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Research Article

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Exosome Therapy for Hair Loss

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Abstract

Hair loss is a widespread condition impacting millions globally, often causing considerable psychological and social stress. Traditional treatments like minoxidil and finasteride face challenges due to variable effectiveness and possible side effects, leading to an interest in innovative regenerative therapies. Exosomes, tiny extracellular vesicles released by diverse cell types, have gained attention for their role in cell communication and their capacity to influence critical biological processes, like inflammation and cell growth. This review delves into the use of exosomes for treating hair loss, elaborating on their mechanisms, such as activating hair follicle stem cells, fostering angiogenesis, decreasing inflammation, and reducing oxidative stress. Findings from both preclinical and clinical research underline their potential to improve hair density, thickness, and scalp condition, with few negative side effects. The review also touches on obstacles like exosome isolation standardization, scalability, and long-term safety, proposing potential solutions, including advancements in exosome engineering and combination therapies. Looking ahead, there's an emphasis on the necessity for extensive clinical trials and the integration of exosome therapy with other regenerative approaches. This treatment showcases a cutting-edge, minimally invasive method with incredible potential to transform hair loss management loss.

Keywords: Exosomes, Hair Loss, Androgenetic Alopecia, Mesenchymal Stem Cells, Regenerative Medicine, Hair Follicle Biology

1. Background

Trams et al. first identified exosomes in 1981, noting the release of small vesicles by cells during the maturation of reticulocytes [1]. Simultaneously, Rose M. Johnstone and her team at McGill University uncovered these vesicles while investigating the removal of transferrin receptors from developing red blood cells [2]. The word "exosome" was first introduced by Johnstone's team in 1987, initiating targeted research into their biological functions [2]. Research on exosomes for hair therapy was initiated in the mid-2010s as scientists explored the regenerative potential of exosomes sourced from mesenchymal stem cells (MSCs). These MSC-derived exosomes were found to harbour growth factors, cytokines, and various signalling molecules that can stimulate dermal papilla cells, essential for hair follicle growth [3]. Exosomes began to be clinically applied for hair restoration between 2016 and 2018, as research revealed their potential to enhance cell proliferation, boost vascularization, and lessen inflammation in the scalp, thereby fostering an ideal environment for hair growth [4].

2. Introduction

Conditions like androgenetic alopecia (AGA), alopecia areata (AA), and telogen effluvium (TE) pose significant treatment challenges. Traditional therapies, including minoxidil and finasteride, exhibit limitations such as variable effectiveness and potential side effects [5,6]. Exosomes, recently recognized for their role, are lipid bilayer-enclosed vesicles produced by almost all cell types, transporting molecular content like proteins, lipids, mRNA, and microRNA (miRNA). They emerge from multivesicular bodies and are released into extracellular spaces, where they modify recipient cells by delivering bioactive molecules [7]. Their involvement in modifying the microenvironment via cell-to-cell communication is well-documented in tissue repair, immune regulation, and disease pathology [8].

Regarding hair loss, exosomes derived from mesenchymal stem cells (MSCs) demonstrate impressive regenerative capabilities. These exosomes are rich in growth factors such as vascular endothelial growth factor (VEGF), insulin-like growth factor 1 (IGF-1), and transforming growth factor-beta (TGF-β), which are essential for the development and cycling of hair follicles (HFs) [9].

Hair follicles experience a cycle of growth (anagen), regression (catagen), and rest (telogen). Dermal papilla cells (DPCs) regulate the transitions between these stages, playing a crucial role in sustaining follicular activity. Disruptions in this cycle, often due to genetic, hormonal, or autoimmune issues, can lead to hair loss disorders [10].

Exosomes affect hair follicle (HF) biology by activating various signalling pathways, such as Wnt/β-catenin, TGF-β, and ERK, which encourage the initiation and prolongation of anagen [11]. Exosomes from adipose-derived stem cells (ADSCs) have been found to stimulate DPC proliferation and migration, resulting in increased follicular density and thickness [12].

