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Review

Stem Cell Applications in Plastic Surgery

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ABSTRACT

In the realm of medicine today, plastic surgery stands out among all internal and surgical fields. This priority stems from the fact that the procedures have their own conceptual and scientific underpinnings. However, the procedures applied must be artistically and technically detailed. An effective and current model shift in plastic and reconstructive surgery applications is made possible by the efficient use of stem cell therapies and applications utilized for the repair and regeneration of the same or other tissues and organs. In the last seven to ten years, stem cell-assisted therapies have become a widely preferred method due to their ability to self-renew and multi-potential differentiation. According to the findings of the studies, adult mesenchymal stem cells provide the ideal stem cell population for practical regenerative medicine, even though the use of embryonic stem cells or induced pluripotent stem cells is very important in clinical studies. However, adipose-derived stem cells (ASCs), which are among the easily accessible cells, have been shown to have the potential to distinguish between mesenchymal, ectodermal, and endodermal lineages. Since ASCs are a plentiful source, diverse across several lineages, simple to collect, and easy to obtain, they might be thought of as a good option in the field of plastic surgery and aesthetics. Adipose tissue is also easier to obtain and propagate as it yields a high number of ASCs per tissue volume. Stem cells have grown more desirable for plastic surgery due to their usage in a variety of aesthetic procedures, such as the treatment of burn scars, breast augmentation methods, defining facial contours, and postponing the onset of indications of aging, particularly on the hands and face. This situation has given promising results in the current preclinical and clinical studies on the use of stem cells in the field of aesthetics. However, prospectively, there is a limited investigation into the efficacy and potential of stem cell-based therapy for use in aesthetic and plastic surgery. This chapter focuses on the state-of-the-art and most recent advancements in stem cell therapies for cosmetic and plastic surgery, as well as the possibilities for tissue engineering and cell-free therapy in this area. Applications in research and medicine, as well as their benefits and drawbacks, are also covered.

Keywords: Adipose-derived stem cells, bone marrow mesenchymal stem cells, embryonic stem cells, mesenchymal stem cells, stem cell, plastic surgery.

The medical specialty of plastic surgery, also known as plastic, reconstructive, and aesthetic surgery, deals with the reconstruction and shaping of various body structures on the face, the removal of this issue following significant tissue loss, and aesthetic interventions like hand surgery, craniofacial surgery, microsurgery, and burn treatment.[1] Essentially, it is split into two parts. Reconstructive surgery is a discipline that includes all surgeries to replace any missing skin, subcutaneous tissue, or bones on the entire body's surface. It is the first major portion of the book. This procedure is mostly done to make sure that any lost tissue is replaced with tissues that are fairly comparable to it. For instance, this field of study includes conditions like cleft lip and palate caused by womb deformity, conjoined fingers (syndactyly), burns following trauma, facial injuries from serious car accidents, various incisions and limb ruptures, and chronic wounds. Plastic surgery makes up the second major category.[2]

This field includes many disciplines. It can present diseases that are not always accompanied by aesthetic perceptions and medical problems that do not only aim for beauty. In addition, a person with large breasts can be corrected or reduced after gigantomastia

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(breast reduction) plastic surgery as a result of weight gain. At the same time, nose surgery (rhinoplasty), which is also performed for aesthetic perceptions, can also occur in breathing problems.[3] It can be seen from the term's origin that it comes from the Greek word "plastikos." Through reshaping, the required shape is achieved. Following this surgical procedure, it is intended to help the patient feel more confident about their new body image. Recent years have seen considerable advancements in the use of stem cells in plastic surgery and regenerative medicine.[4]

Clinical applications have led to a great deal of interest as a result of studies aimed at increasing the use of stem cells in many different disciplines. Therefore, it is becoming the main focus of modern therapeutic treatment approaches. One of the most important factors in the studies is the use of adult stem cells, well-characterized, well-defined cell lines in patients safely and with a standardized treatment approach.[5] The fact that stem cell therapies provide "patient-specific" care is their most crucial quality. In the near future, there will be more certified cell products available due to the growing significance of stem cell research, which will improve their effectiveness and usefulness and lead to a larger distribution of the technology.[6] Plastic surgeons have used human tissues to repair defects caused by unwanted injuries and discovered that a single cell line can be used for tissue regeneration.[7] For stem cell-based tissue coating, it is necessary to consider the types of cells utilized (embryonic stem cells and adult stem cells), the cell sources (autologous and allogeneic), and the source of the tissues (bone marrow, muscle, fat, cartilage, or blood).[8,9]

STEM CELL APPLICATIONS IN PLASTIC SURGERY

The deoxyribonucleic acid (DNA) molecules in cells contain the full biological life program. Unfortunately, it is still unknown what exactly makes such encoded information visible to others. From the development of a fertilized egg to trillions of cells that differentiate and gain new traits simultaneously, the programming in cell division has drawn attention.[10]

