CHRD 2021: Abstract & Poster Submission Form

Submitter Name

Jigneshkumar
First

Vaghasiya
Last

Email

vaghasij@myumanitoba.ca

Research Category:

- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

What was your role in the project?

- ☑ Design
- ☑ Perform Experiments
- ☑ Analyze Data
- ☑ Write Abstract
- ☐

Presenter Status:

- ○ Undergraduate Students
- ○ Masters Student
- ◉ PhD Student
- ○ Post-Doctoral Fellows
- ○ Residents
- ○ Non-Trainee

Title

Intranasal Delivery of Neutralizing Antibody for Oxidized Phosphatidylcholines Prevents Airway Neutrophilia in Allergen Challenged Mice

Background

There is considerable medical interest to develop new therapy for asthmatics in whom symptoms are poorly controlled by conventional therapy. In human and mice, we have shown that allergen challenge induces accumulation of pro-inflammatory oxidized-phosphatidylcholines (OxPCs) in parallel with the emergence of airway-hyperresponsiveness (AHR).

Objective

We hypothesized that E06, a natural IgM antibody that neutralizes pro-inflammatory properties of OxPCs, ameliorates allergen-induced airway inflammation and AHR

Methods

We used house dust mite (HDM)-challenged BALB/c mice (female, 6-8 weeks) that were randomized into different groups (n=4/group): vehicle [PBS]; E06 [1-ug]; E06 [10-ug]. Age-matched allergen-naïve mice were used as controls. PBS/E06 were instilled intranasally (i.n.) 1-hr before each HDM challenge (25 ug/mouse, i.n.) daily for 2 weeks (5 days/week) and 48-hrs after the last treatment, pulmonary function in response to methacholine was assessed using a flexiVENT small animal ventilator. We also performed immunophenotype analysis of inflammatory cells in bronchoalveolar lavage (BALF) using an Attune NxT flow cytometer. Data were analyzed by one-way ANOVA with Dunnett's post-hoc test.

Results

HDM challenge induced a significantly accumulation of inflammatory cells in BALF. Compared to allergen-naïve controls, this included increase in SiglecF+CD11c--positive eosinophils (35-fold), LY-6G+CD11b+-positive neutrophils (3 fold), B220-expressing B cells (10-fold), CD3+-lymphocytes (4-fold), and CD3+CD4+-lymphocytes (6-fold). This accompanied by a significant increase in AHR (ie. 60% and 100% higher methacholine-induced central airway resistance and peripheral lung tissue resistance, respectively). PBS treatment did not affect HDM-induced responses, nor was E06 [1-ug] sufficient to significantly affect HDM-induced inflammation and AHR. Notably, E06 [10-ug] specifically abrogated HDM-induced accumulation of neutrophils and alveolar macrophages in BALF. Moreover, this correlated with upto 17% reduction of methacholine-induced peripheral lung resistance.

Conclusion

Prophylactic treatment of mice with intranasal E06, OxPCs-neutralizing antibody, can abrogate allergen induced airway neutrophilia, which correlates with suppressed peripheral airway responsiveness. This implicates OxPCs as a treatable target for new asthma therapies.

Authors

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Name	Email	Role	Profession
Jignesh Vaghasiya	vaghasij@myumanitoba.ca	Presenting Author	Graduate Student
Sujata Basu	SBasu@chrim.ca	Co Author	Research Associate
Alaina Bagan	bagana@myumanitoba.ca	Co Author	Undergraduate Student
Amir Ravandi	Amir.Ravandi@umanitoba.ca	Co Author	Assitant Professor
Andrew J. Halayko	Andrew.Halayko@umanitoba.ca	Co Author	Full Professor