3. Present Treatments in Hair Loss

Hair loss treatment is one of the common aspects in dermatology clinical practice. From traditional drug therapy to regenerative exosome therapy, hair loss treatments continue to grow into finding the best possible treatment method in terms of hair regeneration. Non-medical treatments can range from dietary supplements from plant sources such as ginseng as a bioactive ingredient, to lifestyles changes with food consumption and shampoos to remove excessive oil or dirt [13]. The following table overviews the present therapies used in clinics.

Treatment Type	Mechanism of Action	Reference
Drug Therapy		
Minoxidil	Vasodilating effect, potassium channel opener and extension duration of anagen phase inducing angiogenesis.	[14]
Finasteride	Androgen affect metabolic changes in the occurrence of androgenetic alopecia, through the inhibition of type II 5-alpha reductase.	[15]
Avodart	Inhibition of type II 5-alpha reductase, although more potent than finasteride.	[16]
Dutasteride	Anti-androgenic medication, by inhibiting type I and II 5-α-reductase to block the production of dihydrotestosterone (DHT).	[17]
Bicalutamide	Nonsteroidal androgen receptor inhibitor.	[18]
Cetirizine	Anti histamine medication, promotes release of prostaglandin-E2 to stimulate effect on hair cycle.	[19]
Clascoterone	Anti-androgen medication by blocking androgen receptor.	[20]
Surgical treatment		
Hair transplantation	Hair extraction from donor site into scalp bald area.	[21]

Strip Follicular Unit Transplantation (FUT) Transplantation	Removal of a thin strip of skin with intact hair from a safe and permanent donor area at the back side of the head.	[22]
	Newest Treatment Methods	
I. Physiotherapy		
Microneedle therapy	Rolling of needles in activation of hair growth genes, stem cells, and the release growth factors.	[23]
Fractional radiofrequency (FRF) therapy	The use of both needles and the delivery of ultra-high-frequency radio waves to increase hair density.	[24]
II. Light therapy		
Photo biomodulation therapy (PBMT) or Low-level laser therapy (LLLT)	Using red and infrared spectrum, wavelength of 600-1000nm targeting nitric oxide and cytochrome C oxidase. These events result in releasing growth factors, cytokines, inflammatory mediators and enhance hair growth.	[25]
CO2 laser	Fractional laser through upregulation of Wnt β-catenin by enhancing drug delivery to promote hair growth.	[26]
Excimer lamp	Used in the treatment of alopecia areta through the induction of T cell apoptosis by ultraviolent B light 290-320nm.	[27]
Absorbable Threads	Insertion of absorbable threads such as polydioxanone and poly-L-lactic acid (PLLA) to promote hair growth.	[28]
Botulinum Toxin	Vasodilatory effect by clearing of DHT from dermal papilla cells (DPCs) by the blocking acetylcholine.	[29]
	Regenerative medicine	
Platelet-Rich Plasma (PRP) therapy	Extraction high numbers of platelets from blood to promote cell proliferation and release of growth factors.	[30]

Table 1: Overview of the Present Treatments in Hair Loss

4. Exosome Mechanism of Action in Hair Regrowth

Exosomes promote the growth and differentiation of hair follicle stem cells (HFSCs) by delivering important miRNAs like miR-100-5p and miR-27b-3p, which activate hair growth pathways [31]. Furthermore, exosomes derived from mesenchymal stem cells (MSCs) have been shown to increase β-catenin expression, a vital regulator of HFSC activation [32]. Sufficient blood supply is crucial for the health and growth of hair follicles. Exosomes rich in VEGF enhance vascularization around hair follicles by promoting endothelial cell proliferation and the formation of new capillaries [33]. This angiogenic effect is supported by preclinical studies, which revealed that scalps treated with exosomes had greater blood vessel density and improved hair regrowth [34].

