

Adult Stem Cells: A Focus On Mscs

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INTRODUCTION

Adult stem cells are those which are derived from developed organs and are named usually by their tissue of origin, for example, neural stem cells. These cells are found endogenously in specialised 'stem cell niches' within the foetal and adult body and serve to repair and rejuvenate damaged and/or aging tissue. Unlike ESCs, adult stem cells are multipotent which means that they can differentiate into multiple cell types but are conventionally restricted to the cell types within their lineage of developmental origin. These stem cells are currently at the forefront of autologous regenerative cell therapies, with Mesenchymal Stem Cells (MSCs) currently being the most widely investigated stem cell type for such therapies. MSCs are found throughout the body (including but not limited to bone marrow, adipose tissue, dental tissue, salivary glands and peripheral blood) making them a relatively easy-to-obtain source of stem cells. MSCs have been shown to differentiate into a range of mesoderm-derived tissues including bone, muscle and adipose tissue, as well as transdifferentiate into ectoderm and endoderm-derived cell types. Importantly, MSCs secrete immunomodulatory factors such as cytokines and growth factors that have been shown to aid in the immune response. Evidence also suggests that these factors may modulate the body's own stem cells to differentiate and repair damaged tissue. Importantly, MSCs express Cluster Of Differentiation (CD) molecules CD73, CD90 and CD105, but lack haematopoietic markers CD45 and CD39 and express low levels of Major Histocompatibility Complex (MHC) I and MHC II. These properties prevent MSCs from inducing an immune response making them an attractive source of stem cells for autologous and allogeneic (cells from a foreign donor) cell therapy. Fat tissue contains a rich supply of MSCs, known as adipose-derived stem cells, commonly obtained from patients through lipoaspiration.

The Stromal Vascular Fraction (SVF) within the lipoaspirate contains a heterogeneous population of cells including red blood cells, endothelial cells, leukocytes and MSCs. The SVF can be obtained through two primary methods: enzymatic isolation or mechanical isolation. Enzymatic isolation incorporates the use of collagenase to break down the lipoaspirate, producing two distinct phases: An adipose phase on the top and an aqueous phase (containing the cellular portion of interest) on the bottom. Centrifugation followed by filtration and lysing of red blood cells yields a population of pure SVF cells. However, in order to be used for human therapy, GMP grade human collagenase must be used, and this is an expensive component. The mechanical isolation process has thus been developed as an alternative method to extract SVF. This process relies on the emulsification of the lipoaspirate in order to mechanically agitate the tissue and release adipose-derived MSCs from adipose stores. This method not only eliminates the need for enzymatic digestion (thus reducing the time and cost associated with obtaining SVF rich in stem cells), but it can be done in a closed system (using a series of sterilized separators and syringe tubing) straight from the patient, eliminating the possibility of cross-contamination as well as the need for cells to be exposed to an artificial culture environment. Induced pluripotent stem cells The discovery of Induced Pluripotent Stem Cells (iPSCs) has been an important breakthrough in the field of stem cell and regenerative medicine. Once a cell is said to be terminally differentiated, it means that the cell has reached its differentiation capacity. However, in 2006, this phenomenon was challenged by a team lead by Shinya Yamanaka, who questioned whether a terminally differentiated cell could be reprogrammed to a pluripotent embryonic stem cell-like state

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