Transcriptomic profiling of non-ischemic cardiomyopathies; what lies beyond sarcomere in characterization of non-ischemic cardiomyopathies?

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BACKGROUND

The application of unbiased omics to discover the molecular basis of non-ischemic cardiomyopathies (NICM) advances our understanding of the pathogenesis of idiopathic cardiomyopathies and opens a new avenue for targeted personalized drug development.

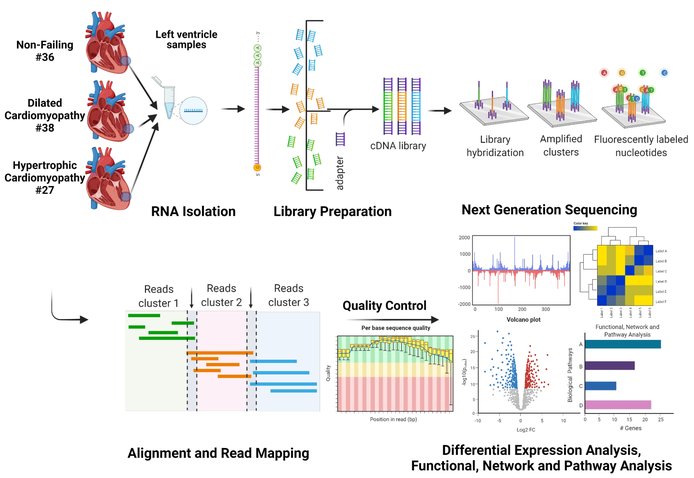
METHODS

We performed a post-hoc analysis on the high throughput gene expression database of the Myocardial Applied Genomics Network that was obtained from the repository site.

Samples were collected at the time of heart transplantation from left ventricular tissues of 36 non-failing (NF) donors, 38 individuals with dilated cardiomyopathy (DCM), and 27 individuals with hypertrophic cardiomyopathy (HCM).

Whole transcriptomic profiles of DCM and HCM were compared with NF controls.

Figure 1) Study Protocol



RESULTS

A total of 101participants (48% female) with median age of 50 years (ranged 21-80 years) were included in the analysis. Participants were age- and sex-matched between DCM, HCM, and NF groups. African Americans comprised 41% of the total study population. With log [fold change] greater than 2, and $p<0.01$, we identified 118 DEGs in DCM vs NF and 84 DEGs in HCM vs NF. More than 50% of these DEGs being overlapping between DCM and HCM.

Figure 2) DEG of DCM vs NF

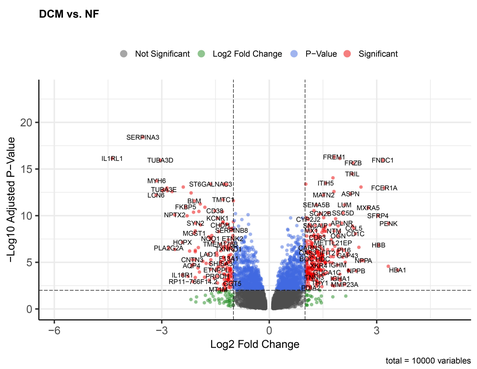


Figure 3) DEG of HCM vs NF

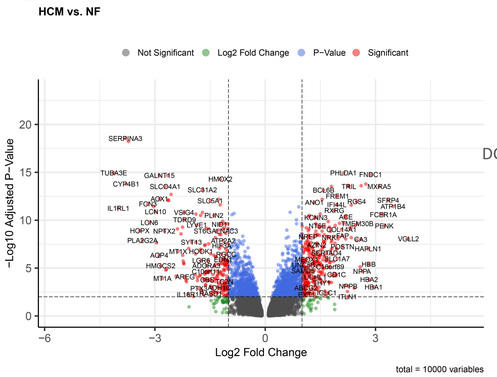


Figure 4) Heatmap of DCM vs NF

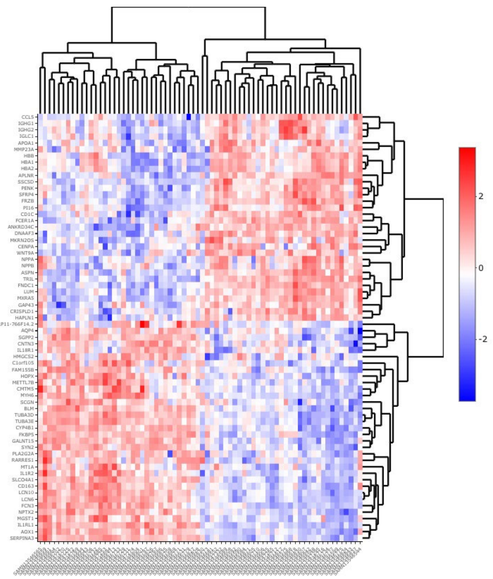
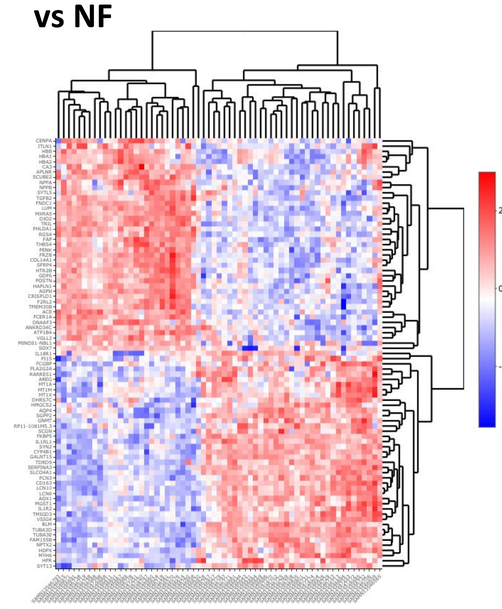
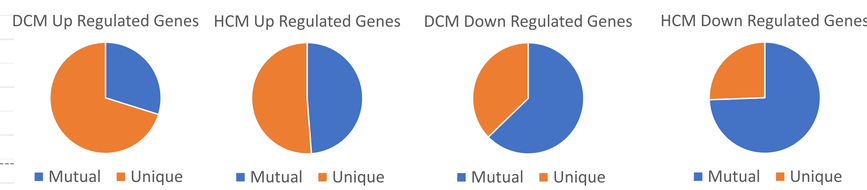


Figure 4) Heatmap of HCM vs NF



Mutual up-regulated genes in DCN and HCM encoded globin proteins, extracellular matrix glycoproteins, proteins involved in angiogenesis, calcium cycling, and natriuretic peptides. Unique upregulated DEGs in HCM were related to growth factors, glucose metabolism, transmembrane proteins involved in NOTCH signaling, and active transportation. Unique upregulated DEGs in DCM were related to the innate immune system and ion transportation. DCM and HCM shared more similarities in terms of downregulated DEG profile including pathways of several tubulin class proteins, oxidoreductase class, and scaffold/adaptor proteins

Figure 5) genes that mutually or uniquely expressed differently in HCM and DCM



CONCLUSIONS

DCM and HCM have several similarities at the transcriptomics level including biomarkers of cardiomyocyte senescence. Biomarkers of metabolism and fibrosis were more dysregulated in HCM, while innate immune response dysregulation was more prominent in DCM.

ACKNOWLEDGEMENT

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