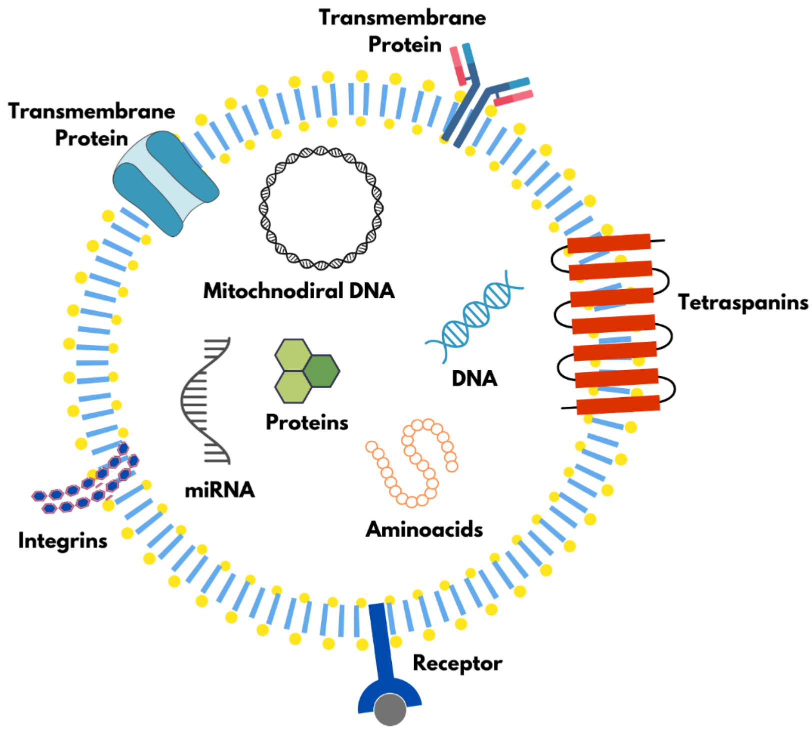

Figure 1: Xosome Diagram

Scalp inflammation is a common feature of conditions such as alopecia areata (AA) and telogen effluvium (TE). Exosomes influence immune responses by lowering levels of pro-inflammatory cytokines like IL-6 and TNF-α while boosting anti-inflammatory cytokines such as IL-10 [35]. This immunomodulatory function assists in restoring a healthy follicular environment. Additionally, oxidative stress can damage follicular cells, leading to hair loss. Exosomes that contain antioxidant enzymes like catalase and superoxide dismutase help reduce oxidative damage and maintain the integrity of HFSCs [36].

Several studies have been conducted in treating androgenic alopecia. A recent study done by L. Dehghani has found exosomes derived from placenta mesenchymal stem cells promoted significant improvements in hair density and reduced hair loss [37]. Another study has found a significant increase in hair density after the use of exosomes in in male patients with androgenic alopecia [38]. Furthermore, a study has shown the difference between the results exosomes and PRP, where exosome results were significantly higher in the improvements of the hair restoration [39].

Preclinical research has confirmed the effectiveness of exosome therapy in animal studies. A study by Zhang et al. revealed that MSC-derived exosomes significantly boosted hair density and follicle size in a mouse model of AGA [40]. Likewise, ADSC-derived exosomes improved HF elongation and DPC activity both in vitro and in vivo [41]. Several clinical trials have explored the potential of exosomes for treating hair loss. For instance, a pilot study involving AGA patients noted a 25% rise in hair density three months after treatment with exosomes from bone marrow MSCs [42]. Another study reported enhanced hair thickness and scalp health in patients treated with exosomes versus those treated with platelet-rich plasma (PRP) [43]. Nonetheless, large-scale randomized controlled trials (RCTs) are necessary to confirm these results and establish standardized protocols for the use of exosomes in hair loss treatment.

