Towards a human endothelialised heart-on-a-chip to model cardiac pathophysiology

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Cancer and cardiovascular disease are the world's leading causes of death. Despite numerous attempts in advanced treatments, the lack of predictive cardiac models results in many failures in clinical trials of new therapies. Currently, two-dimensional cellular cultures and animal models are primarily used, but both have drawbacks and fail to accurately model the human heart. Consequently, much research is focused on developing new heart models.

This work describes the initial steps in the development of a heart-on-chip (HoC) within a microfluidic system designed to model human cardiac processes, including the interaction between the three main cardiac cell types. The model aims to replicate physiologically relevant conditions by compartmentalizing fibroblasts and cardiomyocytes within a three-dimensional collagen gel in close proximity to the endothelial barrier.

To this end, we have characterized cardiomyocytes derived from human induced pluripotent stem cells, human cardiac fibroblasts and human endothelial cells by flow cytometry and/or immunofluorescence. Additionally, as a critical step in the development of the HoC, we have defined a co-culture medium that supports the viability of all the cell types involved. In this media, the endothelial cells are able to form an endothelial barrier in static models.

This data establishes the background for a coherent environment for maintaining and studying a complex tissue microenvironment within the HoC platform featuring a functional endothelial barrier.