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REVIEW

# Exosomes for hair growth and regeneration

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**Exosomes are lipid bilayer vesicles, 30–200 nm in diameter, that are produced by cells and play essential roles in cell–cell communication. Exosomes have been studied in several medical fields including dermatology. Hair loss, a major disorder that affects people and sometimes causes mental stress, urgently requires more effective treatment. Because the growth and cycling of hair follicles are governed by interactions between hair follicle stem cells (HFSCs) and dermal papilla cells (DPCs), a better understanding of the mechanisms responsible for hair growth and cycling through exosomes may provide new insights into novel treatments for hair loss. In this review, we focused on the comprehensive knowledge and recent studies on exosomes in the field of hair development and regeneration. We classified exosomes of several cellular origins for the treatment of hair loss. Exosomes and their components, such as microRNAs, are promising drugs for effective hair loss treatment.**

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[**Key words:** Exosomes; Hair growth; Hair regeneration; Hair follicles; Hair cycle; Dermal papilla cells; Mesenchymal stem cells; Hair follicle stem cells]

Exosomes were discovered half a century ago (1), but the composition of exosomes and molecular mechanisms for vesicle separation and exocytosis remained unknown for a relatively long time. In 2007, a study reported that exosomes derived from mouse and human mast cell lines and primary bone marrow-derived mouse mast cells contained RNAs and miRNAs that could be transferred to other cells. After the exosomes entered new cells, their RNAs were translated to produce new proteins (2). Because exosomes contain bioactive components such as proteins, RNAs, and microRNAs (miRNAs), they convey information to cells to activate or inactivate various functions of receptor cells (3). Exosomes have received extensive attention in recent years because of their numerous physiological and pathophysiological functions (4). In dermatology, research on exosomes involves anti-aging, wound healing, skin tumors, and hair regeneration (5). Among many skin diseases, hair loss, a major disease that affects the appearance of modern people and causes mental stress, urgently requires more effective treatment methods. Owing to the limitations of traditional hair loss treatments (such as oral finasteride, topical minoxidil, and hair transplantation), new treatment options, including hair regenerative medicine, have become popular in recent years (6). With their contents, small size, and transcellular conductivity, exosomes may be a new direction and play an essential role in the treatment of hair loss. After a brief introduction to the definition, isolation methods, and main characteristics of exosomes, this paper reviews the research on hair growth using exosomes from different cell sources, with a view to providing a direction for the development of novel therapies for hair loss in the future, as summarized in Fig. 1.

## EXOSOMES AND EXTRACELLULAR VESICLES

Extracellular vesicles (EVs) are lipid bilayer vesicles, which can be secreted by most types of cells, including bacteria, fungi, plant cells, parasites, and animal cells, indicating a conservative evolution (7). EVs include exosomes, microvesicles and apoptotic bodies. In terms of size, the diameter of exosomes ranges from 30 to 200 nm; the size of microvesicles is 100–1000 nm; the largest is the apoptotic body, which has a diameter from 500 to 2000 nm (8). The process of exosome formation is the most complicated from the perspective of formation mechanism. Exosomes begin to form by the inward budding of the plasma membrane. The inward budding of the early endosomal membrane results in multivesicular bodies (MVBs). Finally, the fusion of the plasma membrane with MVBs allows the release of exosomes outside the cells. Microvesicles are simply produced by budding out of the plasma membrane and without the involvement of endosomes (8). In three types of EVs, apoptotic bodies are released by dying cells, and these vesicles are rarely used in research, probably because of their large and heterogeneous grain size (9). EVs are named as exosomes in most studies, which implies endosomal origin of secretory vesicles.

