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Young Investigators Awards

STEM CELL FACTOR OVER-EXPRESSION IMPROVES CARDIAC FUNCTION AFTER MYOCARDIAL INFARCTION IN SWINE

Special Session
North, Room 120
Sunday, March 10, 2013, 8:15 a.m.-8:30 a.m.

Session Title: Young Investigator Awards Competition: ACCF/Herman K. Gold Young Investigators Award in Molecular and Cellular Cardiology
Abstract Category: Molecular and Cellular Cardiology
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Background: Stem cell factor (SCF), a ligand of the c-kit receptor, is a critical cytokine which contributes to cell migration, proliferation, and survival. It has been shown that SCF expression increases after myocardial infarction (MI) and may be involved in cardiac repair. The aim of this study was to determine whether SCF over-expression by gene transfer improves cardiac function in a large animal model of MI.

Methods and Results: A transmural MI was created by implanting an embolic coil in the left anterior descending coronary artery in Yorkshire pigs. One week after the MI, the pigs received direct intramyocardial injections of either a recombinant adenovirus encoding for SCF, (Ad.SCF, n=9) or β-gal (Ad.β-gal, n=6) into the infarct border area. At three months post-MI, ejection fraction increased by 12% after Ad.SCF therapy, whereas it decreased by 4.2% (P = 0.004) in pigs treated with Ad.β-gal. Preload-recruitable stroke work was significantly higher in pigs after SCF treatment (Ad.SCF, 55.5±11.6 vs Ad.β-gal, 31.6±12.6, P=0.005) indicating enhanced cardiac function after SCF gene therapy. The slope of the end systolic pressure volume loop which was analyzed by pressure volume loops at three months tended to be higher in SCF pigs (Ad.SCF, 2.16±0.59 vs Ad.β-gal, 1.66±0.45, P=0.13). Histological analyses confirmed the recruitment of c-kit+ cells as well as reduced degree of apoptosis one week after Ad.SCF injection. In addition, increased capillary density compared to pigs treated with Ad.β-gal was found at three months and suggests an angiogenic role of SCF.

Conclusions: Local over-expression of SCF post-MI induces the recruitment of c-kit+ cells at the infarct border area and results in improved cardiac function in a pre-clinical model of ischemic cardiomyopathy.