Charting the direct channels of communication between endocrine cells in the human gut

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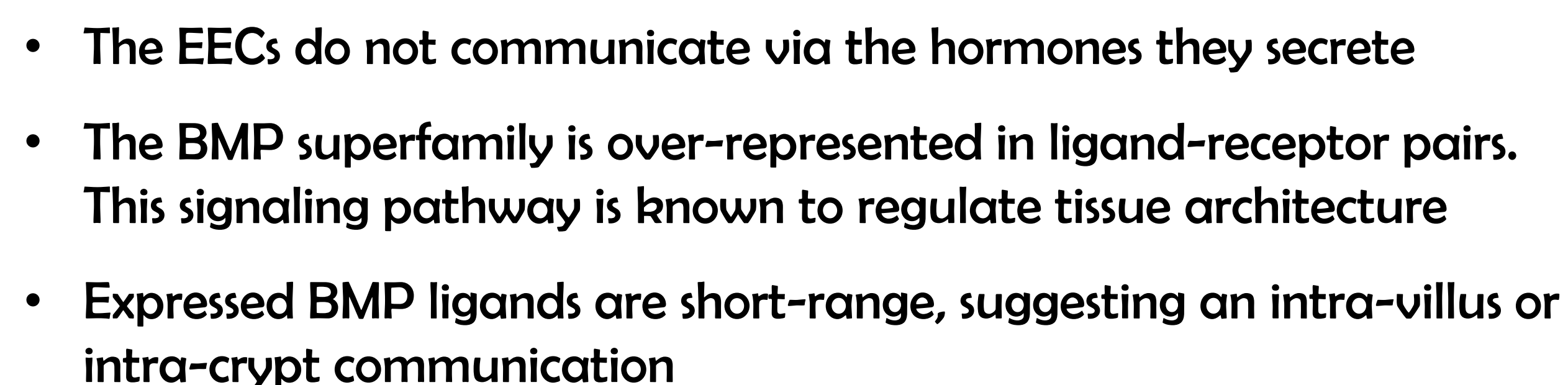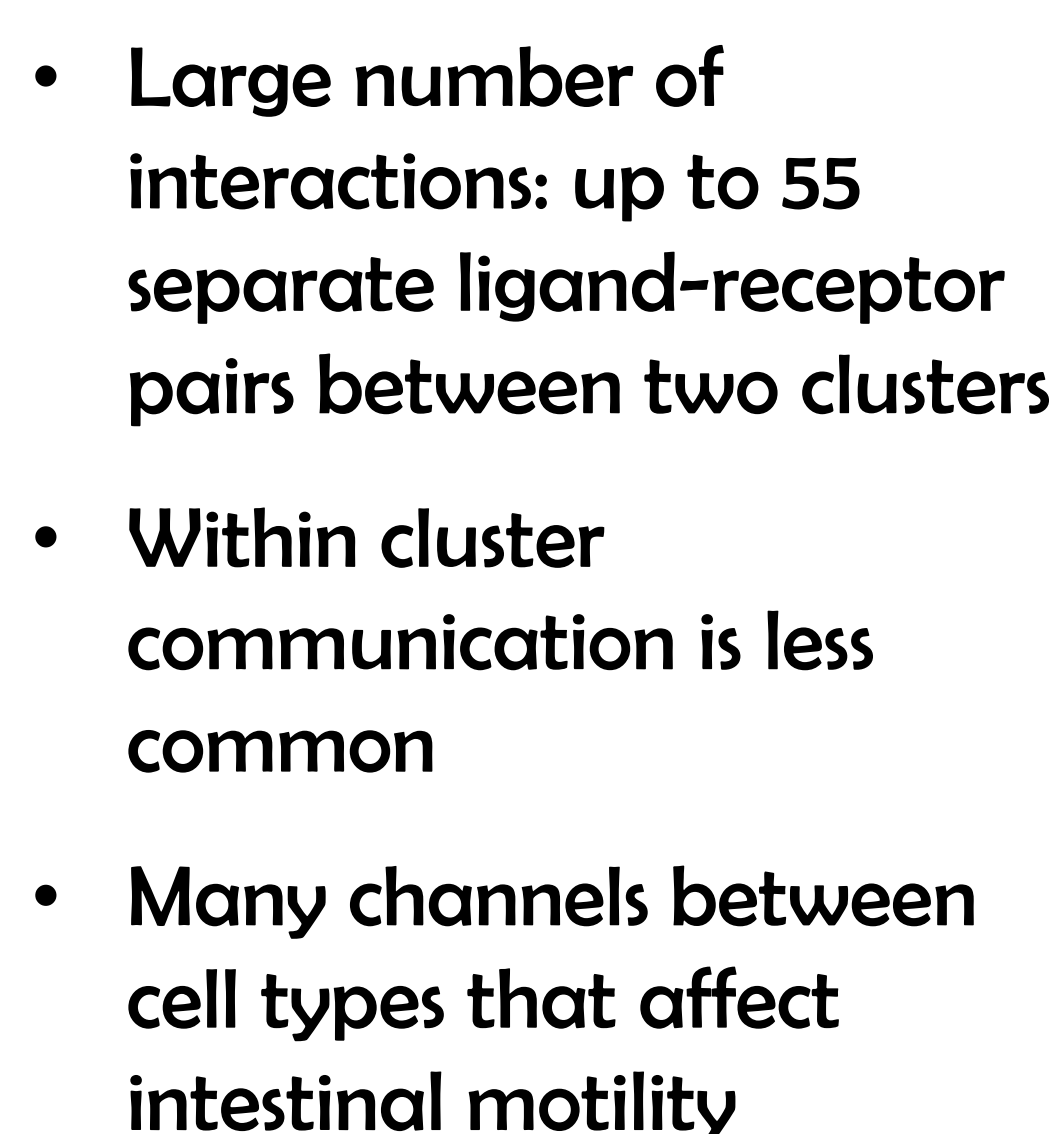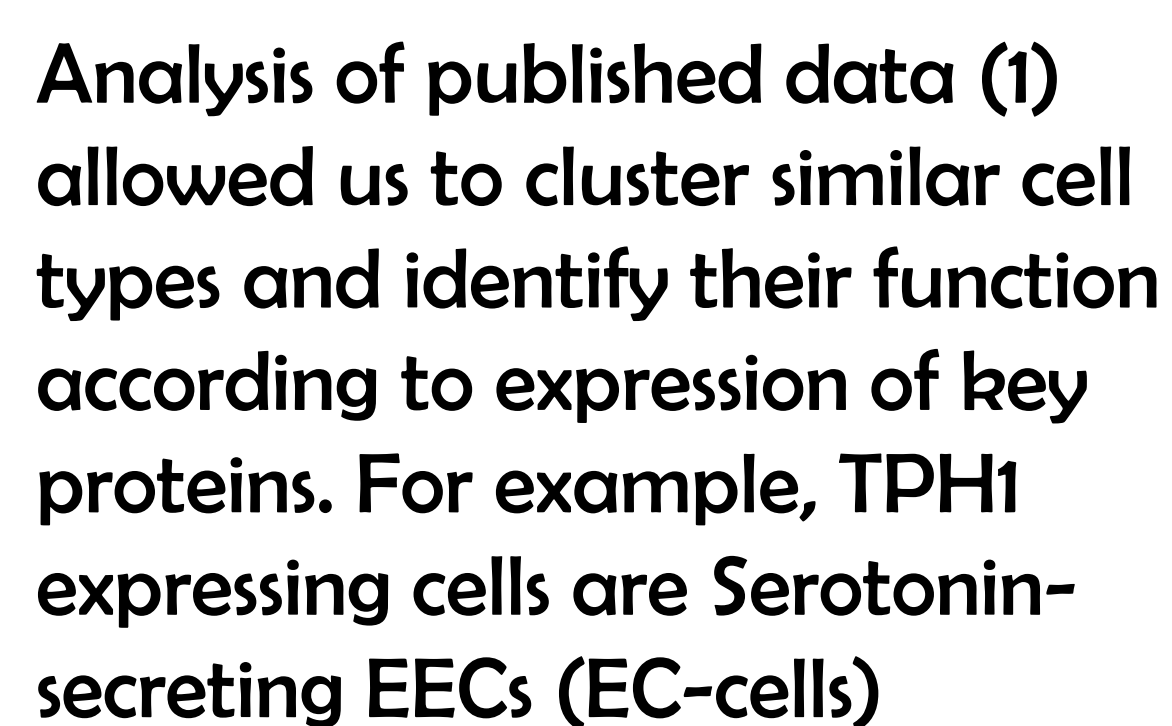
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1 Introduction