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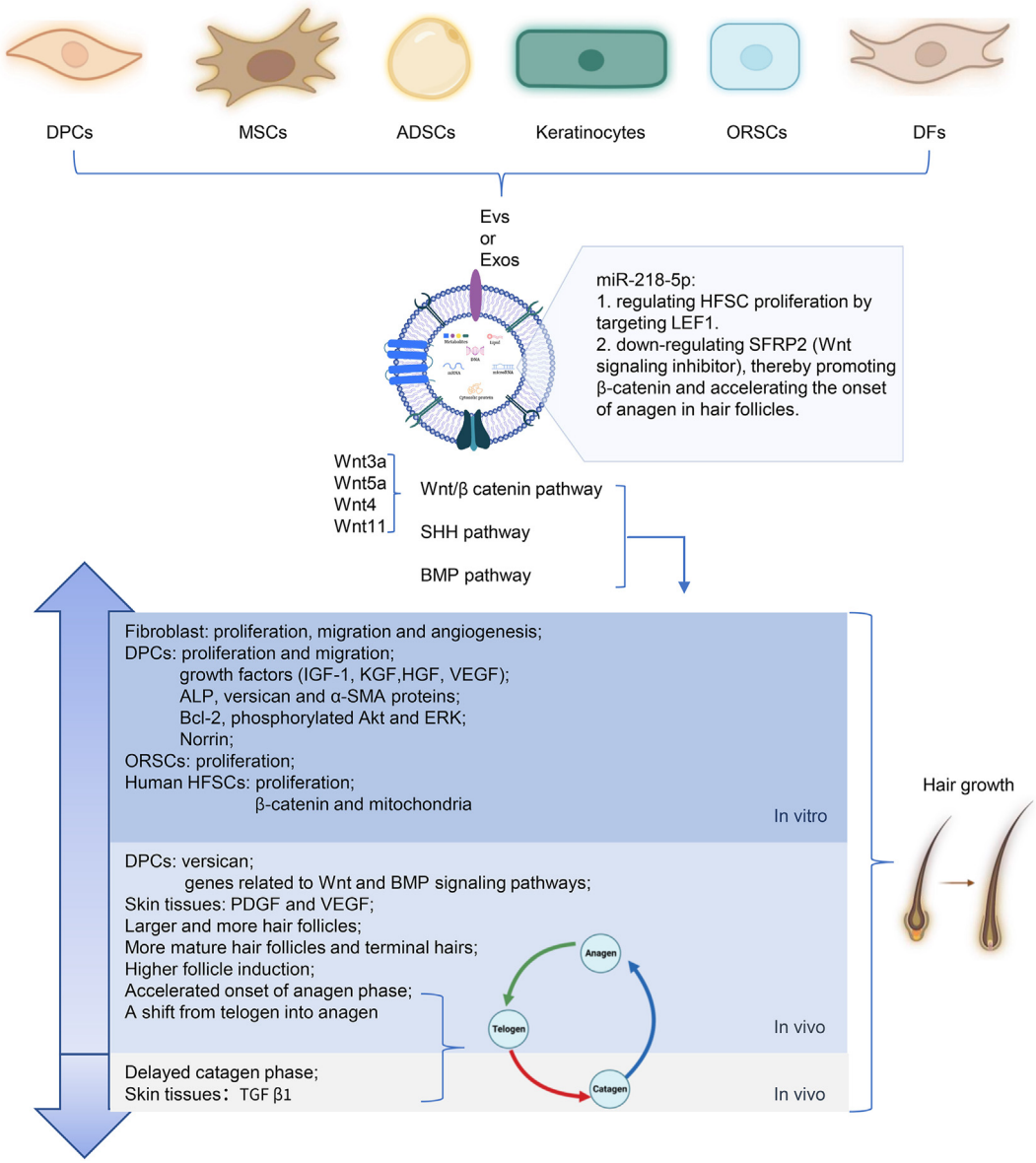



FIG. 1. The schematics of extracellular vesicles (EVs) or exosomes (Exos) derived from cells for hair growth. DPC: dermal papillae cells; MSCs: mesenchymal stem cells; ADSCs: adipose-derived stem cells; ORSCs: outer root sheath cells; DFs: dermal fibroblasts; HFSCs: hair follicle stem cells; LEF1: lymphoid enhancer binding factor 1; SFRP2: secreted frizzled related protein 2; SHH: sonic hedgehog; BMP: bone morphogenetic protein; IGF-1: insulin growth factor; KGF: keratinocyte growth factor; HGF: hepatocyte growth factor; VEGF: vascular endothelial growth factor; ALP: alkaline phosphatase; α-SMA: alpha-smooth muscle actin; Bcl-2: B-cell lymphoma-2; PDGF: platelet derived growth factor; TGF β1: transforming growth factor-β1. The elements in this figure were created with BioRender.com.

