



## **Understanding cardiac failure using engineered biomaterials**

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### **Abstract**

Cardiovascular diseases are a major cause of mortality worldwide. There is a large need to develop in vitro platforms that mimic the tissue environment to understand these cardiovascular diseases. Towards that objective, we aim to develop surface engineering strategies to support the growth of cardiomyocytes. Two different approaches were investigated to modify the surface for culturing cardiomyocytes, which in turn could be used for investigating cardiac hypertrophy. Firstly, we have used keratin from human hair to develop a simple, efficient and cost-effective protocol for culturing cardiomyocytes. The nanoscale coating with keratin was characterized using SEM and AFM. Our optimized protocol for culturing cardiomyocytes yielded 106 cells per heart with minimum use of reagents. Molecular characterization of cardiomyocytes revealed that they can grow and show spontaneous contraction on keratin-coated substrates. Cardiomyocyte differentiation was assessed by immunofluorescence. Cardiac hypertrophy was induced agonist, PE. Signalling proteins such as p-Akt, p-mTOR and transcript levels of genes associated with hypertrophy were up-regulated along with marked increase in protein synthesis on development of hypertrophy. Secondly, we also demonstrate that microscale topography can be used to obtain engineered cardiomyocytes which closely resembles mammalian heart. Cardiomyocytes grown on these micro-ridges showed global alignment and elliptical nuclear morphology. Calcium currents traversed the engineered cardiomyocytes in a directional manner and were responsive to hypertrophic stimuli. Taken together, these results highlight the biocompatibility, suitability and ease of using keratin coated surfaces for neonatal murine cardiomyocyte culture and also emphasize the importance of topography in assessing cardiac function. We describe an economical and efficient protocol for murine cardiomyocyte culture on surfaces coated with keratin. We also validated that our culture protocol can serve as a model for studying cardiac hypertrophy.