

The tuft cell – ILC2 circuit in intestinal physiology

Summary of the project:

The tissue-immune cell interface is critical for the integrity and homeostasis at mucosal barriers, in particular in the gastrointestinal tract. Tuft cells are rare, secretory epithelial cells that generated scant immunological interest until recent reports linked tuft cells with type 2 immunity in the small intestine. The small intestinal tuft cell–ILC2 circuit mediates epithelial responses to intestinal worms and protists by tuft cell gustatory sensing and IL-25-mediated activation of IL-13 secretion by group 2 innate lymphoid cells (ILC2s). Tuft cells have emerged as potential central players in tissue-immune cross-talk due to their capacity to sense luminal signals, including metabolites, and to produce an unusual spectrum of biological effector molecules, including IL-25, eicosanoids, and the neurotransmitter acetylcholine. We hypothesize that the small intestinal tuft cell-ILC2 circuit integrates luminal signals resulting in responses that mediate adaptation to dynamic environmental changes. The goal of this project is to identify luminal signals and molecular mechanisms that mediate circuit activation, and to determine their function in different gastrointestinal tissues, which will lead to a novel conceptual understanding of these pathways in intestinal physiology and in pathologic tissue alterations.