ISSN: 2754-494X

Journal of Dermatology Research Reviews & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

Review of Stem Cell Therapy for Hair Loss

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ABSTRACT

Background: Hair loss (HL) is a disorder that both male and female experience frequently. The most typical kind of hair loss is pattern hair loss, which is also referred to as androgenetic alopecia. Recent years have seen a surge in interest in stem cell-based therapies, which aim to reactivate hair follicle stem cells and so promote the growth, regeneration, and advance of hair follicles. Stem cell transplant, conditioned media made from stem cells, and exosomes made from stem cells are all examples of stem cell-based therapeutic techniques.

Objective: In this review, we will highlight stem cell therapies and hair loss.

Methods: We scoured medical papers and databases including PubMed and Google Scholar for information on Hair Loss, Alopecia areata, Types of stem cells and Stem Cell Therapy. After meticulously screening references from the appropriate literature, which included all of the identified research and reviews, the authors included only the most current or complete study.

Conclusion: Because stem cells can result in follicle regeneration, their use in hair regeneration is promising. It is quite possible to cure nonautoimmune hair loss with stem cell regeneration for a variety of causes. In the future, stem cells and their secretory factors may be used to cure hair loss and alopecia areata.

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Received: July 19, 2024; **Accepted:** July 25, 2024; **Published:** July 31, 2024

Keywords: Hair Loss, Alopecia Areata, Types of Stem Cells, Stem Cell Therapy

Introduction

Alopecia androgenetica, sometimes referred to as men and women pattern hair loss, disturbs around 50% of men and 45% of women in the United States. The progressive thinning of hair, which is most noticeable at the crown and frontal scalp in alopecia androgenetica, is caused by interactions between different hereditary and endocrine variables. People who have Alopecia Androgenetica (AA) experience general psychological trauma as a result of their condition, as many report having a lower quality of life, lacking self-assurance, and having few social associates [1]. Pattern hair loss (PHL), the most prevalent kind of hair loss, affects both women and men relatively often and frequently result in a considerable decline in quality of life1. At the age of 70, male pattern hair loss/androgenetic alopecia (MPHL/AGA) and female pattern hair loss (FPHL) are thought to affect over 80% of Caucasian men and up to 42% of Caucasian women, respectively. Since hair is regarded as a key component of beauty and aesthetic appeal, hair loss has a significant effect on one's sense of self and self-esteem and can trigger depression and other mood disorders. Additionally, some claim that early AGA onset is linked to a higher risk of developing metabolic syndrome and myocardial infarction [2].

The Wnt- β-catenin pathway is believed to be a key player in the aetiology of hair loss. There are currently just 2 FDA-approved treatments for hair loss: finasteride, a selective inhibitor of type II and III 5'-reductase, and minoxidil, a vasodilator. These drugs haven't been perfect, though; both have been linked to issues with efficacy, duration of effect, and a number of significant side effects [2].

PHL is a kind of alopecia that does not leave scars. PHL is distinguished by abnormalities in the loss of hair progenitor cells, whereas hair follicle stem cells (HFSCs) survive. This idea in particular makes PHL a reversible disorder, and modern and cutting-edge treatment methods work to make use of the viability and responsiveness of HFSCs that are already present in order to reverse the pathology of hair loss and encourage hair regeneration. The scientific and clinical community that studies hair regeneration is particularly interested in creating the right signals and environment to reactivate HFSCs and regenerate a hair follicle. Research on hair regeneration has decreased significantly over the past ten years, and one reason for this is the discovery of stem-cell-based therapy, which has resulted in a number of promising preclinical and clinical trials. Recently, a lot of interest has been focused on stem cell transplantation, conditioned medium formed from stem cells, and stem cell-derived exosomes as possible novel agents to alter and augment the signalling pathways that might trigger HFSC reactivation, hair cycle, and hair follicle regeneration [3].

Review

35 million American males and 21 million American females, according to the International Society of Hair Restoration Surgery, are affected by hair loss. Many balding people want to keep their hair, and there is a big potential for assisting these patients, thus there is a demand for more affordable and effective alopecia treatments. Since their inception, invasive procedures like hair transplants and plugs have drawn criticism for their unnatural appearance [4,5].

