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Reduced collagen density in infarcted myocardium facilitates induced pluripotent stem cells (iPSC) engraftment and angiomyogenesis for improvement of left ventricular function

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E xcessive scar production after myocardial infarction (MI) seriously compromises cellular regeneration. This study explores the role of collagen deposition on engraftment of progenitor cells in the myocardium. *In vitro*: A tri-cell patch (Tri-P) consisting of iPSC derived cardiomyocytes (CM), endothelial cells (EC), and mouse embryonic fibroblasts (MEF) was cultured and seeded on isolated peritoneum. The expression of fibrosis related molecules from MEF and the infarcted heart was measured by Western blot and qPCR. *In vivo*: The Tri-P was overlaid on the entire infarcted area at 7 days after MI in overexpressing adenylyl cyclase VI (AC6) and WT mice. A combination of *in vivo* bioluminescent imaging (BLI) and postmortem *ex-vivo* analysis, as well as counting the number of green fluorescent protein positive cells (GFP⁺) was used to assess engraftment efficiency of progenitor cells. Echocardiography was performed weekly. Hearts were harvested for analysis *4* weeks after Tri-P application. MEF were stimulated with forskolin before an anoxia/reoxygenation protocol. *Several fibrosis related molecules* were analyzed. In AC6 mice, infarcted hearts treated with Tri-P showed significantly higher BLI signals and a higher number of GFP⁺ cells as compared with WT mice. Heart function, which progressively improved from week 2 to week 4, was associated with reduced left ventricular fibrosis in AC6 mice as compared to WT mice after MI. The application of a Tri-P in AC6 mice with decreased collagen and sparsely distributed connective tissue showed significantly higher iPSC engraftment and subsequent angiomyogenesis in an infarcted area.

Biography

Yigang Wang has completed his medical degree in 1983, PH. D in1997 and have been in academic research ever since. He is an associate professor in the Department of Pathology and Laboratory Medicine, University of Cincinnati. He has served as an editorial board member of several journals in the U.S. He has published more than 50 papers in reputed journals. Over the past 2 decades, his research focus has been in three areas: 1) Protection of the ischemic myocardium testing cardioplegic solutions for cardiac ischemic injury and their effect on hemodynamic changes; 2) Ischemic preconditioning against ischemia/reperfusion injury, its molecular mechanisms, and signaling pathways; 3) Progenitor cell based therapy for treatment of myocardial infarction.

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