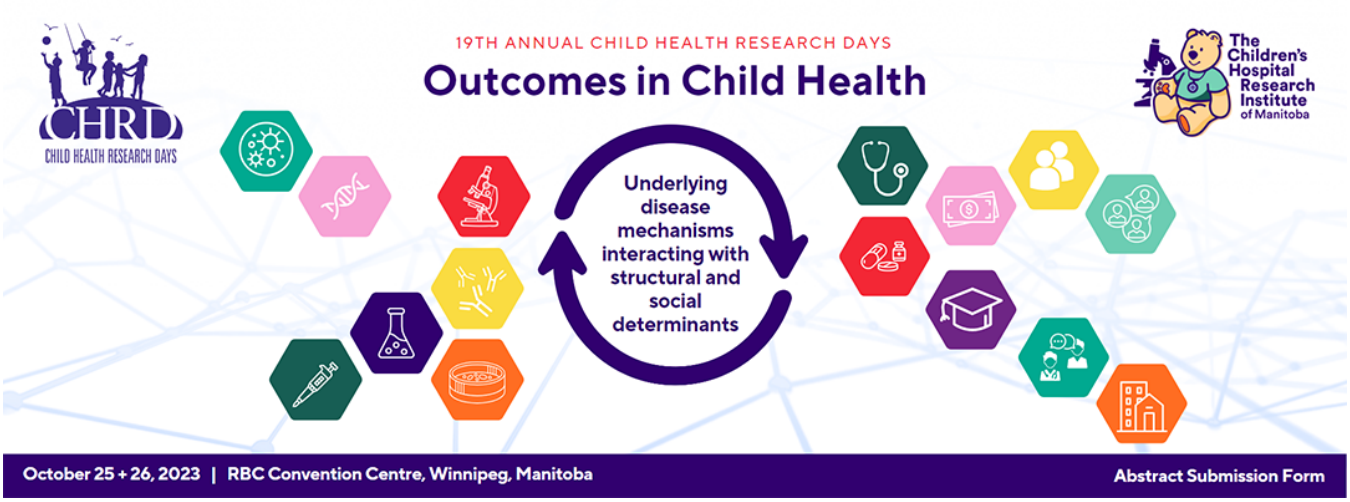

CHRD 2023: Abstract Submission Form

Submitter Name
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Presenter Status
Non-Trainee

Research Category
Basic Science

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Title
Pro-inflammatory role of oxidized phospholipids in Tumor Necrosis Factor induced gene transcription and efficacy of glucocorticoid treatment

Background
Inhaled glucocorticoids (GCs) are the primary controller therapy for asthma as they suppress persistent inflammation. GCs can stymie pro-inflammatory inducible gene transcription through trans-repression of the NF-kB transcription factor. We have shown that oxidized phosphatidylcholine (OxPAPC) in asthmatic patients is pro-inflammatory. We investigated OxPAPC effects on NF-kB-induced gene transcription, and the inhibitory effects of GCs.

Objective
To investigate the effect of OxPAPC on NF-kB-induced gene transcription, and the inhibitory effects of GCs.

Methods
NF-kB luciferase reporter human bronchial epithelial cells, 3kBU BEAS-2B were treated with tumor necrosis factor (TNF) (10ng/mL, 5 hrs). NF-kB inducible transcription was measured by Firefly Luciferase Assay (n=5). Some cultures were also pre-treated with fluticasone propionate (FP). Other cultures were pre-treated with OxPAPC (40 or 80ug/mL) prior to TNF, or TNF/FP. Data were analyzed by one-way or two-way ANOVA.

Results

TNF triggered a 110 percent increase in NF-kB dependent gene activation. FP decreased TNF-induced luciferase activity in a concentration-dependent manner (maximum suppression 45±20% with 10-5M FP). OxPAPC alone was not sufficient to induce NF-kB dependent transcription, however, OxPAPC pre-treatment increased TNF luciferase activity (19.71±7.10). OxPAPC did not prevent inhibitory effects of FP, but NFkB-induced luciferase activity remained higher after OxPAPC-TNF-FP (16863±5355) compared to FP-TNF (7607±3806).

Conclusion
GCs inhibit TNF-induced NFkB-dependent gene transcription in human airway epithelial cells. OxPAPC and TNF synergistically activate NFkB-induced gene transcription, resulting in persistence of higher transcriptional activity. This suggests that OxPAPC may contribute to persistent steroid refractory inflammation in asthma.

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