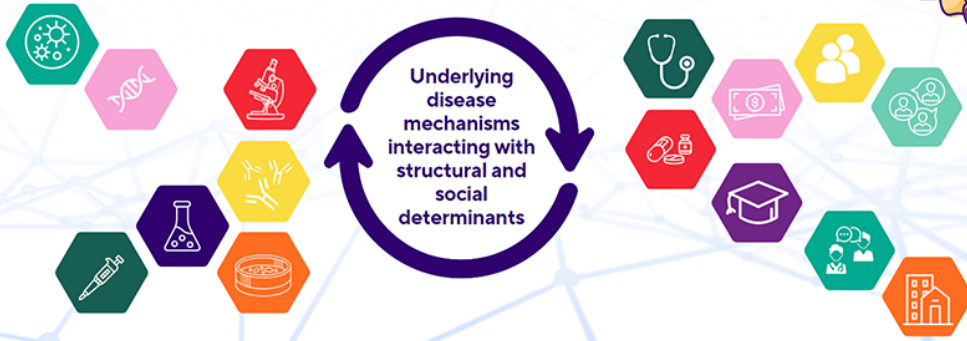




19TH ANNUAL CHILD HEALTH RESEARCH DAYS
Outcomes in Child Health



October 25 + 26, 2023 | RBC Convention Centre, Winnipeg, Manitoba

Abstract Submission Form

CHR D 2023: Abstract Submission Form

Submitter Name

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Presenter Name

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Presenter Status

Masters Student

Research Category

Basic Science

Role in the project

Design
Perform Experiments
Analyze Data
Write Abstract

Title

Do EpOMEs and DiHOMEs cause Airway Smooth Muscle Contraction?

Background

Oxylipins are lipid mediators found within the lung and can regulate airway function, especially in Asthma. Well known oxylipins including Prostaglandins and leukotrienes can mediate Airway Smooth Muscle (ASM) contraction or relaxation. However, the function of most oxylipins in the lung remains unknown (Figure 1.). EpOMEs (epoxy-12-octadecenoic acid) and DiHOMEs (dihydroxy-12-octadecenoic acid), which may activate TRP channels, are found in the lung following exposure to pollutants, but remain unexplored in the context of ASM contractility.

Objective

Our objective is to discover whether EpOMEs and DiHOMEs use TRP channels to cause ASM contraction.

Methods

Human ASM were loaded with a calcium indicator dye and changes in calcium after addition of 9,10-EpOME, 12,13-EpOME, 9,10-DiHOME, 12,13-DiHOME was measured. Allyl-isothiocyanate (TRP activator) and Histamine were used as a positive control. Phosphorylated Myosin Light Chain (p-MLC) was measured as a surrogate for contraction via Western Blotting. Data was analyzed via One-Way ANOVA and GraphPad.

Results

Intracellular calcium concentration was increased in ASM by 10 μ M of 9,10 EpOME (117 η M \pm 74), 12,13

EpOME (424 η M \pm 246), 9,10 DiHOME (20 η M \pm 11), 12,13 DiHOME (58 η M \pm 29). Contextually, control elicited a small increase (12 η M \pm 1), whereas positive controls Allyl-isothiocyanate and histamine caused a 630 η M \pm 96 and 542 η M increase, respectively. P-MLC abundance compared to control was increased following treatment with 9,10 EpOME (35%), 12,13 EpOME (102%), 9,10 DiHOME (80%), 12,13 DiHOME (39%). Contextually, Histamine and Allyl-isothiocyanate had a 45% and 54% increase, respectively.

Conclusion

EpOMEs and DiHOMEs all caused calcium release and increased p-MLC, but with variable responses. This data gives strong evidence to suggest that EpOMEs and DiHOMEs are possible contractile agonists. Upcoming experiments will look at whether EpOMEs or DiHOMEs use TRP channels for calcium release and downstream contractile functions. Further evidence is needed to understand the mechanism of this response and whether these molecules can be targeted as a therapeutic for Asthma.

