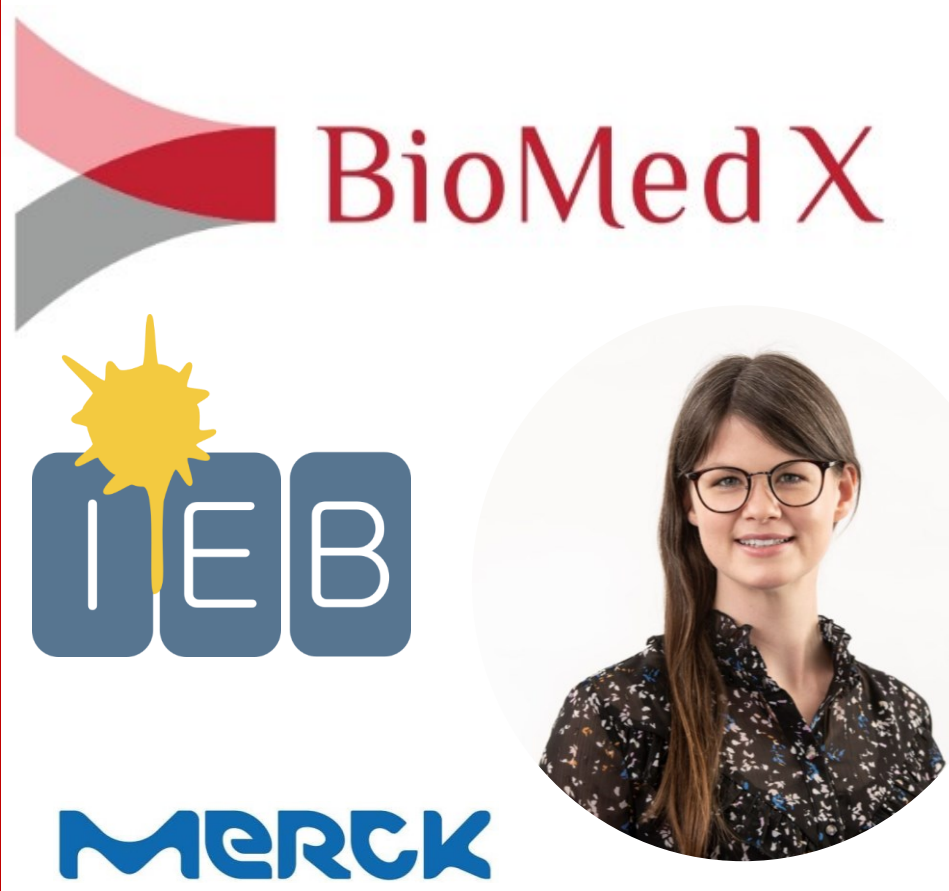


Human intestinal organoid co-culture model with tissue-derived immune cells uncovers novel immune-epithelial interactions

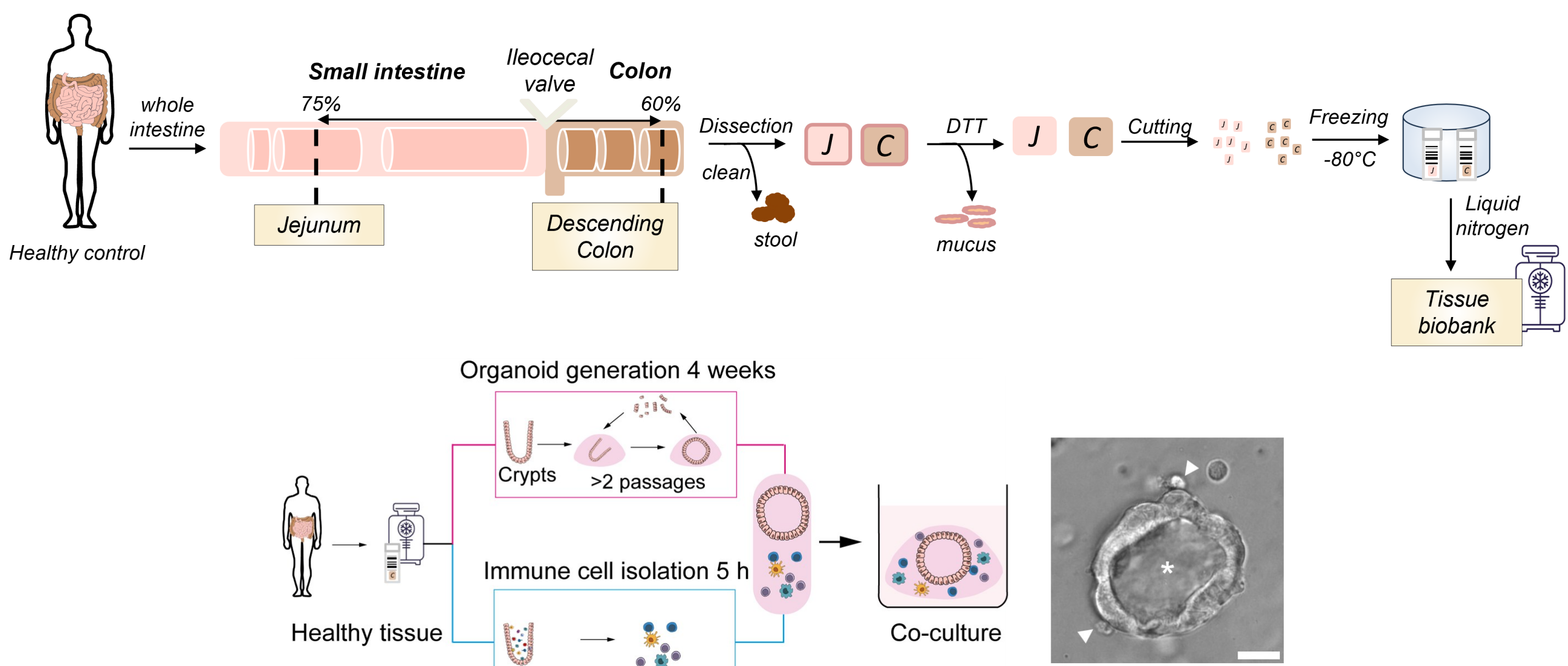
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Background