Only when dosages are consistently taken are over-the-counter pharmaceutical medications, such as minoxidil and Propecia, effective therapy options. Vasodilation occurs when minoxidil is administered topically to the scalp skin, increasing the amount of nutrients and oxygen that reach the follicles. Finasteride works by inhibiting 5 alpha-reductase, which lowers the amounts of DHT around the follicles. Due to teratogenic adverse effects during pregnancy, this medication is only suitable for use in men. Spironolactone, a less effective inhibitor, has been attempted on females, although there are adverse effects to take into account, including hyperkalemia, headaches, breast soreness, and tiredness. The abrupt cessation of such medications would result in the continuing of hair loss at a pace similar to that seen before the usage of the medications [5].

The use of bone marrow stem cells, fat cells, and mesenchymal cells from the base of existing follicles, as well as embryonic umbilical stem cells, is now being researched to see whether it is possible to restore the hair. Future therapies for hair loss include other methods such stem cell-derived nutritional medium and stem cell-derived exosomes [5].

Types of Stem Cells for Hair Regeneration:

The degree of flexibility determines how stem cells are categorized. They may be divided into four categories: totipotent, pluripotent, multipotent, and adult stem cells, which are a subset of the multipotent stem cell category (Figure 1). Currently, research on hair regeneration has focused more on the use of pluripotent and multipotent stem cells as well as stem cells derived from adipose tissue [6].

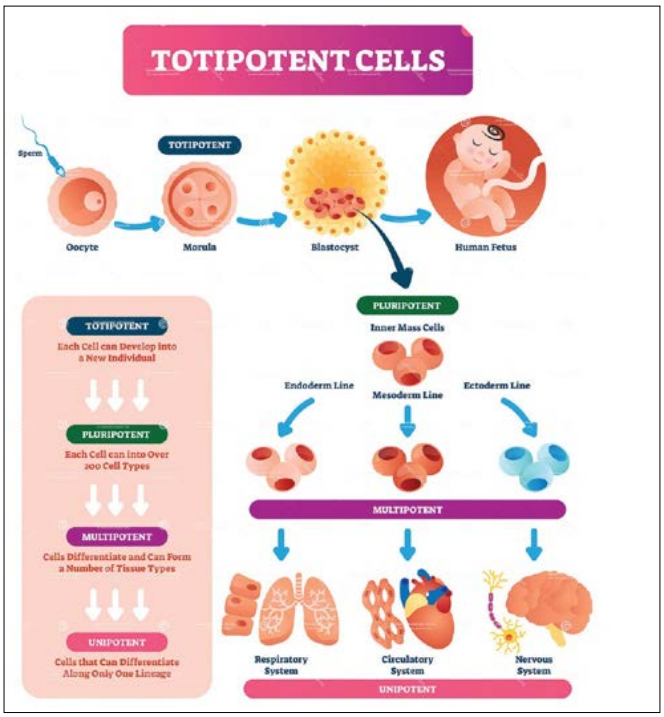

Figure 1: Cells multiply and specialize as the embryo develops naturally, starting with the fertilized egg and ending with the blastocyst. The inner cell mass of the blastocyst is where pluripotent embryonic stem cells are produced. Multipotent stem cells are confined to just giving birth to cells of their particular germ layer and are discovered in the developing embryo or produced from pluripotent stem cells [7]

Autologous Stem Cells

In order to stimulate hair follicle regeneration, autologous dermal papillae (DP) cells are being explored as a sort of cellular treatment for alopecia. To encourage the development of hair follicle lineages, pluripotent stem cells may be used. Even though an autologous transplant is thought to be the gold standard, its application is restricted due to a dearth of data and the lower viability of cells made available through this method. Techniques are now being developed to increase the viability of autologous stem cells from hair follicles [8].

Adipose-Derived Stem Cells

Because they may possess few immunogenic characteristics, the best cell population for regenerative medicine appears to be ADSCs. They can quickly differentiate into various cell lines, are multipotent, and are very simple to get. They have a lot of angiogenesis potential as well. These cells have resembled pericytes, vascular smooth muscle cells, and mural cells found in the perivascular regions. These cells are susceptible to vesicular endothelial growth factor (VEGF) and are involved in the formation of blood vessels [8].

