MG53 and diabetic cardiomyopathy

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MG53 is a striated muscle-specific protein. Its expression is significantly increased in the myocardium of several animal models with metabolic disorders. Mice with cardiac-specific overexpression of MG53 (MG53 h-TG) displayed a phenotype that closely resembles that of diabetic cardiomyopathy (DCM). At 20 weeks of age, MG53 h-TG mice developed ventricular hypertrophy, fibrosis and dysfunction, which were associated with compromised energy substrate utilization, increased lipid accumulation and insulin resistance. Interestingly, in addition to desensitizing the insulin signaling pathway, MG53 can be recruited to the promoter of PPARα and regulates its activity. The upregulation of PPARα and its target genes by MG53 contributes to the increased lipid uptake and utilization by cardiac myocytes. These unexpected results revealed a novel role of MG53 as a transcriptional regulator. We subsequently performed ChIPseq analysis to identify more target genes of MG53. Our findings underscore MG53 as an important therapeutic target for the treatment of diabetes and associated cardiovascular complications.