Cardiomyocytes of Mice
A New Way to Examine the Function of Mutant MYBPC3 Expression in Cardiomyocytes of Mouse

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Rationale: Alterations to the cardiac regulatory light chain (RLC) phosphorylation state correlate with many types of cardiac disease including familial hypertrophic cardiomyopathies (FHC’s) and heart failure (HF) post myocardial infarction (MI). However, little is known regarding the role of RLC phosphorylation in regulating the cardiac muscle contraction mechanics during shortening. Objective: Determine the mechanical effect of altered cRLC phosphorylation on the force-velocity characteristics of cardiac muscle.

Autosomal dominant mutations in myosin binding protein C (MYBPC3) account for up to 30% of myofibrillar mutations causing Hypertrophic Cardiomyopathy (HCM). We used Spontaneous Oscillatory Contractions (SPOC) to compare the performance of isolated cardiomyocytes from heterozygous MYBPC (+/-) and homozygous MYBPC (-/-) and wild type (+/+) mice. Our aim is to identify changes in their contractile parameters. SPOC is a physiological state that is intermediate to full contraction and relaxation. The stable auto-oscillatory properties of SPOC are well suited to precise measurements of contraction and relaxation.

Preliminary evaluations reveal there is: (1) a progressive prolongation in both the relative lengthening and shortening periods from MYBPC++/+ to MYBPC++/- and MYBPC-/-; (2) MYBPC++/- exhibits faster rates of lengthening than MYBPC++-/+; (3) MYBPC-/- displays significantly depressed rates of shortening compared to MYBPC+-/+ and MYBPC++/+.

These findings suggest significant systolic dysfunction in MYBPC-/- associated with severe hypertrophic remodelling. Perhaps, more importantly MYBPC++/- exhibits diastolic dysfunction consistent with previous reports examining SPOC in human HCM at the 56th Biophysical Society Meeting. We conclude that SPOC can objectively assess the functional state of heart muscle fibres in this mouse model.