However, tracing the origin of vesicles often lacks conclusive evidence; for example, the fusion of MVB with the cell surface is a very dynamic process that is often not captured by conventional electron microscopy (10). Instead of exosomes, some studies have directly used the broader definition of EVs. Some articles have even suggested using the term small EVs (sEVs) to define membrane structured vesicles with a diameter less than 200 nm (9). The specialized formation process of exosomes results in their inclusion of cell surface proteins and other biological substances (e.g., proteins, lipids, and metabolites) (9). Exosomes carry proteins and RNAs and mediate intercellular communication, thus affecting normal and pathological conditions. Currently, especially in the field of regenerative medicine, most studies are focused on the potential of exosomes. In this review, subsequent occurrences of the term EVs refers to the most widely studied type of EVs, i.e., almost equivalent to the definition of exosomes.

## ISOLATION AND CHARACTERIZATION OF EXOSOMES

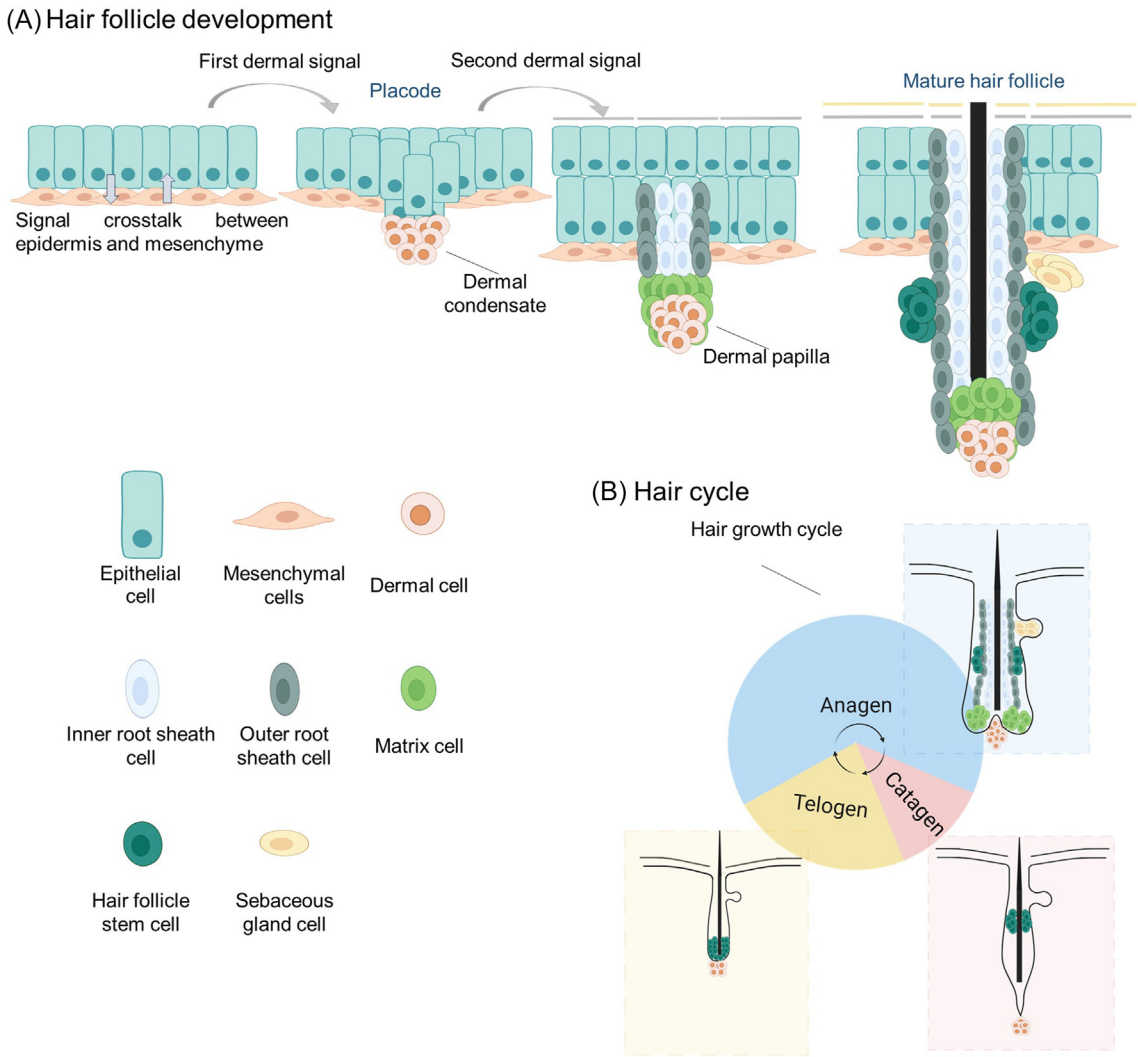
Currently, there are several exosome isolation methods, including ultracentrifugation, ultrafiltration, polymer precipitation, size-exclusion chromatography, immunoaffinity capture, and microfluidics-based techniques (11). According to a review (12) in which 126 articles were counted to analyze exosome isolation methods, ultracentrifugation is the most widely used method to isolate exosomes from the culture media of mesenchymal stem cells (MSCs), accounting for approximately 54 %, followed by the use of commercial kits, accounting for 27 %.