There are no established tissue regeneration techniques for ADSC-assisted hair transplantation at this time. The capabilities of autologous cell suspensions in the Rigenera System, which were derived from the mechanical fragmentation of subcutaneous and adipose tissue from the occipital region, were examined by Zanzottera et al. To increase growth factors, the cell solution was applied to the region receiving the hair transplant. Even two months after the treatment, it was noted that microdamage healed more quickly and transplanted hair grew more quickly, with a shorter telogen phase [9].

Additionally, the effectiveness of ADSC-conditioned medium was examined in 27 female patients with female pattern HL. For 12 weeks in a row, this group applied ADSC-conditioned media using a microneedle roller. A phototrichographic investigation showed no adverse effects (including pain) and a statistically significant improvement in hair density and thickness [2].

Embryonic Stem Cells

Human ESCs (hESCs) were stimulated in culture to produce hair-inducing DP-like cells after first producing brain cells. When implanted beneath the skin of mice, DP-like cells generated from hESC display markers that are commonly expressed in adult human DP cells and are able to promote the formation of hair follicles. The necessary markers were expressed when these hESC-derived dermal papilla-like cells were inserted into the dermal papilla of freshly created hair follicles. They are not suitable for this objective, however, because they cannot be collected in adequate quantities and lose their potential to trigger hair follicle growth when cultivated. Functional hESC-DP cells can encourage greater hair production to treat alopecia [8].

Cord Blood Stem Cells

A gel-like material called Wharton's jelly can be found in the vitreous humour and inside the umbilical cord. It has developed into a reliable source of stem cells because to its extensive availability from numerous donors, painlessness and lack of risk to the donor. Additionally, there are no moral concerns, it has a low immunogenic potential, and it is simple to grow and differentiate. Additionally, the risk of infection is negligible [8].

Discussion

The hair progenitor cells are thought to be diminished in hair loss, while the hair follicle stem cells are still present and active. Therefore, bringing these hair follicle stem cells back to the anagen phase may be able to stop the loss of hair and regrow it. The development of the hair growth is dependent on a number of things. Proteins, which are necessary for the formation of hair, blood flow, which carries nutrients to the follicle, oil production, which keeps hair lustrous and prevents brittleness, and growth factors, which promote hair development and maintain active and productive follicles, are some of these variables. Alopecia and hair loss might result from a lack of any of these components [5].

Over 4700 clinical trials funded by the National Institutes of Health (NIH) are currently being conducted in an effort to understand all the pathways and potential applications of stem cell therapy. There are two different kinds of stem cell sources: mesenchymal stem cells from other sources, such bone marrow, adipose tissue, or the actual hair follicle, and embryonic stem cells from the umbilical cord. In an effort to find a more successful therapy for alopecia, research has been done on each one of these crucial variables. The significance of chemical signals in follicular physiology has been studied as one aspect. Chemical signals like Wnt and Noggin were examined by researchers at Rockefeller University. Examples of chemicals that induce stem cells to start differentiating into hair follicles include these signals. If no signals are given to the follicle, follicular degeneration begins, which results in the cessation of hair development. The signals used in this process and how to influence the signal system in their favor are the subject of some study. Researchers from the University of California, Los Angeles (UCLA) have shown that two medicines, RCGD423 and UK5099, have distinct effects on and activation mechanisms in mesenchymal stem cells isolated from hair follicles, which send information from the outside to the cell's nucleus. The cell signaling pathway Janus kinase (JAK)-signal transducer and activator of transcription (STAT) is activated by RCGD423. The increased lactate generation that results from JAK-STAT activation promotes the activation of hair follicle stem cells and accelerates hair growth. UK5099 prevents pyruvate from accessing mitochondria, which would otherwise cause a cell to produce lactate. It has been demonstrated that this lactate generation stimulates the proliferation of hair follicles and hair cells [5,10].

In certain trials, stem cells have been injected directly into the scalp to promote growth. The protrusion of the hair follicle was biopsied by Gentile et al. Fat is eliminated after trimming the punch biopsies to a 2 mm width. To separate the cells, the residual tissue is centrifuged in 1.2 ml of ordinary saline. The resultant suspension and cells are injected into the target region to a depth of 5 mm. When the hair density of AA patients was compared to controls, it was found that there had been an improvement. Studies like this highlight the enormous potential stem cells may hold for the creation of specialized therapies [11].

