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Research Article

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Stem Cell therapy for Hair Loss

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Abstract

Stem cell research has made significant strides since its inception, with applications expanding into regenerative medicine and therapeutic treatments for various conditions, including hair loss. The discovery of hematopoietic stem cells (HSCs) in the 1960s and the advent of induced pluripotent stem cells (iPSCs) in 2006 have propelled the field into new frontiers. Stem cell-based therapies for hair loss focus on regenerating hair follicles, with sources ranging from adipose-derived stem cells (ADSCs) to hair follicle mesenchymal stem cells. These approaches leverage the unique properties of stem cells, including self-renewal and differentiation, to address androgenetic alopecia and other conditions. Stem cells promote hair growth by activating dermal papilla cells, stimulating follicular regeneration, and enhancing hair density. Techniques such as intradermal injections combined with growth factors and vitamins further optimize therapeutic outcomes. This review highlights the mechanisms, sources, and applications of stem cells in hair loss treatment, emphasizing their potential to revolutionize hair restoration therapies.

Keywords: Stem cells, Hair loss, Regenerative medicine, Induced pluripotent stem cells, Mesenchymal stem cells, Adipose-derived stem cells, Hair follicle regeneration, Androgenetic alopecia, Dermal papilla cells, Hair restoration therapy

1. Background

Interest in stem cell research surged after its discovery by Ernest McCulloch and James Till in the 1960s, establishing the groundwork for regenerative medicine [1]. Early funding focused on basic research, but investments increased substantially in the late 1990s with the advent of human embryonic stem cell (ESC) technology. The field gained further momentum in 2006 when Shinya Yamanaka introduced induced pluripotent stem cells (iPSCs), reducing ethical concerns and opening new therapeutic possibilities [2]. Human embryonic stem cells may be utilized to address various conditions, including Parkinson's disease, spinal cord injuries, and diabetes [3]. Results indicate a rising growth rate for the stem cell market, with the global market size valued at US$297 million in 2022. It is projected to expand at a compound annual growth rate of 16.8% between 2022 and 2027. This growth is fueled by factors including successful clinical trials, increased funding for stem cell research, an expanding number of technologies and facilities in cell therapy, and heightened demand for regenerative medicine [4].

2. Introduction

In the 1970s, stem cells made their debut in medicine, specifically hematopoietic stem cells (HSCs), which were used in bone marrow transplants to address blood disorders such as leukemia and aplastic anemia [5]. The therapeutic applications of stem cells have broadened to encompass treatments for Parkinson's disease, diabetes, spinal cord injuries, and cardiovascular conditions. Mesenchymal stem cells (MSCs) are extensively researched for their regenerative and anti-inflammatory [6]. The creation of iPSCs in 2006 transformed the field, allowing for developing therapies tailored to individual patients [2]. Research into stem cells for treating hair loss started in the early 2010s, highlighting the potential of adipose-derived stem cell (ADSC) therapies in both preclinical and clinical trials. These therapies focus on regenerating hair follicles and promoting hair growth in conditions like androgenetic alopecia [7]. Additionally, studies using iPSCs to develop hair follicles that can naturally grow through the skin may significantly advance hair restoration [8].

3. Stem Cell Mechanism and Method of Application in Hair Loss

To understand the mechanism of stem cell-based therapies, three distinctive perspectives shape the direction of their use; this includes the hair growth mechanism, extraction of stem cells from

various sources, and method of application. From multipotent sources to adipose tissue-derived stem cells, various sources are yet under investigation to consider superior based on the response of the hair regeneration.

3.1 Hair Growth Cycle: Underlying Mechanism

In the focus of the dermal papilla, from its control of the hair growth and direction, it lies at the base of the hair follicle, and it's rich with multipotent stem cell hair [9]. With its self-renewal and differentiation properties, it serves as the homeostasis of the skin barrier. The hair growth cycle consists of three phases. The first step is the anagen phase, where it holds much of the active hair growth and lasts from 2-6 years. The hair grows into the dermal papilla downward into the follicle and up to 1 cm every month. Second is the catagen phase, which lasts 1-2 weeks, where the hair shaft experiences death and is pushed upward as it separates from the follicle in a two- week transitional phase and enters into the last phase of telogen. In the inactive third phase of telogen, it can last for four months before the hair starts to grow, lasting two to seven years. For the hair to start back to the anagen phase, it should be near a supply of stem cell bulge for the cycle to continue in the direction of hair regeneration. Factors that can affect hair growth are the disruption of β-catenin signaling, by prolonging the catagen phase and preventing the anagen phase [10,11].

3.2 Stem Cell Sources for Extraction of Use

Stem-cells range from sources where continuous self-renewal and differentiation are the core of their existence. With its rich nature and independence of self-growth and promotion, it could be held as a new home for the organ maturation. Regenerative sources are classified based on plasticity and range from pluripotent stem cells to multipotent ones, such as: umbilical cord, adipose tissue, hair follicles, bone marrow, etc. In the following section, further details will be discussed.

3.2.1 Mesenchymal Stem Cells (MSCs): Mesenchymal stem cells are first discovered through bone marrow and continue to be extracted from adipose tissues, peripheral blood, lung, placenta, umbilical cord, and pulp [12,13]. Through its paracrine and immunomodulatory effects on tissue regeneration. Such effects are growth factors, which include hepatocyte growth factor (HGF), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), etc. A study has shown the use of dermal sheath cup cell (DSCs) and dermal papilla cells (DPCs) from mice and humans cells in vivo, where they differentiate into bone, adipose, and cartilage, and they show superiority to other MSCs [14,15]. They tend to form and aggregate into spheres and act as hair bulbs in vivo.