The characteristics of exosomes include diameter, morphology, and surface antibodies. The diameter and morphology of exosomes can be confirmed by electron microscopy, nanoparticle tracking analysis, and dynamic light scattering (13). The purity of exosomes can be measured by detecting their surface antibodies. Surface

antibodies can be detected by staining, immunoblotting, or proteomics analysis (14). The surface antibodies contained in exosomes are related to their formation. Since the formation of MVBs and exosomes is regulated by the endosomal sorting complex required for transport (ESCRT) protein, exosomes in principle contain the ESCRT protein and its accessory proteins (such as Alix and TSG101) (15). CD63, CD9, and CD81 are proteins of the tetraspanin family that are usually found in exosomes (16). In contrast, proteins related to the Golgi apparatus and endoplasmic reticulum are absent from exosomes (17).

## HAIR FOLLICLE DEVELOPMENT AS WELL AS HAIR GROWTH AND MAINTENANCE

As shown in Fig. 2A, a series of signals between epithelial and mesenchymal cells lead to changes in both cell populations that eventually differentiate into mature hair follicles. The crosstalk between the two cell types may be largely governed by exosome-mediated transport, which will be discuss later. The emergence of a first dermal signal in the dermis results in the formation of




Signals involved in hair follicle development and hair growth

| Process | Placode | Dermal condensate | Dermal papilla | Proliferation and downward growth of epithelium | Differentiation of the hair shaft | Hair growth cycle |
|---|---|---|---|---|---|---|
| Signals | Wnt (β-catenin, Wnt10b), SHH | Wnt (β-catenin, TOPGAL), SHH | Wnt, BMP (BMP4) | SHH | BMP (Bmp2,BMP4), Wnt (TOPGAL, LEF1) | Wnt (Wnt10b, Wnt10a), SHH |

FIG. 2. Hair follicle development and hair cycle. Crosstalk between epithelial and mesenchymal cells through exosomes largely governs the development of hair follicles (A) and hair cycles (B). TOPGAL: T cell transcriptional factor (Tcf) optimal promoter (TOP)-beta-galactosidase. The elements in this figure were created with BioRender.com.

thickenings of some parts of the epidermis, called placodes. Signals from the epithelial cells of the placode then cause some cells in the mesenchyme to aggregate, forming dermal condensate. The second dermal signal from the dermal condensate causes the epithelial cells of the placode to proliferate and invade the dermis, eventually surrounding the dermal condensate to form the dermal papilla (DP). Further proliferation and differentiation of epithelial cells result in the formation of the mature hair shaft (18). Activation of the Wnt signaling pathway in the dermis may be involved in the formation of the first dermal signal. In the presence of Wnt signaling, β-catenin degradation in the cytoplasm is inhibited and β-catenin translocates to the nucleus, where it participates in the formation of transcriptional complexes and activates the transcription of target genes (19). Wnt paracrine signaling molecules function during early follicle formation and promote placode development. In animal experiments, Wnt10b (20) and nuclear β-catenin (21) are significantly upregulated in placodes. Conversely, loss of β-catenin gene function in the mouse epidermis leads to the failure of placode development (22). Induction of dermal condensation may require Wnt signaling. TOPGAL, a β-galactosidase gene directly stimulated by β-catenin, is expressed in the dermal condensate and follicular epithelium (23). Meanwhile, dermal condensates cannot be successfully developed without epithelial β-catenin (22). Another essential protein involved in epithelial–mesenchymal signaling in the placode is sonic hedgehog (SHH) (24). SHH is dependent on Wnt signaling and is required for follicular epithelial proliferation and the development of dermal condensates into the dermis (25). Proliferation and downgrowth of the epithelium are dependent on the second dermal signal, which is activated by SHH (26). BMP and Wnt signaling are vital for hair shaft differentiation. The highest expression of Bmp4 was observed in the DP. Outside the dermis, Bmp4 is expressed in hair shaft progenitors in the distal hair matrix and Bmp2 is expressed in differentiating hair shaft cells in the precortex. They participate distally in proximal proliferation and differentiation (27). TOPGAL expression is observed when hair shaft precursor cells begin the process of terminal differentiation. These cells also express the LEF1 protein (23), which is an integral part of the Wnt signaling pathway.

