Title: The effects of an oxygen gradient on cardiomyocyte morphology

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Abstract
Cardiovascular diseases (CVD) cause the majority of mortality worldwide, with heart ischemia as the primary contributor to premature deaths globally. In heart ischemia, an occluded blood vessel restricts the flow of oxygen and nutrients into a part of the myocardium, leading to ischemia. An oxygen gradient, an ischemia border zone (iBZ), forms between the normal and the ischemic myocardium. Existing research has uncovered iBZ to be prone to arrhythmia and to cause less force compared to normal myocardium. However, the effects of the iBZ on cellular and molecular levels remain unclear. The human induced pluripotent stem cell-derived cardiomyocytes (iPS-CMs) combined with organ-on-chip technology provides a powerful tool to study the cellular and molecular aspects of iBZ.

This work aims to
1) Model the iBZ using an in-house developed oxygen gradient chip.
2) Study how the oxygen gradient affects iPS-CMs morphology.

We use luminescence-based oxygen sensing to monitor the formation of the oxygen gradient in the chip. OxyGenie cell culture platform is used to maintain the correct temperature and to supply oxygen on the chip. The chip has two gas inlets, which deliver different oxygen concentrations, in our study either 0-19% or 0-5%. It has been demonstrated that an oxygen-gradient forms as expected in an empty chip. Formation of the gradient will be also demonstrated with iPS-CMs plated on a chip. The effects of oxygen gradient on the expression of cardiac specific sarcomeric proteins are assessed by immunocytochemistry. In addition, it has been shown earlier that uniform hypoxia decreases nuclei size and disrupts sarcomere structure. Thus, the aim is also to assess how these changes occur in an oxygen gradient.