

### **Inflammatory bowel disease at single-cell and sub-cellular spatial resolution**

CosMx Spatially Molecular Imaging (SMI) (NanoString) is a recently developed technology that enables spatially resolved profiling of tissue at molecule-level resolution at an unprecedented scale (up to 1,000 RNA analytes). We applied scRNA-seq and CosMx SMI to investigate the molecular basis of Ulcerative colitis and Crohn's disease: chronic inflammatory bowel diseases (IBD) that show a perplexing heterogeneity in manifestations and response to treatment.

Patients exhibited a notably high diversity in the myeloid compartment. Besides resident macrophage subsets (M0 and M2), we found a variety of activated macrophages including classical (M1) and new inflammation-dependent alternative (IDA) macrophages, as well as intestinal neutrophils in three transcriptional states. Sub-epithelial IDA macrophages expressed NRG1, which promotes epithelial differentiation. By contrast, IDA macrophages not expression NRG1 were expanded within the submucosa and in granulomas, in proximity to inflammatory fibroblasts, thereby potentially promoting macrophage activation.

Overall, our study emphasises the diversity and plasticity of the intestinal myeloid compartment where macrophages sense and respond to unique tissue microenvironments, and perhaps contribute to heterogeneity in IBD through an interplay of unique transcriptional signatures and tissue distribution.

Reference: Garrido-Trigo et al. (2022)

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