The hair growth cycle is illustrated in Fig. 2B. The hair growth cycle can be divided into anagen, catagen, telogen (and exogen). The anagen phase is a growing period lasting 2 to 6 years, during which epithelial cells continue to proliferate and form hair shafts (28). The telogen phase is a resting period lasting approximately 3 to 5 months, after which hair falls out (exogen). The catagen phase is a transitional period between the anagen and telogen phases that lasts for approximately 3 weeks. During the catagen phase, hair growth ceases (29). The hair growth cycle is inseparable from Wnt and SHH signaling. Wnt10b and Wnt10a are expressed at the onset of anagen (20) and Shh is expressed in the inner root sheath cells of anagen follicles (26).

Two cell types, hair follicle stem cells (HFSCs) and dermal papilla cells (DPCs), are vital for the cycle and maintenance of hair follicles, as shown in Fig. 2B. HFSCs are located in the hair follicle bulge and provide epithelial cell pools (29). In the anagen phase, HFSCs grow downward to form transient-amplifying progenitor matrix cells, where they form internal hair follicles and shafts (30). DP is located at the bottom of the hair follicle and originates from the mesenchyme, where DPCs of mesenchymal cell origin are morphologically and structurally distinct from the epithelial cells of the hair follicle. DPCs maintain the growth of epithelial cells, whereas epithelial cells require the help of DPCs to organize into complex hair structures (31). During the telogen-to-anagen transition, DP signals stimulate the hair germ and activate resting HFSCs, after which cells at the bottom of the follicle begin to proliferate and form new hair filaments. During the anagen and telogen phases, DP remains morphologically intact and approach the bulge upward (32).

## HAIR LOSS TREATMENT IN CELL THERAPY AND THE USE OF EXOSOMES

As early as 1997, transplanted cells (containing DPCs) could be used for hair regeneration in animal models for the treatment of hair loss (33). When freshly prepared hair buds or primary mouse keratinocytes were mixed with active rat DPCs and transplanted into nude mice, hair follicles formed in the reconstructed skin, whereas no hair follicles formed in the reconstructed skin when hair buds or keratinocytes were mixed with dermal fibroblasts. The hair-inducing activity of DPCs was retained; however, this activity was rapidly lost during *in vitro* culture (34). In our laboratory, some studies have been conducted on the restoration of the hair-inducing ability of DPCs *in vitro* through the PI3K/Akt pathway (35) or electrical stimulation (36). However, the transplantation of DPCs still involves issues such as cell number and origin, which limit their application in the field of hair loss treatment. Obtaining a sufficient number of cells for transplantation is challenging. In addition, the immune response brought about by transplantation and the ethical issues associated with transplantation must be considered. Studies have shown that the main mechanism involved in tissue repair during cell transplantation therapy is related to the paracrine activity of cells (37). EVs released by cells are involved in intercellular communication by transferring functional proteins and RNAs to neighboring cells, thereby mediating various biological responses. Cell-secreted EVs are promising for the development of novel cell-free therapies that may overcome the limitations and risks associated with cell therapy (37).

