CHRD 2024: Abstract Submission Form

Presenter Name
Folayemi Olayinka-Adefemi

Presenter Status
PhD Student

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
PI3kδ Hyperactivation (APDS) In B Cells Drives Lung Architecture Breakdown and Airway Dysfunction.

Background
Activated PI3Kdelta-Syndrome(APDS) is a congenital immune deficiency caused by PI3KD gene mutations and is characterized by severe immunodeficiency, recurrent respiratory disease and bronchiectasis starting in early childhood. While B-cell dysfunction is known to occur in the lymphoid tissues of patients with the disease, its impact on the respiratory tract is unclear.

Objective
This study aims to investigate if PI3Kδ hyperactivation in B-cells can disrupt lung function. We hypothesize that PI3Kdelta-mediated dysregulated B-cells in the lungs impair antibody production, lung immune cell/cytokine responses and airway function.

Methods
In a quantitative study, 15 genetically modified mice (PI3KδGOF//B) with the PI3Kδ gene mutation mimicking APDS in humans, and control/WT group (no mutation) were assessed at 12 weeks for airway function and lung histopathology at steady state. Mice were subsequently challenged for experimental asthma (using house dust mite) to recapitulate airway. Tests done included Airway hyper-responsiveness (AHR), Lung histopathology, antibody assessment by ELISA, and immune cell/cytokine analysis using the laser-based test, Flow cytometry. Data were statistically analyzed using ANOVA and students T-test ($p<0.05$).

Results
Lungs of PI3KδGOF//B mice at steady state and in asthma showed increased Total airway resistance (Rrs)($p= 0.0001$), Tissue damping (G)($p= 0.0001$) and Elastance (H)($p= 0.015$) when compared to control group.
Histopathology revealed a compromised lung tissue architecture in the mutants following asthma challenge marked by an increase in airway inflammation(H&E)($p= 0.03$), mucus ($p= 0.005$) and collagen deposition($p= 0.06$) in the airways.
Lung immune cell assessment in the mutant revealed the expansion of B-cells ($p= 0.040$) which expressed the suppressive markers PDLI($p= 0.020$) and interleukin IL10 at baseline($p= 0.004$) and in disease($p= 0.01$).
IgE antibody levels were decreased($p=0.016$) while IgM ($p=0.010$) was increased in the mutants, characteristic of a compromised antibody response.

Conclusion
The results support our hypothesis that APDS in B cells undoubtedly disrupts lung homeostasis and impairs airway function.

Do you have a table/figure to upload?
No

Authors

Name	Email	Role	Profession
Folayemi Olayinka-Adefemi	olayinkf@myumanitoba.ca	Presenting Author	Graduate
Mojdeh Matloubi	matloubm@myumanitoba.ca	Co Author	Graduate
Ambrosia Smith-Brunetta	smithbra@myumanitoba.ca	Co Author	Graduate
Peyton Malcom	malcomp@myumanitoba.ca	Co Author	Graduate
Milad Sabzevary-Ghahfarokhi	sabzevam@myumanitoba.ca	Co Author	Graduate
Lianyu Shan	Lianyu.Shan@umanitoba.ca	Co Author	Graduate
Sen Hou	Sen.Hou@umanitoba.ca	Co Author	Graduate
Sujata Basu	Sujata.Basu@umanitoba.ca	Co Author	Graduate
Andrew Halayko	Andrew.Halayko@umanitoba.ca	Co Author	Full Professor
Abdelillah Soussi-Gounni	Abdel.Gounni@umanitoba.ca	Co Author	Full Professor
Aaron Marshall	Aaron.Marshall@umanitoba.ca	Co Author	Full Professor