

BONE MARROW STROMAL CELLS: CELL BIOLOGY & CLINICAL APPLICATIONS

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INTRODUCTION: Bone marrow is the tissue where hemopoiesis occurs in close contact with the stromal microenvironment, which support haemopoietic stem cell growth and differentiation. The bone marrow stroma is composed of a variety of different cell types providing structural and functional support for hemopoiesis: endothelial cells, adipocytes, smooth muscle cells, reticular cells, osteoblasts and stromal fibroblasts. Among these cell types, stromal fibroblasts have a peculiar biologic relevance. They are in fact able to support hemopoiesis, to differentiate towards osteogenic, chondrogenic and adipogenic lineage and to form a bone structure complete of hemopoietic marrow in in vivo assays. Their in vitro clonogenic counterpart is represented by Colony Forming Units-fibroblasts (CFU-f), which in turn give rise to Bone Marrow Stromal Cells (BMSC) and Mesenchymal Stem Cells (MSC), possibly corresponding to a single cell population. Hemopoietic stem cells commitment, differentiation and proliferation need complex interactions with the marrow environment which is mostly cellular, with relatively little extracellular matrix compared to the collagenous scaffolds in most other organs. BMSC in particular provide the absolutely essential support for hemopoiesis through both direct contact with cell surfaces and stromal cell derived soluble mediators. In vivo bone formation by CFU-f derived fibroblasts has been strikingly demonstrated and therefore these cells are considered a progenitor compartment for endosteal osteoblasts, responsible for the maintenance of bone turnover throughout life.

BMSC can be easily isolated from iliac crest bone marrow aspirates. Nevertheless, a step of extensive in vitro expansion is required to obtain a consistent number of cells available for both reconstruction and repair of mesodermally

derived tissues, given the low frequency of BMSC in a marrow sample. Moreover, their use for gene and cell therapy of skeletal diseases requires the long-lasting engraftment of BMSC endowed with a residual proliferation potential sufficient to sustain the low, but continuous, bone turnover in adulthood. The maintenance of their stem properties and the possibility to reprogram their commitment is therefore a field of primary interest given their potential use in regenerative medicine.

Cell therapy of bone lesions by ex vivo expanded osteogenic progenitor is passing from the phase of experimental animal model to the phase of clinical trials. Bone is repaired via local delivery of cells within a scaffold. Extremely appealing is the possibility of using mesenchymal progenitors in the therapy of genetic bone diseases via systemic infusion. There are experimental evidences that mesenchymal progenitors delivered by this route engraft with very low efficiency and do not produce relevant and durable clinical effects. Under some conditions where the local microenvironment is either altered (i.e. injury) or under important remodelling processes (i.e. fetal growth) engraftment of stem and progenitor cells seems to be enhanced.

DISCUSSION & CONCLUSIONS:

Although multilineage differentiation potential of this cell population is supported by a substantial amount of experimental evidences, a better understanding of the mechanisms, which control differentiation, is required for their exploitation in therapy of human diseases. Furthermore, a better understanding of their engraftment mechanisms will hopefully extend the field of therapeutic applications of mesenchymal progenitors.