3D histological competent human tissues in vitro for reliable OoC devices

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In order to fulfill the potential of Organ on Chip (OoC) technology as a partial replacement for animal models, it is essential to develop tissue and organ models that accurately reproduce the composition and organization of the extracellular space. While significant progress has been made in integrating sophisticated miniaturized instruments for on-chip control and sensing, the current design and implementation of tissue-engineered constructs for use on chips is lacking. The widespread use of exogenous materials as cell scaffolding, coupled with limited control over the microenvironment at the single-cell level, greatly undermines the trustworthiness and physiological relevance of OoC models. To ensure robustness and reliability, OoC devices should consider not only the three-dimensional nature of the tissue but also the spatiotemporal presentation of molecular cues and the morphophysical characteristics of the cell microenvironment in (patho-)physiology. In this context we established a bioengineered-inspired strategy for producing 3D human tissue and organ equivalents in vitro, with histological competence. Leveraging the pivotal role of stromal fibroblasts and the stroma itself in physiological and pathological tissue genesis, we have developed viable 3D tissue equivalents where cells are cultured within their own extracellular matrix (ECM). Furthermore, we have designed a microfluidic platform to culture these 3D tissue analogs in a controlled environment. By adopting this approach, we have successfully created functional OoC models in which cells are surrounded by endogenous ECM, faithfully replicating the cell-cell and cell-ECM interactions observed in vivo. These models effectively recapitulate patho-physiological characteristics of organ diseases and morphogenesis as well as their response to an exogenous stimulation.