Heart failure comprises of clinically distinct inciting causes but a consistent pattern of changes in myocardial gene expression suggests that unifying biochemical mechanisms underlie disease progression. With the recent revolution in deep sequencing technology, up to 75% of the human genome is now known to be transcribed to RNA. Estimates for the number of long non-coding RNAs (≥200 nucleotides) reach up to 10,000. This project aims to discover whether the myocardial expression of lncRNAs changes in the failing heart.

Paired-end RNA-seq from total RNA isolated from stretched and non-stretched neonatal mouse cardiomyocytes was carried out to generate 36-40 million 76-mer sequence reads per sample. Mechanically stretching myocytes with equibiaxial stretch apparatus mimics pathological hypertrophic cardiomyopathy.

Two lncRNAs, MIAT and MALAT-1, were found to have significantly increased expression in stretched cardiomyocytes relative to the non-stretched. MIAT and MALAT-1 have previously been associated with increased risk of myocardial infarction and metastatic cancers respectively, but never before with heart failure.

In addition, five novel transcripts were identified in our RNA-seq that showed differential expression in stretched cardiomyocytes compared with controls. These are regions of the genome that are currently unannotated and potentially transcribe novel lncRNAs. Differential transcript expression was validated by RT-qPCR.

Subsequent in vitro and in vivo experiments will seek to understand the role of these lncRNAs in cardiac biology and how they could contribute to the progression of this complex disease.