Biological Characteristics of MSCs

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Abstract: Recent advancements in tissue engineering and regenerative medicine have highlighted MSCs as a potential source of cells which would differentiate to a variety of tissue tailored to individual needs. This chapter briefly outlines the current status of MSCs, focusing on their biological characteristics and potential for clinical applications.

3.1 Surface Markers and Paracrine Characteristics

3.1.1 Surface Markers

MSCs have been defined by their plastic-adherent growth and subsequent expansion under specific culture conditions, by a panel of nonspecific sur-
face antigens and by their *in vitro* and *in vivo* differentiation potential. MSC transdifferentiation into myocytes, osteoblasts, adipocytes and chondrocytes by different inducers have been widely demonstrated. In contrast, human fibroblasts cannot transdifferentiate into other lineage cells, except fibrocytes. A CD (cluster of differentiation) molecule is a kind of membrane antigen associated with cell development, differentiation and activation. MSCs have been identified as expressing CD29, CD44, CD90, CD105, and lacking hematopoietic lineage markers and HLA-DR (Dominici et al, 2006). In general, MSC refers to bone marrow-derived cells, while similar populations can also be obtained from other tissues, such as adipose umbilical cord blood and peripheral blood, connective tissues of the dermis, and skeletal muscle. The biological characteristics of MSCs derived from other tissues are not the same as those from bone marrow. Hereby we discuss the surface markers of bone marrow-derived MSCs.

Multiple studies have focused on the identification of specific surface markers on MSCs, in an effort to effectively isolate MSCs. For instance, a high expression of CD105, CD73, and CD90 is used as one of minimal criteria to identify human MSCs. Scores of monoclonal antibodies have been raised in an effort to provide reagents for the characterization and isolation of human MSCs. It has been demonstrated that at least three types of surface markers are expressed on MSCs (Jootar et al, 2006) (Table 3.1), including adhesion molecules, extra-cellular matrix proteins, cytokine and growth factor receptors. In addition, a series of antibody binding sites exists on the membrane of human MSCs, including prolyl-4-hydroxylase, vimentin, desmin, nestin, CD13, collagen IV, osteopontin, osteonectin, bone sialoprotein II and endogenous alkaline phosphatase to name a few. The expression of these cell markers depends not only on species, original tissues and individuals MSCs, but also on the different status of the cell cycle. For rat MSCs, there is high expression of CD44, CD90, c-kit and stemcell antigen-1 (sca-1) (Xie et al, 2006; Uemura et al, 2006) and low expression of CD34, VE-cadherin, Flk-1 and c-met (Uemura et al, 2006). MSCs in different generations may present different antigen, i.e., nestin as an immature marker will be gradually absent during subsequent passages.

Surface markers of MSCs can be changed after transdifferentiation. For example, rat MSCs, after specific induction, can differentiate into cells with the Schwann cell (SC) phenotypes according to their morphology and immunoreactivities to SC surface markers including S-100, glial fibrillary acidic protein (GFAP) and low-affinity nerve growth factor receptor (p75). The expression of surface markers can also decrease or increase during the differentiation, and some surface markers indicate a differentiation potential, as integrin subunits $\alpha_{10}$, a potential marker to predict the chondrogenic differentiation state of MSCs.