Atopic Dermatitis Skin Biopsies Have High Numbers of Activated Mast Cells that Are Inhibited by Antolimab (AK002) After Stimulation Ex Vivo

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- **Methods**: Antolimab (AK002) is a novel, humanized, non-fucosylated IgG1 monoclonal antibody to Siglec-8.
- **Results**: Activated mast cells were elevated in number and were basally activated in AD. Human skin mast cells express the inhibitory receptor Siglec-8, and treatment with AK002 significantly reduces IL-33/TSLP mast cell activation as evidenced by decreased surface markers of activation and cytokine production.

- **Conclusions**: Mast cells appear to be important in AD, and targeting mast cells via Siglec-8 with antolimab may represent a novel therapeutic approach to the treatment of AD and other allergic diseases.

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**Background**

- Loss of epithelial barrier integrity is a critical step in the development of atopic dermatitis (AD) whereby the alarmin cytokines IL-33 and TSLP activate inflammatory cells such as mast cells (MCs) (Figure 1).
- While MCs have been shown to be elevated in AD, there is need for further characterization of their pathogenic role.

**Methods**

- Single-cell suspensions were prepared by enzymatic & mechanical digestion of fresh biopsies from patients clinically diagnosed with AD (n=6) or non-diseased control subjects (n=10).
- Multi-color flow cytometry was performed to quantify immune cells and evaluate the activation state of eosinophils & mast cells as shown in Figure 4.
- Mast cells were FACS-sorted from AD biopsies or non-diseased skin tissues followed by overnight incubation with or without PMA/ionomycin.
- Cell-free supernatants were collected the following day and cytokines were quantified using meso scale discovery (MSD) system.

**Results**

- The following cytokines were analyzed: IL-4, IL-5, IL-6, IL-10, IL-13, IL-18, GM-CSF, INFγ, TNFα, CCL2, CCL3, CCL4, and VEGF.

**Conclusions**

- Human skin mast cells express the inhibitory receptor Siglec-8, and activation of mast cells via FcεRI is inhibited with antolimab.
- Mast cells are elevated in number and are basally activated in AD biopsies with high levels of surface-bound IgE.
- Antolimab inhibits IL-33/TSLP-mediated MC activation in AD skin biopsies, suggesting antolimab can broadly inhibit multiple modes of mast cell stimulation including, IgE, IL-33, and TSLP.
- Mast cells appear to be important in AD, and targeting mast cells via Siglec-8 with antolimab may represent a novel therapeutic approach to the treatment of AD and other allergic diseases.