

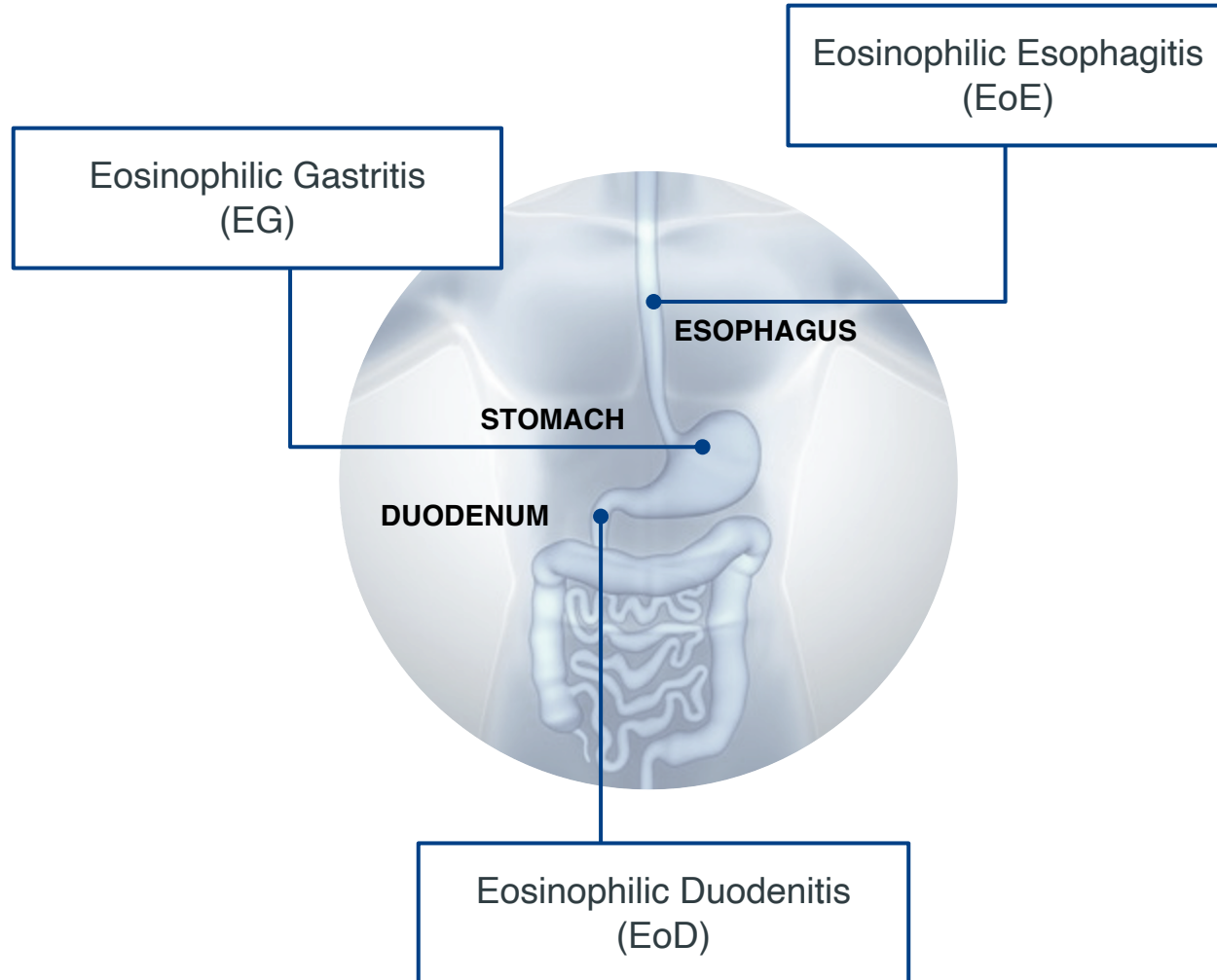
# EGID Biopsies Have Functionally Distinct and Activated Mast Cells That Contribute to Disease Pathogenesis and Are Inhibited By an Anti-Siglec-8 Antibody, Antolimab (AK002)

