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COMMENTARY

# Prospect of Adipose Tissue Derived Mesenchymal Stem Cells in Regenerative Medicine

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**Abstract:** Adipose tissue derived mesenchymal stem cells (AT-MSCs) have similar properties to the previously characterized bone marrow mesenchymal stem cells (BM-MSCs). However, adipose tissue is easier to get in larger volumes, the procedure is less painful and at lower risks, and yield more stem cells compared to bone marrow. Moreover, considering the various differentiation and angiogenic potentials, the ease in collecting the samples, and the immuno-suppressive properties, adipose tissue stem cells are very promising for regenerative medicine, and therefore will be the preferred source of MSCs for future clinical use.

**Keywords:** mesenchymal stem cell, multi-potent, niche, immunosuppressive

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## Introduction

Regenerative medicine is classified into cell therapy that does not require a scaffold, and tissue engineering that requires a scaffold and bioactive substances such as growth factors; though both need stem cells, either the controversial embryonic stem cells or adult stem cells.[1]

Adult stem cells can be found in all tissues and organs, where they maintain homeostasis and respond to injury. In the tissues and organs, adult stem cells are located in stem cell niches, which provide supporting micro-environment in the form of other cells and regulatory signals that interact with and regulate the stem cells and stem cell derived progenitors.[2]

There are various sources of stem cells, such as bone marrow, umbilical cord blood, adipose tissue,[3] peripheral blood, muscle, dermis, synovial membrane, periosteum, and trabecular bone;[4] and this article will especially address adipose stem cells.

## Definition of Adipose Stem Cells

Adipose stem cells are adult stem cells that have similar properties to the previously characterized bone marrow mesenchymal stem cells or mesenchymal stromal cells (BM-MSCs), and can be isolated from adipose tissue stromal vascular fraction (SVF) that are alternatively called adipose stromal compartment.[5,6] Therefore, they are also called processed lipo-aspirate (PLA) cells[6] or adipose tissue derived mesenchymal stem cells (AT-MSCs).

Until recently, bone marrow is still the main source of stem cells.[3] However, compared to bone marrow, adipose tissue can be obtained in larger volumes, at lower risks,[5] less painful, and easier to get as it is the waste product of liposuction. Moreover, in bone marrow, BM-MSCs are few, and the number is declining with age. The number of BM-MSCs per nucleated bone marrow cells is one per $10^4$, $10^5$, and $10^6$ in newborns, in teenagers, and in older individuals respectively.[7] In human bone marrow aspirate, the frequency is 1–20/$10^5$.[8] In addition, adipose tissue gave more AT-MSCs compared to bone marrow per gram (5,000 vs. 100–1,000). Therefore, adipose tissue will be the preferred source of MSCs for future clinical use.[5]

## Characterization of AT-MSCs

Both bone marrow and adipose tissue MSCs are multipotent, bear similar CD markers and under proper stimulation in vitro can be differentiated into various kinds of cells. Adipose tissue MSCs have multi germ-line potential and can be differentiated into cells of the mesodermal lineage such as osteogenic, chondrogenic, adipogenic, and myogenic lineages, and even into cells with neuron-like morphology that expressed neuronal proteins.[6] In addition, AT-MSCs can differentiate into endothelium and have angiogenic capacity.[9]

However, AT- MSCs differ from BM-MSCs in the fact that they were found to be positive for CD49d and negative for CD106 (hematopoesis related marker), while the opposite was observed on bone marrow MSCs.[6]

The International Society for Cellular Therapy has defined minimal criteria for the so called bone marrow or other tissue MSCs, i.e:[10]

- The cells should adhere to plastic when they are cultured under standard culture conditions in tissue culture flasks.
- When measured by flow cytometry, 95% or more of the cell population should express CD105, CD73 and CD90, and lack the expression of CD45, CD34, CD14 or CD11b, CD79a or CD19 and HLA class II (only 2% positive or less).
- The cells should be able to differentiate into osteoblasts, chondroblasts and adipocytes, when they are cultured under standard differentiating conditions.

Vast evidence showed that the cell origin of AT-MSCs was a mixed population of activated pericytes or alternatively called 'vascular stem cells' (VSC) at various stages of differentiation.[5,7] Therefore, some researchers found that fresh or early passages of AT-MSCs beared CD 34, a fact that opposed the minimal criteria that were proposed by The International Society for Cellular Therapy, though the CD34+ cells decreased upon further passages.[5,11] The decrease in CD34+ cells is supposed to be due to CD34 down regulation rather than cell death.[5]

The CD34 is long known as the marker for hematopoietic stem cells (HSCs) and endothelium, though some HSCs were shown to be CD34-. Further, the CD34+ and CD34- HSCs can differentiate into one another,[5,12] as in the case of CD34+ and CD34- AT-MSCs.[5,9]

## Biological Activity of AT-MSCs

A very interesting property of bone marrow as well as adipose tissue MSCs is their immuno-suppressive properties as was shown in the efficient control of

graft-versus-host disease that was associated with allogeneic hematopoietic transplantation.[13]

The immuno-suppressive properties targeted both primary and secondary T cell responses that were not antigen specific, and mediated through both soluble factors and cell contact. The soluble factors might include IDO, hepatocyte growth factor, transforming growth factor $\beta$, IL-10, prostaglandins, and nitric oxide. However, some evidence showed that these immunosuppressive properties did not eventually avoid their rejection.[14]

## The Role of AT-MSCs in Regenerative Medicine

Considering the wide differentiation potential of AT-MSCs in-vitro, it is highly supposed that in the future AT-MSCs can replace the role of BM-MSCs in regenerative medicine, where animal[15–17] and human studies for AT-MSCs and BM-MSCs,[4,18,19] have been conducted.

In regenerative medicine, AT-MSCs and BM-MSCs may play a role in various areas such as in orthopedic surgery i.e. in bone and cartilage tissue engineering,[4,15,16,18–20] stroke and neurological diseases,[1,21] cardiovascular disease,[9] urology,[1] etc.

In conclusion, considering the various differentiation and angiogenic potentials, the ease in collecting the samples, and the immuno-suppressive properties, adipose tissue stem cells are very promising for regenerative medicine.

## Disclosure

The author reports no conflicts of interest.

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