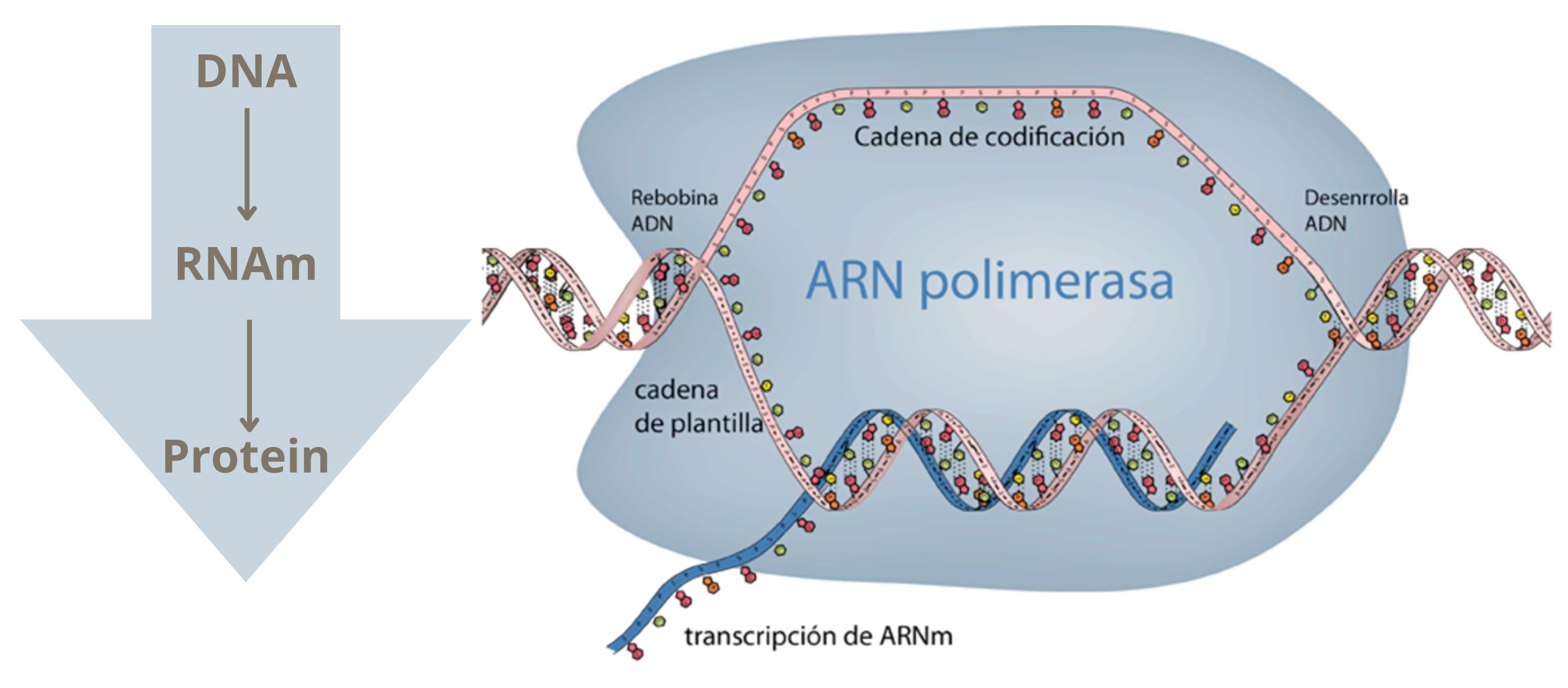


CAN SINGLE-CELL TRANSCRIPTOMICS GUIDE US TO BETTER UNDERSTAND TUFT CELLS FUNCTION?

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INTRODUCTION

The intestinal epithelium contains tuft cells, a rare cell type (<0.5%) with chemosensory and immune functions. Their role is not fully understood, but they may secrete IL-25 and produce acetylcholine. Single-cell RNA sequencing (scRNA-seq) allows detailed analysis of their gene expression and functional diversity.