There is clear evidence that exosomes play a role in organ generation. One study by Jiang et al. (38) indicated that exosomes mediate epithelial–mesenchymal crosstalk during organ (tooth) development. Epithelial exosomes induce mesenchymal cell differentiation, and mesenchymal exosomes induce epithelial cells to produce basement membranes and other proteins necessary for organ formation (38). This indicates that exosomes, or the molecular content they transport, may be involved in the treatment of diseases or tissue growth and regeneration. Likewise, as an organ, the generation of hair follicles and the maintenance of their morphology and function are the result of epithelial–mesenchymal crosstalk. Therefore, it is hypothesized that exosomes have a positive effect on hair follicles.

As mentioned above, the Wnt signaling pathway is critical for hair follicle development and hair growth. Data have shown that Wnt ligands secreted by the hair follicle epithelium are required for adult hair follicle growth, providing new insights into potential targets for the treatment of hair loss (39). As for how Wnts travel in the extracellular space, it has been shown that Wnts are secreted on exosomes during both Drosophila development and human cells, and that exosomes carry Wnts on their surfaces to induce Wnt signaling activity in target cells (40). It has been found that the Wnt3a protein can be detected exteriorly using $CD63^{+}$ exosomes derived from bone marrow MSCs, which lead to downstream fibroblast proliferation, migration, and angiogenesis *in vitro* (41). Exosomes isolated using ultracentrifugation show significantly reduced exterior Wnt3a detectability; however, exosomes isolated using polyethylene glycol (a type of polymer precipitation) can retain exterior Wnt3a detectability and downstream Wnt/β-catenin activity (41). It has been shown that Wnt4 is delivered by exosomes derived from human umbilical cord MSCs (hucMSCs), and Wnt4 induces angiogenesis and β-catenin activation in endothelial cells, which may be an essential mechanism of skin wound healing (42). Another study evaluated 3,3′-diindolylmethane (DIM), a natural small molecule involved in the repair of hucMSCs. The results showed that DIM promoted the stemness of hucMSCs by increasing Wnt11 autocrine signaling in exosomes (43). Consistent

with the above theories, intradermal injection of MSC-Evs into C57BL/6 mice demonstrated an increase in Wnt3a and Wnt5a, which may contribute to the activation of human HFSCs, leading to the onset of the anagen phase (44). Furthermore, MSC-EV treatment resulted in higher versican expression than in the control group (45). According to other findings, versican expression was higher in DPCs in the anagen phase, but significantly lower in the catagen phase (45), suggesting that MSC-EV treatment leads to the initiation of the anagen phase of DPCs. Immunohistochemical analysis in one study (46) showed that β-catenin and Shh levels were upregulated in mouse skin after subcutaneous injection of exosomes derived from DPCs (DPC-Exos) into mice. *In vitro*, DPC-Exo treatment stimulated the expression of β-catenin and Shh in outer root sheath cells (ORSCs) (46). These findings demonstrate that DPC-Exos stimulate the anagen phase of the hair growth cycle.

miRNAs are small non-coding RNA segments that affect gene expression by enhancing the degradation of mRNAs and preventing their translation. Because of their small size (approximately 19–24 nucleotides) and long half-life, miRNAs continuously regulate complex cell behaviors. Skin morphogenesis and hair growth cycle are inseparable from the miRNA-dependent regulation of gene expression (47). miRNA delivery strategies, including exosomes, have been extensively reviewed (48). As an essential component of paracrine signaling, exosomes can mediate communication between distantly isolated cells by transferring various biomolecules, including miRNAs, between donor and recipient cells (49). Yan et al. (50) found that miR-22-5p contained in DPCs-Exos could regulate HFSC proliferation by targeting LEF1, a fundamental transcription factor in the Wnt signaling pathway that determines hair growth by promoting the translocation of β-catenin. In addition, Hu et al. (51) observed that miR-218-5p was significantly upregulated in DP spheroid–derived exosomes, and that exosomes with high miR-218-5p expression accelerated the onset of anagen in hair follicles. miR-218-5p regulates hair follicle development by downregulating the Wnt signaling inhibitor SFRP2, thereby promoting β-catenin and forming a positive feedback loop. Similar results were reported by Zhao et al. (52), who demonstrated that SFRP2 is a direct target of miR-218-5p. The expression of miR-218-5p inhibits the expression of SFRP2, which activates the Wnt signaling pathway and acts as a dynamic regulator of hair follicle development.