Table/Figure File

Iceberg figure oxylipins final.pdf

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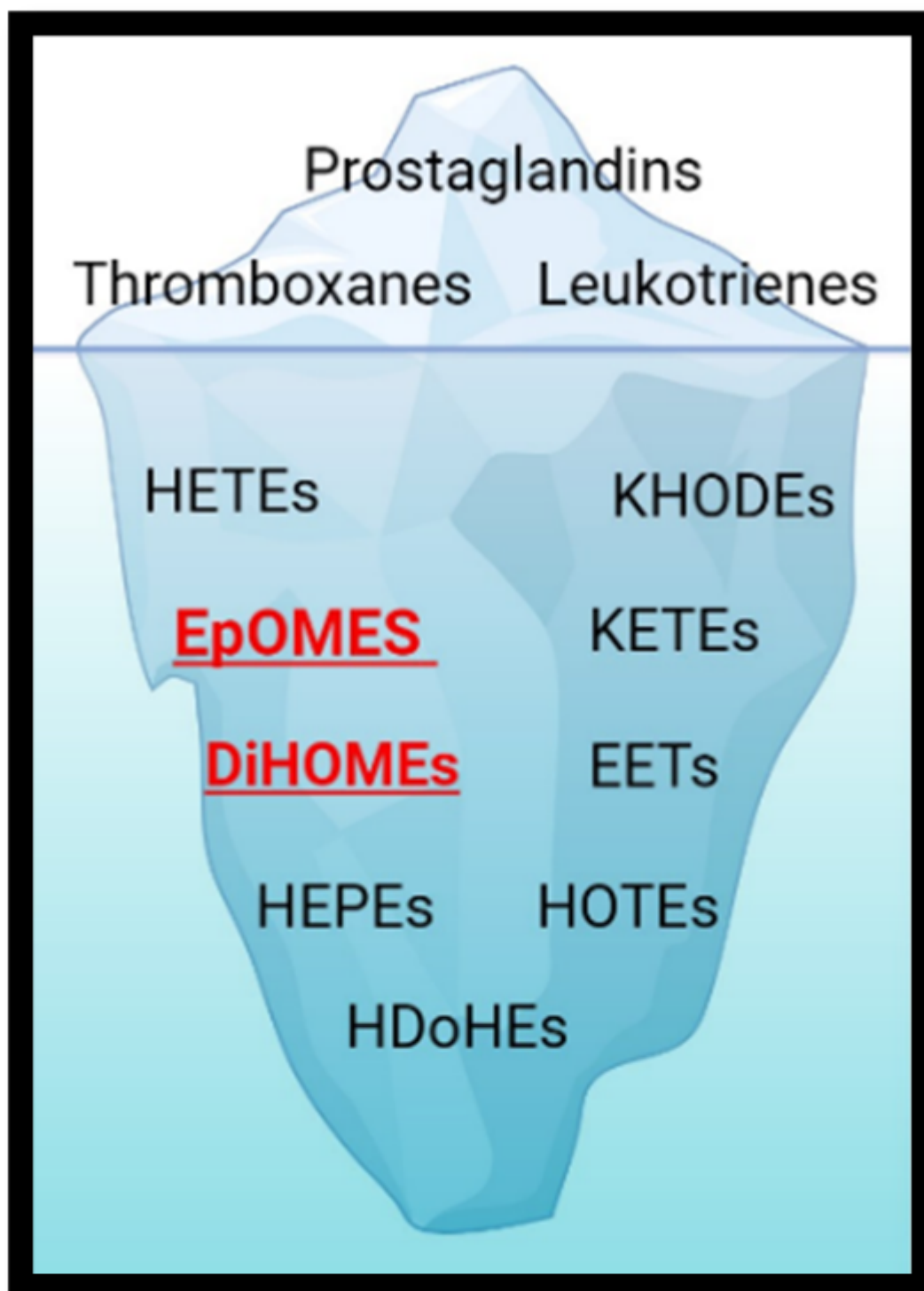


Figure 1. Iceberg concept showing the lack of knowledge on many lipids found in the lungs of asthmatics.