

### **MEETING ABSTRACT**



# B cell Semaphorin 4c expression mitigates the airway hyperresponsiveness and acute inflammation which characterize allergic airway disease

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*From* Canadian Society of Allergy and Clinical Immunology Annual Scientific Meeting 2014 Ottawa, ON, Canada. 23-26 October 2014

#### Background

Semaphorin signaling proteins, initially examined in the context of neuronal axon development, have recently been implicated as regulators of immune cell migration. Our laboratory has determined that expression of Semaphorin 4C (Sema4C) is strongly induced on B cells exposed to Th2 stimulation, and we seek to elucidate its mechanism of controlling allergic airway disease.

#### Methods

Wild-type and Sema4C<sup>-/-</sup> mice were sensitized intraperitoneally using 100  $\mu$ L OVA (0.5 mg/mL ovalbumin and 4 mg/mL aluminum hydroxide in PBS) on days 0 and 14, and were challenged intranasally using 20  $\mu$ L OVA (10 mg/mL ovalbumin in PBS) from days 28 to 30. Sacrifice and analysis of Airway Hyperresponsiveness via flexiVent was performed on day 31. Serum IgE and IL-10 expression levels were measured by ELISA. B cells were phenotyped by fluorescence-activated cell sorting (FACS). B cell motility was measured by migration assays.

#### Results

Please see figure 1.

#### Conclusions

Semaphorin 4C regulates the allergic airway disease through immune synapse-governed cytoskeletal rearrangements in B cells, and minimizes the inflammatory cellular lung infiltration that contributes to airway hyperresponsiveness.

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Published: 18 December 2014

#### doi:10.1186/1710-1492-10-S2-A26

Cite this article as: Lei *et al.*: B cell Semaphorin 4c expression mitigates the airway hyperresponsiveness and acute inflammation which characterize allergic airway disease. *Allergy, Asthma and Clinical Immunology* 2014 **10**(Suppl 2):A26.

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IL-4, and IL-21 for 24 hours (A-D), or 72 hours (E-H). I-L. Sema4C<sup>-/-</sup> (KO) B cells have aberrant actin cytoskeletal structural organization. **M.** KO mice have narrower airway diameter than WT mice. H&E staining of WT (n=6) and KO (n=5) lungs with Allergic Airway Disease (AAD). **N**. KO mice with AAD had a greater percentage of lung-infiltrating lymphocytes (CD4+ T cells, CD19+ B cells, and CD138+ plasma cells) than WT mice. Lymphocytes were recovered using Bronchoalveolar Lavage. **E.** KO mice with AAD had higher serum OVA-specific IgE levels than WT mice. **F.** KO mice with AAD had lower serum IL-10 levels than WT mice.