ABSTRACT SUBMISSION FORM

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SEX + GENDER

Exploring the role of sex and gender on health research

CHILD HEALTH RESEARCH DAYS

CHRD 2020: Abstract Submission Form

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Title
Oxidized Phosphatidylcholine Causes Airway Narrowing: Novel Indication for Airway Hyperresponsiveness in Asthma

Background
Asthma is a chronic lung disease characterized by excessive airway narrowing that affects 12% of Canadian children. Oxidative stress, a feature of asthma, causes the peroxidation of phosphatidylcholine a major phospholipid in lung cells and extracellular fluids. Oxidized phosphatidylcholines (OxPCs) are pro-inflammatory and accumulate in the lungs of mice and humans after inhaled allergen challenge. We have shown that OxPCs trigger ryanodine receptor-mediated intracellular Ca2+ flux in human airway smooth muscle cells.

Objective
Here, we test the hypothesis that OxPCs cause airway narrowing under control of pathways that regulate cytoplasmic Ca2+ flux in human airway smooth muscle.

Methods
Murine thin-cut lung slices (TCLS) and phase-contrast video microscopy were used to assess airway narrowing. Real-time changes in airway lumen area were recorded for 3 min, after exposure to OxPC (ie. oxidized 1-palmitoyl-2-arachidonoyl-sn-glycero-3-phosphocholine, 80 µg/ml) in the presence and absence of extracellular Ca2+. To determine the role of intracellular Ca2+ stores, TCLS were pre-treated with ryanodine channel inhibitors (ryanodine (100 µM) and caffeine (25 mM)). NIH/Scion Image J software was used to determine changes in airway lumen area.

Results
OxPC (80ug/mL) induced significant, 15% airway closure, compared to non-oxidized phosphatidylcholine. As a positive control, 0.1 µM methacholine induced 25% airway constriction. In the absence of extracellular Ca2+, OxPC did not induce any airway narrowing, while methacholine-induced airway closure was 60% lower than in presence of extracellular Ca2+. When TCLS were pre-treated with ryanodine receptor

inhibitors (ryanodine or caffeine), OxPC-induced airway narrowing was completely abrogated, whereas MCh-induced airway closure was unaffected.

Conclusion
These findings demonstrate that OxPCs mediate airway narrowing via influx of Ca2+ from both the extracellular source and the ryanodine receptor regulated stores of the sarcoplasmic reticulum. This implicates a role of OxPCs in airway hyperresponsiveness, a hallmark feature of asthma.

Theme:
Basic Science

Do you have a table/figure to upload?
No

Are you willing to participate in Goodbear's Den?
Yes

Presenter Status:
Undergraduate Students

What was your role in the project?
Perform experiments, and analyze data

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