Cardiac repair achieved by bone marrow mesenchymal stem cells/silk fibroin/hyaluronic acid patches in a rat of myocardial infarction model

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\textbf{A R T I C L E I N F O}

- **Article history:**
  - Received 16 March 2012
  - Accepted 10 April 2012
  - Available online 8 May 2012

- **Keywords:**
  - Heart
  - Cardiac tissue engineering
  - Mesenchymal stem cell
  - Silk(HA)

\textbf{A B S T R A C T}

Bone marrow mesenchymal stem cells/silk fibroin/hyaluronic acid (BMSC/SH) patches were implanted into myocardial infarction (MI) rat hearts to investigate the efficacies of them on enhancing left ventricular (LV) remodeling and cardiac repair. 45 rats were divided into four groups: Sham, MI (MI hearts, induced by a cryo-injury technique), SH and BMSC/SH (MI hearts with implantations of SH and BMSC/SH patches, respectively). After eight weeks of post-implantation, the patches for the SH and BMSC/SH groups were intact and well adhered on the MI zones with no and minor immunological responses, respectively, examined by a CD68 marker, while severe inflammation on the zones was observed for the MI group. The SH group showed the efficacy of cardiac repair on MI zones. Moreover, BMSC/SH group significantly improved the wall thickness of LV, assessed by echocardiography, and had high viability of delivery BMSC, largely reduced apoptosis, significantly promoted neo-vascularization and stimulated the secretions of various paracrine factors such as VEGF, examined by real-time PCR, in MI zones compared with those of the SH and MI groups. In conclusion, the therapeutic efficacies of using BMSC/SH patches for repairing MI hearts were demonstrated by showing the advantages of both bioactive SH patches and BMSC-based therapy.

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\section{1. Introduction}

Myocardial infarction (MI), a leading cause of heart failure, results in injury of myocardium, gradually losing cardiac tissues and impairing left ventricular (LV) functions [1]. In order to repair injured myocardium, BMSC therapy using various techniques such as intra-coronary infusion has been investigated in animal models or clinical trials [2–6]. Although BMSC therapy for MI hearts of various animals have shown by reducing the size of the infarcted area and improve cardiac functions [2], the results in clinical studies for improving LV functions and heart remodeling of MI hearts by BMSC-based therapy are conflicts [3–6]. The conflict results of BMSC therapy in MI hearts in various investigations may be due to low survival rates of delivered BMSC in MI microenvironments [5–7]. To improve the efficacy of BMSC therapy for MI hearts, developing a new biomaterials (e.g., hydrogels or cell patches) for cardiac repairs such as increasing survival rates of BMSC and improving angiogenesis in MI hearts is worth investigating [2,6–8].

Many biopolymer-based cardiac patches for restraining infarcted LV or repairing MI hearts include synthetics polymeric materials such as nitinol mesh (e.g., Paracor device), poly(lactide-co-epsilon-caprolactone), PGCL scaffold) and polyester urethane urea (PEUU) [8–10]. However, the non-biodegradable synthetic biomaterials or degraded microparticulate may trigger inflammatory and foreign body responses [8–10]. Although implantation of degradable collagen scaffolds for the treatments of cryo-injured MI rat hearts improve vascularization responses in the scaffolds and MI zones, the implanted scaffolds trigger moderate inflammatory responses (e.g., CD45\textsuperscript{+} marker) and macrophages in the cryo-injured and the scaffold zones after two months of implantation [11]. Recently, peptide fibers or hydrogels with or without MSC encapsulation to enhance heart remodeling and improve functionalities of MI hearts have been reported and reviewed [7,12,13]. Although treatments of MI hearts using injectable hydrogels to

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