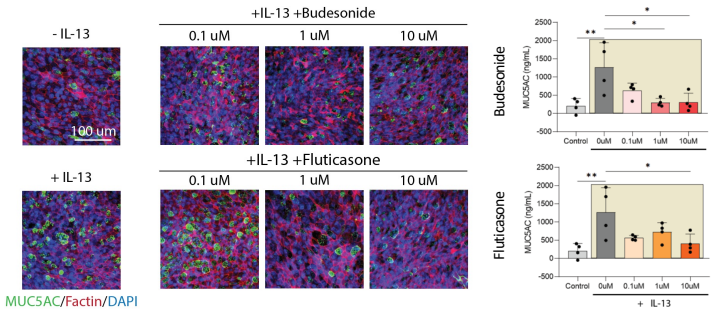
AeroLung is a customized, high-throughput aerosol delivery system that enables uniform exposure across and entire plate and supports dose–response delivery.





Modeling inhaled corticosteroid

Inhaled corticosteroids (budesonide, fluticasone) were delivered using AeroLung in the IL-13 stimulated asthmatic epithelium. These therapeutics significantly reduced MUC5AC secretion and goblet cells hyperplasia, mirroring clinical responses.



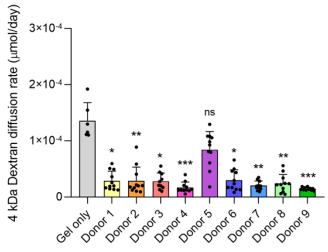
Conclusion

The integrated IFlowPlate384–AeroLung platform enables scalable modeling of healthy and IL-13–stimulated asthmatic airway epithelium with physiologic aerosol delivery, revealing sex-dependent differences in disease features and therapeutic response.

Phase 0 clinical trial on plate

IFlowPlate384 enables studying sex and donor-specific differences in asthma phenotypes such as mucus production, and response to corticosteroid efficacy using epithelial cells from male and female donors with and without estradiol, progesterone, and testosterone.

Donor	Sex	Age	Ethnicity
Donor 1	Female	73	African-American
Donor 2	Female	67	Caucasion
Donor 3	Female	18	Caucasion
Donor 4	Female	70	Caucasion
Donor 5	Female	41	African-American
Donor 6	Male	12	Caucasion
Donor 7	Male	44	Asian
Donor 8	Male	55	Caucasion
Donor 9	Male	32	Black



References

1. Jozani, K. A., et al. The Canadian Journal of Chemical Engineering, 2023.
2.Rajasekar, S., et al. Adv Mater, 2020.