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# Eosinophilic Gastrointestinal Diseases (EGIDs)

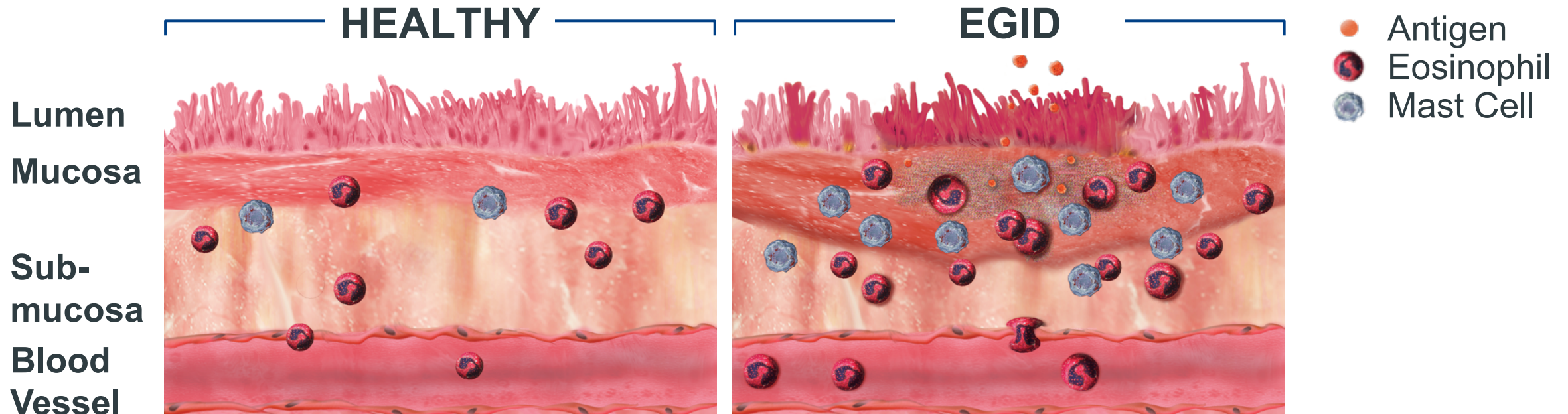


## EoE, EG, EoD

### Chronic Eosinophilic Inflammation of the Esophagus, Stomach, or Duodenum

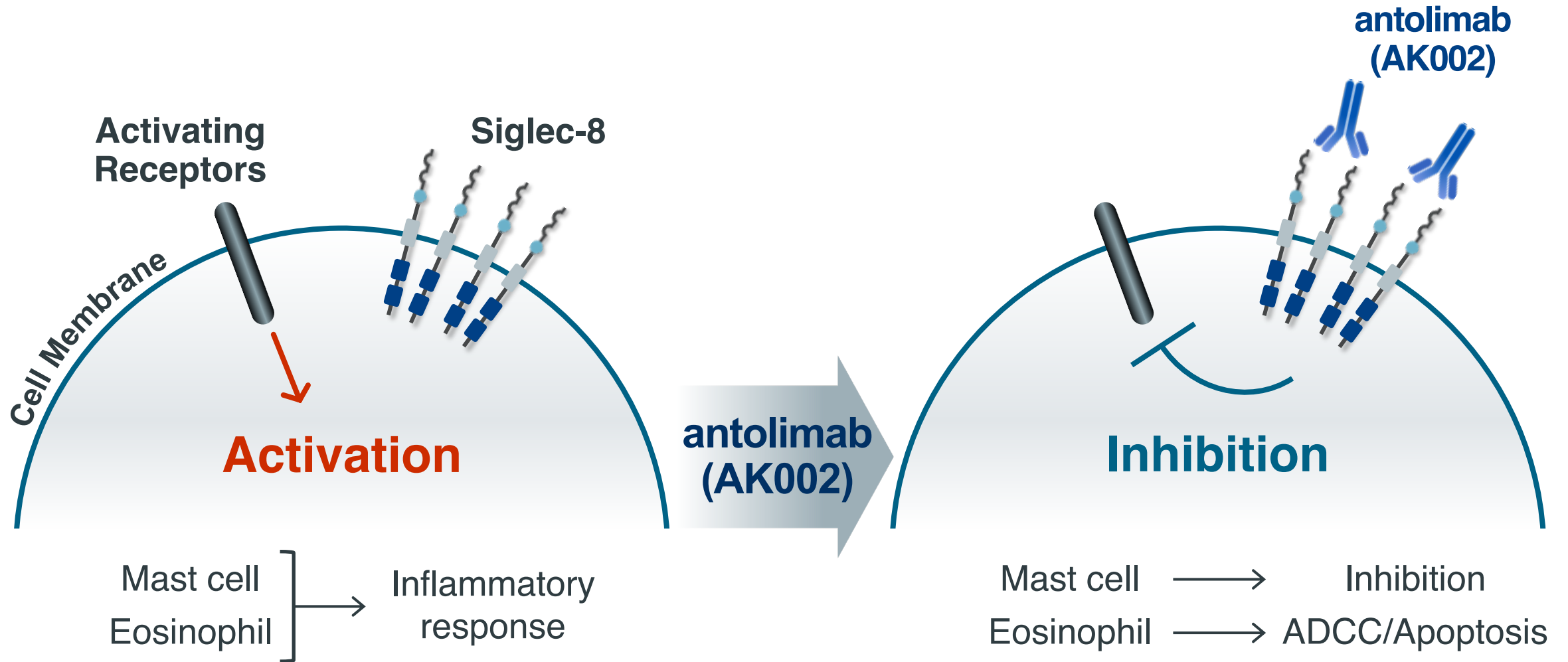
- Eosinophils and mast cells are important drivers of disease
- Symptoms: abdominal pain, nausea, early satiety, loss of appetite, bloating, abdominal cramping, vomiting, diarrhea, and dysphagia
- No FDA approved treatment for EoE, EG, or EoD
- Current standard of care: diet and/or steroids

# Eosinophils and Mast Cells Drive EGID Pathogenesis



- EGIDs are characterized by antigen-mediated eosinophil and mast cell infiltration in the esophagus (EoE), stomach (EG), and duodenum (EoD)
- Despite the evidence of mast cell involvement in EGIDs, the mechanism by which they contribute to disease pathogenesis has yet to be established in human tissue

