The emerging role of mesenchymal stem cells in tissue engineering

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Letter to editor

Mesenchymal stem cells (MSCs) are pluripotential stem cells with high capacity of self-renewal and expansion, with differentiation potential to various cells including osteoblasts, chondrocytes, adipocytes, endothelial cells, nerve cells, heartmyocytes,hepatocytes and pancreatic cells.[1] The approach of reconstructive medicine and tissue engineering demands designing biocompatible scaffolds, clinical use of which has the lowest level of side effects without provoking immunological response, along with the use of stem cells with the least clinical complications despite high capacity in repair of the damages. Due to the high expansion ability and multi-lineage differentiation potential of MSCs, especially because of their prominent immunomodulatory role, these cells can be used as a tool for cell and gene therapy applications to treat many degenerative congenital abnormalities and diseases.[2, 3] Clinical studies show high capacity of MSCs in improvement of allogeneic stem cell transplantation and in reducing chronic GVHD complications. In fact, these cells exert their anti-inflammatory and immunomodulatory effects through activation of T suppressor lymphocytes and secretion of a number of immunomodulatory agents. On the other hand, these cells identify the damaged area by their paracrine effects, are implanted there and accelerate the repair process of the damaged area by secreting a number of factors.[4, 5] So far, acceptable results of the successful use of MSCs have been reported in treating a number of human diseases in animal models of disease, such as osteogenesis imperfecta, spinal cord injuries, Parkinson's disease and stroke. However, the development of routine clinical application of MSCs in humans is subject to further investigation on physiological and pathological models of other mammals and monitoring the results.[1] Studies have shown that MSCs isolated from various tissues have high capacity to differentiate into human hepatocytes, similar to embryonic stem cells (ESCs). Meanwhile, due to higher differentiation and reduced tumor igenic capacity, the use of MSCs has attracted more attention in comparison with ESCs. In several studies, differentiation capacity of MSCs into hepatocyte-like cells and hepatocytes, which play a role in liver regeneration, has been studied.[6] Hepatocyte-like cells with biological and metabolic functions, as appropriate, have been differentiated from human MSCs, and can remain active for 21 days on three-dimensional cell scaffolds.[7] Based on another study, it has been found that the global pattern of gene expression in MSC-derived hepatocyte-like cells is significantly different from that in more un differentiated MSC.[8] MSC-derived hepatocytes, in addition to expressing specific markers such as albumin, AFP, CK-18 and CK-19, should be biologically active, and this can be verified by expression of cytochrome P450 enzymes (sub-units CYP1B1 and CYP2B6). Cytochrome P450 enzymes, playing an important role in metabolism of drugs and carcinogens, are highly expressed in active MSC-derived hepatocytes and hepatocyte-like cells.[9]

Another application of MSCs in tissue engineering is the approach of using these cells

to differentiate into bone cells to treat extensive bone damages due to trauma or degenerative pathological injury. Because of limited donations for autologous bone transplantation, tissue engineering has been discussed for the repair of bone defects using three-dimensional scaffolds designed for MSC expansion and differentiation. In fact, designing a scaffold capable of acting as a proper support for cell attachment and proliferation, differentiation induction to bone cells and providing a porous space for communication between the bone cells produced is an essential topic to achieve the goal of regenerative medicine for bone. In a clinical application, the scaffold and MSCs can be placed under the skull bone of mice to evaluate the ability of MSCs to form bone cells. Our research results indicated enhanced repair of maxillary sinus bone tissue by using MSCs. In fact, histomorphological studies showed generation of osteoblasts capable of forming an osteoid matrix using biphasic HA/TCP matrices.[1, 10] However, the application of tissue engineering in repair of bone defects has some limitations due to low number of stem cells isolated from bone marrow aspiration. Additional studies are required on clinical use of different scaffolds for expansion and differentiation of MSCs and monitoring the status of implanted MSCs.

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