Single-cell RNA sequencing identifies pathogenic characteristics of T cells in eosinophilic esophagitis

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The clusters of CD8+ cells contain

other clusters are distinct

Geometric Mean of Shared TCRB

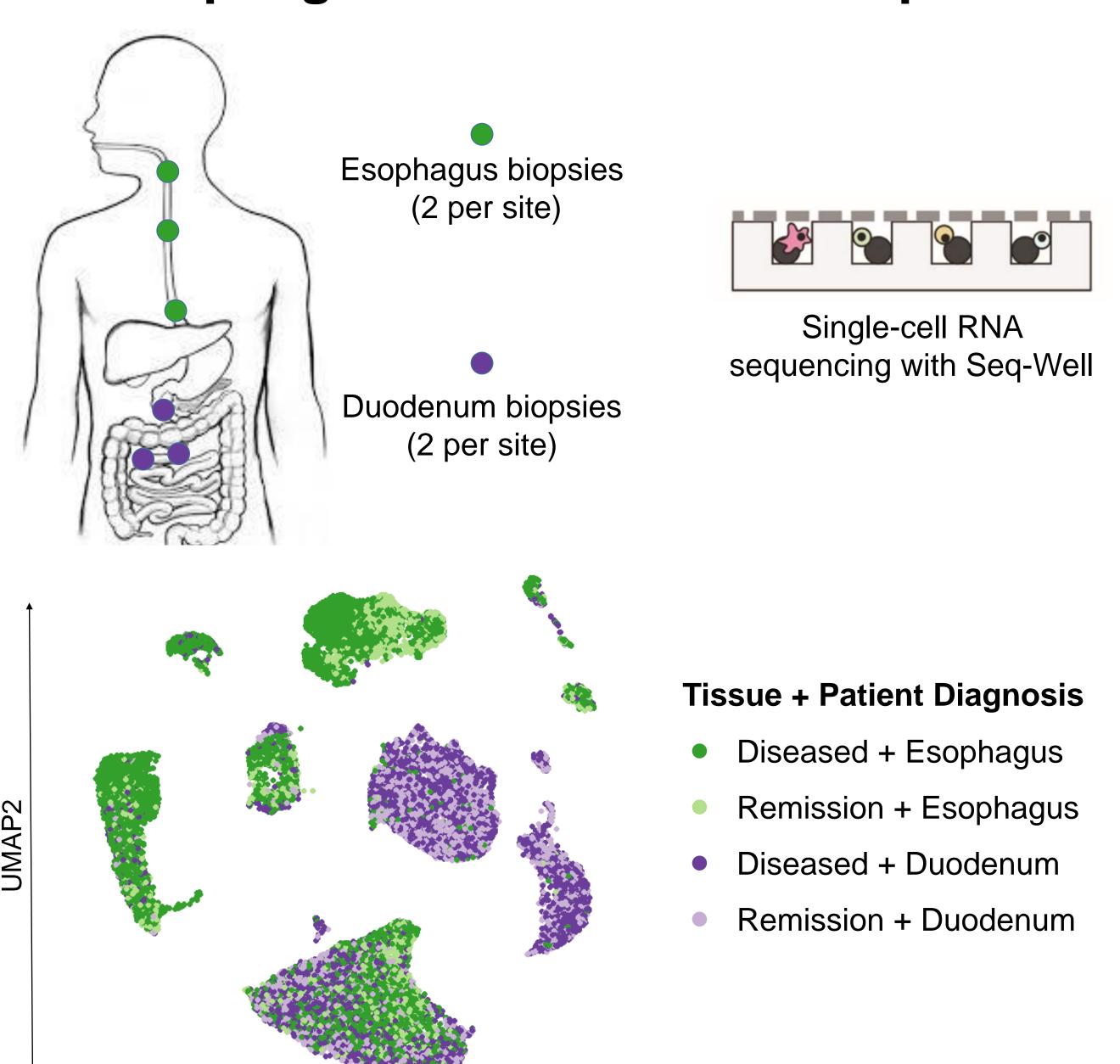
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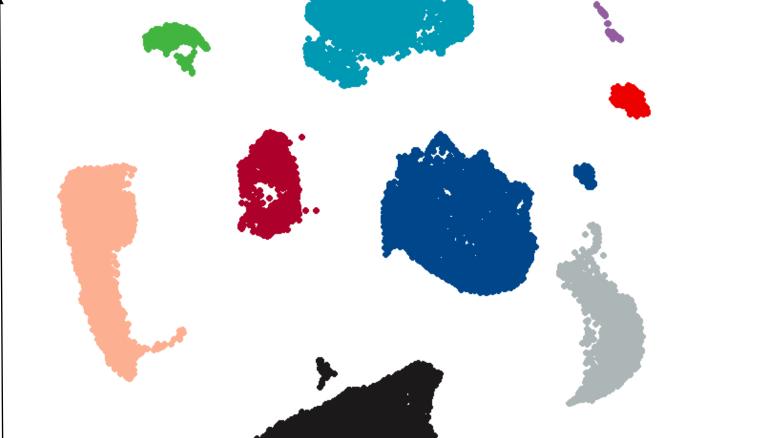
expression