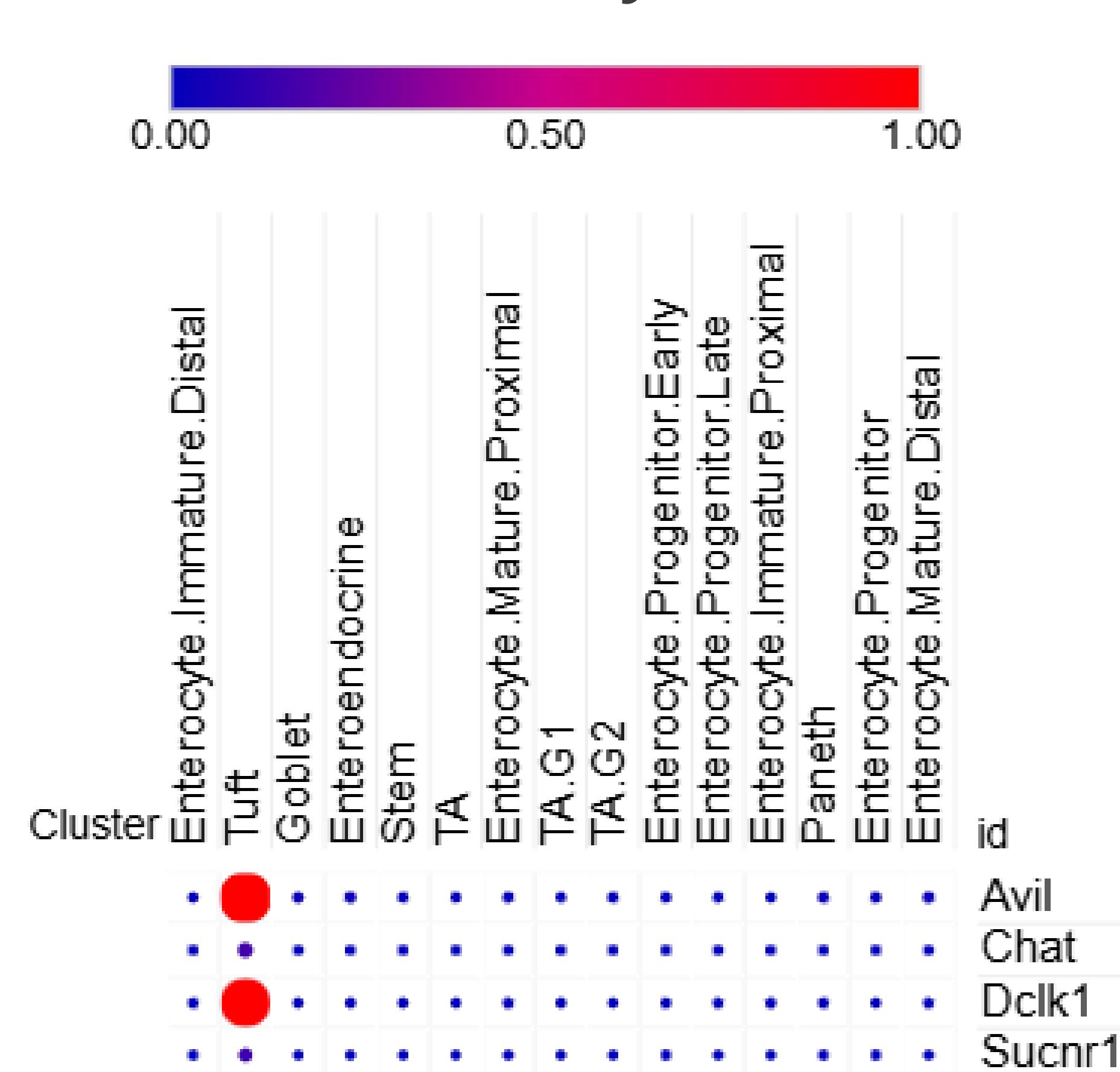


OBJECTIVES

- To characterize the gene expression profile of intestinal tuft cells using scRNA-seq.
- To investigate non-neuronal cholinergic signaling via acetylcholine synthesis.
- To explore alternative immunomodulatory pathways beyond IL-25 signaling.

