ABSTRACT SUBMISSION FORM

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Exploring the role of sex and gender on health research

CHILD HEALTH RESEARCH DAYS

CHRD 2020: Abstract Submission Form

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Title
IGFBP3 Modulates Lung Pathophysiology In An Allergen-Specific Manner In Murine Models Of Asthma

Background
Insulin like growth factor binding protein (IGFBP)-3 binds insulin-like growth factor-I (IGF-I) and plays a role in asthma pathogenesis. Extracellular IGFBP-3 prevents activation of IGF-1 induced cell proliferation. Intracellularly acts through nuclear hormone receptors and nuclear ligands. Transforming growth factor-β and tumor necrosis factor-α associated with lung inflammation also increase IGFBP-3 expression.

Objective
Literature suggest that IGFBP3 can prevent asthma. We tested the hypothesis that IGFBP3 overexpression modulates change in murine lung function induced by ovalbumin (OVA) or house dust mite (HDM).

Methods
Female 8-9 week old mice overexpressing human IGFBP-3 (phosphoglycerate kinase (PGKBP3) and their wild type were sensitized with intraperitoneal OVA (2ug, Day 1 and 11) then challenged with intranasal OVA (50ug, Day 11, 18 and 19) OR challenged with intranasal HDM extract (25µg, 5 days/week for two weeks). Lung function was assessed at 72 hours after final allergen challenge using a Scireq flexiVent small animal ventilator

Results
Baseline lung function were no different for PGKBP3 and WT mice (n=6).
In WT mice, OVA and HDM exposure showed similar increase in Newtonian resistance (Rn), 54% and 52% ($p<0.001$), tissue damping (G), 192% and 185 % ($p<0.0001$) and tissue elastance (H), 53% and 54% ($p<0.001$) in response to 25 and 50 mg/mL MCh challenge.
PGKBP3 mice were refractory to the effects of OVA sensitization and challenge, as all parameters of lung function were unchanged compared to allergen naïve PGKBP3 mice.
In contrast, IGFBP3 overexpression conferred no protective effect for HDM challenge. HDM-challenged

PGKBP3 and WT showed significant increase of Rn, G and H compared to naïve controls.

Conclusion
IGFBP3 overexpression prevents asthma pathophysiology in mice sensitized and challenged with OVA, but is without effect in mice challenged with HDM. These findings clearly support our hypothesis that IGFBP3 plays a selective role in modulating inflammatory pathways induced by different allergens.

Theme:
Basic Science

Do you have a table/figure to upload?
No

Are you willing to participate in Goodbear's Den?
No

Presenter Status:
Non-Trainee

What was your role in the project?
all the above

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