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Cardiac Differentiation of Bone Marrow-Derived Stem Cells and Regeneration of Infarcted Myocardium

Do Sun Lim
Korea University

Myocardial infarction is a leading cause of morbidity and mortality in civilized countries. Because cardiomyocytes do not regenerate after birth, loss of cardiomyocytes leads to regional contractile dysfunction and necrotized cardiomyocytes in infarcted ventricular tissues are progressively replaced by fibroblasts to form scar tissues.

Recent studies have reported that many adult tissues contain populations of stem cells that have the capacity for self-renewal. Especially bone marrow is the major source of adult stem cells. Bone marrow contains two kinds of stem cells, hematopoietic stem cells(HSCs) and mesenchymal stem cells(MSCs). MSCs give rise to multiple mesodermal tissue types, including bone and cartilage, tendon, muscle, fat, and a marrow stromal connective tissue which supports the differentiation of hematopoietic stem cells by addition of extrinsic bioactive factors and microenvironment effects. Culture conditions, in vitro, can play a critical role in addressing their fate. For example, in response to 5-azacytidine, MSCs differentiate into cardiomyogenic cell in vitro. We investigate that MSCs differentiate into cardiomyocytes and express cardiac markers when co-cultured with neonatal rat cardiomyocytes or when cultured with mixed cytokines in vitro. In rats, transplantation of rat bone marrow cells directly into cryo-injured heart improved heart function with increased cardiac myocyte cells and angiogenesis in the scar. MSCs from bone marrow injected directly into rat hearts also gave rise to cardiomyocytes. We demonstrate whether transplanted MSCs or MSCs treated with 5-azacytidine into infarcted myocardium can be survival and regenerate infracted myocardium. Viable cells tagged with DAPI found in host myocardium. And we found that transplanted cells were differentiated into heart cells using immunohistochemical analysis. These results suggest that the safe and efficient method to differentiate MSCs into cardiomyocytes for myocardial regeneration. In infracted hearts in adult mice, cardiomyocytes and vascular cells can be formed in vivo from circulating mouse bone marrow stem cells and these stem cells also give rise to cardiomyocytes after direct injection into damaged heart tissue. Highly purified HSCs in lethally irradiated mice contributed to the formation of cardiomyocytes and endothelial cells in ischemic hearts. Very recently, it has been reported that bone marrow hemangioblasts contribute new vessels to the post-ischemic myocardium and strikingly, that c-kit-positivie bone marrow hematopoietic stem cells differentiate into cardiomyocytes, endothelium, and smooth muscle when injected into a post-ischemic ventricular wall. Transplantation of human bone marrow hemangioblasts into rat heart formed new vasculature but not cardiomyocytes, and improved cardiac function. Although the formation of vascular cells such as endothelial cells may not appear directly relevant to the attempts to repair damaged hearts, it should be noted that an adequate blood and oxygen supply for newly seeded cardiomyocytes is critical for their survival. There are still open questions for clinical application of bone marrow-derived stem cells, therapeutic possibilities using stem cells should be optimistic.