A mechanically active 3D gut-on-chip to study intestine-microbiome-tumor interactions

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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].
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 [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 and vascular layers separated by ECM 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. Complex microbiota communities collected from healthy and pathological tissues were introduced in the gut-on-chips to evaluate the influence of different bacterial consortia on intestinal epithelium integrity.
In parallel, we developed a tumor-on-chip device consisting of patient-derived tumor spheroids embedded in ECM gel and different therapies were tested on-chip. The two modules will be integrated to study the role of gut microbiota in shaping immune system and anti-tumor therapy.

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