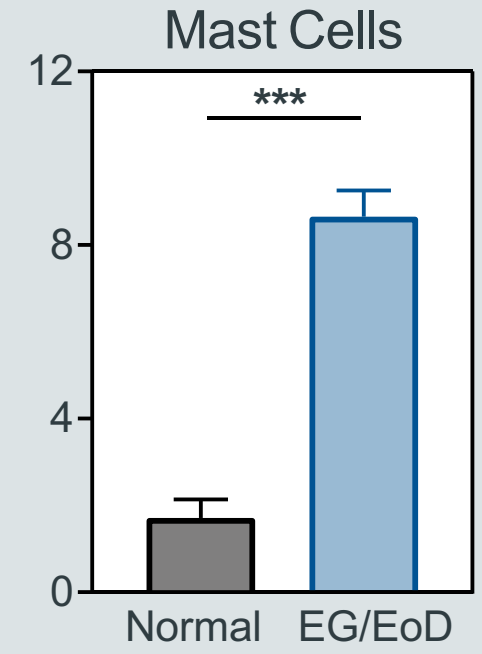
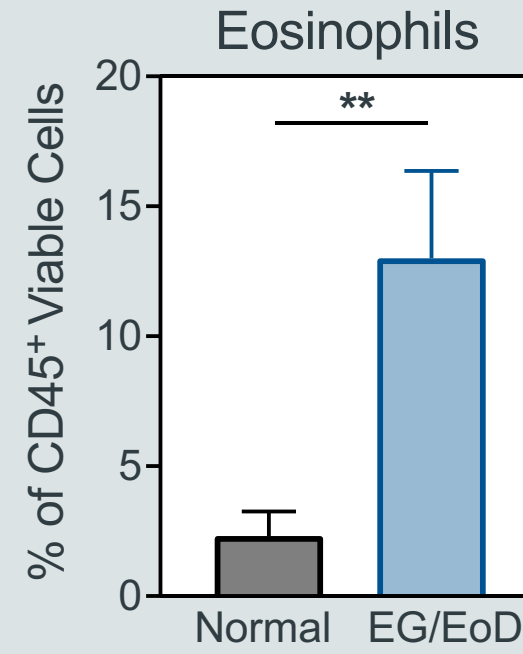
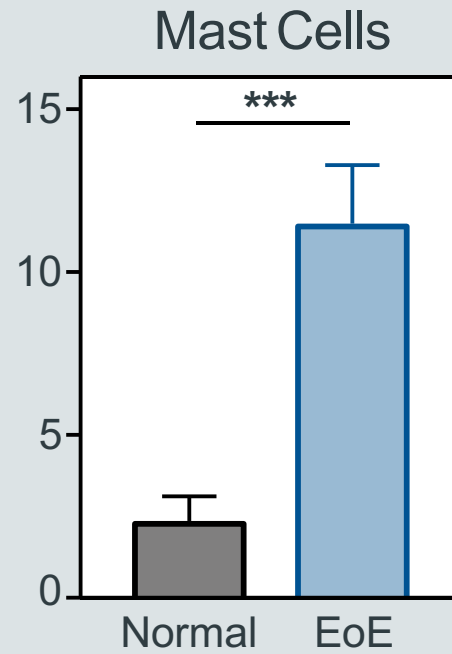
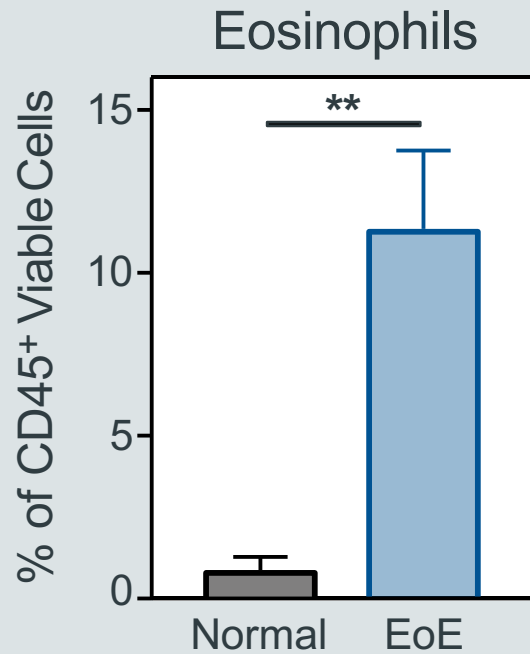
# Antolimab Targets Siglec-8 on Eosinophils & Mast Cells



