Engineering 3D heart tissues using hPSC derived cardiac cells

The main function of the heart is to pump the blood through the body, via the contraction of the cardiomyocytes (CMs) that constitute the cardiac tissue. CMs are the cells in the cardiac tissue that produce the contraction force. The contraction force is a factor that determines the maturity of the CMs. A high contraction force means more mature CMs and more mature CMs on a tissue is a more representative of the adult human heart.

The 2D models don't resemble tissue structure and organization of the human heart. Therefore we need to go 3D. Scientists have shown that 3D models have the advantage of mimicry the tissue organization, functions and cell interaction. The current gold standard 3D cardiac model validated by different scientific groups is the engineering heart tissues (EHT). With EHTs we can measure contraction force of 3D tissues.

We have successfully developed a medium throughput platform that fits in a 12 well plate (A). Where we can make 36 EHTs using hPSC-CMs (B). The contraction force of the 3D Cardiac tissues is analyzed with a custom made software that identifies the displacement of the tissues and that distance, later on, is converted to force. This software automatically goes through the stack of folders with the recordings of the EHTs and gives as a result 3 graphs (Displacement, the force of contraction and speed) and excel file with all the data for further analysis (C). The cell line that we used is a Double Reporter of mRubyII-α-Actinin and GFP-NKX2.5 (DRRAGN), which allows live recording of sarcomere movement and alignment of cardiac cells (D).

Establishing this platform would allow to assess the maturation of the CMs by using different culture medium, electrical stimulation and co-culture of different cells, to obtain an in vitro 3D cardiac tissue that is most representative of the human heart.