3.2.2 Adipose-derived stem cells (ASCs): With its minimal immunogenic properties and easy to obtain, adipose derived stem cell is favored to be the ideal regenerative medicine and angiogenesis potential. Immature adipocyte lineage cells drive follicular stem cell activation and the production of platelet derived growth factor (PDGF). Strong synchronicity between adipose derived stem cells and hair growth cycle was found [16]. Adipose derived stem cells (ASCs) are usually used in alopecia androgenetic (AA), due to its reduced side effects when used in male/female hair loss [17]. A study was done by Fukuoka, 2015, have found hair growth and increase after treatment of both male and female patients [18].

3.2.3 Embryonic Stem Cells and Cord Stem Cells: With limited research in the use of pluripotent stem cell extraction, studies on embryonic stem cells have found its capacity of continuous self-renewal in developing cells of the adult body and in hair follicle regeneration. With its formation from human embryonic stem cells (hESCs), neural cells are activated into hair-inducing DP, acting similarly to adult human DP cells to encourage hair growth. A study has found the extraction of neural crest cells promotes cell proliferation and induces growth factors by activating DPCs and hair follicle stem cells [19]. Wharton's jelly in umbilical cord has good source of stem cells and minimal risk of infections [15]. In 2015, Li et al, have found cord blood- derived multipotent stem cell (CB-SC) as a new form of umbilical cord source and different from other mesenchymal stem cells (MSCs) functionally and genetically. It was also found that it promoted hair generation [20]. An in vitro model was found successful in reducing hair loss in mice as well as inflammation [21].

3.2.4 Hair Follicle-Derived Mesenchymal Stem Cell: In hair anatomy and growth cycle, one of the main parts that gained focus when treating hair loss is the hair bulge. The bulge of the hair is the powerhouse due to its properties, such as the presence of epithelial and mesenchymal cells, its contribution to maintaining hair growth, and the generation of interfollicular epidermis, sebaceous glands, and follicle structure. One study has found that the extraction of hair follicle stem cells by mechanical centrifugation and punch biopsy was able to improve hair density and hair count above the goal baseline of the research [22]. Other advantages of hair follicle stem cells use are the decrease of hair loss and inflammation around hair follicles [21].

4. Stem Cell Application in Hair Loss

After extraction and preparation of stem cells, the method of application consists of using gauge needles throughout the scalp and spaced 1 cm apart or in a specific alopecic area. Through intradermal direction and a volume of 0.02 ml, some clinical practices combine vitamin B1, vitamin H, vitamin C, vitamin B6, Vitamin E, coenzyme Q10, and other amino acids, as well as the use of mesotherapy during administration. Patients who feel pain during the procedure prefer to use anaesthesia with lidocaine to suppress or block the supraorbital nerve and greater occipital nerve.

The course can be given per month in six to eight months, as well as depending on the severity of the alopecia, and in men, finasteride is administered to support during or after treatment is completed [23].

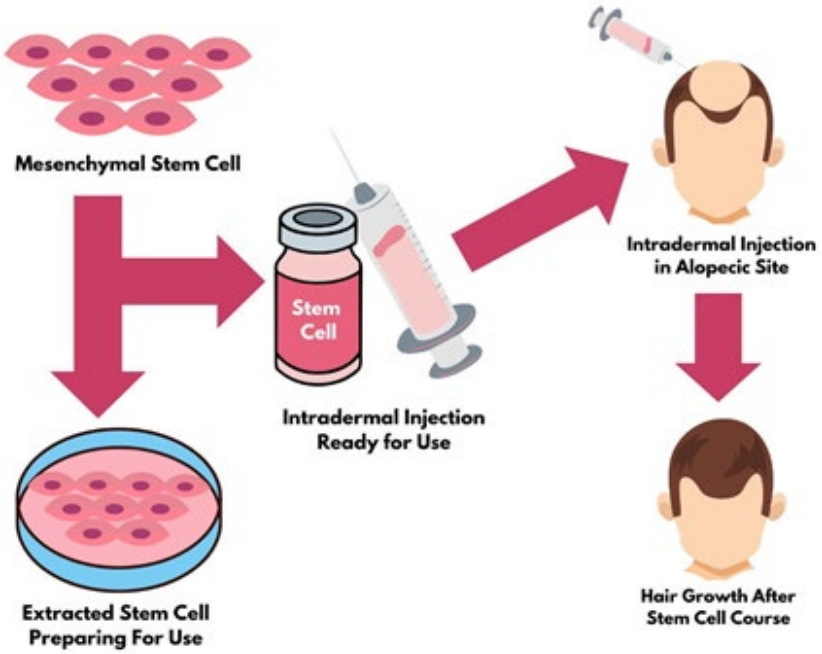

Figure 1: Stem Cell Use in Hair loss Treatment

After extraction from the donor site and prepared for use, stem cells are applied through intradermal injection in the alopecic site or throughout the scalp and result in the promotion of hair growth and regeneration.

5. Conclusion

With its success and exploration of use in various specialties in medicine, stem cell implications are continuing to grow significantly in treating and maintaining dermatological conditions. In hair loss conditions, stem cell results are promising, and engaging in clinical practices and patients' satisfaction with their results. Various sources of stem cell extraction seem to be the continuing drive for studies in choosing which of the best donor sites is providing an everlasting outcome in hair regeneration. Whereas the method of applications seems to act best through intradermal injection, due to the stability of nature as well as the effective course of use. However, further studies can be done to widen the horizon of its method of application in diverse settings for the future of cosmeceuticals and accessibility.

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