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CARDIAC PATCH LOADING MSCS OVEREXPRESSING T β 4 PROMOTES REPAIR OF THE INFARCTED MYOCARDIUM BY ENDOGENOUS REGENERATIVE MECHANISMS

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Recent studies suggest that the epicardium plays an important role in cardiomyogenesis during development, while it becomes quiescent in adult heart. Thymosin beta 4 (T β 4) has an effect on activating the epicardium. However, effectiveness of T β 4 administration is unsatisfactory. Therefore, this study prepared cardiac patch and investigated efficiency of activating the epicardium by T β 4 released sustainedly from the cardiac patch. Mesenchymal stem cells (MSCs) isolated from bone marrow of rats and mice were transfected with T β 4. T β 4 release from the cells was determined with an acquity ultra-performance liquid chromatography system. For preparing of cardiac patch, the cells transfected with T β 4 and Flag were seeded on PLACL/collagen membrane formulated by electrospinning. The survival and proliferation of the cells on the nanofibers were examined after treatment with hypoxia. In MI models of rats and Wt1*CreERT2*^{+/+}, R26*mTmG* mice, the patches were implanted on the epicardium of the infarcted region. In rat models, differentiation of the epicardium-derived cells (EPDCs) and the engrafted MSCs towards cardiomyocytes and vascular cells was examined by Wt1 immunostaining and Flag labeling. In transgenic mouse models, the activated EPDCs expressed GFP. At four week after implantation of the patches, cardiac function was improved significantly, scar area in the infarcted region was reduced obviously. EPDCs increased in subepicardium and myocardium, and some Wt1⁺ cells and GFP⁺ cells expressed CD31, α -SMA or cTnT. Moreover, c-kit⁺ cells were observed in subepicardium and myocardium, and a few of them expressed CD31, α -SMA or cTnT. Flag labeling showed that some engrafted MSCs migrated into subepicardium and myocardium. These results suggest that T β 4 released from the transfected MSCs in PLACL/collagen nanofibrous patches may effectively attenuate left ventricular remodeling and improve cardiac function by activating the epicardial cells and recruiting endogenous stem cells. Our finding provides a novel strategy for myocardial regeneration by enhancing the endogenous regenerative mechanisms.

References:

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Biography

Yu-zhen Tan is a Professor in Department of Anatomy, Histology and Embryology at Shanghai Medical School of Fudan University. She completed her MD at Nanjing Medical University, China and; PhD at Shinshu University School of Medicine, Japan. In 1999, she became a Professor of Shanghai Medical School of Fudan University. She firstly designed and synthesized the self-assembling peptide modified with RGDSP, and investigated effects of the peptide carrying stem cells on repairing the infarcted myocardium. She was also first to investigate effects of the PCL/gelatin nanofibrous patch on repairing the infarcted myocardium after transplantation on the epicardium. Her research interests include "Stem cell differentiation and cardiovascular regenerative medicine".

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