

# Adult tissue resident or somatic stem cells

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1 Building on earlier observations in the 1960s relating to bone marrow-derived cell populations, in the 1990s the term 'mesenchymal stem cell' (MSC) was used in relation to therapy, based on observations that some of these cells, under the right conditions, could differentiate into cell types relating to musculoskeletal, adipose and other tissues. In 2005 the International Society for Cellular Therapy (now the International Society for Cell and Gene Therapy; ISCT) proposed that these cells be termed multipotent 'mesenchymal stromal cells' with the same abbreviation MSC, and that the term mesenchymal stem demonstrate stem cell activity by clearly stated criteria'. They

4 went on to describe minimum criteria in 2006: adherence to plastic, expression of certain surface markers (CD105, CD73 and CD90) but a lack of expression of others (CD45, CD34, CD14 or CD11b, CD79  $\alpha$  or CD19 and HLA-DR) and, finally, the ability to differentiate into osteoblasts, adipocytes and chondroblasts in vitro, often described by authors as trilineage differentiation. The importance of nomenclature relates to the mechanism by which such cells might achieve a clinical effect. The earlier term mesenchymal 'stem' cell implies that cells directly contribute to repair and regeneration by differentiation, whereas using the term 'stromal' can encompass paracrine and secretory behaviour, in which cells are envisaged to work with other cells to influence the outcome of repair and regeneration (Figure 4.3). As a consequence, the term mesenchymal 'stem' cell has been highlighted as a cause of potential confusion, whereby patients might wrongly infer that the cell constitutes

5,6 a 'stem cell therapy'. In 2019, the ISCT gave continued support for the term mesenchymal stromal cell but recommended that it be: supplemented with the tissue source of the cell; intended unless rigorous evidence for stemness exists; associated with robust functional assays demonstrating properties. A further consideration is the manufacture and delivery of such cells. MSCs can be isolated from bone marrow (iliac crest aspiration) or from subcutaneous fat (liposuction/lipoaspiration). Cells can be delivered at the point of care, using bedside systems, or isolated in vitro on the basis of their adherence to plastic and subsequently

further characterised. Therefore, they can be used shortly after extraction or after expansion of their numbers by in vitro culture. Furthermore, MSCs can be differentiated into the desired lineage in vitro by addition of suitable growth factors and chemicals. The wide variety of cell type, source and manufacturing process represent important opportunities for treatment.

Cell culture Osteoblast Chondrocyte Adipocyte In vitro trilineage differentiation Figure 4.3 Proposed characteristics of mesenchymal stromal cells relevant to tissue engineering and regenerative medicine. Mesenchymal stromal cell Interaction with inflammatory and immune processes B-cell Macrophage Natural killer cell Dendritic cell T cell

the understanding of which will be greatly improved by molecular biology techniques and functional assay. In terms of agreed nomenclature, a report on consensus has described key parameters in the abbreviation DOSES: D – donor, O – origin tissue, S – separation method, E – exhibited characteristics, S – site of delivery. The relative ease of cell acquisition has meant that autologous MSCs have been used in clinical settings and they represent a great opportunity for new treatment development. Before widespread adoption, more translational research is required to understand and refine the therapeutic mechanism of action and conduct well-designed clinical trials to establish the evidence of effectiveness. Adult tissue resident or somatic stem cells

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