Mesenchymal Stem Cells

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Introduction

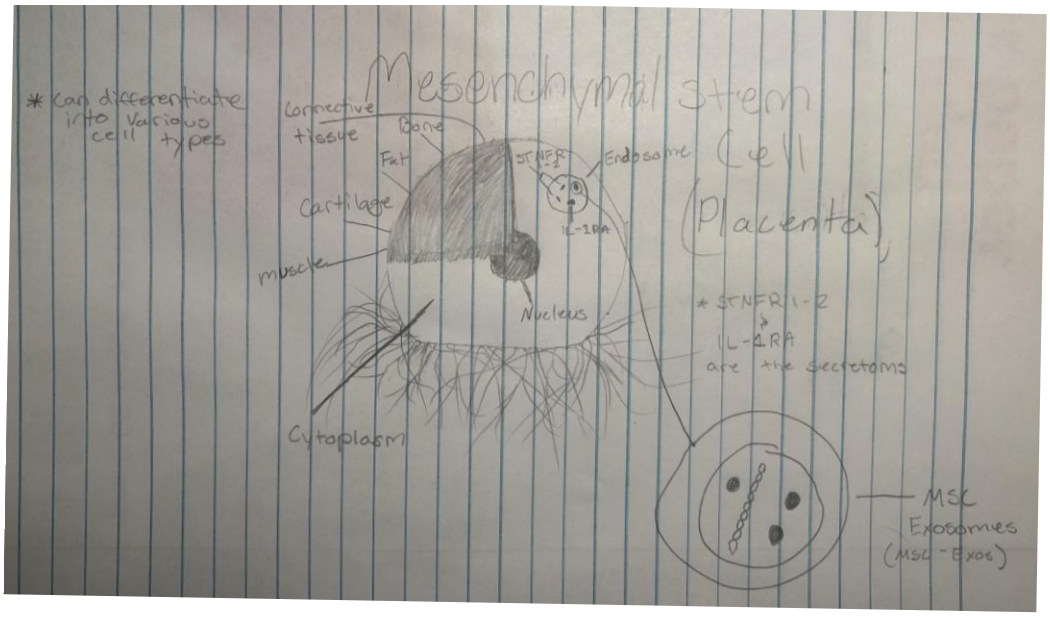
Mesenchymal stem cells (MSC) were first discovered in 1976 by Alexander Friedenstein and his colleagues. The cells were derived from bone marrow and were found to have anti-inflammatory and immune regulatory properties. Clinic testing of cultured MSCs was found to have additional properties. The medical use of MSCs has been investigated in over 950 trials and is still being investigated today. The first uses for MSC can be found as early as 1993 when infusion into patients began. Since the MSC has treated over 10,000 patients in controlled clinical settings (4). MSC was primarily harvested from human bone marrow, however, new locations for harvesting have become apparent. Adipose tissue, umbilical cord tissue and the placenta are also places where MSC can be found within the body (4). Each source of MSC is thought to be renewable except umbilical cord tissue where the MSC is discarded at birth. MSC has immense potential in intercellular and intracellular signaling, and the growing field of MSC research is helping increase its uses in cell therapy.

Body

Mesenchymal stem cells have been used in various diseases and conditions. Additionally, MSC can be found in processes like childbirth and other body processes that involve intercellular signaling. One of the more recent uses of MSCs was during the Covid 19 pandemic, where they were used in preventing or attenuating the cytokine storm in a patient's lungs. Covid 19 was a virus that started in December 2019 and ended in 2020 with the availability of the vaccine. The virus caused a cytokine storm which can lead to severe acute respiratory syndrome. A cytokine storm within the lungs can cause dysfunction of the air exchange and acute respiratory distress syndrome (3). MSC has two primary functions which include immunomodulatory effects and additionally MSC has differentiation abilities. MSC can secrete distinct types of cytokines.

Cytokines are created via paracrine secretion into the extracellular environment (1). It then makes direct interactions with immune cells, which leads to immunomodulation. Then the immunomodulatory effects of MSC are activated when the TLR receptors within the MSC are activated by pathogen associated molecules (3). The immunomodulating function of MSCs was the main contributor to the efficiency of the treatment and the transplantation of MSCs showed positive results when treating Covid 19. For transplantation, the MSGs were contained within a saline with the total amount being 1x10^6 cells per kilogram of weight. The time for injection was defined as when symptoms worsened. An injection of MSC must be performed for forty minutes at a rate of 40 drops per minute (3).

Inflammatory bowel disease (IBD) is known for its complexity and being a multifactorial disease associated with genetics. IBD can take different forms, however, the most common one is ulcerative colitis. These disorders can result in intestinal barrier destruction, which can increase vascular permeability. The increase can lead to auto-immune activation and mucosal tolerance failure (2). In addition to cytokine mediation, MSC can secrete extracellular vesicles containing micro vesicles, and exosomes that can regulate intercellular communications and inflammation (2). Cultured MSCs can differentiate into more specialized cells such as osteocytes and adipocytes which play a part in bone remodeling and inflammation regulation (5). A clinical trial of evolving mice was conducted to observe the efficacy of MSCs in treating chronic colitis. The results showed that the severity of blood weight loss after treatment with MSC was severely moderated when compared to the control group (2). There was a decrease in bleeding and a significant level of mucosal damage was reduced. MSC also showed an improvement in healing tissue when compared to the control group (2).



The figure above shows an MSC located within the placenta. Along with differentiation the MSC is also capable of self-replication. MSC can differentiate into other general cells and tissues such as muscle, cartilage, fat, bone, and connective tissue (5). Within the cytoplasm of the cell exists an endosome which contains anti-inflammatory cytokines and chemokines. It also contains the MSC exosomes which is the part of the cell primarily used for chemical cell to cell communication. The MSC exosomes are lipid lined nano vacuoles that contain genetic material growth factors along with mitochondria and other proteins (5). Multipotent stem cells possess limited proliferation potential; however, they have capabilities such as expandability, hypo-immunogenicity, and tissue regeneration. A fitting example of MSC's cell to cell communication abilities can be seen during pregnancies. The macrophage during an autoimmune disease secretes pro-inflammatory cytokines that bind to designated receptors located on the native cell (1). The contents of the MSC endosome are released into the extracellular space where they modulate the immune response. The factor receptors sTNFR1 and 2 bind themselves to cytokines preventing them from binding to the native cell. Since there is no cytokine signaling the immune response is suppressed (1).

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