# Eosinophils and Mast Cells Are Increased in EoE, EG, and EoD Biopsies

## Esophageal Tissue

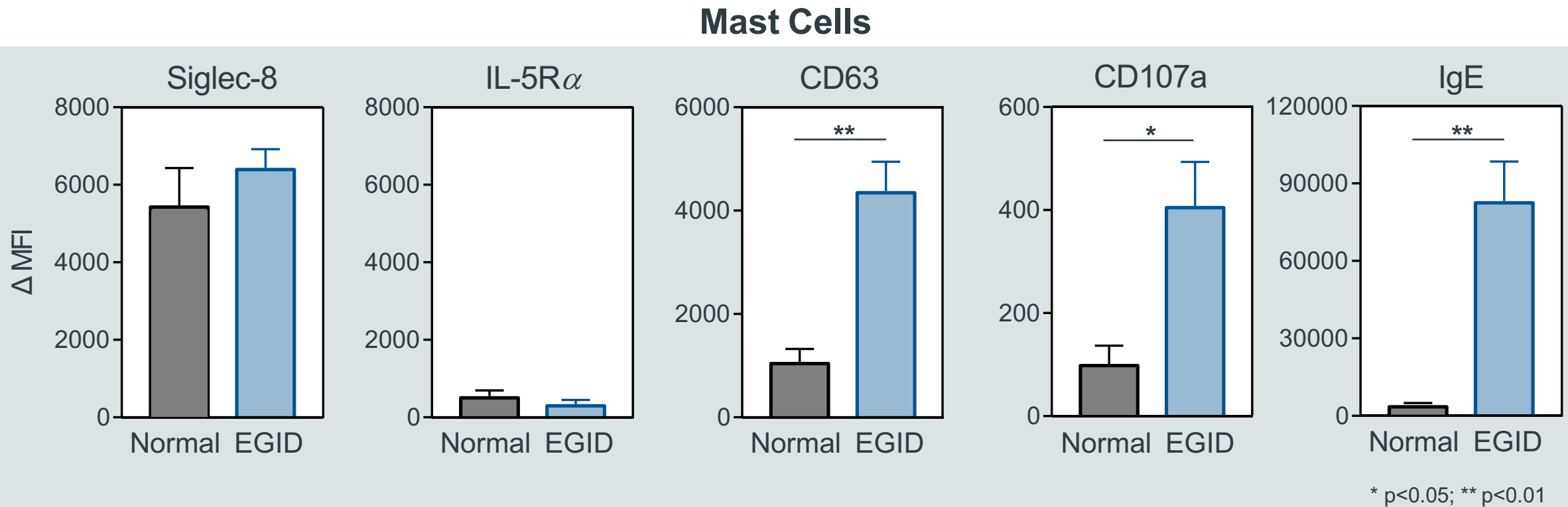
## Gastric Tissue



Increased numbers of eosinophils and mast cells are found across EGIDs

