Building blocks of the human heart

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STELLINGEN BEHOREND BIJ HET PROEFSCHRIFT:

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1. Patient-specific hiPSC-CMs and tissue models have the potential to advance basic research on the one hand and contribute to personalized and regenerative medicine, on the other. This thesis
2. hPSC-CMs do not display all of the morphological and functional characteristics of adult cardiomyocytes. This needs to be taken into account when studying late-onset cardiovascular diseases but also mechanisms that are based on the highly specialized contraction machinery or gene splicing variants only expressed postnatally. This thesis
3. The 2D microenvironment in which hPSC-CMs are cultured does not entirely recapitulate the complex dynamics and properties of the human heart. This thesis
4. There is clear evidence that including non-cardiomyocyte cell types in multicellular cardiac tissue mimics *in vitro*, is essential to advance current disease models, which primarily focus on monotypic cultures of cardiomyocytes, neglecting other cellular components of the myocardium. This thesis
5. The human heart contains an estimated 2 to 3 billion cardiac muscle cells and they represent >70% of its volume but they account for fewer than one third of the total number of cells in the heart. Tirziu, D., Giordano, F.J. & Simons, M., 2010. Cell Communications in the Heart. Circulation, 122(9), pp.928–937.
6. It is becoming clear that in solid organs different cell types sense different stimuli and integrate their responses to them. Thus, no cell is an island, particularly in the heart. Tirziu, D., Giordano, F.J. & Simons, M., 2010. Cell Communications in the Heart. Circulation, 122(9), pp.928–937.
7. Cardiac endothelial-myocardial interactions play a central and indispensable role in global cardiac organ growth, contractile performance, and rhythmicity. Brutsaert, D.L., 2003. Cardiac Endothelial-Myocardial Signaling: Its Role in Cardiac Growth, Contractile Performance, and Rhythmicity. Physiological Reviews, 83(1), pp.59–115.
8. Both electrophysiological and molecular data suggest that cardiac fibroblasts and myocytes are in direct contact and part of a syncytial network afforded by the conglomerate of connexin 43 and 45 hemichannels. Kakkar, R. & Lee, R.T., 2010. Intramyocardial Fibroblast Myocyte Communication. Circulation Research, 106(1), pp.47–57.
9. It is an exciting time for the study of fibroblast biology. Particularly in the heart, the characterisation of the embryological origin of the cardiac fibroblast and the discovery of a fibroblast cardiogenic programme have been paradigm-shifting, demonstrating that the cardiac fibroblast is unique among fibroblasts, as well as being functionally relevant for both regeneration and pathological remodelling. Furtado, M.B. et al., 2016. View from the heart: cardiac fibroblasts in development, scarring and regeneration. Development (Cambridge, England), 143(3), pp.387–397.
10. If I have the belief that I can do it, I shall surely acquire the capacity to do it even if I may not have it at the beginning. Mahatma Gandhi (1869-1948). Everything is possible as long as you put your mind to it.
11. You don't need to limit yourself anymore. You've opened your heart. Now open your mind. Look around. See all the possibilities. The more open you become, the more creative you'll be – in work, in play, in love, in life. The more creative you are, the more possibilities you'll see. Melody Beattie. Journey to the Heart. Published in March 1996. Learn to be open-minded and you will be surprised at how many possibilities you have in front of you.
12. The important thing is not to stop questioning. Curiosity has its own reason for existing. Albert Einstein (1879-1955). Curiosity is the most powerful thing that keeps us alive.