**REGULATION OF ANGIOGENIC RESPONSE IN DIABETIC MYOCARDIUM**

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Our earlier studies showed that AKAP12 and Thioredoxin-Interacting Protein (TXNIP) interfere with HSPA12B-induced angiogenic signaling in ischemic myocardium. HSPA12B appears to play an essential role in myocardial angiogenesis, which is impaired during diabetes. This study explores the impact of HSPA12B overexpression on heart function, neovascularization, and downstream target proteins, AKAP12, Thioredoxin-1 (Trx-1) and VEGF, in non-diabetic (ND) and diabetic (D) animals following myocardial infarction (MI). Co-immunoprecipitation followed by immunoblot analysis showed significant increase in HSPA12B/AKAP12 association in diabetic group suggesting that diabetes impairs HSPA12B availability triggering impairment of angiogenesis. This result was also confirmed by docking analysis (insilico models). Trx-1 activity along with HSPA12B and VEGF expression was increased in DHSPMI and NDHSPMI compared to respective controls. Both AKAP12 and TXNIP appeared to be down-regulated in HSPA12B-treated groups compared to controls. Echocardiography demonstrated increased fractional shortening and ejection fraction 4 weeks post-MI in DHSPMI-treated rats compared to DLZMI. Increased capillary and arteriolar density in DHSPMI compared to DLZMI was obesrved by morphometric analysis. In addition Picrosirius red staining documented decreased fibrosis in DHSPMI vs. DLZMI myocardium.

Conclusion: Therefore overexpression of HSPA12B enhances neovascularization and cardiac function following MI in diabetic animals by down-regulating AKAP12/HSPA12B association, resulting in increased HSPA12B, Trx-1 and VEGF. These findings support a role for HSPA12B gene therapy in mitigating the morbid expression of ischemic heart disease in the setting of diabetes.