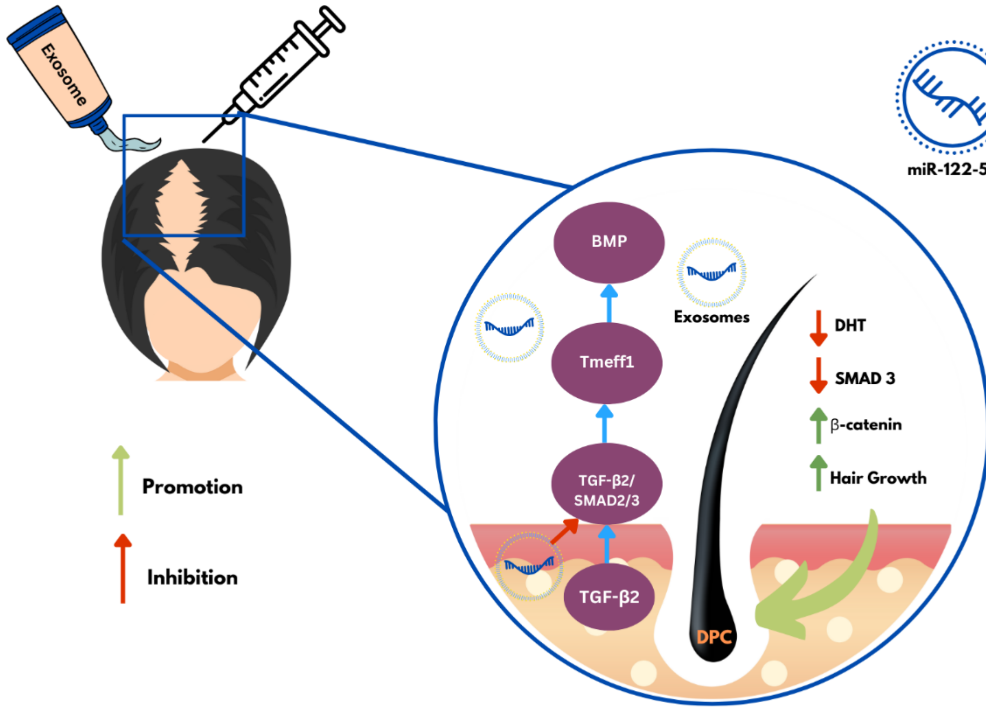

Figure 2: Mechanism of Adipocyte Stem Cell-Derived Exosome Through Topical and Intradermal Applications. ASC-Exo-miR-122-5 inhibits SMAD 3 which results in the inhibition of dihydrotestosterone (DHT) in dermal papilla cells (DPCs) and promotes cyclin, β-catenin to regenerate hair growth [44].

5. Methods of Application

Exosomes can be delivered via topical solutions or intradermal injections into the scalp. Intradermal delivery ensures direct interaction with hair follicular structures, enhancing therapeutic outcomes [45]. Topical formulations are gaining popularity due to their non-invasive nature, though their efficacy may be limited by penetration barriers. Combination therapies, such as exosomes with microneedling or low-level laser therapy (LLLT), have shown synergistic effects, further improving hair regrowth outcomes [46].

Despite promising results, several challenges hinder the widespread adoption of exosome therapy such as variability in exosome isolation, purification, and characterization methods complicates reproducibility across studies [47]. Exosomes are sensitive to storage conditions, requiring optimized preservation techniques to maintain their bioactivity [48].

The production of clinical-grade exosomes on a large scale remains a technical and economic challenge [49]. Although exosomes are generally considered safe, potential risks, such as immune reactions or off-target effects, warrant thorough investigation [50].

6. Conclusion

Exosome therapy is a revolutionary method for treating hair loss, utilizing their regenerative and anti-inflammatory characteristics to promote follicular health. Although initial findings are promising, thorough clinical studies are crucial to tackle current issues and validate this therapy as a standard choice. Combining exosomes with other regenerative techniques offers significant potential to transform hair restoration.

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