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Mini Review

Current Approach for Keratin-Mediated Hair Growth

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ABSTRACT

Keratin, an essential structural protein in epithelial cells, plays an important and complex role in hair growth and regeneration. In addition to its recognized structural features, keratin plays a role in several biological processes important for hair follicle development, Dermal Papilla (DP) cells, by releasing paracrine factors, direct the migration and differentiation of stem cells into matrix cells, which ultimately commence follicle formation. Keratin synthesis in the hair cortex is essential for the mechanical strength and structural integrity of the hair shaft. Recent research has revealed that keratin-based biomaterials, specifically keratin derived from human hair, can promote therapeutic approaches, including keratin injectable, keratin-based microneedle patches and keratin microspheres, have demonstrated encouraging results in promoting hair growth and wound healing. This review provides information of current approaches of keratin-based treatments to improve hair growth.

Keywords: Cytokeratins; Keratin; Dermal papilla

INTRODUCTION

Hair growth begins in the bulb located in the basal area of the hair follicle. Cell division and differentiation emerge within this compartment to establish the various components of the hair follicle. The hair is a pathway responsible for the generation of the hair follicle through the movement and specialization of stem cells [1-3]. The hair follicle undergoes a series of cycles consisting of anagens, catagens, and telogen. These cycles are controlled by various growth hormones, cytokines, and signaling molecules [4]. Keratin is essential for generating intermediate filaments in epithelial cells and preserving the structural integrity of the cells. Keratin is the main structural protein of hair and plays a core role in determining the mechanical properties of hair [5-8]. Hair is composed of layers, and the cuticle is made up of thin, transparent cells that form overlapping scales. It strengthens the mechanical restoring power of hair and protects it from damage caused by external factors. The cortex, which comprising the most of the hair, is the intermediate layer consisting of elongated cells loaded with keratin fibers and melanin pigments, and the cortex gives hair durability and flexibility. Medulla is located in the central layer of the hair [9]. During hair growth, Dermal Papilla (DP) cells release multiple paracrine substances that promote stem cell movement in the prominent region of the Outer Root Sheath (ORS) cell. The migrating cells transform into cells that can multiply rapidly, and then they proceed to differentiate into cells that produce the matrix, which in turn initiates the creation of hair. During this procedure, a significant quantity of keratin is produced within the cortex [1-3]. Keratin filaments are deposited and reorganized by keratin-related proteins and establish structural stability through intermolecular and intramolecular disulfide bonds [10]. Cell apoptosis begins in the epithelial strands during the movement from anagen phase to the regression phase of the hair cycle [11]. The apoptotic cells are then cleared by macrophages and surrounding epithelial cells by phagocytosis. Ultimately, keratin remains as the main protein in hair [12].

Recent studies have shown the effectiveness of keratin-based biomaterials in stimulating hair growth. Injecting keratin produced from human hair into the dermal area of skin has been shown to promote the development of hair follicles and stimulate hair growth in mice [11]. This review introduced the important function of keratin in the process of hair growth and regeneration, as well as the possible advancement of therapeutic methods based on keratin.

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LITERATURE REVIEW

Keratin-mediated hair growth and its underlying biological mechanism

Our previous research has shown that keratin plays important role in hair growth, extending beyond its structural function. Keratin actively supports the proper development and growth of hair follicles by influencing several biological processes, such as stem cell activation, differentiation, and signalling. Research suggests that keratin can interact with cells involved in hair germ formation in extracellular environment of the cells, stimulating their activity and promoting hair development. Specifically, keratin contributes to the aggregation of DP cells and the development of hair follicle germ cells, which express P-cadherin in ORS cells. This influence arises from keratin-induced local micro environmental change. Injecting keratin into the dermis area of skin boosts the condensation of DP cells and aids in formation of secondary hair follicle germs, ultimately promoting hair growth in mouse models. This mechanism involves the deposition of keratin exposed from TGF-β2 induced apoptotic ORS cells, a role similar to the natural exposure of keratin during the hair growth cycle. TGF-β2 expression occurs during the late anagen phase, leading to apoptosis in ORS cells in the catagen phase. The keratin released by apoptotic ORS cells plays a vital role in initiating the transition between telogen and subsequent anagen phases. At the start of the anagen phases, secondary germ formation by ORS cells expressing P-cadherin, accompanied by the condensation of DP cells. This series of changes ultimately supports and promotes hair growth [11].

Keratin microspheres as potential tool for targeting follicular growth

This study involved the production of keratin microspheres utilizing keratin derived from wool. The research demonstrated the efficacy of these microspheres have the substances that promote hair development. The keratin microspheres have the capability to infuse the epidermal barrier. During a study with seven weeks old male C57BL/6 mice, significant regrowth of hair was detected in the group threated with keratin microspheres after 20 days of applying the therapy to the skin. The results of this treatment were compared to those of the minoxidil group. Gene profiling result demonstrated that the application of keratin microspheres in the upregulation of genes associated with the growth of hair follicles, cell proliferation, and wound healing. Simultaneously, the treatment downregulated genes linked to aging and inflammation, suggesting that the treatment has anti-inflammatory and regenerative properties. This study also conducted using DP cells have verified an increase cell proliferation and the expression of hair growth-related markers [13].