Background

- Eosinophilic esophagitis (EoE) is an allergen-triggered condition in which eosinophils are recruited to the esophagus, causing inflammation.
- Like other allergic diseases, treatment for EoE relies primarily on antigen avoidance.
- The mechanisms through which the local microenvironment supports inflammation in EoE remain largely unknown.
- To better understand the tissue ecosystem of EoE, we utilized single-cell RNA sequencing to perform a single-cell genomics analysis of the types and functions of cells manifest within esophagus and duodenum biopsies from patients with EoE.

Approach: Single-cell RNA sequencing of esophagus and duodenum biopsies





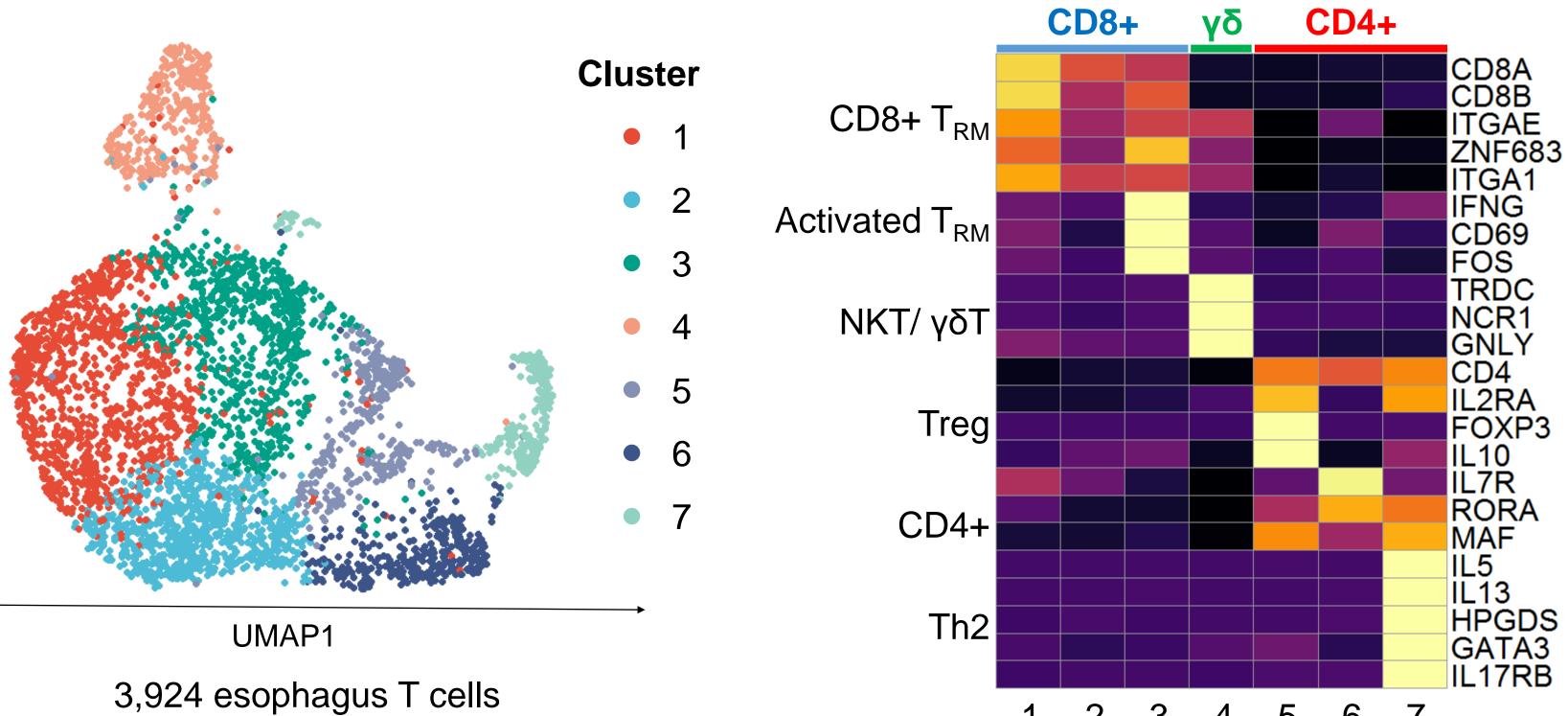
24,245 total cells

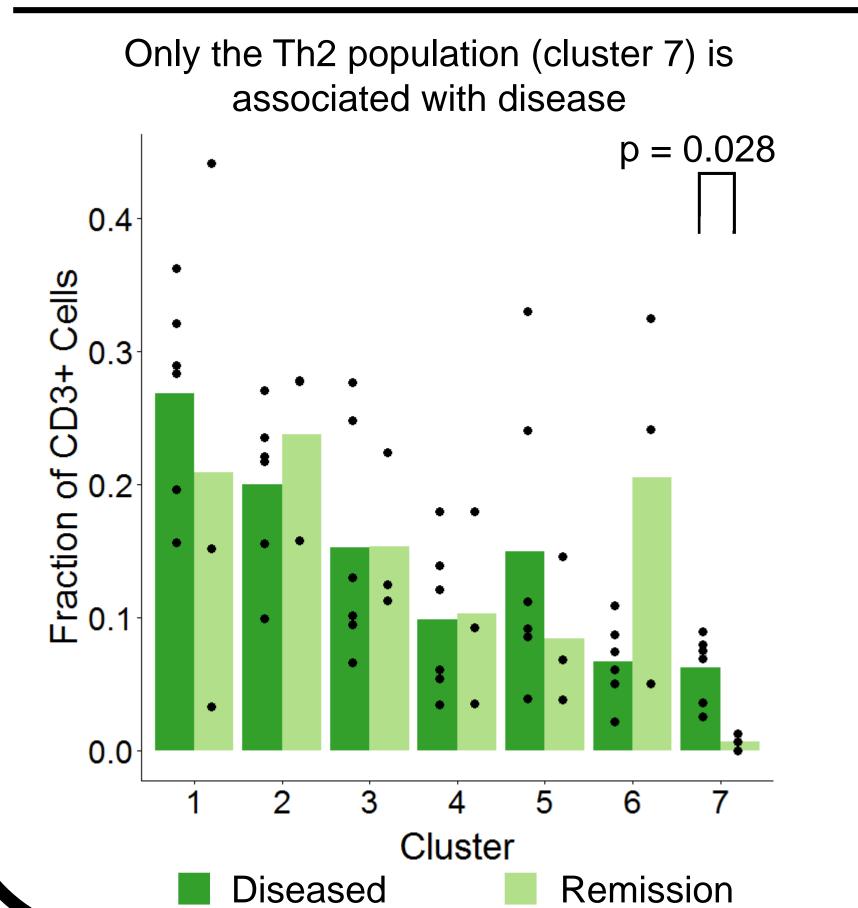
UMAP1

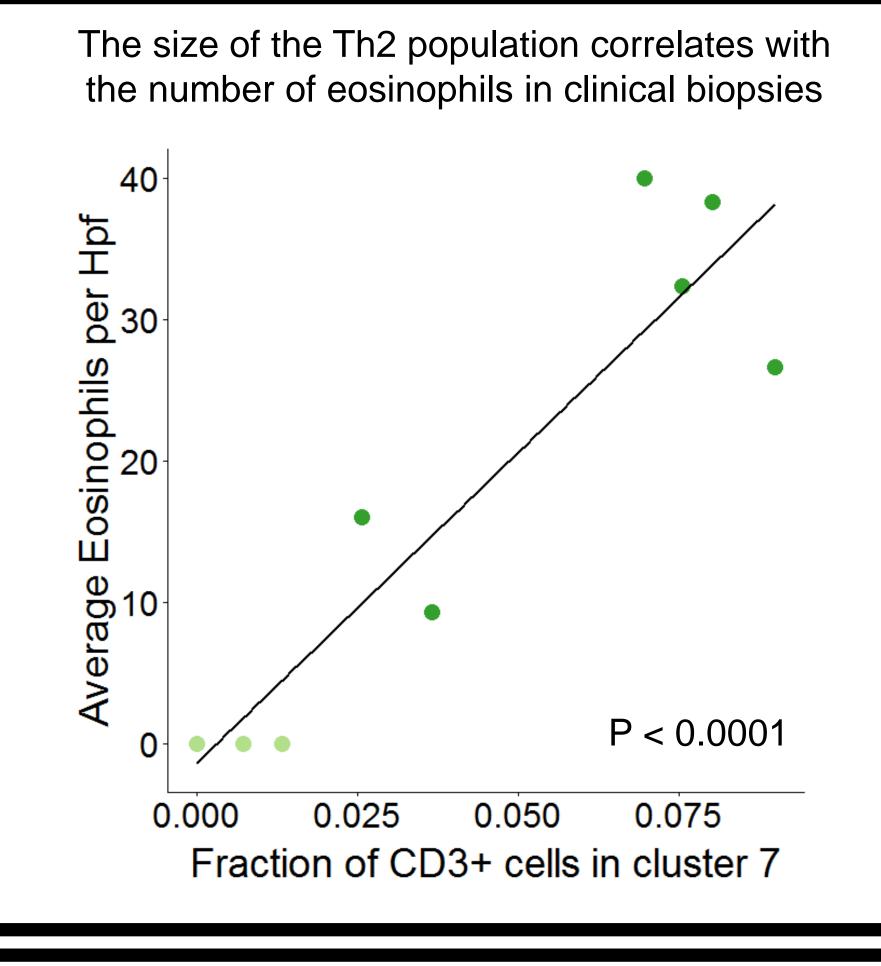
Cell Phenotype

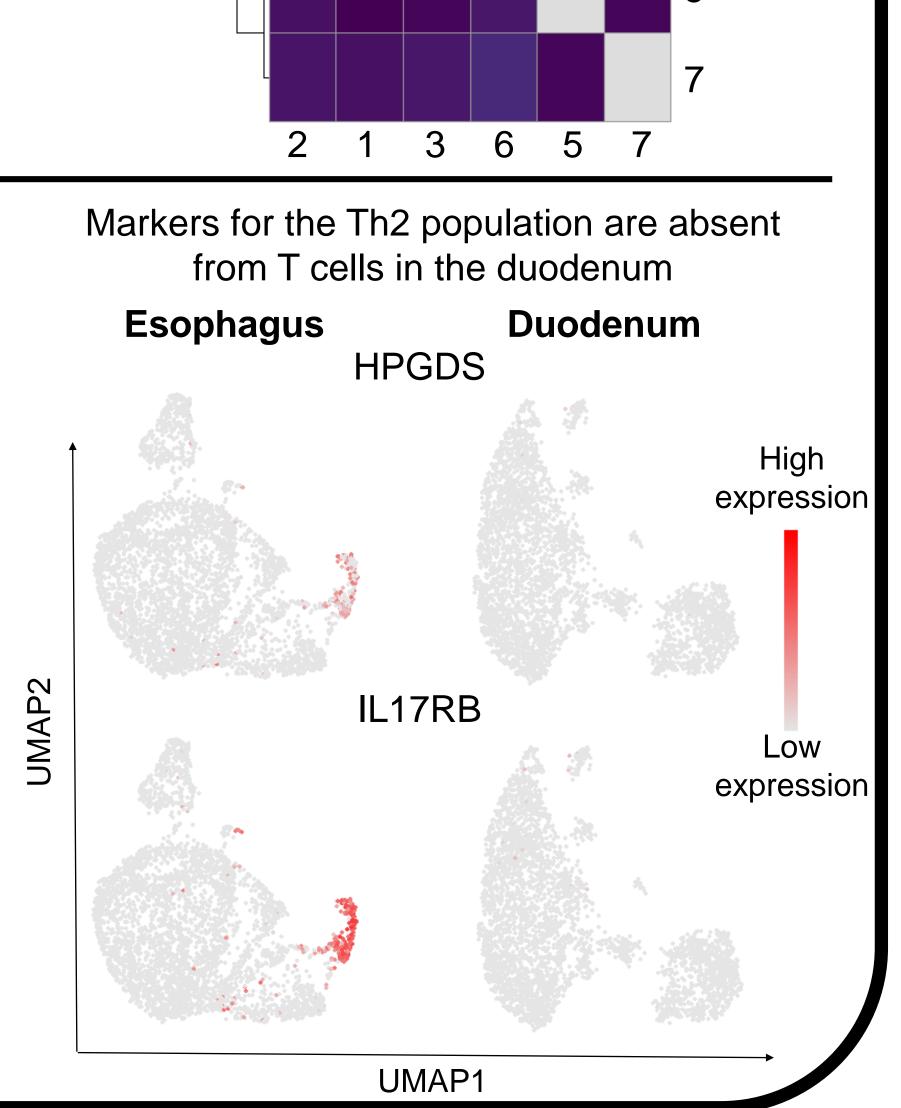
- Duodenum Epithelium
- Endothelium
- Eosinophil
- Esophagus Epithelium
- Fibroblast
- Mast Cell
- Myeloid Cells + B Cells Plasma Cell
- T Cell
- UMAP1