Our body's aged and dying cells are replaced by newly formed cells. Yet, the body also makes unique defense cells to combat outside antigens. For vision, secretion, and respiration, cells in the pancreas, eyes, and lungs undergo differentiation. A "stem cell" is the earliest mother cell of all cells in a live organism. These cells have the capacity to develop into several cell types.[11] Stem cells are cells that have the ability to multiply indefinitely, self-renew, differentiate into other cells, and repair damaged tissue. Stem cells can be obtained from undifferentiated cells that can self-renew by continuing to divide in an organism for a long time, forming undifferentiated cells. In other words, cells with the potential to differentiate into different cell types and self-renew are called stem cells. The cells in our body such as muscle cells, liver cells, skin cells, etc. have a specific purpose and when these cells divide, they form a cell just like themselves.[12] However, unlike these cells, stem cells do not have a defined function. Therefore, they can transform into different cell types according to the signals they receive. The most important factors in determining this seem to be genes and external stimuli. When death or damage occurs in any cell population in our body, stem cells transform into the cells needed.[13] Since they are plentiful and easily accessible, multiply by differentiating into a variety of cell types, and can be safely and efficiently transplanted into both autologous and allogeneic recipients, they are chosen in regenerative medicine applications. According to their capacity for differentiation, stem cells are classified as totipotent, pluripotent, multipotent, oligopotent, and unipotent. Theoretically able to develop into a creature are totipotent stem cells. The first totipotent cell that has the capacity to differentiate into every type of cell that makes up an organism is the zygote. Via the creation of the placenta, extra-embryonic umbilical cord, amniotic sac, Wharton's gel, and multipotent, pluripotent, and unipotent cells, respectively. Pluripotent cells can develop into any type of germ tissue (endoderm, ectoderm, mesoderm). They can form fetal and adult cell types, but not organisms.[14,15]

Pluripotent stem cells can differentiate only to a lesser extent. Throughout the body, they can only differentiate into a few different cell types. When the right conditions and signals are present, they have the capacity to differentiate in the lab into a considerably greater diversity of cell types. In higher organisms, unipotent cells are cells with the capacity to differentiate into a single cell type. They assist in tissue regeneration as well, but in order to repair severe tissue damage, pluripotent stem cells are needed.[16,17]

Stem Cell-Assisted Wound Recovery Process

The intricate process of wound healing involves several interactions between cells, cytokines, and extracellular matrix. Several stem cell-based wound healing methods have been developed over the past few decades, some of which have been used in clinical settings. Both fibroblasts and bone marrow mesenchymal stem cells (BMSCs) have demonstrated outstanding wound-healing effects with significant collagen and growth factor production. Adipose-derived stem cells (ASCs) may be helpful in critical limb ischemia wounds due to their angiogenic characteristics. By encouraging the secretion of various cytokines that promote macrophage recruitment, fibroblast chemotaxis, collagen production, granulation tissue formation, and improved angiogenesis, ASCs play a significant role in the wound recovery process.[18,19]

Enhancing Burn Healing and Reducing Scarring through Stem Cell Therapy

Mammalian skin does not regenerate spontaneously and the final outcome of mammalian wound healing results in scarring. Scars are morphologically characterized by irregular collagen deposits. Recently, various scar reduction techniques have been developed. Therapeutic amounts of cells can be applied directly to the target wound, which has an effect on wound healing.[20] The duration of inflammation during wound healing is closely related to the degree of scarring. Adipose-derived stem cells may be a potential therapeutic tool for extreme scarring due to their anti-inflammatory and immunosuppressive effects. This approach may provide a more complete and useful regenerative process, similar to scarless wound healing. In the near future, this ASC-based treatment could become a new therapeutic option in wound management to ensure complete healing without any visible scar formation.[21]

Stem Cell Applications in Tissue Engineering

In biotechnology-based research, there have been many integrated clinical studies and research between tissue engineering and plastic surgery. Plastic surgeons can nowadays obtain stem cell sources from various tissues in the body. Circulating stem cells, i.e. hematopoietic stem cells, have a potentially unlimited bank of cells with great differentiation potential, obtained through minimally invasive procedures.[22]

Mesenchymal stem cells (MSCs) derived from bone marrow and adipose tissue are another useful source. Autologous mesenchymal stem cells with scaffolds show improved wound healing. Adipose-derived stem cells can be easily removed from the patient/human body using various liposuction techniques. Providing a sufficient number of stem cells to the defect can trigger local regeneration and healing processes. It can be difficult to find scaffolds suitable for these cell lines. The scaffold must have multiple functional roles such as cell adhesion, promoting the desired proliferation, and differentiation, and preventing the migration of the implanted cell in order to achieve good results.[23]

Rejuvenation with Stem Cell Application with Fat Graft Technique

Degenerative pathways play a large role in the aging process, specifically the loss of soft tissue volume. Due to the aging population, the desire to seem young, and the availability of minimally invasive procedures, there is a rising demand for cosmetic procedures. One of the most often utilized anti-aging procedures in plastic surgery is the fat injection method.[24] It can help repair defects and strengthen soft tissues. Specific side effects caused by immune responses have not been reported with the use of autologous tissue. However, simply injected fat can be absorbed at any time and the degree of absorption is difficult to predict. For liposuction to work well, it can be improved by using cell-assisted lipotransfer (CAL). CAL is a technique that combines concentrated ASC with aspirated fat to create an ASC-enriched fat graft. This approach significantly improves the survival of the fat graft.[25] Thus reducing the adverse effects of fibrosis and cyst formation. BSCs can promote fat graft survival through neovascular sprouting. Bone marrow MSCs and circulating progenitor cells upregulate the production of angiogenic growth factors and increase the number of new blood vessels formed in the grafted fat, improving graft survival.[26]

