Engineered cardiac model systems for dilated cardiomyopathy

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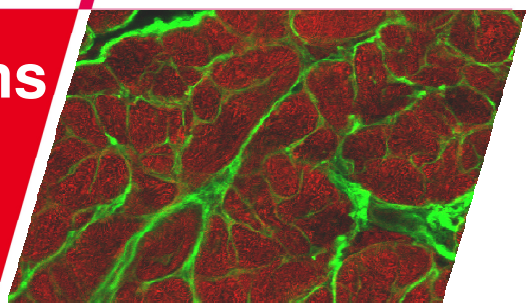
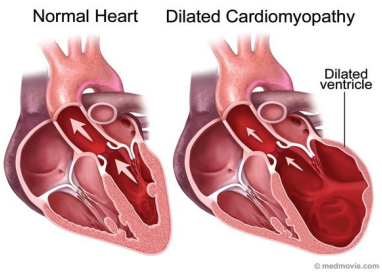


Introduction

Dilated cardiomyopathy (DCM) is characterized by diminished contractile function and progressive enlargement of the heart. It is the leading cause of heart failure and DCM patients suffer from arrhythmia and risk a sudden death[1]. The goal of this project is to develop an engineered cardiac model system of healthy and dilated cardiac tissue to perform studies on the effect of DCM on mechanical properties resulting from changes in cell-cell and cell-matrix interactions.



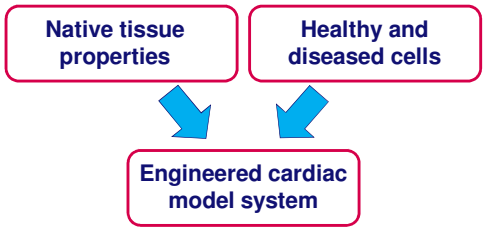


Fig 1. Project overview: To create an engineered cardiac model system, we will characterize the native environment of cardiomyocytes in healthy and diseased tissue. Furthermore HL-1 murine cardiomyocytes will be used as healthy cells, and they can be transfected or treated with drugs to induce 'disease'.

Native Tissue properties

The composition, architecture and mechanical properties of healthy and diseased cardiac tissue from mouse models, as well as from human cardiac biopsies, will be determined to mimic the native environment of cardiac cells in engineered cardiac models system.

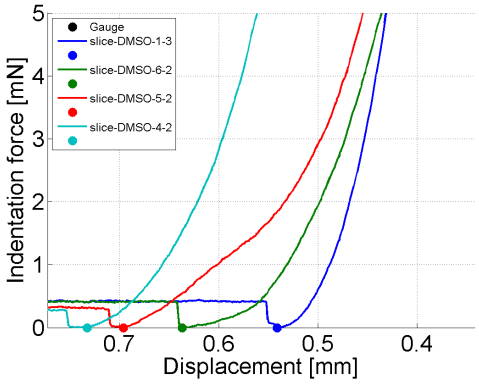


Figure 2: Results of initial indentation tests on porcine myocardium.

Tissue stiffness will be determined using indentation tests (fig. 2), which can be related to the matrix composition, as determined by histology (fig. 3). Furthermore, tissue composition in both healthy and diseased myocardium will be studied by performing immunohistochemistry.

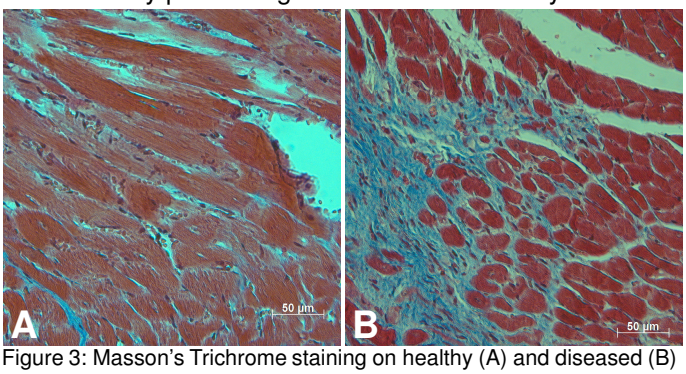


Figure 3: Masson's Trichrome staining on healthy (A) and diseased (B) mouse myocardium with cells in red and collagen in blue. Diseased tissue had more collagen an a more chaotic structure compared to healthy tissue.

Healthy and diseased cells

The HL-1 murine cardiomyocyte cell line, will be used to develop our engineered cardiac model system. Since this cell line has been studied in 2D only[2,3], we will start by investigating the application for making 3D constructs (fig.4).

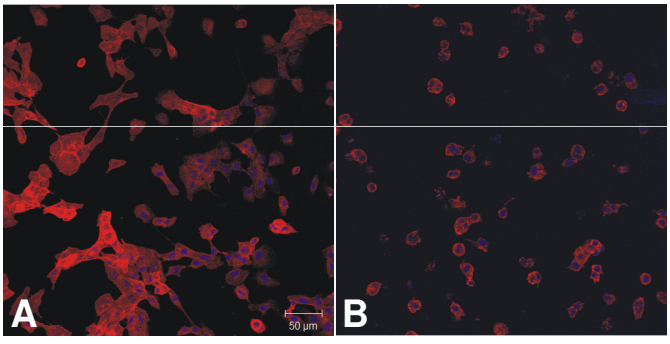


Figure 4: HL-1 cells in 2D (A) and in a 3D hydrogel (B) stained for actin in red and nuclei in blue. HL-1 cells in 2D have a more spread morphology and more stress fibers, compared to 3D, where the cells have a more round morphology.

Future Research

Different mouse models for DCM will be characterized by immunohistochemistry and indentation tests to provide input for the engineered cardiac model system. The HL-1 cardiomyocytes will be used make 3D cardiac tissue models to perform studies on the effect of DCM on cell-cell and cell-matrix interactions.

[1] Taylor et al. *Orphanet.J.Rare.Dis.* 2006.
[2] Claycomb et al. *Proc.Natl.Acad.Sci. 1998.*
[3] White et al. *Am.J.Physiol.Heart.Circ. Physiol,* 2004