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Literature Review of Adipose-derived Mesanchymal Cells from History to Approaches

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Abstract

Context: After about 40 years from the discovery of bone marrow stem cells, the adipose stem cells (ASCs) were identify and the applications of these cells in different fields including the medical and biomedical fields have always attracted the attention of the scientists. The great quantity of stem cells obtained from adipose tissue allows the scientists to rapidly apply these primary cells without culture expansion.
Evidence Acquisition: Human has different types of fat tissues and each has its own applications, which means that the ASCs are harvested from different niches and each could be applied for different purposes. There are also specific biomarkers on the surface of the stem cells which is specific for every kind of these cells and the ASCs have also their own surface markers which help to easily detect.
Results: Already the ASCs are clinically applied in many other purposes but the first clinical application of ASCs was reported in 2004 for the treatment of traumatic calvarial deficiency in a 7-year-old girl. However in the last decade a huge number of studies has been done on ASCs and the ASCs are used for different reasons and in different medical fields including the treatment of cardiovascular and immune diseases, for healing the wound scars and also is applied for skin rejuvenate, radiation injury, scar remodeling, and skin engineering.
Conclusions: This review was to focus on the roles of ASCs in different applications and also provide the researcher general information about the history and current applications of ASCs. We found that the ASCs have a potential role to be used for the treatment of different sorts of disorders, with the less side effects and is also a new approach toward new remedies.

Keywords: Review, Adipose-Derived Stem Cell, Application

1. Context

1.1. History

The first report of stem has always been controversial, but on the 1st of February 1961, Till and Mc Culloch established the foundation for stem cell sciences, while they were working on radiation therapy for cancer treatment in the early 60s in Canada, they have published their findings as "Cytological demonstration of the clonal nature of spleen colonies derived from transplanted mouse marrow cells" (1). However, Sabin et al. were among the first authors who have published an article and stated that there is a common stem cell for all the blood white cells which is the main hypothesis of further studies (2).

For the first time, in 1868, the term "stem cell" was defined by a German scientist, Ernst Haeckel, who was a supporter of Darwin's evolution theory, he used the term "stem cell" as the unicellular ancestor of all multicellular organisms and as the fertilized egg, which gives rise to all cells of live organisms (3). Then this term has been referred to the embryotic cells that give rise to more specialized cells, in 1981, Evans and Martin conducted separate studies and derived pluripotent cells from the mice embryotic cells, which was the first embryonic stem cells (4).

The popular idea of mesenchymal stem cells, which was first expressed by Caplan 1991, is referred to the studies of Goujon in 1869, in that study they transplanted the bone marrow (BM) to the heterotopic anatomical sites, which resulted in de novo generation of ectopic both bone and marrow (5). Then further studies have been conducted to establish and find the new features of the mesenchymal cells, afterwards, in 1970, Friedenstein developed fibroblast colonies from bone marrow and spleen cells, he found that these cells are introduced by single cells known

as colony-forming unit fibroblastic (CFU-Fs) (6). Later on, he reported that bone marrow contains determined osteogenic precursor cells with high potential to differentiation and the in vitro transplantation of BM stromal cells led to generation of skeletal tissues (7).

Pittenger stated that these adult stem cells could be induced to differentiate totally into the adipocytic, chondrocytic, or osteocytic lineages and were identified that, when expanded to colonies, they can retain their multilineage potential (8). First, the original designation of this class of stem cells as "mesenchymal" was based on the theory that multiple tissues beyond skeletal lineages could be produced by postnatal MSCs, including skeletal muscles, myocardium, smooth muscle, tendon, etc. (9). Caplan in 2007 has published an article in which he suggested the cell therapy using the mesenchymal stem cells as a treatment of some disorders including myocardial infarcts, graft-versus-host disease (GVHD), cartilage and meniscus repairs, stroke, Crohn's Disease, and also spinal cord injuries, moreover he explained the biological basis for the in vivo functioning of MSCs through development and aging (10).

Over the last decade, great interests have been made towards the adult stem cell field. In 2002, Zuk et al. has published their article in which they declared the potential of the adipose-derived stem cells (ASCs) to differentiate to neuronal-like cells of the ectodermal lineage, which was further confirmed by other studies of other researchers (11).

Afterward other studies that confirmed the potential of ASCs to differentiate to various cells including neurons, oligodendrocytes, Schwann cells and epidermal lineage cells have added value to the theory that ASCs may be pluripotent cells rather than multipotent (12, 13).

The first clinical applications of ASCs on human were reported in 2004, among those reports, Lendeckel et al. reported the use of autologous ASCs and fibrin glue to cure the traumatic calvarial deficiency in a 7-year-old girl and he finally reported bone formation after three months (14); in addition, the ACSc were used for treatment of different diseases including Crohon's disease, urinary incontinence and GVHD (11). These sorts of clinical applications demonstrate the wide range of ASCs use.

