**CARDIAC SPECIFIC OVER-EXPRESSION OF MEMBRANE-ASSOCIATED HUMAN STEM CELL FACTOR IMPROVES CARDIAC FUNCTION IN DIABETIC MICE**

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Objective: The aim of the present study was to investigate the effects of cardiomyocyte-specific over-expression of human membrane-associated stem cell factor (M-hSCF) on cardiac function in streptozotocin (STZ)-induced diabetic mice.Background: Diabetes induces cardiomyocyte loss and interstitial fibrosis causing diabetetic cardiomyopathy. We recently demonstrated that the cardiac-specific over-expression of M-hSCF improves cardiac function and survival after myocardial infarction. However, the effects of cardiac specific M-hSCF over-expression on cardiac function in diabetic mice are not known.

Methods: Wild-type (WT) and the inducible cardiac-specific M-hSCF transgenic (hSCF/ tTA) mice were treated with STZ to induce diabetes. Six weeks after STZ treatment, cardiac function was measured by echocardiography and in vivo left ventricle (LV) pressure-volume analysis. Morphology and histology of the heart were also assessed.

Results: Basal cardiac function was not significantly different between WT and hSCF/tTA control groups. However, both LV systolic (maximum dP/dt, end-systolic pressure, end-systolic pressure-volume relationship) and diastolic function (minimum dP/dt, end-systolic pressure-volume relationship) was significantly improved in hSCF/tTA compared to WT mice 6 weeks after STZ injection. Using tissue Doppler imaging, diabetic WT mice showed an impaired diastolic function including lower Ea/Aa ratio and higher E/Ea ration compared to controls. But the diastolic function was significantly improved in diabetic hSCF/tTA compared to WT mice. Moreover, both heart to body weight ratio and heart weight to tibia length ratio were significantly preserved in diabetic hSCF/tTA mice compared to WT.

Conclusions: Cardiomyocyte-specific over-expression of M-hSCF improves cardiac function in STZ-induced diabetes.