Mesenchymal cells have been exploited as a source of stem cells in other investigations. Hardy explains how adult mesenchymal cells and embryonic stem cells can be employed to produce new hair or aid in adult new growth. Hair follicles are a possible donor location for the collection of stem cells to be employed in the replacement or regeneration of damaged hair due to the capabilities and availability of mesenchymal stem cells [12].

The replacement of dead scalp follicles by stem cells as well as the use of growth factors and other chemicals to reawaken dormant follicles are other topics of recent research. In the treatment of AA, Li et al. found at stem cells not as a replacement but as an addition to existing hair follicles. AA is the most frequent autoimmune condition that causes hair follicle destruction and loss. In this study, researchers offered "stem cell educator therapy," which involves circulating a patient's autologous blood with multipotent stem cells (cord blood stem cells, CB-SC) and then returning the patient's blood to them after the "education" process. It was found that this therapy caused the transforming growth factor-beta (TGF-β) to create a ring around the hair follicle, shielding it from the immune system. This illustrates yet another possible use of stem cells for controlling hair development in alopecia [13].

The crucial molecules in the multistage morphogenesis of tissues were seen by Lei et al. These molecules' activation and inhibition shed light on how stem cells are trained to form particular three-dimensional tissue architectures. In this situation, it appears that adult skin cells and stem cells, particularly those found in hair follicles, have the potential to be used in regenerative medicine. The success of the future stem cell research depends on our ability to comprehend how cells interact to form three-dimensional structures [14].

Elmaadawi et al. studied the safety and efficacy of the autologous bone marrow-derived mononuclear cells (BMMCs) including stem cells in comparison to follicular stem cells (FSCs) obtained from the unaffected scalp areas in 20 patients with AA and 20 patients with AGA. All patients underwent one treatment session with autologous stem cells (BMMCs or FSCs) that were injected intradermally. Evaluation by immunostaining and digital dermoscopy 6 months post-treatment demonstrated significant improvement of both conditions with no significant difference between treatment groups and no adverse events [15].

Gentile et al. examined the autologous mature stem cell isolation from patient-own biopsy specimen and scalp injection in 11 patients. They revealed that 29% of the individuals who received the injection had an increase in hair density. This shows that stem cells may be injected to increase hair growth, but further research is needed to determine if this is due to the activation of dormant stem cells already in the body or to new cell growth regeneration. Studies demonstrate a 0.4%–2% increase in density in people receiving 5% minoxidil. It has been demonstrated that a technique like platelet-rich plasma (PRP) injection may enhance hair density by about 29% [5,11].

It was shown by Al-Ghadban et al. that adipose tissue has the capacity to develop into adipose-derived regenerative cells. Their research showed that, over a three- and six-month period, injecting adipose-derived regenerative cells close to regression follicles increased hair growth and density. The focus of the other research fields is on the bioactive chemicals found in stem cells. Hair development is also influenced by growth factors, chemokines, cytokines, and other regulatory proteins. The identification of these elements and their use can also aid in reversing the hair follicle regression. The paracrine factor, which is one specific molecule, is part of the stem cells' signaling system. Rich media used in the vicinity of the follicles can promote follicle development and reverse its latent inactivity [15].

There are a lot of restrictions on stem cell treatment for hair loss. The way the cells were prepared and how many were utilized in the research were not standardized. The interval between treatments and if the stem cell injection is permanent have not been studied. There hasn't been any research on the advantages of one type of donor stem cell, such adipose tissue, over others, including bone marrow or hair follicles. Finally, there are no great treatments for extreme hair loss. There are no standards for extraction methods. Future research must address each of these concerns [5].

Conclusion

Because stem cells can result in follicle regeneration, their use in hair regeneration is promising. It is quite possible to cure nonautoimmune hair loss with stem cell regeneration for a variety of causes.

In comparison to current treatment modalities, stem cell therapies have fewer side effects and appear to be effective in both men and women. Stem cell-based therapy could be the way of the future for hair regrowth.

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