## CELL SOURCES OF EXOSOMES INVOLVED IN HAIR GROWTH AND REGENERATION

**DPC-derived exosomes** In the current exosome studies in the field of hair, exosomes derived from DPCs are widely used in hair studies. DPCs are mesenchymal cells with adult stem cell properties that regulate hair follicle development by interacting with epithelial cells and play an essential role in the hair growth cycle (53).

In a study by Zhou et al. (46), human two dimensional cultured DPC-Exos were injected into the dorsal skin of mice in the telogen and anagen phases. The results showed that hair follicles treated with DPC-Exos were larger and more numerous than those in the control group (injected with PBS). The injection of DPC-Exos accelerated the onset of the anagen phase and delayed the catagen phase. These results suggested a hair growth-promoting role for exosomes. In another study by Kwack et al. (54), human DPC-Exos obtained in a three-dimensional (3D) culture promoted the proliferation of DPCs and ORSCs and increased the expression of growth factors in DPCs. Mice in the anagen phase of hair follicle development were injected with 3D DPC-Exos or PBS. After different time periods, 3D DPC-Exos-treated hair follicles remained in the anagen phase, whereas hair follicles injected with PBS were in the catagen or telogen phase. After different periods of topical injection of 3D DPC-Exos or PBS into mice in the telogen phase, 3D DPC-Exos-treated hair follicles accelerated the onset of the anagen phase, whereas mice injected with PBS remained in the telogen phase. These suggested a positive effect of 3D DPC-Exos on hair growth. Next, the researchers explored the effect of 3D DPC-Exos on hair regeneration. Human DP spheroids were treated with 3D DP-Exos or PBS and co-transplanted with epidermal cells from fetal mice into the skin of nude mice, showing significantly higher follicle induction in the former than in those treated with PBS. 3D DP-Exos also increased the expression of DP signature genes and genes related to the Wnt and BMP signaling pathways. We have studied the effect of exosomes derived from human DPCs on hair follicle organoids and discussed their role in hair regeneration. We found that treatment of exosomes isolated after culturing DPCs in a 3D oxygen-permeable device increased hair follicle sproutings, upregulated IGFbp5 expression, and downregulated TGFβ2 expression in hair follicle organoids (4). In this study, hair follicle organoids were prepared from the dorsal skin of embryonic mice (55,56).

**MSC-derived exosomes (or EVs) and adipose-derived stem cell-derived exosomes** In addition to exosomes derived from DPCs, hair growth-promoting effects of exosomes derived from MSCs have been reported. MSCs are adult stem cells originally identified in the bone marrow (57). Adipose-derived stem cells (ADSCs) are subordinate to MSCs and are obtained from adipose tissue (58). MSCs strongly secrete exosomes. MSCs encapsulate functional proteins or regulatory RNAs in exosomes, and the phospholipid layer of exosomes activates rapid signaling pathways (59). Rajendran et al. (44) used the culture media of mouse bone marrow MSCs to prepare extracellular vesicles (MSC-EVs). The results revealed that treatment with MSC-EVs increased the proliferation and migration of DPCs, as well as the levels of Bcl-2, phosphorylated Akt, and extracellular signal-regulated kinase. In addition, MSC-EV treatment increased the expression of VEGF and IGF-1 in DPCs. The intradermal injection of MSC-EVs into mice resulted in a shift in the hair growth cycle from telogen to anagen. Moreover, treatment with MSC-EVs increased Wnt signaling and versican expression in the dorsal skin of mice.

Nilforoushzadeh et al. (60) compared the effects of different concentrations of exosomes derived from human ADSCs and platelet-rich plasma (PRP) on the proliferation, migration, and expression of alkaline phosphatase (ALP), versican, and smooth muscle alpha-actin (α-SMA) in human DPCs. The results showed that for 100 μg/ml of ADSC-Exos, the expression of ALP, versican, and α-SMA proteins increased 1.2-, 2-, and 3-fold, respectively, compared to the control group. ADSC-Exos at 100 μg/ml significantly promoted the proliferation and migration of DPCs compared to the same concentration of PRP-Exos. In addition to the aforementioned ability to promote hair growth, ADSCs have been shown to contribute to hair follicle regeneration in our lab (61). Mixing human DPCs, mouse embryonic epithelial cells, and ADSCs resulted in hair follicle germ-like aggregates. Compared to hair follicle germ without ADSCs, the involvement of ADSCs significantly increased the expression of genes related to hair morphogenesis and effectively produced hair shafts when transplanted into nude mice. Wu et al. (62) isolated ADSC-Exos from mouse-derived ADSCs. In the ADSC-Exos group, the dermal and epidermal cells were treated with ADSC-Exos and co-transplanted into the skin of nude mice. In the control group, only dermal and epidermal cells were transplanted into nude mice. Two to three weeks after transplantation, the ADSC-Exos group generated more mature hair follicles and terminal hairs than the control group. In addition, skin tissue in the ADSC-Exos group was found to have higher expression levels of PDGF and VEGF, while TGF β1 levels were lower than in the control group. Shiekh et al. (63) designed OxOB and a gel composed of antioxidant polyurethane with sustained oxygen release