Intestinal epithelial cells function as a protective barrier towards potential harmful luminal content. They release immune regulators to attract basally residing immune cells to initiate immune responses and control inflammation. Loss of intestinal barrier integrity, and alterations in intestinal immune cell function is correlated with gut dysbiosis, cancer and inflammation processes like e.g. autoimmune diseases. However, interactions between lamina propria immune cells and intestinal epithelial cells are poorly understood due to the lack of a relevant human *in vitro* model.

Experimental setup



Diverse mix of LP-derived immune cells

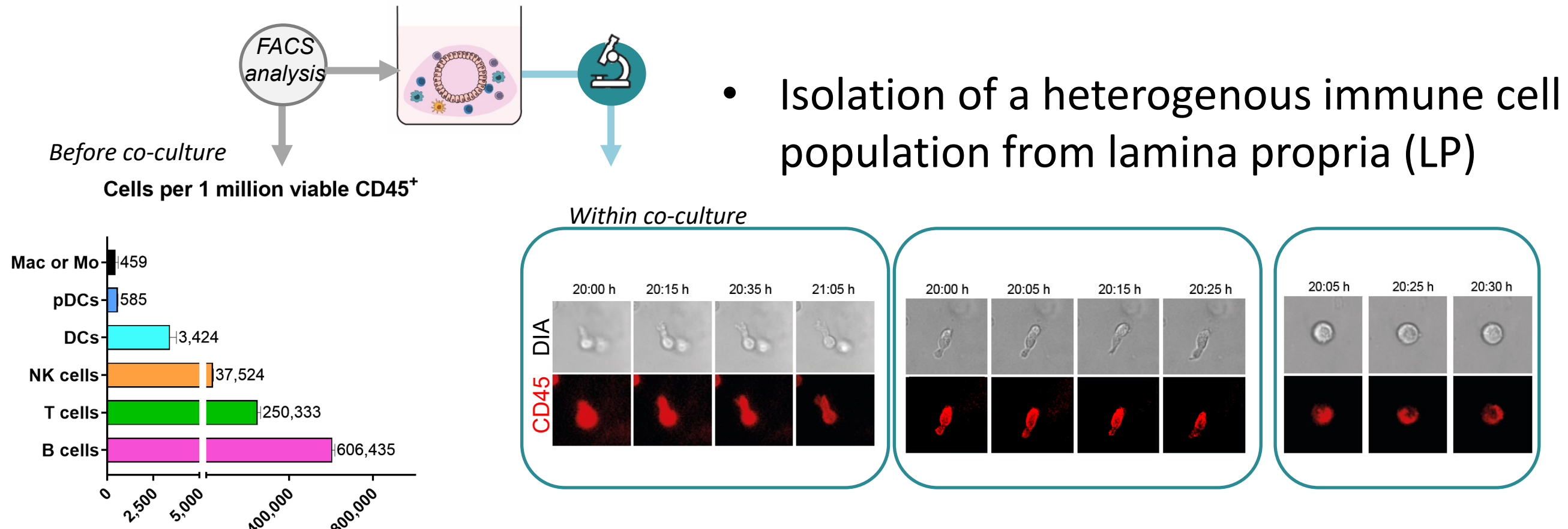
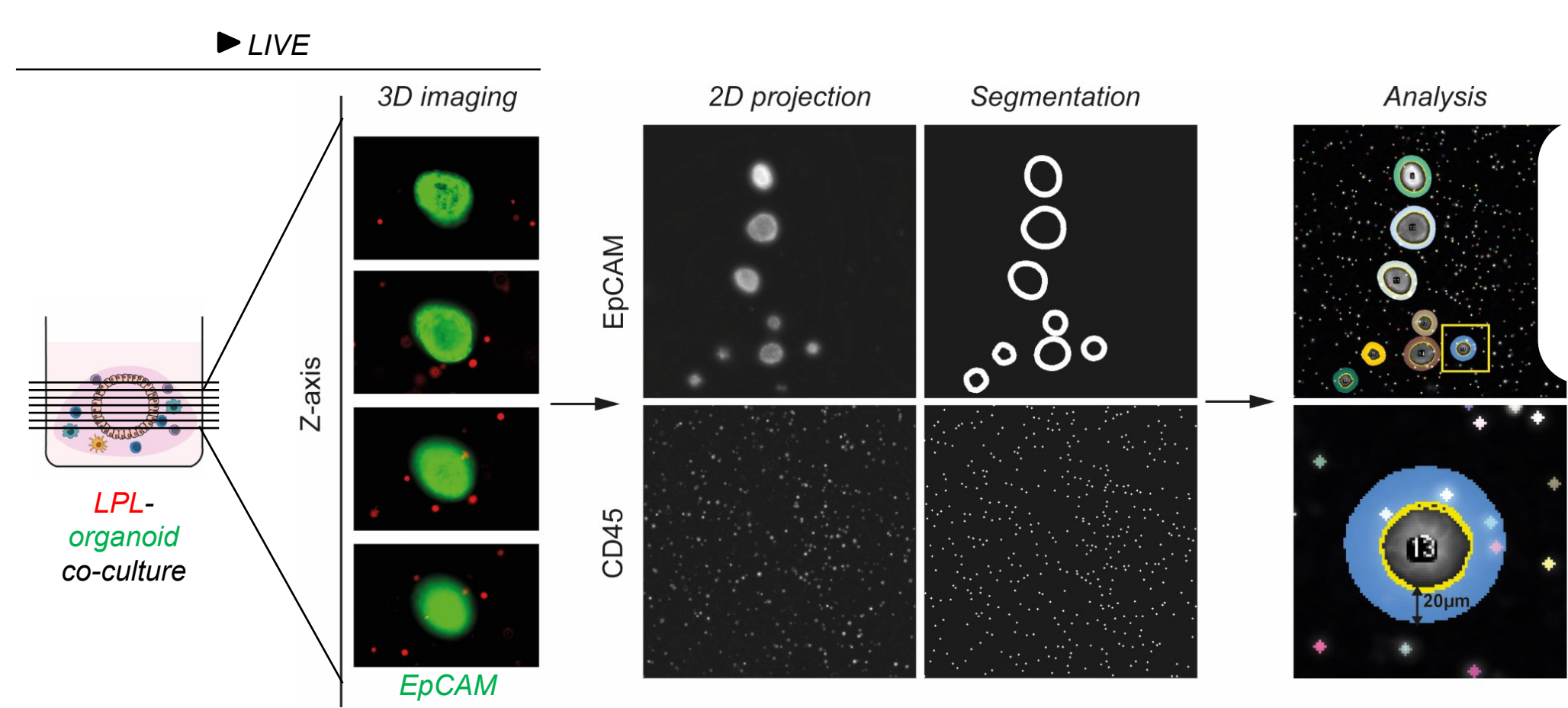
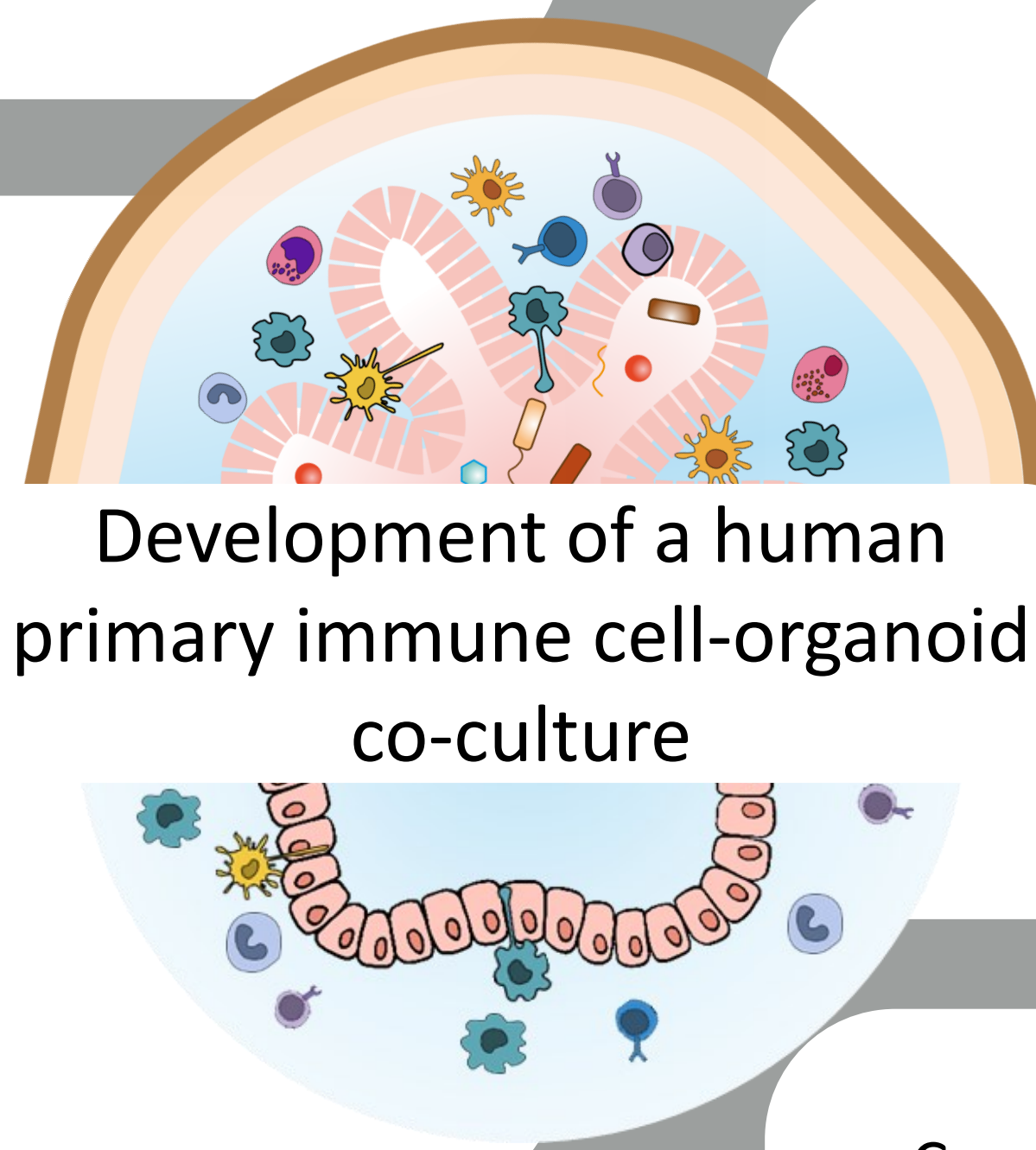


