**Phenotypic Characterization of Inflammatory Bowel Disease Biopsies Reveal That Mast Cells Are Significantly Elevated and Activated In Patients with Ulcerative Colitis**

Bradford A Youngblood, Melissa Butuci, Tina Davis, Alan L Xu, Julia Schanin, Emily C Brock, Bhupinder Singh, Henrik S Rasmussen, Amy Holman, Richard Drake, Kathryn Peterson, and Ann D Flynn

1 Allakos Inc. Redwood City, CA; 2University of Utah, UT

**BACKGROUND**

- Accumulation and activation of mast cells and eosinophils have been implicated in the pathogenesis of several chronic inflammatory gastrointestinal (GI) diseases, including eosinophilic gastrointestinal diseases (EGIDs) and inflammatory bowel disease (IBD).
- Despite the strong association of mast cells and eosinophils in IBD, no further characterization of these cells has been performed.
- Here, we aimed to quantify and evaluate the activation state of mast cells and eosinophils in non-diseased control patients as well as characterized the production of cytokines from human tissue mast cells.

**METHODS**

- Single-cell suspensions were prepared by enzymatic digestion of fresh colon biopsies from patients with IBD or non-diseased control colon tissue.
- Multi-color flow cytometry was performed to identify and evaluate the activation state of mast cells and eosinophils.
- Mast cells were FACS-sorted from non-diseased human colon tissue to evaluate cytokine production from mast cells after overnight stimulation with PMA/ionomycin.
- The inhibitory activity of lirentelimab was evaluated using human colon mast cells stimulated with LPS and IL-10.

**RESULTS**

- The expression of the cell degranulation marker CD107a was significantly increased on mast cells from UC biopsy tissue compared to CD and non-diseased colon tissue mast cells.
- The expression of the mast cell degranulation marker CD107a was significantly increased on mast cells from UC biopsy tissue compared to CD and non-diseased colon tissue mast cells.
- However, unlike mast cells in allergic disease, IgE expression was unchanged between UC, CD, and non-diseased colon mast cells which suggests a non-IgE-driven mechanism of mast cell activation in IBD.

**CONCLUSIONS/DISCUSSION**

- Mast cells and eosinophils may play a significant role in driving the pathogenesis of ulcerative colitis through the production of inflammatory mediators.
- Siglec-8 is highly expressed on mast cells and eosinophils in IBD tissue, thus antibodies that target the Siglec-8 receptor, such as lirentelimab (AK002), represent a potential novel targeted approach to IBD treatment.

**Figure 8. Siglec-8 is Highly Expressed on Mast Cells and Eosinophils in IBD Tissue**

**Figure 9. Human GI Tissue Mast Cells Produce Multiple Pro-inflammatory Cytokines Associated with IBD**

**Figure 10. Lirentelimab (AK002) Suppresses Cytokine Production from Human GI Tissue Mast Cells**


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