A therapeutic microneedle patch made from hair-derived keratin for promoting hair regrowth

This study has shown the efficacy of a removable microneedle patch Hereditary Motor Neuropathies (HMN) composed of keratin extracted from human hair in stimulating hair regrowth. This study aimed to develop a system that is easy for users to use and that improves the effectiveness of alopecia treatment. The purpose of the HMN was to achieve a continuous release of extracellular vesicles, exosomes, and the small molecule UK5099. This was done by combining UK5099-loaded PLGA nanoparticles and hair-derived keratin into a transdermal delivery system based on microneedles. This patch combined Mesenchymal Stem Cell (MSC)-derived exosomes with the small molecular medicine UK5099, resulting in improved therapeutic effectiveness and decreased dosage requirements. Using a mouse model, researchers found that applying the patch twice over six days led to enhanced pigmentation and hair regrowth, surpassing the effectiveness of traditional subcutaneous injection or topical applications. The utilization of a keratin hydrogel with strong mechanical properties and the ability to release drugs over an extended period, in combination with microneedles, enabled a transdermal drug delivery method that not only provided long-term biocompatibility with surrounding tissues but also ensured continuous drug release. This study highlights the potential of keratin produced from hair for treating alopecia and wound healing. This study provides a non-invasive and effective therapeutic technique [14].

DISCUSSION

Recent investigations have directly shown that keratin plays a substantial biological role in facilitating hair growth and regeneration, surpassing its structural function. Nevertheless, the exact processes by which keratin triggers the condensation of DP cells and the formation of hair germs cells are still not fully understood. Prior study, including our study, has demonstrated that DP cell condensation can be stimulated by keratin-induced mechanical change of basement membrane surrounding hair forming cells, along with reduction in the rigidity of basement membrane when keratin is present [11]. These findings indicate that keratin treatment causes the change of partial stiffness of basement membrane, which in turn affects cell-Extracellular Matrix (ECM) interactions. The presence of keratin, which is released by apoptotic ORS cells induced by TGF-β2, can impact the mechanical characteristics of the surrounding environment and the interactions between cell-ECM. This keratin may serve as a signal for the condensation of DP cells and the activation of hair follicle stem cells. Additional investigation into the process of keratin-mediated mechanotransduction is necessary to fully understand these mechanisms. The review article emphasizes the important biological function of keratin in stimulating hair growth and regeneration. Future studies should prioritize investigating the methods by which keratin interacts with the basement membrane. This study will enhance our comprehension of the biological functions of keratin and mechanics behind hair growth, ultimately leading to the development of novel treatment approaches to stimulating hair growth.

CONCLUSION

Keratin is essential for biological processes of hair development and regeneration. Recent research has demonstrated that keratin not only serves a structural function but also actively contributes to a range of activities including stem cell activation, proliferation, differentiation, and signalling. Studies have demonstrated the efficacy of keratin-based biomaterials in stimulating hair growth and facilitating wound healing. For instance, the introduction of keratin produced from human hair and the application of keratin microneedle patches in mice model have demonstrated the ability to stimulate the development of hair follicles and enhance hair growth. In addition, it has been discovered that keratin microspheres stimulate the activation of genes associated with the growth of hair follicles and wound healing. Future research should focus on investigating the mechanisms by which keratin interacts with the basement membrane and devising new treatments based on these findings.

REFERENCES

1. Panteleyev AA, Jahoda CA, Christiano AM. Hair follicle predetermination. J Cell Sci. 2001;114(19):3419-3431.
2. Fujie T, Katoh S, Oura H, Urano Y, Arase S. The chemotactic effect of a dermal papilla cell-derived factor on outer root sheath cells. J Dermatol Sci. 2001;25(3):206-212.
3. Huelsken J, Vogel R, Erdmann B, Cotsarelis G, Birchmeier W. β-Catenin controls hair follicle morphogenesis and stem cell differentiation in the skin. Cell. 2001;105(4):533-545.
4. Alonso L, Fuchs E. The hair cycle. J Cell Sci. 2006;119(3):391-393.
5. Soma T, Tsuji Y, Hibino T. Involvement of transforming growth factor-β2 in catagen induction during the human hair cycle. J Invest Dermatol. 2002;118(6):993-997.
6. Mesa KR, Rompolas P, Zito G, Myung P, Sun TY, Brown S, et al. Niche-induced cell death and epithelial phagocytosis regulate hair follicle stem cell pool. Nature. 2015;522(7554):94-97.
7. Greco V, Chen T, Rendl M, Schober M, Pasolli HA, Stokes N, et al. A two-step mechanism for stem cell activation during hair regeneration. Cell Stem Cell. 2009;4(2):155-169.
8. Hibino T, Nishiyama T. Role of TGF-β2 in the human hair cycle. J Dermatol Sci. 2004;35(1):9-18.
9. Yang FC, Zhang Y, Rheinstädter MC. The structure of people's hair. PeerJ. 2014;2:e619.
10. Fuchs E, Green H. Changes in keratin gene expression during terminal differentiation of the keratinocyte. Cell. 1980;19(4): 1033-1042.
11. An SY, Kim HS, Kim SY, Van SY, Kim HJ, Lee JH, et al. Keratin-mediated hair growth and its underlying biological mechanism. Commun Biol. 2022;5(1):1270.
12. Ito M, Cotsarelis G. Is the hair follicle necessary for normal wound healing? J Invest Dermatol. 2008;128(5):1059-1061.
13. Bejaoui M, Heah WY, Oliva Mizushima AK, Nakajima M, Yamagishi H, Yamamoto Y, et al. Keratin microspheres as promising tool for targeting follicular growth. ACS Appl Bio Mater. 2024;7(3): 1513-1525.
14. Yang G, Chen Q, Wen D, Chen Z, Wang J, Chen G, et al. A therapeutic microneedle patch made from hair-derived keratin for promoting hair regrowth. ACS Nano. 2019;13(4):4354-4360.