2. Evidence Acquisition

2.1. The Adipose Tissues and Their Roles

Macroscopically, there are at least five different types of adipose tissues including the bone marrow, mammary, mechanical, brown, and white adipose tissues that each has its own specific biological roles. The bone marrow adipose tissue works as an energy reservoir and the source of cytokines for osteogenic and hematopoietic actions. The brown adipose tissue is thermogenic tissue through the expression of a unique uncoupling protein that short circuits the mitochondrial pH gradient and surrounds the major organs such as heart, aorta, gonads , kidneys as well as the newborn infants, and will disappear by aging as humans mature. Mammary adipose tissue provides the needed nutrients and energy for the breast fed baby and is regulated by hormones. Mechanical adipose tissues including the palmar fat pads and the retroorbital, support the specific organs such as eye, hands etc. The white adipose tissue stores energy and provide protection. Now, there is a larger appreciation of the white and other adipose tissues roles as the endocrine organs. Adipose secretions cause physiological and pathological effects (15).

2.2. Mesanchymal Stem Cells Morphology

Human MSCs act as the reservoirs of reparative cells without tissue specific features. Different signals are resulted in cell mobilization and differentiate to connective tissue lineages cells, which include damage in the tissues such as fracture, necrosis, inflammation, tumors and trauma (16).

Mesenchymal stem cells are morphologically known by a small cell body containing a large, round nucleus with a prominent nucleolus, which is by surrounded finely spread chromatin particles and a few cell processes that are long and thin. The cell body holds a small amount of Golgi apparatus, rough endoplasmic reticulum, mitochondria, and polyribosomes. The cells, which are long and tinny, are widely spread and the nearby extracellular matrix is occupied by a few reticular fibrils but is lacking of the other types of collagen fibrils (17). Most of MSCs have spindle-like fibroblastic shape with a single nucleus. These cells proliferate at around day 7 of culture and progressively grew to form small colonies. Then the colonies increasingly grow in size by interconnection of the cells. The colonies become union 21-28 days after plating, this time is depended on the proliferating ability of each cell and sample (18). Moreover, the MSCs morphological appearance ranges from spindle shaped to polygonal and cuboidal in various sizes (19).

Generally the physical properties of the extracellular matrix define the cell function as well as its behaviors. For instance, previous studies showed that human mesenchymal stem cells that were allowed to adhere, flatten and also spread, differentiated in to the osteogenic cells while the cells which were unspread and round gave rise to the adipocyte cells (20).

2.3. Detecting Mesanchymal Stem Cells

Adult tissues contain particular stem cell niches supplying the replacement cells during normal cell turnover and tissue renewal after trauma or any sort of harms. The epidermis, hair, and the gastrointestinal tract all are proper models of tissues with niches containing stem cells that can supply these cells throughout typical cellular turnover (21).

Mesanchymal stem cells were originally isolated from the bone marrow stroma but lately these cells have been detected in various tissues, including fat, cord blood and epidermis (22). MSCs have been isolated from a variety of tissues including adipose tissue, tendon, periodontal ligament, synovial membranes, trabecular bone, bone marrow, embryonic tissues, the nervous system, skin, periosteum, muscle, first-trimester blood and fetal pancreas (16, 21, 23).

The International Society for Cellular Therapy (ISCT) has introduced a number of standards to define human mesenchymal stem cells (hMSCs) for laboratory investigations and preclinical studies, these standards include: adherence to plastic surface of plate in standard culture conditions, they also have the capacity of in vitro differentiation to osteoblasts, adipocytes, and chondroblasts and they also could express specific surface antigen, which we will explain more in the following sections (24).

There is also an other general approach which is used to isolate all kinds of MSCs which have previously isolated from different niches by using the Dulbecco's Modified Eagle Medium (DMEM), in this method the collagenase is dissolved as the result the digestion times would be limited to a maximum of 1 hour at 37°C and stem cells isolation as soon as possibly following the euthanasia, another advantage of this method is the use of culture medium at temperatures not lower than the temperature of the laboratory (21).

2.4. Mesanchymal Stem Cell Bio Markers

The mesenchymal stem cells have common surface markers such as CD44+, CD90+, and CD105+, but there is no surface marker that exclusively defines MSCs and expresses on the MSCs surface. These surface antigen expression allows for rapid detection of the MSCs, according to the ISCT protocol, to identify the MSCs, the cells should be CD105+, which is known as the endoglin, recognized by the MAb SH2, the other CD antigens that are commonly expressed by these cells are the CD73 and CD90 which are known as the ecto 5' nucleotidase and Thy-1, respectively. Moreover the lack of hematopoietic antigen expression, including CD45, CD19, CD14, is an additional criterion of MSCs detection (21, 24, 25).