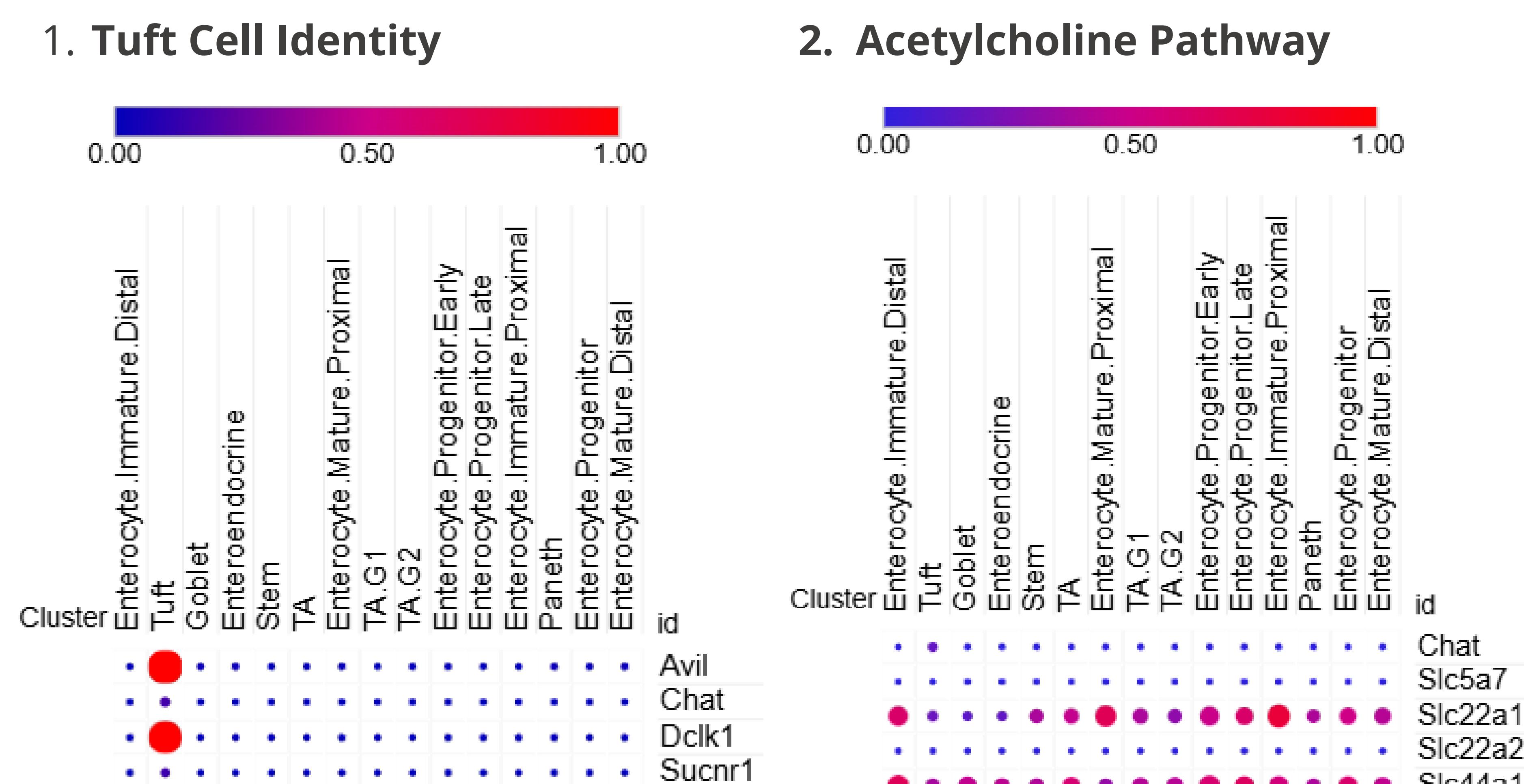
RESULTS

1. Tuft Cell Identity

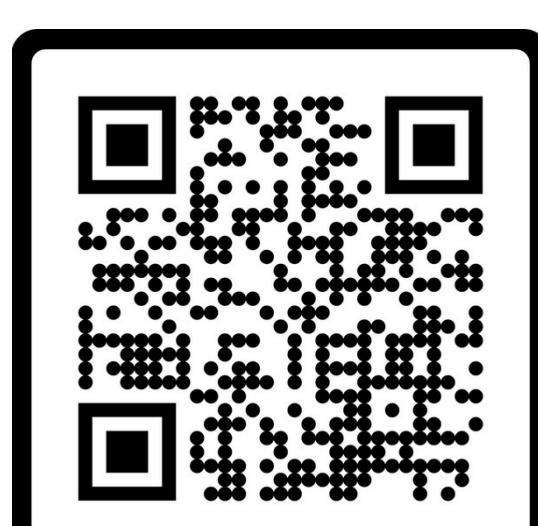


Data and plots from: Broad Institute – SCP44: Small Intestinal Epithelium (accessed via Single Cell Portal).

