

Lymphatic endothelial progenitor cells and VEGF-C loaded with self-assembling peptide nanofibers promote lymphangiogenesis in infarcted myocardium

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Lymphatic vessels play a crucial role in draining excess fluid and transport macromolecular substances from extracellular spaces. Dysfunction of lymphatic vessels may cause lymph edema and chronic inflammation, leading to fibrosis of the local tissue. This study investigated efficiency of transplantation of lymphatic endothelial progenitor cell (LEPCs) and sustained release of VEGF-C from self-assembling peptide (SAP) on promoting lymphangiogenesis after myocardial infarction (MI). CD34+VEGFR-3+ EPCs were isolated from rat bone marrow. Sustained release of VEGF-C from SAP nanofibers (SAPNs) was detected with ELISA. Compatibility of SAPNs with the cells was accessed with transmission electron microscopy and EB/ AO staining. After rat MI models were established with ligation of the anterior descending branch of the left coronary artery, SAP carrying the cells and VEGF-C was injected at the border of the infarcted region. At four week after transplantation, the survival and differentiation of the cells labeled with GFP were examined, and repair of the infarcted myocardium was evaluated. Under induction with VEGF-C, CD34+VEGFR-3+ EPCs could differentiate into lymphatic endothelial cells. The cells spread well along SAPNs. SAPNs protected the cells from apoptosis in the condition of hypoxia, and released VEGF-C sustainedly. After transplantation, cardiac function was improved significantly. The number of the survived cells increased, and some cells differentiated into lymphatic endothelial cells. Density of lymphatic vessels increased, and cardiac edema was reduced. Moreover, angiogenesis and myocardial regeneration were enhanced. These results suggest that SAPNs load LEPCs and release VEGF-C effectively. VEGF-C released from SAPNs induces differentiation of LEPCs towards lymphatic endothelial cells. Loading stem cells and releasing growth factor with SAPNs is a promised strategy for MI therapy. References: 1. Wang Q L, Wang H J, Li Z H, Wang Y L, Wu X P and Tan Y Z (2017) Mesenchymal stem cell-loaded cardiac patch promotes epicardial activation and repair of the infarcted myocardium. *J Cell Mol Med.* 21:1751–66. 2. Zhou P, Tan Y Z, Wang H J and Wang G D (2017)

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