Using inter-cellular communication maps to facilitate network medicine

Lejla Potari-Gul[1], Dezso Modos[1,2], Denes Turei[3], Alberto Valdeolivas[3], Matthew Madgwick[1,2], Julio Saez-Rodriguez[3], Tamas Korcsmaros[1,2]

Earlham Institute, Norwich, UK[1]; Quadram Institute, Norwich, UK[2]; Heidelberg University, Heidelberg, Germany[3]

Ulcerative colitis (UC) is an inflammatory bowel disease (IBD), which affects the colon and the rectum. During the pathogenesis of the disease, both the intracellular and the intercellular interactions are rewired. A recent study published single-cell RNA-seq data of healthy, inflamed and non-inflamed UC colon. We combined this dataset with OmniPath, an integrated resource of curated intracellular and the intercellular interactions we developed earlier. We analyzed the intercellular interactions between 5 cell types (dendritic cell, macrophage, regulatory T cell, myofibroblast, Goblet cell), compared healthy colon and non-inflamed UC, and explored the downstream intracellular signaling processes affected by the intercellular communications between cells.

Results revealed that cells were connected to each other in both conditions, however, the intercellular signaling diverged among cell types and between the same pair in different conditions as well. In healthy condition, cells were tightly communicating to dendritic cells which are the main antigen-presenting cells. In contrast, during UC, cells were more connected strongly to T reg cells, and activate their receptors, hence causing various downstream signalization.

We examined the interaction between myofibroblast and regulatory T cells and found ligands and receptors expressed only in one condition (healthy or non-inflamed UC - called condition-specific receptors). Analysing the downstream signaling from the condition-specific receptors on T cell surface, MAPK and TLR2/6, TLR7/8 pathways were discovered in healthy while TLR4 and TLR3 pathways in diseased Treg cells. We have built up a pipeline to predict not only cell type but also condition-specific effects on intercellular communication, therefore, facilitate the identification of potential drug targets on cell type level.

References and useful links

http://omnipathdb.org

Turei *et al, Nature Methods*, 2016

Smilie *et al, Cell*, 2019