Regenerative Biology and Medicine: A Science Whose Time Has Come

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We are at the dawn of regenerative biology and medicine, using stem cells and progenitor cells to replace irreversibly damaged tissues and organs. In this presentation, we will illustrate this by reviewing some new discoveries in relation to myocardial regeneration, using adult stem cells derived from the bone marrow. To optimize the therapeutic strategy in using the bone marrow stromal cells (MSCs) for cardiovascular tissue repair, we studied their pathophysiological roles in myocardial infarction.

MSCs of Lewis rats were isolated and expanded using Caplan's method. They were labeled with pMFG-LacZ retrovirus-mediated reporter gene and then used for bone marrow transplantation. The MSCs were injected intravenously into isogenic recipient rats. These cells homed in to the bone marrow of the recipients. One week later, they were randomized to left coronary artery ligation (LCA) or sham operation group. The labeled MSCs were recruited from bone marrow via circulation, and migrated to the infarcted myocardial segments, but not to non-infarcted myocardia. Immuno-histochemical stains for cardiomyocyte specific *troponin I-c* were positive for some of these labeled MSCs, while others became endothelial cells and myofibroblasts. These findings indicate that MSCs can be recruited by signals from injured tissue, migrate to the damaged area where they undergo *in situ* differentiation to participate in tissue repair.

The MSCs also have unique immunologic properties as they are tolerogenic to T cells encountered. We repeated the marrow transplant experiment described above, except this time we did a xenotransplantation by using mice as donors, and rats without immunosuppression as the recipients. Amazingly the labeled mice MSCs survived in rats without evidence of rejection. Furthermore, the mice MSCs were able to be recruited to the infracted myocardium of the rat hosts, and undergo *in situ* differentiation, producing a stable mouse/rat cardiac chimera.

The clinical implications of these findings for the emerging new treatments of myocardial infarction and heart failure, which continues to be the leading cause of mortality and morbidity in developed and emerging nations, will be discussed.

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