Since the MSCs are isolated from different niches, which are classified as adipose-derived stem cells (ASCs), bone marrow-derived-stem cells (BM-MSCs), periodontal ligament-derived stem cells (PDL-SCs), trabecular bone-derived-stem cells (TB-MSCs), synovial membrane-derived stem cells (SM-MSCs), periosteum-derived stem cells (P-MSCs), muscle-derived stem cells and satellite cells (M-MSCs), skin stem cells (SSCs), Wharton's Jelly stem cells (WJ-MSCs), miscellaneous stem cells and so forth. Each of these MSCs express specific markers on the cell surface (21, 26).

2.5. Adipose-Derived Stem Cells Bio Makers

Adipose-derived stem cells (ASCs) are differentiated into different lineages including endodermal, ectordermal and mesodermal lineages. According to the study by Zuk et al., these cells express the following antigens: CD13, CD29, CD44, CD71, CD90, CD105/SH2. SH3 and STRO-1, while these cells do not express hematopoietic lineage markers including CD12, Cd16, CD31, CD34, CD45, CD56, CD61E, CD104 and CD106 (11).

3. Results

3.1. Isolation and Clinical Application of Adipose-derived Stems Cells

Stem cells are used alone or in combination with scaffolds to regenerate the tissues and in some cases the organs, this approach is quiet a new one in medical sciences, Correct selection of the MSCs source is crucial in order to obtain a more efficient treatment (21).

The MSCs are commonly isolated form aspiration of the bone marrow isolated from the superior iliac crest of the pelvis, the tibial and femoral, thoracic and lumbar spine (27).

The transplantation of allogeneic stem cells and autologous into patients, through local delivery or systemic infusion is a model of haematopoietic stem cell transplantation, which has been applied for the treatment of leukemia and other malignances for few years. The bone-marrow derived stem cells have been used for the cardiovascular, lung fibrosis treatments, bone and cartilage repairs as well as spinal cord injuries repairs (27). According to the available collected data so far, engineered cardiac muscles tissue, bone and cartilage are the most suitable candidates for clinical use (21). A potential clinical feature of MSCs is related to their anti-inflammatory and immunosuppressive effects. The previous studies showed that MSCs prevent acute graft versus host disease (GVHD) without any side effects, which was a millstone of transplantation (28).

Adipose-derived stem cells are a subtype of MSC, which could be isolated by less invasive techniques and in larger

quantities compared with other MSCs that are used for the tissue engineering. White adipose tissues are rich of multipotent stem cells, while the number of ASCs and the potential to differentiate are reduced in brown adipose tissues, so the with adipose tissues are a proper reservoir to isolate the ASCs. In humans the largest numbers of ASCs are recovered from the arm as compared with the thigh, abdomen, and breast areas (15).

These sorts of MSCs are collected from elective liposuction procedures under local anesthesia, during which a hollow blunt-tipped cannula attached to gentle suction, was penetrated into the subcutaneous space through 1-cm-incisions. The cannula was moved through the adipose part and mechanically disrupting the fat tissue (21, 29). Through tumescent liposuction, surgeons infuse a saline solution containing anesthetic and/or epinephrine to the subcutaneous tissues via a cannula and then remove both the liquid and tissue by suction. The procedure generates finely minced tissue fragments, which the size depends on the dimensions of the cannula (15).

Nowadays, the applications of ASCs in tissue regeneration are very impressive. Most of the researches are focused on the ischemia revascularization, cardiovascular tissue regeneration, bone and cartilage repairs as well as urinary tract reconstructions (11).

In a study by Lu et al. they have stated that the adipose-derived stem cells have greatly improved the blood supply of flap necrosis with different patterns and the histological findings demonstrated that this has been achieved by direct differentiation on adipose-derived stem cells to the endothelial ones as well as the growth factors released by these cells (30).

In 2007, Kim et al. has stated when the ASCs are co-cultured with human dermal fibroblast, would enhance the proliferation of the fibroblasts by both direct contact and indirectly will affect the expression of type I collagen in fibroblasts, this phenomenon should be consider in wound healing (31). Also in another study in 2009 the application of ASCs in the field of plastic and reconstructive surgery has been proposed and the authors explained that the ASCs have a potential to regenerate the skin and epithelial layer of the human body (32).

Moreover the effect of the ASCs in reducing the UVB-induced wrinkles was positive and the anti-wrinkle effects of the ASCs is proven by increasing the collagen production by human dermal fibroblasts (33). Generally the ASCs have great potential for applications in repair of skin scars, rejuvenation of aging skin and aging-related skin lesions (34).

4. Conclusions

According to the findings of the other authors and previous literature on ASCs, we found that the ASCs have a potential role to be used for the treatment of different sorts of disorders, with the less side effects and is also a new approach toward new remedies. Since 2000, there is a surging interest toward the ASCs and the clinical applications and the positive and effective results were reported in different studies.

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