A mechanically active 3D gut-on-chip for intestine-microbiome co-culture

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Introduction

It is now evident that the gastrointestinal bacteria contribute in shaping the immune system in both physiological and pathological conditions [1]. Traditional in vitro co-culture models fail to recapitulate the underlying mechanisms [2]. Owing to the ability to recreate complex multicellular architectures in finely controlled dynamic environments, 3D-microfluidic culture systems represent promising tools to overcome these limitations [2-3].

Theory and Experimental procedure

Early gut-on-chip devices, based on 2D cellular monolayers seeded on thin porous PDMS membranes, demonstrated that a peristalsis-like mechanical actuation plays a crucial role in the maturation of the model [2]. More recently, the recapitulation of a 3D microenvironment proved increased faithfulness to the in vivo condition in terms of shape, and functionality thanks to the use of ECM-like gels [4]. Here we report a novel gut-on-chip device combining for the first time a 3D architecture with a controlled mechanical actuation. The device is composed by two layers: a cell culture compartment, containing epithelial (Caco-2 and HT-29 MTX co-culture) and vascular (HMEC-1) layers separated by fibrin gel, and an actuation chamber. Once the pressure in the actuation chamber increases, a controlled uniaxial strain (10%, 0.2Hz) is transferred to the cellular construct mimicking peristalsis. Imaging-based assays and RNAseq were used to evaluate cells viability, barrier functionality and epithelial maturation after 7-9 days of culture. Preliminary co-culture experiments using complex microbiota communities collected from healthy and pathological tissues were performed using the proposed platform.

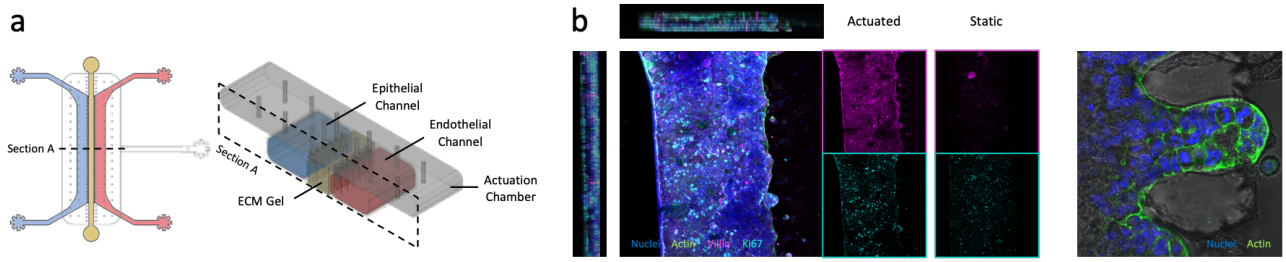

Figure 1 a) 3D mechanical active gut-on-chip design. b) Mechanical actuation increases epithelium proliferation (Ki67) and maturation (Villin) and favors the formation of 3D villi-like structures.

Results and Discussion

Complete epithelial and endothelial tubules were obtained and characterized on chip. Noteworthy, mechanical actuation increased epithelial cells proliferation (Ki67) and maturation (Villin) and favored the spontaneous formation of 3D villi-like structures.

Conclusion

The developed 3D gut-on-chip device is suitable to assess the influence of peristalsis-like mechanical deformations on epithelium development and functionality. Mechanical actuation could also play a crucial role for long term co-culture experiments between human intestinal cells and bacteria complex communities.

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References

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