properties, and loaded it with ADSC-Exos. In diabetic rat models, OxOB and ADSC-Exos promote the formation of mature epithelial structures with hair follicles.

**Exosomes (or EVs) derived from other cell types** In the study of exosomes for hair loss, in addition to the cells mentioned above, one study of keratinocyte-derived exosomes has been reported by Ogawa et al. (64). They reported that exosomes secreted by HaCaT cells (human keratinocytes) could activate β-catenin and mitochondria in human HFSCs and induce their proliferation, thus promoting hair growth (64). In addition, human ORSC-derived exosomes (ORSCs-Exos) could also be used as a promising approach to promote hair inducibility in human DPCs and improve the therapeutic outcome of hair loss. According to the findings of Nilforoushzadeh et al. (65), ORSCs-Exos at a concentration of 100 μg/ml significantly promoted the proliferation and migration of DPCs. The expression of ALP, versican, and α-SMA proteins increased 2.1-, 1.7-, and 1.3-fold, respectively, in DPCs treated with ORSCs-Exos compared to the control group. Le Riche et al. (66) have reported the effects of EVs isolated from activated human dermal fibroblasts (DFs) on DPCs and hair follicle growth. It was found that DPCs treated with this type of EVs could secrete norrin, a non-Wnt ligand that activates the β-catenin pathway in human hair follicle keratinocytes. They also showed that DF-EVs are potent activators of DPCs and promote elongation of hair follicles *ex vivo*.

## CURRENT LIMITATION OF EXOSOMES IN CLINICAL APPLICATIONS

The use of exosomes in various medical fields has attracted increasing interest from researchers; however, there are still limitations to their clinical application. There is a lack of a uniform gold standard for the origin, isolation, purification, identification, and storage; furthermore, clinical applications require a high degree of controllability and standardization (67). The precise quantification of exosomes and effective concentration methods are also of interest because ensuring that sufficient quantities or concentrations of exosomes enter the body for clinical use is challenging. Therefore, when using exosomes for hair loss treatment on the scalp, there is a need to improve the existing protocols and standardize procedures for exosome production to increase exosome yield and ensure their purity and safety.

Another limitation is that cellular and animal experiments are not fully representative of the human level, and the mechanisms of hair growth and regeneration in humans may be much more complex. Therefore, it is essential to construct animal models that more closely resemble human hair follicles and skin. Furthermore, owing to the different functions of exosomes in physiological conditions (68), further studies are needed to elucidate the mechanisms by which exosomes promote hair growth and regeneration as well as exosome-mediated signaling pathways *in vivo* in specific pathological settings, such as alopecia. More data are required to support the modes of administration and assessment methods in humans.

## CONCLUSION AND PERSPECTIVES

Exosomes have been widely studied owing to their long shelf life, simple storage conditions, long intracellular communication distances, and low risk of immune responses, making them superior to direct cell therapy (69). Here, we present the mechanisms and related studies of exosomes in the promotion of hair growth and regeneration. Because of their paracrine role, exosomes are involved in a variety of physiological and pathological processes in hair follicles. As intercellular messengers, exosomes shuttle between the cells and participate in tissue repair and regeneration. Exosomes produced by DPCs, MSCs, ADSCs, keratinocytes, ORSCs, and DFs exhibit hair growth-promoting and regenerative properties that are expected to address the problem of hair loss. However, there are still some limitations in this field that need to be addressed. Further studies are needed to investigate the strategies associated with exosomes to improve their clinical efficacy in the field of hair growth.

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