Stem Cell Applications Prevent Allotransplantation Rejection

For replacing various tissue defects, composite tissue allografts can be a perfect option for reconstruction following trauma, tumor removal, congenital malformation correction, etc. Yet, it has been demonstrated that immunosuppressants might have negative side effects on composite tissue allografts. In order to minimize the systemic toxicity of immunosuppressants, stem cells may therefore aid to create lifetime tolerance following transplantation.[27]

It has been demonstrated that immunosuppressive regimens used in conjunction with bone marrow transplantation (BMT) increase transplant survival. Multipotent progenitor cells that can develop into several mesenchymal cell types can be found in the bone marrow.[28] Bone marrow stromal cells, bone marrow progenitor cells, or bone marrow MSCs are the names given to these cells.[29] These stem cells have the capacity to control the production of T cell subsets and anti-inflammatory cytokines.[30] Combining temporary immunosuppression with MSC or ASC infusion can increase long-term transplant acceptance, prolong allograft survival, and induce immunological tolerance.[31]

In conclusion, clinical advances using various stem cells have shown great promise for opening up new cell therapy strategies in plastic surgery. More clinical research is needed for stem cell therapy to become a more established standard of care, but more research is also needed to determine the fate of transplanted cells and to sort the cells needed to determine clinical impact. In addition, the potential for tumor growth and the long-term consequences of these cells, which are considered side effects of cell transplantation, should also be demonstrated. A Good Manufacturing Practices facility is essential for the safe collection, testing and cryopreservation of cells. The fundamental benefit of stem cell therapy is that it does not require potentially risky surgical procedures or result in long-term morbidity at the donor site. In particular for elderly individuals, it can lower surgical risks. Skin grafting and flap surgery, which include removing any kind of tissue from the donor site and replacing it at the recipient site with an unbroken blood supply, can be quite taxing on the patient or necessitated by their overall health. Several plastic surgeons continue to conduct more research with diverse stem cells. In the future, when many techniques are used in maxillofacial surgery, MSCs will play a critical role in preventing tissue loss due to infection, trauma, tumors, and congenital diseases. Their immunomodulatory, differentiation, and migratory abilities for the treatment of diseases make MSCs particularly suitable for clinical use. There is a risk of morbidity at the donor site when significant volumes of autologous tissue are transplanted to restore function and appearance. Mesenchymal stem cells could eventually have a wide range of uses in the maxillofacial area. To produce strong proof, more preclinical and clinical trials are required. Adult pluripotent stem cells must be easily accessible and thoroughly described in order for their plasticity to be of meaningful clinical benefit. To increase the frequency and precision of these events, it is necessary to identify the molecular pathways driving cell line modifications if pluripotent qualities are to be attained by *ex vivo* manipulations leading to differentiation. Whether the process of divergence and division will always take place in the absence of unfavorable genetic modifications that could cause aberrant differentiation and even carcinogenesis is a risk that has to be understood. If pluripotent stem cells are found *in vivo*, their surroundings, behavior during proliferation and/or differentiation, and capacity to gather at damage sites will be crucial factors in determining how they are used in medicine. Additionally, it motivates medical professionals and researchers to stimulate supposedly dormant pluripotent stem cells through in vitro or *in vivo* manipulation. This should motivate researchers to investigate whether this triggers unchecked proliferation and/or differentiation processes akin to those seen when embryonic stem cells are implanted *in vivo*. Adult stem cells can be taken from the patient, preventing an undesirable immune reaction, which is perhaps one of their most significant benefits. The fact that many degenerative diseases have poorly understood underlying mechanisms, however, complicates the situation. It is unclear whether stem cells or other cell lines derived from them have comparable flaws. Despite the fact that numerous centers across the world are conducting various clinical trials, many practical and scientific concerns still need to be resolved before large-scale clinical trials can be logically organized. Finding the bare minimum of cells necessary for an organ or tissue to perform better is crucial in the beginning. Next, the question of how many stem cells are required to restore a tissue or organ arises. How long are the replacement cells functional? Second, it will be crucial to determine the chemoattractants that injured tissues or organs emit in order to draw BMSCs to the area. So, it is essential to have a solid grasp of stem cell biology. To address the issues and concerns that have developed or may arise in human stem cell therapy, more research and studies are required. Despite all of these concerns, the method of removing stem cells from each patient, increasing their number, and then reinjecting them back into the patient appears to have much greater benefits when the drawbacks of treatments like organ transplantation and immunosuppressive medications are taken into account. The hope that stem cell therapy can treat diseases for which there is now no efficient and effective therapeutic approach is the basis of research. Future stem cell therapies aim to treat and permanently cure diseases that currently seem "incurable," that is, treatable.

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