Image analysis tool

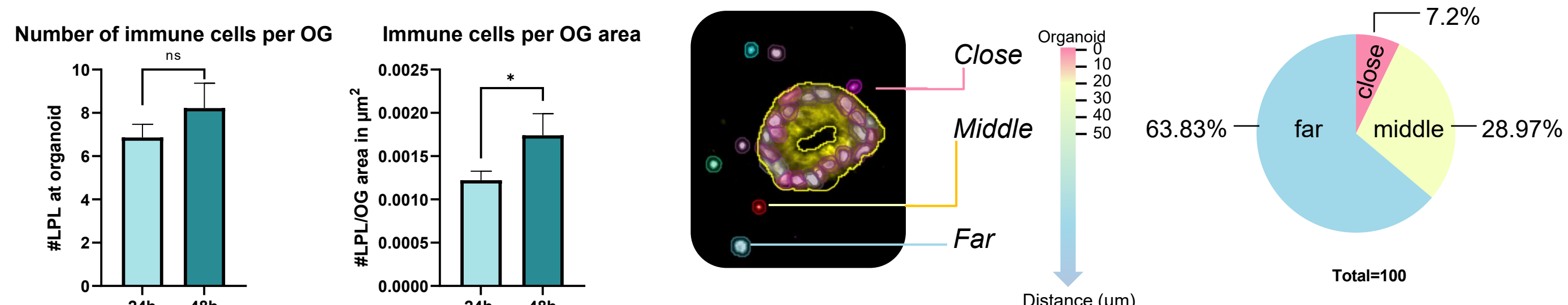


Development of a human primary immune cell-organoid co-culture



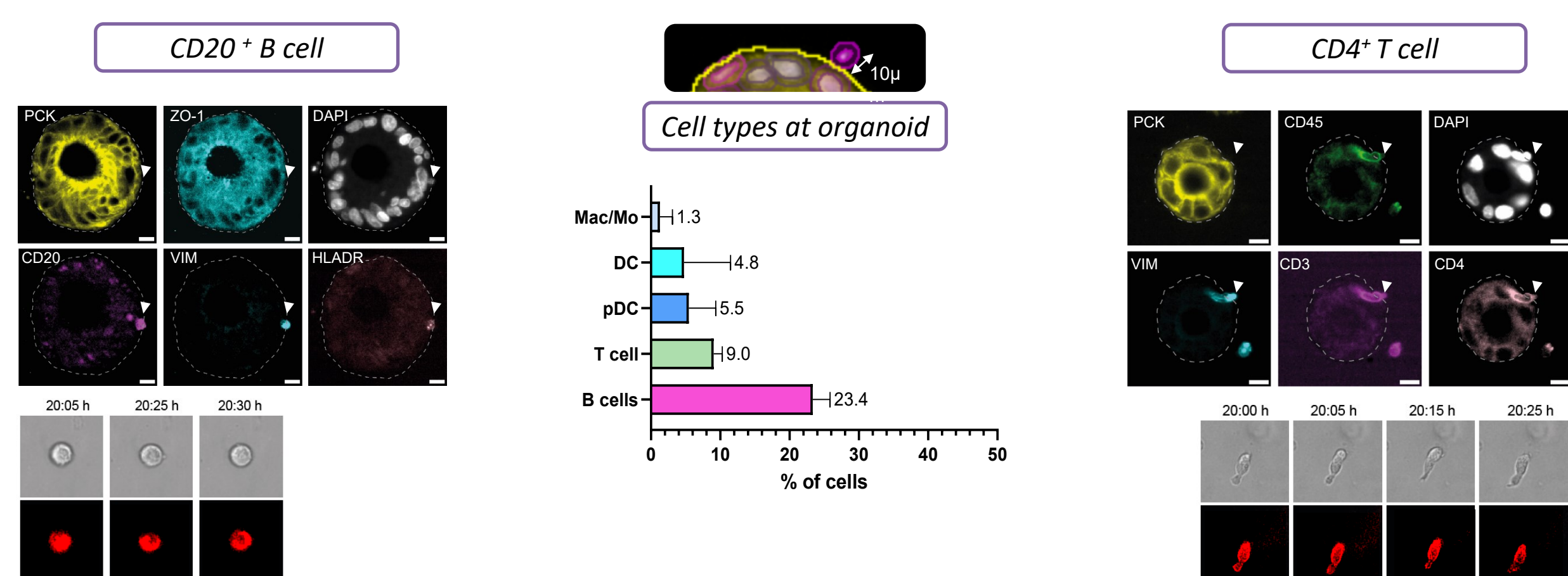
Immune cells migration

- Immune cells migrated towards organoids



Interacting immune cells

- Interacting cells were mostly B and T cells



Research question

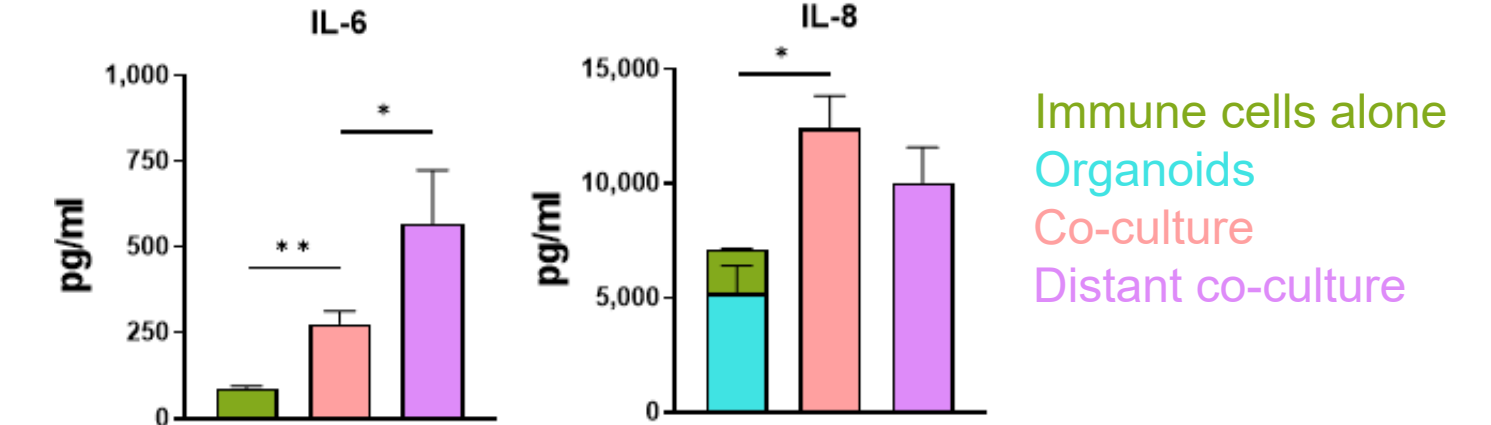
- Can cryopreserved human intestinal biopsies serve as cell source to establish a functional co-culture model?
- What are the interaction dynamics and which cells do interact in the co-culture model?
- How does this interaction change the expression profile of the different cell types?

Key findings

- Human LP-derived immune cells remain functional in a co-culture with organoids
- Migration of immune cells towards organoids
- Co-culture introduces major changes in expression profile of both the epithelial and immune cells
- Cell-cell communication revealed plasma cells as major players

