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Investigating the role of Semaphorin3E in the regulation of immunoglobulin E in HDM-induced asthma

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Background:

Asthma affects millions of people in Canada, including children. Semaphorin3E (Sema3E) is a protein that plays a critical role in immunity to diseases, including asthma. Previously, we reported that mice deficient in Sema3E showed disease exacerbation, and importantly, an elevated serum level of Immunoglobulin E (IgE), during House Dust Mite (HDM)-induced asthma. Because IgE is known as a critical driver of asthma, we hypothesize that Sema3E regulates IgE production in HDM-induced asthma.

Objective:

To investigate the mechanisms through which Sema3E regulates IgE production in HDM-induced asthma.

Methods:

Asthma was induced intranasally *by* treating mice with 25 µg of HDM or saline for two weeks. Mice were sacrificed at 48 hours after the last treatment and the spleens and lungs harvested. Flow cytometry was used to assess the frequencies of IgE-producing B cells, germinal centre B cells, BCL-6, and follicular $CD4^+$ T helper cells.

Results:

We found significantly higher percentages of IgE-producing B cells ($B220^+IgE^+$) in the lungs (but not in the spleens) of *Sema3e*$^{-/-}$ mice compared to wild-type (WT) mice following HDM exposure, suggesting that IgE is produced locally in these mice during HDM-induced asthma. Interestingly, we also found increased percentages of $B220^+GL7^+FAS^+$ GC B cells in the lungs of *Sema3e*$^{-/-}$ mice compared to WT mice. This was associated with increased percentages of lung $CD3^+CD4^+ICOS^+PD1^+$ follicular $CD4^+$ T helper cells (that provide key signals needed by antigen-specific B cells to differentiate into high-affinity antibody-producing cells) and BCL-6 (required for formation and maintenance of GC) in *Sema3e*$^{-/-}$ mice compared to WT control mice.

Conclusion:

Collectively, our data show that in *Sema3e*$^{-/-}$ mice, increased Tfh cells, and a concomitant increase in the GC formation could be contributing to the excessive IgE production and disease exacerbation observed in HDM-induced asthma. Thus, Sema3E could be a critical regulator of IgE in asthma.