



USING FGF21 AS A BIOMARKER FOR HEART FAILURE

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Background

Because of the heavy energetic demand of the heart, heart failure often features deficiencies in energy production. In a mouse model, mitochondrial dysfunction in cardiomyocytes leads to dilated cardiomyopathy (DCM), where the heart is enlarged and incapable of pumping sufficiently. It is thought that mitochondrial damage is also present in human dilated cardiomyopathies. Other previous research has linked Fibroblast growth factor 21 (FGF21) to mitochondrial damage in the nervous and skeletal muscle systems, suggesting its potential use as a serum biomarker for heart failure.

Hypothesis

If FGF21 is linked with mitochondrial damage in heart failure, failing heart tissue should produce high levels of FGF21 which could then be secreted into the blood stream. Serum FGF21 levels should correlate to FGF21 levels in the heart, allowing serum FGF21 to be used as a diagnostic serum biomarker for DCM.

Methods

Transcription factor A for mitochondria knockout (*Tfam KO*) mice were compared to wild type (*Tfam WT*) mice. Heart, liver, and blood samples were collected from mice 14-22 days postnatal (P14-P22). In collaboration with Dr. Drakos' lab, human serum and left ventricle tissue was provided for testing. RNA was isolated from tissue to determine FGF21 gene expression. Serum FGF21 levels were measured using an ELISA assay.

Results

Compared to *Tfam WT*, *Tfam KO* mice had a 200-fold increase in FGF21 gene expression in the heart. Both genotypes had similar FGF21 gene expression levels in the liver. Serum FGF21 levels were higher in *Tfam KO* mice than *Tfam WT* mice. P22 *Tfam KO* mice exhibited higher variability in FGF21 serum levels than their P14 counterparts. In human heart tissue, FGF21 gene expression was slightly higher in DCM patient samples compared to controls. Human serum FGF21 levels in DCM patients were higher controls, but no direct correlation was observed between FGF21 gene expression in the heart and serum FGF21.

Conclusion

DCM results in elevated serum FGF21 levels in both mice and humans, and elevated FGF21 gene expression in the heart, especially in a mouse model with mitochondrial damage. The weak correlation between serum FGF21 and FGF21 gene expression in the heart suggests that FGF21 may not be a direct biomarker for heart failure.