

Master Project Proposal

For students with a background on Molecular Biology, Bioengineering or related areas

Title: Alternative splicing in heart disease

Synopsis:

Heart failure is a major public health issue. Yet, the cellular and molecular mechanisms that trigger cardiovascular diseases are largely unknown. To date, basic research work has been hampered by lack of appropriate models. The recent emergence of patient-derived induced pluripotent stem cells (hiPSCs) that can be differentiated into functional cardiomyocytes holds great promise as an exciting new approach for cardiac disease modelling.

Determining whether cardiomyocytes differentiated in vitro from hiPSCs (hiPSC-CMs) recapitulate cardiac-specific characteristics is currently an area of intense research. Recent evidence is revealing a critical role of alternative splicing in cardiac development and heart disease. Thus, understanding how alternative splicing contributes to regulation of cardiac gene expression will help elucidate the mechanisms underlying human heart failure.

Main objectives:

1. Induce cardiomyocyte differentiation in vitro from iPSCs derived from patients with heart disease;
2. Using RT-PCR and fluorescence microscopy, compare gene expression patterns in cardiomyocytes derived from control and patient iPSCs.

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Bibliography:

Lan F et al. Abnormal calcium handling properties underlie familial hypertrophic cardiomyopathy pathology in patient-specific induced pluripotent stem cells. *Cell Stem Cell*. **12**, 101–113 (2013). URL: <http://dx.doi.org/10.1016/j.stem.2012.10.010>

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