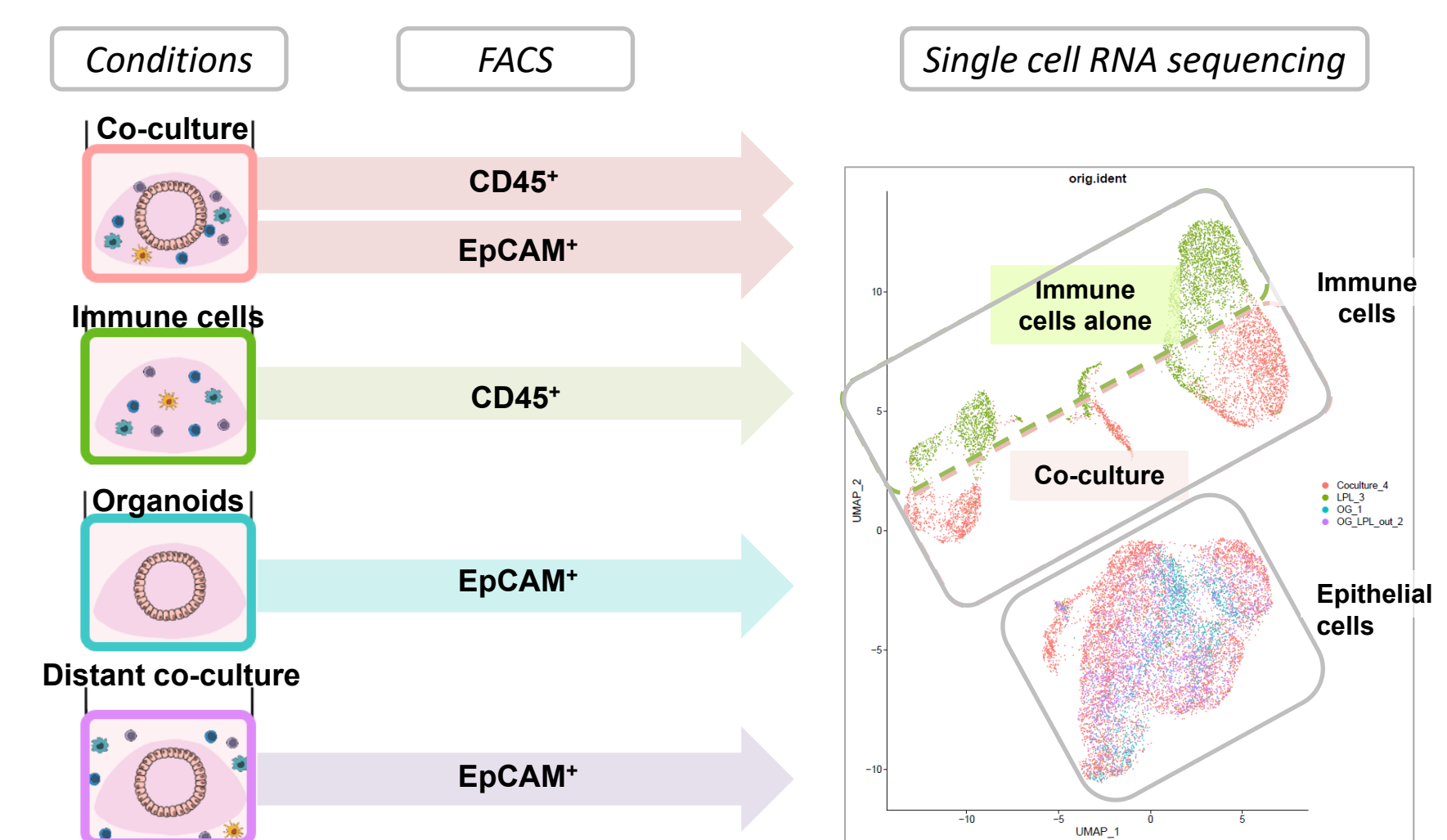
Cytokine release

- IL-6 release was increased upon co-culture
- IL-8 release was highest in co-culture



