Development of biomimetic models of intestinal tissue: guiding cellular self-organization through biofabrication techniques

Epithelial tissues contain three-dimensional (3D) microstructures that guide cell self-organization at the tissue level. In the small intestine, crypts and finger-like villi microstructures improve its absorbance function, provides specific microenvironments and compartmentalizes cell types [1–3]. Despite its physiological relevance, tissue architecture and multicellular population are neglected in the standard *in vitro* models, thus compromising their predictive capabilities [4]. Our efforts in addressing these shortcomings by including key elements to mimic the native tissue *in vitro* will be discussed in this talk. First, this will include strategies to promote cell's self-organization capabilities giving rise to crypt-villus domains on 2D monolayers [5], and strategies to engineer cell spatial positioning through micropatterning. Then, our approach to include the 3D architecture of the tissue will be addressed. In here, light-based biofabrication techniques to produce 3D villus-like structures [6,7] will be discussed. Finally, I will introduce our biofabrication proposal to produce tissue engineered models that include the epithelial and the stromal compartments [8]. Improving the prediction capabilities of cell-based assays is a growing strategy to lead to more efficient drug development processes. As 2D-based systems are showing their limits, new 3D strategies are gaining acceptance among the scientific community [9]. Our approaches aim to further accelerate this trend by providing feasible strategies to routinely incorporate 3D multicellular structures at the tissue level in cell culture systems.

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