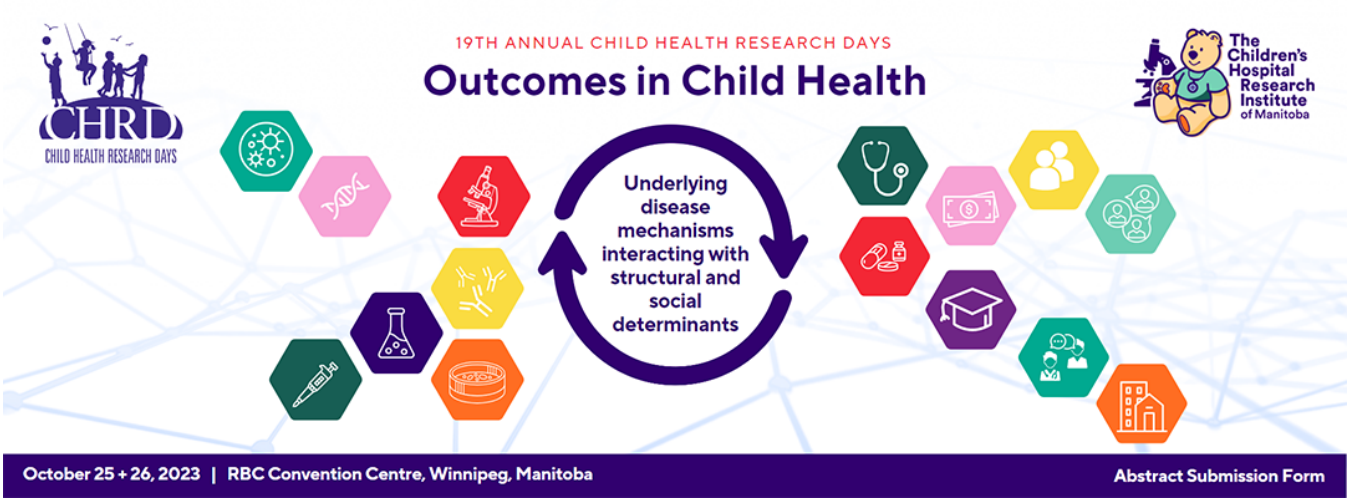

CHRD 2023: Abstract Submission Form

Submitter Name
Mojdeh Matloubi

Presenter Name
Mojdeh Matloubi

Presenter Status
PhD Student

Research Category
Basic Science

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Title
Airway epithelial cell (AEC)-derived Sema3E alleviates airway hyperresponsiveness and remodeling in a sex-dependent manner in allergic asthma

Background
Recent studies have highlighted the potential therapeutic role of Sema3E-plexinD1 in ameliorating asthma severity by reducing airway hyperresponsiveness (AHR), inflammation, and airway remodeling. RNAseq data have indicated that airway epithelial cells (AEC) are the primary source of Sema3E in the lungs. Moreover, the Severe Asthma Research Program (SARP) has revealed a strong association between AEC-Sema3E and severe asthma in humans. We have observed a significant decrease in the level of Sema3E in the airway epithelial layer and bronchoalveolar lavage fluid (BALF) along with the severity of asthma from mild to moderate and severe in humans, correlating with reduced FEV1 and compromised lung function.

Objective
AEC-derived Sema3E is crucial in maintaining airway homeostasis in allergic asthma.

Methods
AEC-specific Sema3E inducible transgene (Sema3E Stopfl/fl/ Scgb1a1tm1(cre/ERT), and wild-type (Sema3E Stopfl/fl) mice were subjected to tamoxifen and HDM acute allergen protocol. AHR parameters were measured using the FlexiVent ventilator. Transgene expression of Sema3E in the lung was visualized by immunofluorescence staining and Real-Time PCR. Moreover, Sirus-red and Periodic acid–Schiff staining were used to visualize collagen deposition and mucus production, respectively. Flow cytometry

was used to analyze cell suspensions from lung tissue, spleen, BALF, and blood.

Results
At the baseline, we observed enhanced Sema3E mRNA expression within the lung tissue but not in the colon upon tamoxifen treatment. Furthermore, the number of immune cells in the lung, spleen, blood, and BALF was similar in tamoxifen-treated compared to non-tamoxifen-treated AEC-Sema3E, Sema3E-Stopfl/fl, and Scgb1a1-Cre mice, indicating that the baseline state is not altered. AEC-specific Sema3E overexpression significantly reduced airway resistance compared to Cre- mice, specifically in male mice. Moreover, AEC-Sema3E overexpression decreased airway EC hyperplasia, with a 25% reduction in mucus production and a 50% reduction in sub-epithelial fibrosis.

Conclusion
airway epithelial-derived Sema3E is critical in reducing AHR and tissue remodeling in allergic asthma.

Authors

Name	Email	Role	Profession
Mojdeh Matloubi	matloubm@myumanitoba.ca	Presenting Author	Graduate
Lianyu Shan	lianyu.shan@umanitoba.ca	Co Author	Other
Ifeoma Okwor	ifeoma.okwor@umanitoba.ca	Co Author	Other
Latifa Koussih	latifa.koussih@umanitoba.ca	Co Author	Other
Abdelilah S. Gounni	abdel.gounni@umanitoba.ca	Co Author	Full Professor