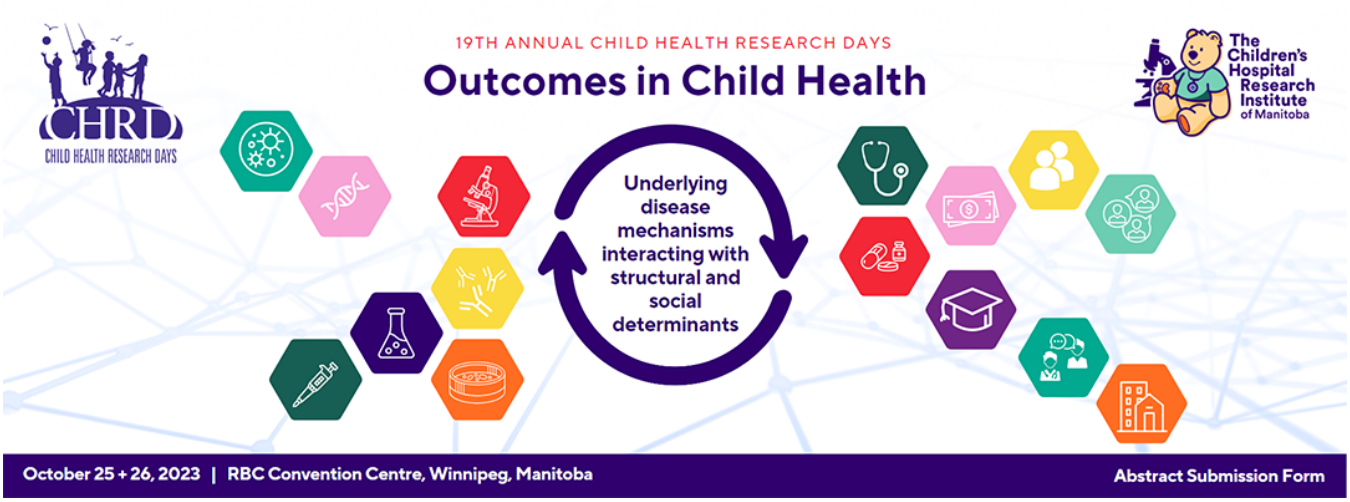

CHRD 2023: Abstract Submission Form

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Presenter Status
PhD Student

Research Category
Basic Science

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Title
B-Cell Specific Activated Pi3kδ Syndrome (APDS) Compromises Lung Homeostasis & Airway Function.

Background
Activating mutation of the PI3Kδ gene in humans causes APDS. This disease is characterized by severe immunodeficiency and recurrent respiratory disease first occurring in infancy or childhood (0–10 years of age), followed by bronchiectasis and autoimmunity in later years. Defects in this gene significantly impact B-cell function in lymphoid tissue yet the B-cell-specific effects of this mutation in the respiratory tract are unknown.

Objective
To determine how B cell-specific PI3KδGOF//B gain-of-function (APDS) mutation impacts lung homeostasis and function.

Methods
The Immune cells, cytokines and lung function of PI3KδGOF//B mutant mice at baseline and in an experimental asthma disease (using House Dust Mite) were examined using Flow cytometry, Cytology, Immunohistology and Airway Hyper-responsiveness (AHR) tests. Data were analyzed using Turkey's multiple comparisons of means test (significance = $p<0.05$).

Results
The lungs of PI3KδGOF//B mice show an increase in the suppressive cytokine, IL10 from B cells at baseline ($p= 0.016$) and in disease ($p= 0.011$) compared to control-(WT) mice. They also express the

innate immune cell markers CD5 and CD43. IL10+ Plasma cells were elevated in their lungs (p= 0.030), bronchial lymph node (p= 0.030) and spleen (p= 0.020). Cytology of the lungs and Bronchoalveolar cells indicated an expansion of Eosinophils (p=0.016, 0.040). The pro-inflammatory cytokines IFN□ and IL17 were unremarkably however, the anti-inflammatory cytokine IL4 was decreased (p= 0.020) further supporting the hypothesis of a suppressed state in the lung. IgE antibody levels were decreased(p=0.016) while IgM(p=0.010) was increased, characteristic of a compromised antibody response. Immunohistology of the lungs revealed a two-fold increase in mucus and collagen deposition (Airway damage) while AHR revealed a more resistant lung (Rrs) in mutants compared to WT.

Conclusion
The Results indicate that B cell-specific APDS drives the expansion of IL10-producing-B cells in the lungs giving it a suppressive phenotype which invariably disrupts lung homeostasis and airway function.

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