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* and *in vivo* co-culture models suffer from intrinsic limitations [2-3]. 3D-microfluidic culture systems may overcome these limitations, because they recreate complex multicellular architectures in a finely controlled dynamic environment [3-4].

Theory and Experimental procedure

In early gut-on-chip devices, relying on 2D cellular monolayers seeded on thin porous PDMS membranes, peristalsis-like mechanical actuation demonstrated to play a crucial role in model maturation [3]. More recently, the recapitulation of a 3D microenvironment proved increased faithfulness to the *in vivo* condition in terms of shape, functionality, and polarity thanks to the use of ECM gels [5]. Here we report a novel gut-on-chip device combining for the first time a 3D architecture with a controlled mechanical actuation. The device contains 3 independent culture units. Each unit is composed by two chambers: a cell culture compartment, containing epithelial (Caco2 and HT29 MTX cell co-culture) and vascular (HMEC1 or HUVEC) layers separated by a collagen-based gel, and an actuation chamber. Once the pressure in the actuation chamber increases, a controlled uniaxial strain (10%, 0.15Hz) is transferred to the epithelium layer, enhancing its maturation. Imaging-based assays and transepithelial electrical resistance (TEER) on-chip measurements were used to evaluate cells viability and barrier functionality after 5-7 days of culture. Complex microbiota communities collected from healthy and pathological tissues were introduced in the gut-on-chips to perform co-culture experiments and evaluate the influence of different bacterial consortia on intestinal epithelium integrity.

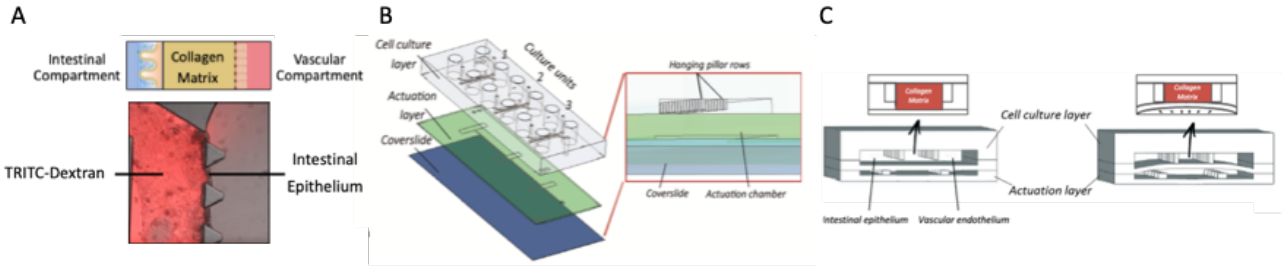

Figure 1: A) Schematic section of the static 3D gut-on-chip device and dextran permeability assay experimental image. B) Platform schematic of the mechanically active 3D gut-on-chip device. C) Working principle of the mechanically active 3D gut-on-chip device.

Conclusion

The developed 3D gut-on-chip devices represent good intestinal models to study the interaction between human intestinal cells and bacteria complex communities. Moreover, the mechanical active device can be used to investigate the importance of peristalsis-like mechanical deformations on epithelium development and functionality and allows to perform long-term co-culture experiments.

References

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