Refined Methods for Transcriptome Analysis in Cardiomyopathy. A. Cullen, (MD, SOM), M. Taylor, L. Mestroni, S. Graw, D. Grine, G. Storm, S. Gao, and S. Chen, Human Medical Genetics and Genomics, Cardiovascular Institute and Adult Medical Genetics Program, Department of Cardiology, and MD Program, University of Colorado, Denver, CO.

**Purpose of Study:** Sweet et al. (2018) reports that severity of heart failure (HF) symptoms and left ventricular dysfunction determine current HF treatment. An approach based on underlying biology may ultimately facilitate a precision medicine approach to HF\(^1\),\(^2\). Using the same data from this 2018 study, we developed a novel modification for bioinformatic analysis of differentially expressed genes (DEG’s) between ischemic cardiomyopathy (ICM), dilated cardiomyopathy (DCM), and non-failing (NF) heart tissue. Our process also permitted easy adjustment of statistical parameters in DEG analysis of this and other datasets. **Methods Used:** RNA-seq from 13 ICM, 37 DCM, and 14 NF control human left ventricular samples with expression data for 57974 genes. Matlab analysis began with purging data of missing and nonsensical entries. We first aimed to replicate the analysis of Sweet et al. Initial replicate lists mostly match the list of Sweet et al., but current efforts to adjust for age and gender to create more complete matching are underway. In DEG identification, we also adjust threshold stringency for a) fold-change and b) mean absolute change between ICM, DCM, and NF gene expression levels to identify smaller, more focused DEG sets. We will also present results of bioinformatic validation testing on a newly generated human heart tissue transcriptome dataset.

**Summary of Results:** Using the DEG cutoff conditions of the 2018 study, we largely replicated its gene lists, but are aiming for more exact matching through age and gender adjustment. With subsequent varying cutoff conditions for mean and fold-change, we produced narrower DEG lists for pathway analysis. Applying the same algorithm to a new, larger dataset will test repeatability. **Conclusions:** Our bioinformatic pipeline provides for flexible adjustment of DEG identification parameters, allowing for tailored generation of DEG lists. Pathway analysis, with verified repeatability across multiple datasets, enables discovery of the underlying biology of HF due to ICM and DCM.

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