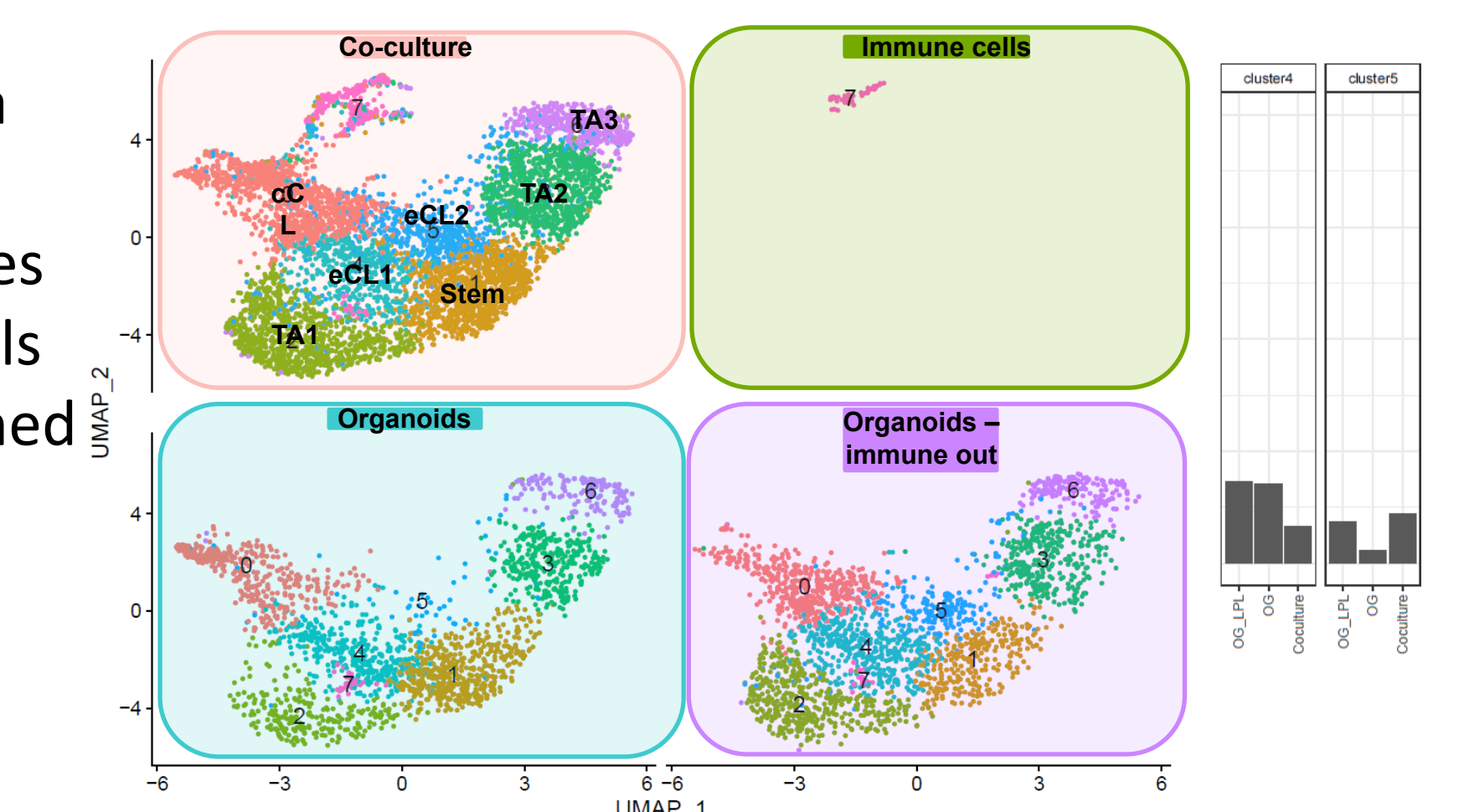
scRNA-seq of sorted co-cultured cells

- All major immune cell types and could be identified
- Epithelial cells were devoid of goblet cells