The enteroendocrine system produces hormones secreted in the stomach, colon, and small intestine, comprising <5% of the epithelial cells (1). The hormones affect target tissues such as the pancreas, central nervous system and the intestine, and coordinate digestion, absorption, nutrient disposal, gut motility, and appetite.

However very little is known regarding the communication between enteroendocrine cells themselves. We set to identify the channels of communication between different types of enteroendocrine cells by utilizing single cell mRNA-Seq data of human enteroendocrine cells.

2 The Intestinal Epithelium

The luminal surface of the small intestine of the gastrointestinal tract, absorbs useful substances into the body and restricting the entry of harmful substances.

Gut hormones are produced by enteroendocrine cells (EECs), which are scattered throughout the epithelial layer of the gut wall.

3 Single-Cell mRNA Clustering Characterization

EECs are rare and scattered along the gut epithelium, making single-cell mRNA seq an ideal tool to study them.

Analysis of published data (1) allowed us to cluster similar cell types and identify their function according to expression of key proteins. For example, TPH1 expressing cells are Serotonin-secreting EECs (EC-cells)

4 Significant p-values rank visualization

CellPhoneDB is a publicly available repository of curated receptors, ligands, and their interactions that was designed to identify ligand-receptor pairs within and between clusters of single cell mRNA-seq data (2). Below is an interaction matrix between cell types.

Some interesting features include

- Large number of interactions: up to 55 separate ligand-receptor pairs between two clusters

- Within cluster communication is less common

- Many channels between cell types that affect intestinal motility

5 Significant Interactions Network

Biological analysis of the network of ligand-receptor pairs:

- The EECs do not communicate via the hormones they secrete

- The BMP superfamily is over-represented in ligand-receptor pairs. This signaling pathway is known to regulate tissue architecture

- Expressed BMP ligands are short-range, suggesting an intra-villus or intra-crypt communication

Warning: CellPhoneDB has limited reliability, and gives the same weight for signaling or inhibition of signaling, and does not consider the level of gene expression (2).

6 Summary

Human EECs signal to other EECs mostly by BMPs and not via the hormones they secrete to target cells. EECs likely communicate within a single villi/crypt, and not across long distances. Most communication is between cells regulating gut motility.

In general, it is possible to identify patterns of communication between different cell types using single cell mRNA seq, and to reach meaningful biological conclusions.

References

1: "High-Resolution mRNA and Secretome Atlas of Human Enteroendocrine Cells", Joep Beumer et al., Cell 181, 1291–1306, June 11, 2020

2: "CellPhoneDB: inferring cell–cell communication from combined expression of multi-subunit ligand–receptor complexes", Sarah A. Teichmann and Roser Vento-Tormo et. al. NATURE PROTOCOLS |VOL 15 | APRIL 2020 | 1484–1506