Th2 cells are enriched in the esophagus of diseased patients These T cell clusters correspond to known T cell Unsupervised clustering identifies seven major populations of T cells in the esophagus overlapping TCRβ sequences, while the phenotypes



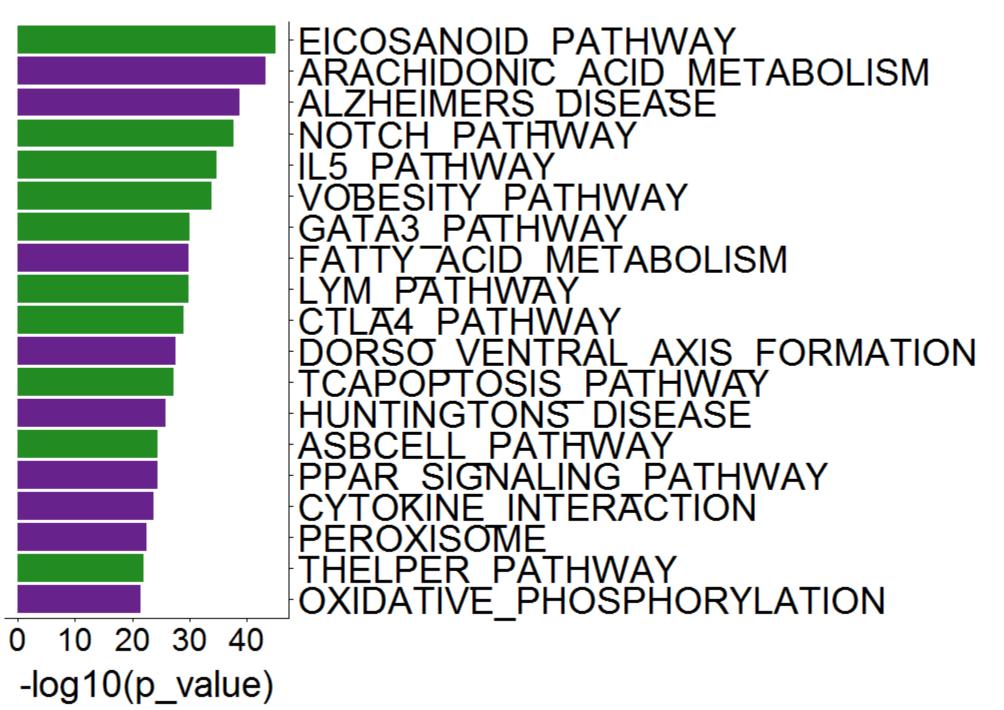






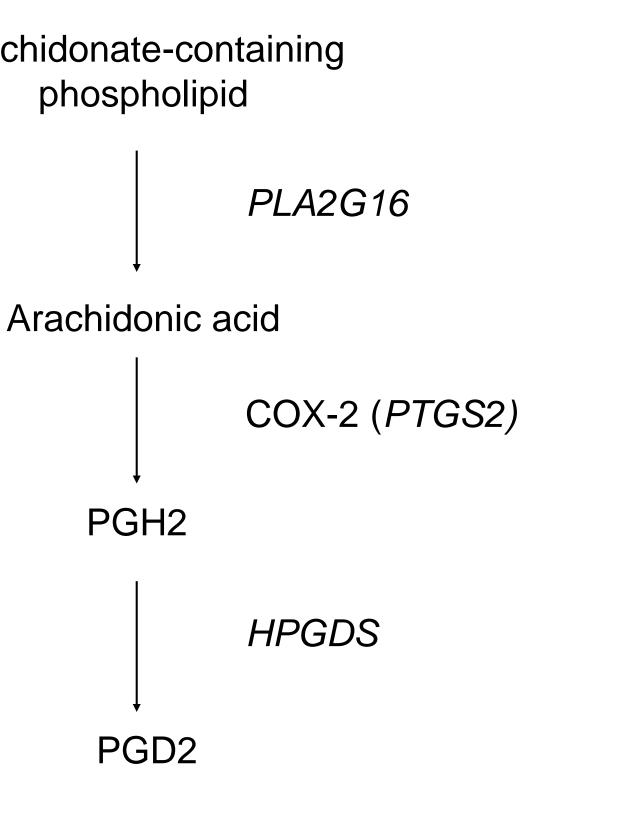
Metabolic characteristics of Th2 cells suggest synthesis of prostaglandin-D2

The most upregulated pathways in Th2 cells relative to other T cells are arachidonic acid metabolism and eicosanoid synthesis

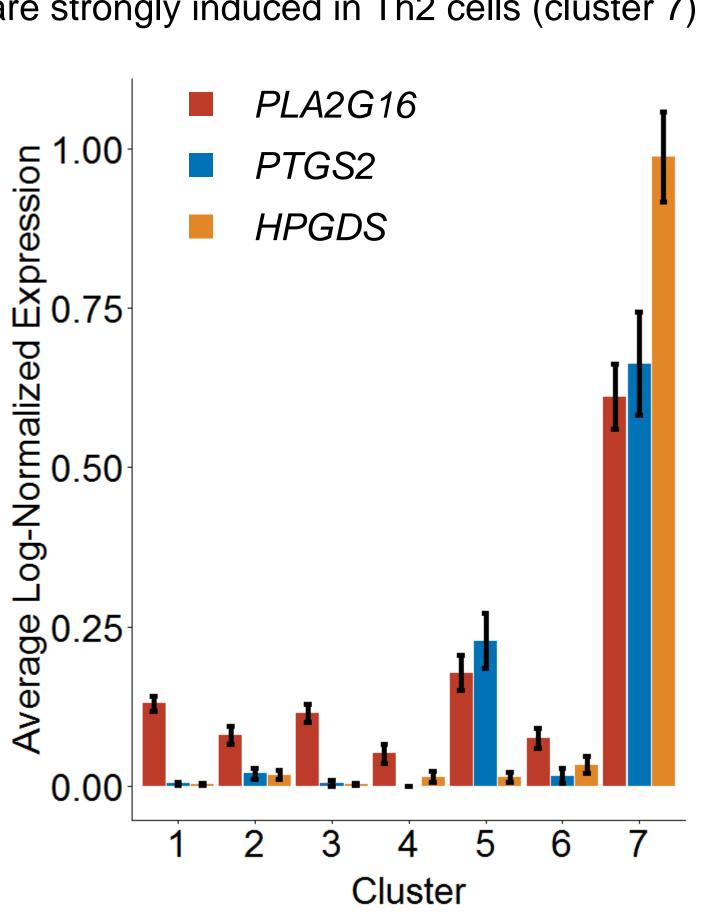


BIOCARTA

Arachidonate in phospholipids can be metabolized to prostaglandin-D2 Arachidonate-containing



Genes associated with prostaglandin-D2 synthesis are strongly induced in Th2 cells (cluster 7)



Summary

- We present a single-cell genomics analysis of 24,245 cells from the esophagus and duodenum biopsies of patients with EoE.
- We identify a clonal population of Th2 cells in the esophagus biopsies of diseased patients that expresses common Th2 mediators and whose size correlates with the number of eosinophils detected in tissue biopsies.

KEGG

Gene signatures corresponding to eicosanoid synthesis and arachidonic acid metabolism are upregulated in Th2 cells, suggesting that prostaglandin-D2 synthesis by Th2 cells contributes to eosinophil recruitment and inflammation in EoE.

Acknowledgements

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