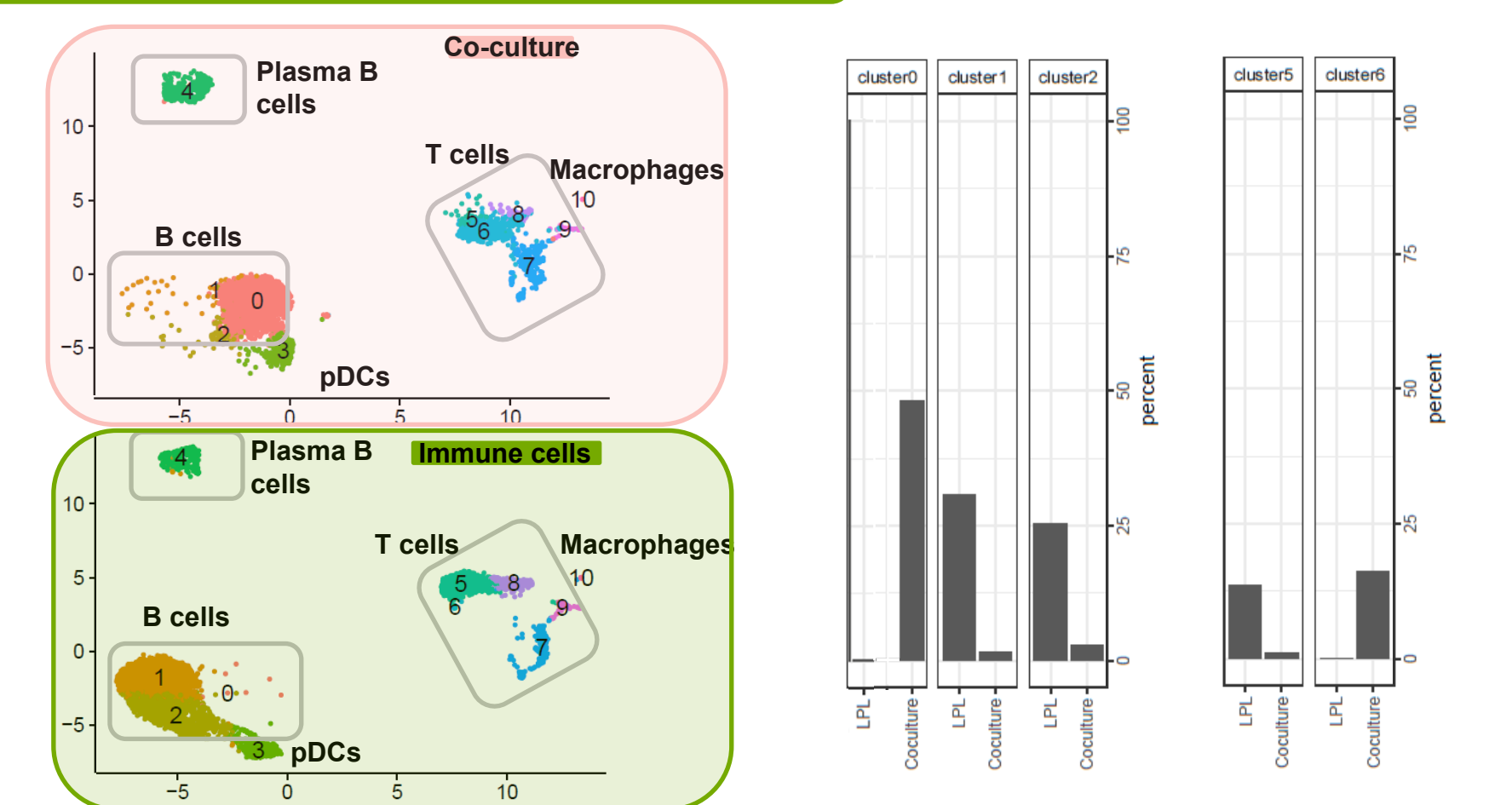
Epithelial cell scRNA-seq analysis

- Co-culture induced a shift towards more proliferative cell types
- EpCAM+ immune cells identified and enriched upon co-culture

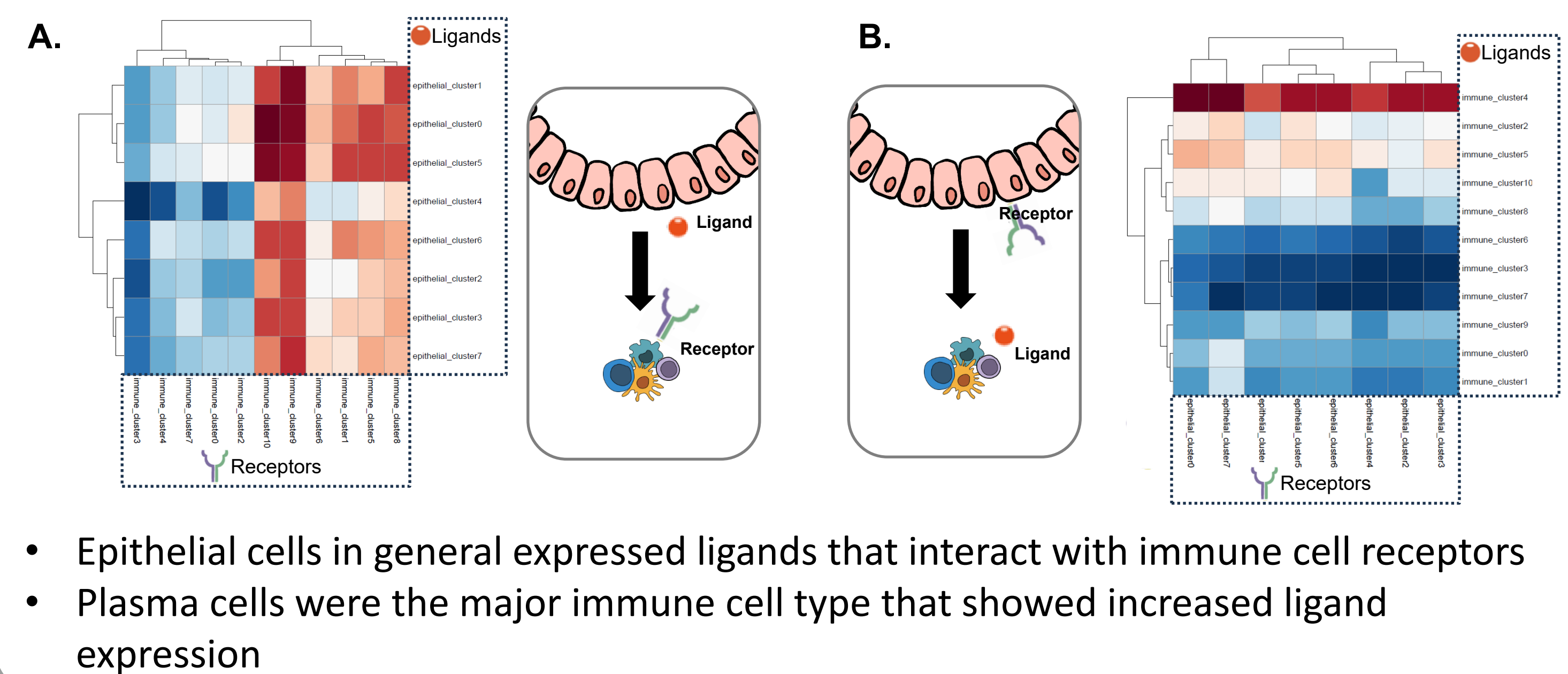


Immune cell scRNA-seq analysis

- Co-culture with epithelial cells introduced major changes in B and T cell expression profile
- Major shifts in cluster sizes



Cell-cell communication



- Epithelial cells in general expressed ligands that interact with immune cell receptors
- Plasma cells were the major immune cell type that showed increased ligand expression