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ADIPOSE DERIVED MESENCHYMAL STEM CELLS ENHANCE CARDIAC FUNCTION AFTER MYOCARDIAL INFARCTION VIA PARACRINE EFFECT

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Objectives To determine if intramyocardial transplantation of adipose-derived mesenchymal stem cells (ADSCs) promotes cardiac function of infarcted hearts, and to determine the role of myocardial differentiation and paracrine effect in the cardioprotection of ADSCs

Methods Mouse myocardial infarction (MI) model was established with ligation of the left anterior descending coronary artery (LAD) to create anterior wall infarction of the left ventricle. ADSCs from GFP transgenic mouse of passage 3 were enriched and their surface markers were identified by flow cytometry. ADSCs were induced by osteogenic media, adipogenic media and chondrogenic media for 21 days. The ADSCs were intramyocardially injected to the border zone of post-MI hearts. At the same time, conditioned medium (CM) collected from cultured ADSCs was intramyocardially injected to infarcted hearts. Cardiac function was detected after 4 weeks by echocardiography (GE vivid 7 dimensions). At the same time, immunocytohistology was performed to identify newly formed GFP+ cardiomyocytes with a-actinin+staining in the post-transplanted heart tissue.

Results ADSCs showed high expression of CD90, CD73, CD44, CD105 and low expression of CD45, CD34. Chondrogenesis, osteogenesis and adipogenic differentiation of ADSCs were confirmed on day 21 with toluidine blue, von Kossa and Oil Red O staining, respectively. Left ventricular fraction shortening (FS) and ejection fraction (EF) were significantly decreased after MI (FS, pre-MI vs after MI: $62.9 \pm 6.3\%$ vs $21.2 \pm 2.2\%$; EF, $90.2 \pm 5.2\%$ vs $46.4 \pm 2.9\%$, $p < 0.05$). With ADSC transplantation, FS and EF of infarcted hearts were significantly increased compared with control hearts (FS, $35.3 \pm 4.5\%$; EF, $68.7 \pm 8.6\%$). With condition medium injection, FS and EF of infarcted hearts were also significantly increased compared with control hearts (FS, $32.7 \pm 3.7\%$; EF, $62.3 \pm 4.9\%$), which is comparable to those of ADSC transplantation. No newly formed GFP+/a-actinin+ cardiomyocytes were found in the heart tissue.

Conclusions Intramyocardial transplantation of ADSCs significantly promotes cardiac function after Myocardial Infarction. The underlying mechanism for the cardioprotection of ADSC transplantation is possibly through paracrine factors of ADSCs rather than myocardial regeneration.