

## The Biology and Therapeutic Applications of Mesenchymal Stromal Cells

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Mesenchymal cells in the bone marrow that form bone tissue were first described by Friedenstein and colleagues in the 1960s. Since then they have been shown to be adult stem cells in that they can both self-renew (ie form daughter stem cells) as well as differentiate *in vitro* and *in vivo* into tissues of the skeletal system including bone and tendon. This mesodermal differentiation capability has been used to repair bone and tendon injuries in both preclinical models and in clinical trials. Mesenchymal stem cells are rare cells and, in order to obtain sufficient numbers for laboratory studies and clinical trials, *ex vivo* expansion in tissue culture is required. This allows large numbers of the progeny of mesenchymal stem cells to be obtained and these cells are called mesenchymal stromal cells (MSCs). They form part of the endothelial wall and are thus present in all vascularised tissues and represent one form of pericyte. In addition to their ability to heal damaged organs of the skeletal system, MSCs are protein factories which secrete proteins that have immunomodulatory, proangiogenic and anti-apoptotic properties and which act in a paracrine fashion on their target organs. This has led to their use in clinical trials in a wide range of diseases, many of them unrelated to the tissues of the skeletal system. MSCs from different tissues share characteristic (but not unique) cell surface membrane markers, mesodermal differentiation ability and immune modulatory capacity but differ in their gene expression. Recently a unique molecular signature of MSCs has been described which should prove useful in identifying MSCs more precisely. Much work on MSCs is required to determine their clinical efficacy, their optimal source, dose, route of administration, frequency of administration and potential side-effects, although to date they appear to be remarkably safe cells.