



Enhanced engraftment and repairing ability of human adipose-derived stem cells, conveyed by pharmacologically active microcarriers continuously releasing HGF and IGF-1, in healing myocardial infarction in rats

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One of the main cause of ineffective cell therapy in repairing the damaged heart is the poor yield of grafted cells. To overcome this drawback, rats with 4-week-old myocardial infarction (MI) were injected in the border zone with human adipose-derived stem cells (ADSCs) conveyed by poly(lactic-co-glycolic acid) microcarriers (PAMs) releasing hepatocyte growth factor (HGF) and insulin-like growth factor-1 (IGF-1) (GFsPAMs). According to treatments, animals were subdivided into different groups: MI_ADSC, MI_ADSC/PAM, MI_GFsPAM, MI_ADSC/GFsPAM, and untreated MI_V. Two weeks after injection, a 31% increase in ADSC engraftment was observed in MI_ADSC/PAM compared with MI_ADSC ($p < 0.05$). A further ADSC retention was obtained in MI_ADSC/GFsPAM with respect to MI_ADSC (106%, $p < 0.05$) and MI_ADSC/PAM (57%, $p < 0.05$). A 130% higher density of blood vessels of medium size was present in MI_ADSC/GFsPAM compared with MI_ADSC ($p < 0.01$). MI_ADSC/GFsPAM also improved, albeit slightly, left ventricular remodeling and hemodynamics with respect to the other groups. Notably, ADSCs and/or PAMs, with or without HGF/IGF-1, trended to induce arrhythmias in electrically driven, Langendorff-perfused, hearts of all groups. Thus, PAMs releasing HGF/IGF-1 markedly increase ADSC engraftment 2 weeks after injection and stimulate healing in chronically infarcted myocardium, but attention should be paid to potentially negative electrophysiological consequences.

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