2. Acetylcholine Pathway



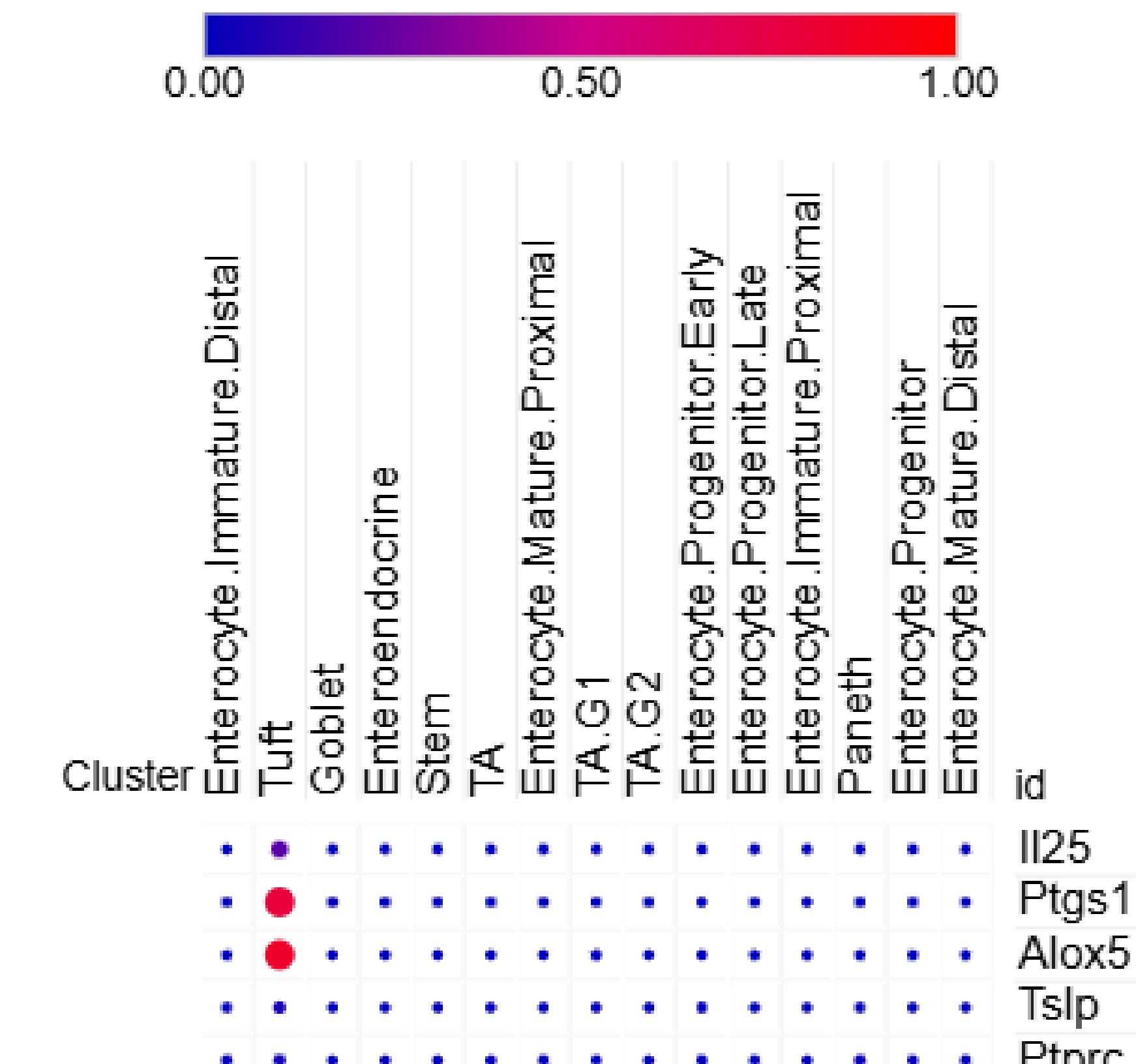
EXPLORE THE INDIVIDUAL TRANSCRIPTOMIC PROFILE OF TUFT CELLS



By scanning this QR code, you will access the interactive heatmap from the SCP44-Small Intestinal Epithelium dataset on the Single Cell Portal (Broad Institute), where you can visualize gene expression data for our genes of interest at single-cell resolution.

Each cell in the heatmap represents an individual intestinal epithelial cell from mouse organized by cell type. The last columns correspond to tuft cells. Blue indicates no expression, while red indicates the highest relative expression level.

3. Alternative Immune Functions



CONCLUSIONS

- Single-cell transcriptomics of intestinal tuft cells validated known markers (*Avil*, *Dclk1*, *Sucnr1*), although none showed absolute expression. A combination of markers is recommended for accurate identification.
- *Chat*, was exclusively expressed in a tuft cell subset, confirming their ability to synthesize acetylcholine. However, none of the analyzed choline transporters seem to explain choline uptake, suggesting the existence of uncharacterized mechanisms.
- Tuft cells may contribute to immune regulation via IL-25-independent pathways, particularly through eicosanoid biosynthesis, indicating a constitutive and heterogeneous immunomodulatory potential.
- These findings were obtained under physiological (non-inflamed) conditions. In pathological contexts such as infection, tuft cell numbers and functions are expected to change significantly.