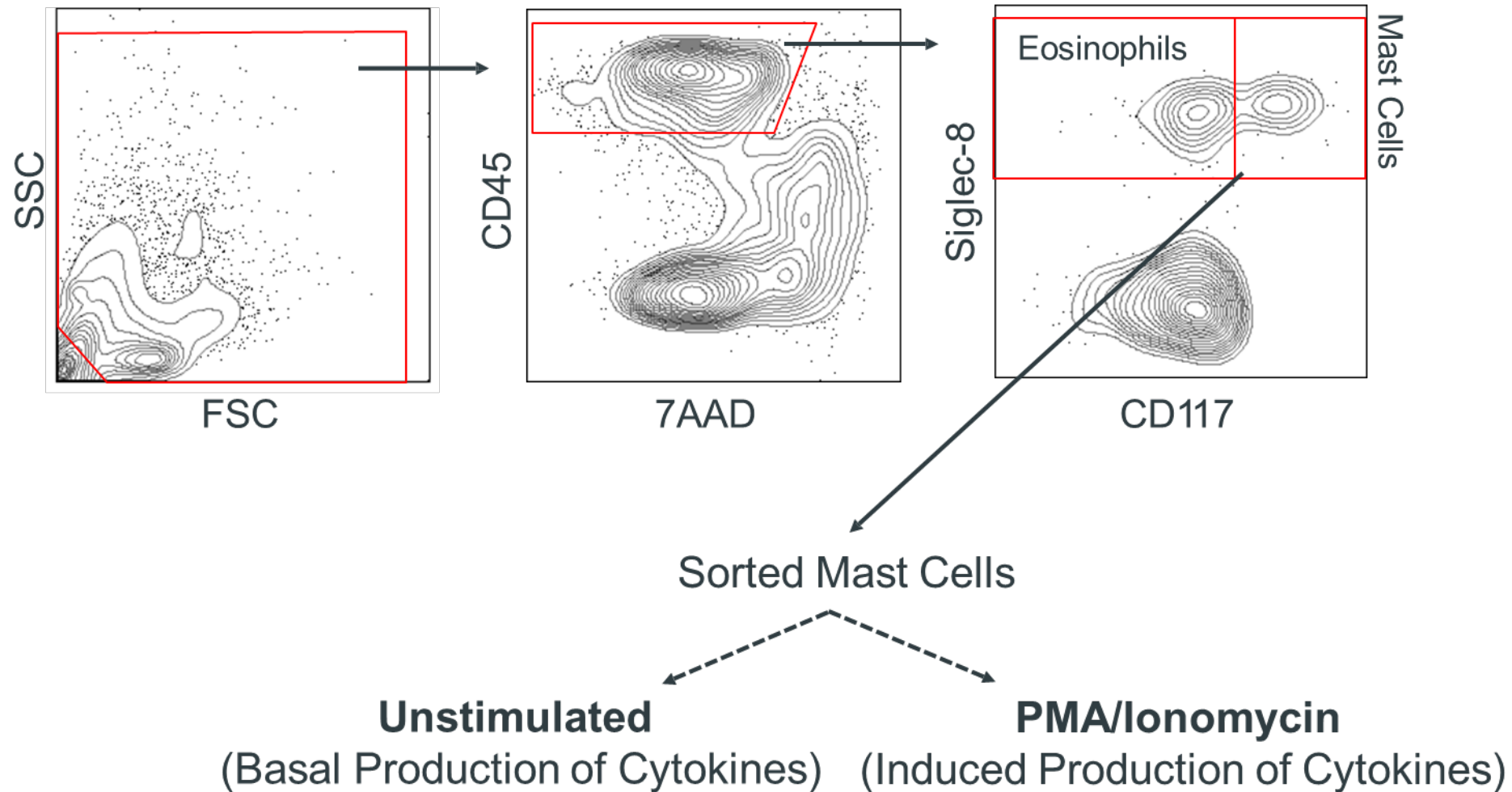


# Mast Cells Are Activated in Upper and Lower EGIDs



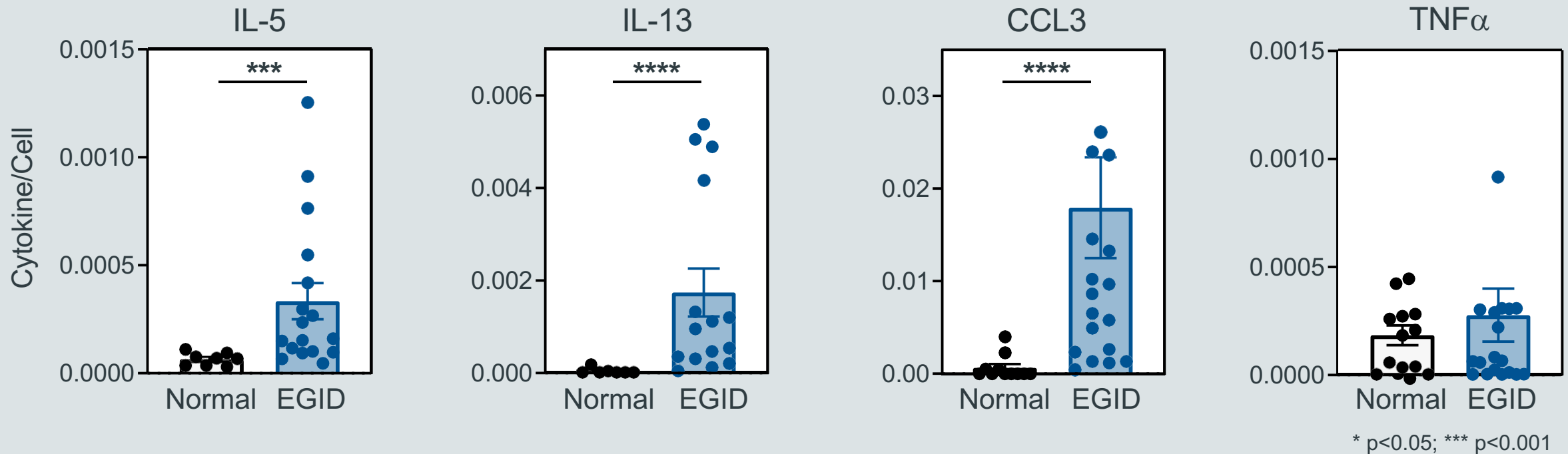
**Mast cell activation is seen in EoE, EG, and EoD biopsies**

