Modelling inflammatory bowel disease in human intestinal organoids using a high-throughput workflow

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Inflammatory bowel diseases (IBD) are characterized by chronic inflammations of the gastrointestinal tract during which the intestinal mucosal barrier gets damaged. Until today, mice models have been used to unravel the complex interactions involved in IBD, yet they often fail to predict human responses. In recent years, organoids have emerged as a game-changing tool for disease modelling and drug screening. These organoids are three-dimensional, miniaturized and simplified versions of an organ that mimic some of the key features of the native tissue *in vitro*. Traditional organoid culture methods consist of embedding these structures in solidified extracellular matrix (ECM) thus introducing an intrinsic lack of reproducibility and creating are highly heterogeneous organoid populations. To overcome these challenges, we used Gri3D®, an innovative hydrogel-based ultra-dense U-bottom shaped microcavity array platform. Gri3D® enables the generation of a single organoid in each microcavity in suspension-like conditions, without a solid ECM, allowing organoid cultures standardization. Combined with a high-content imaging ImageXpress® Micro Confocal system, organoids were live-monitored over time to track key IBD related phenotypes at a single-organoid level. We report the induction of intestinal inflammation on healthy human rectal organoids using pro-inflammatory cytokines (TNF-α and Il-1β). Upon treatment, the epithelial barrier was disrupted and further assessed by immunostaining of tight junctions. Interestingly, treated organoids show slower growth rate and decreased budding capacity. We demonstrate here the use of Gri3D® as a robust and high-throughput in vitro platform for human GI organoid-based IBD modelling.