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Stem Cell Regenerative Potential Combined with Nanotechnology and Tissue Engineering for Myocardial Regeneration

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Abstract: The stem cell-based therapy for post-infarction myocardial regeneration has been introduced more than a decade ago, but the functional improvement obtained is limited due to the poor retention and short survival rate of transplanted cells into the damaged myocardium. More recently, the emerging nanotechnology concepts for advanced diagnostics and therapy provide promising opportunities of using stem cells for myocardial regeneration. In this paper will be provided an overview of the use of nanotechnology approaches in stem cell research for: 1) cell labeling to track the distribution of stem cells after transplantation, 2) nanoparticle-mediated gene delivery to stem cells to promote their homing, engraftment, survival and differentiation in the ischemic myocardium and 3) obtaining of bio-inspired materials to provide suitable myocardial scaffolds for delivery of stem cells or stem cell-derived factors.

Keywords: Cell transplantation, myocardial infarction, myocardial regeneration, nanoparticles, nanotechnology, stem cells.

1. INTRODUCTION

Coronary heart disease (CHD) and its major manifestation, the myocardial infarction (MI), represent the leading cause of death and disability worldwide. Although pharmacological treatments existing today (such as thrombolytic agents, angiotensin-converting enzyme inhibitors, β-blockers, statins, etc) and surgical procedures (coronary artery bypass surgery, percutaneous coronary intervention, cardiac catheterization) improve the survival rate of the patients with CHD, none of this therapy can replace the cardiac tissue lost after infarction. Thus, alternative approaches aimed to induce myocardial regeneration are critical needed. The replacement of infarcted tissue with new functional cardiomyocytes together with the stimulation of angiogenesis using stem cells have been proposed as a potential therapy for MI and heart failure [1]. Embryonic stem cells [2] and adult stem cells such as bone marrow stem cells [3], skeletal myoblasts [4], adipose-derived stem cells [5-7] and cardiac stem cells have been investigated for their ability of cardiac repair. The studies performed in animal models have demonstrated therapeutic benefits of the adult stem cells for myocardial infarction [8]. Unfortunately, to date the functional improvements observed in almost all clinical trials pointed out the absence of long-term relevant differences between infarcted myocardium with and without cellular transplant due to the low survival of transplanted cells into damaged myocardium [9, 10].

In this context, the clinical benefits are only transient and largely attributed to transplanted cell-associated paracrine effects in stimulating angiogenesis and protecting surviving cardiomyocytes [11]. More recently, the strategies that envisage the use of stem cells regenerative potential combined with the emerging innovative nanotechnology concepts provide promising opportunities for myocardial regeneration.

This review summarize the application of nanotechnology in stem cell research starting from cell labeling based on contrast-enhancing nanoparticles to track its fate after cellular transplant to nanoparticle-mediated gene delivery to genetically manipulate stem cells to generate an expression product and to support the survival and differentiation of cells in the ischemic myocardium and ending with the use of nanostructured bio-inspired materials to provide suitable myocardial scaffolds for delivery of stem cells or stem cell-derived factors (Fig. **1**).

2. NANOPARTICLE-BASED STEM CELLS TRACKING AFTER TRANSPLANTATION IN INFARCTED MYOCARDIUM

In order to follow the efficacy of stem cell transplantation in time, it is essential to track the fate of stem cells after *In vivo* administration. Therefore, there was a need for reliable cell labeling to allow the non-invasive in-vivo imaging of transplanted cells and to examine the migration, survival and proliferation of stem cells in the same animal over the time [12, 13]. Recently, the developments in the field of nanotechnology offer new opportunities for labeling and tracking of stem cells and it is expected to play a key role in establishing the appropriate time and concentration of cells for transplantation and also, the mechanisms that mediate the effects of transplanted stem cell on myocardial regeneration [14, 15]. Different types of stem and progenitor cells have

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