# Gating Strategy and Method for Sorting and Activating Mast Cells from GI Tissue



# EoE, EG, and EoD Mast Cells Basally Produce Th2 Inflammatory Mediators

## Mast Cells

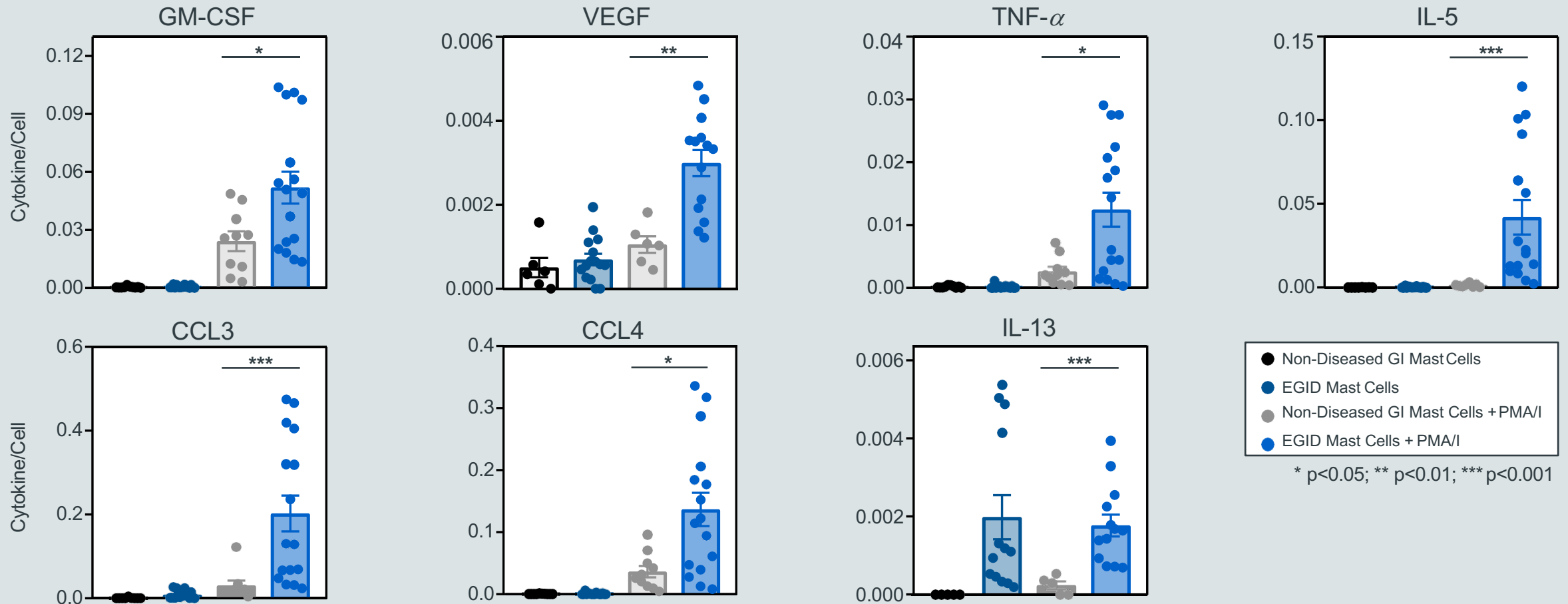


Mast cells from EGID tissue have a functionally distinct cytokine profile

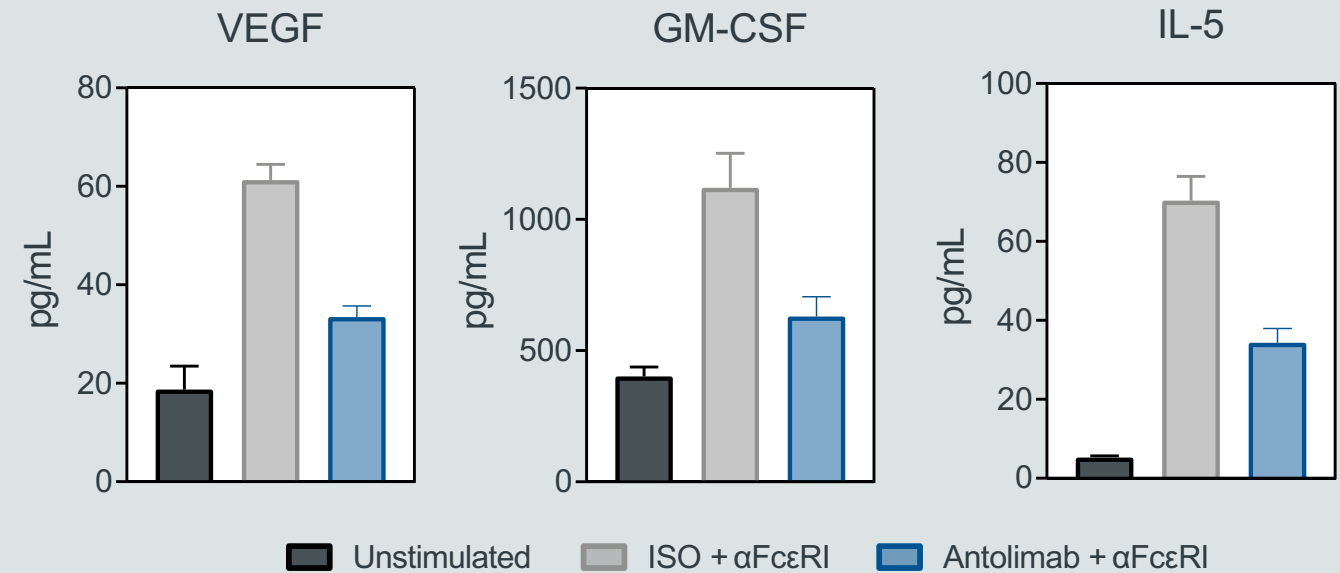
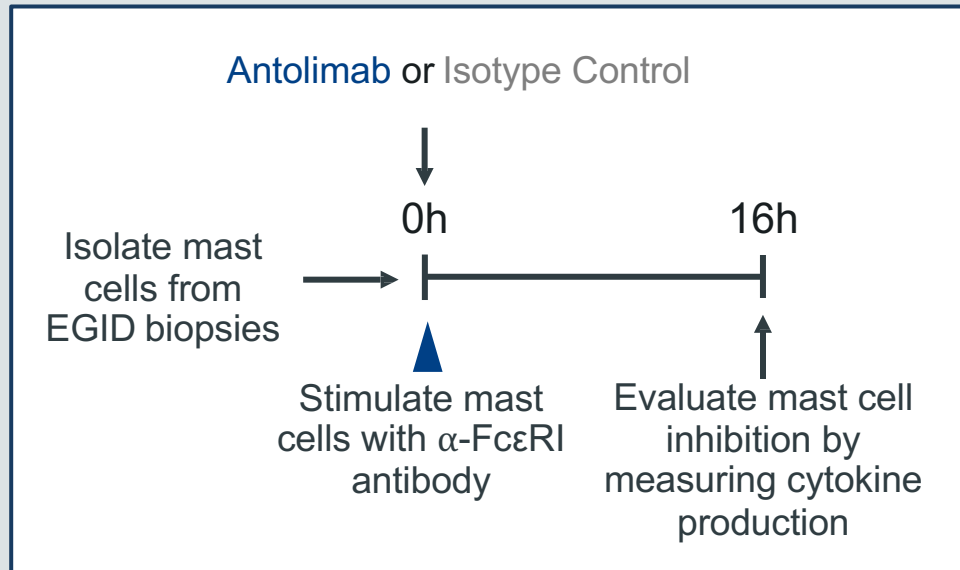


# EGID Tissue Mast Cells Produce Increased Levels of Inflammatory Cytokines Upon Stimulation

## Mast Cells



# Antolimab Inhibits Cytokine Production Induced by IgE/FcεRI Activation of EGID Biopsy Mast Cells



# Summary

- Elevated and activated mast cells are found across EGIDs, including EoE, EG, and EoD
- Mast cells from EGID tissue basally produce Th2 cytokines that are associated with T cell activation and eosinophil and mast cell recruitment
- Upon stimulation, EGID mast cells produce higher levels of mediators compared to non-diseased GI tissue mast cells, suggesting mast cells from EGID tissue have increased pathogenic potential
- IgE/FcεRI activation of EGID tissue mast cells induces mediator production that is inhibited by antolimab
- Targeting both mast cells and eosinophils may be needed to significantly reduce inflammation in EGIDs