Diabetic Mesenchymal Stem Cells Therapy for diabetic heart

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Introduction: Mesenchymal stem cells (MSCs) have the potential for treatment of diabetic cardiomyopathy; however, the repair capability of MSCs declines with age and disease. MSCs from diabetic animals exhibit impaired survival, proliferation, and differentiation and therefore require a strategy to improve their function. The aim of the study was to develop a preconditioning strategy to augment the ability of MSCs from diabetes patients to repair the diabetic heart.

Methods: Diabetes was induced in C57BL/6 mice (6 to 8 weeks) with streptozotocin injections (55 mg/kg) for 5 consecutive days. MSCs isolated from diabetic animals were preconditioned with medium from cardiomyocytes exposed to oxidative stress and high glucose (HG/H-CCM).

Results: Gene expression of VEGF, ANG-1, GATA-4, NKx2.5 MEF2c, PCNA, and eNOS was upregulated after preconditioning with HG/H-CCM, as evidenced by reverse transcriptase/polymerase chain reaction (RT-PCR).Concurrently, increased AKT phosphorylation, proliferation, angiogenic ability, and reduced levels of apoptosis were observed in HG/H-CCM-preconditioned diabetic MSCs compared with nontreated controls. HG/H-CCM-preconditioned diabetic-mouse-derived MSCs (dmMSCs) were transplanted in diabetic animals and demonstrated increased homing concomitant with augmented heart function. Gene expression of angiogenic and cardiac markers was significantly upregulated in conjunction with paracrine factors (IGF-1, HGF, SDF-1, FGF-2) and, in addition, reduced fibrosis, apoptosis, and increased angiogenesis was observed in diabetic hearts 4 weeks after transplantation of preconditioned dmMSCs compared with hearts with nontreated diabetic MSCs.

Conclusions: Preconditioning with HG/H-CCM enhances survival, proliferation, and the angiogenic ability of dmMSCs, augmenting their ability to improve function in a diabetic heart.