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HUMAN HAIR FOLLICULAR STEM CELL (HHFSC) IN HUMAN HAIR FOLLICULAR AGING

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Abstract

Aging is considered an inevitable change at different levels of genome, cell, and organism, from the accumulation of DNA damages to imperfect protein homeostasis, altered cellular communication, and exhaustion of stem cells. The decline of regenerative capability caused by the aging process may significantly impact the quality of hair. The aging process affects the hair color, quantity, and quality. Hair becomes thinner and weaker, along with hair graying. These signs of aging may significantly impact some people's quality of life and lead to depression, anxiety, and other serious mental health problems. In terms of microscopic, the biological problem of aging hair affects biochemical and molecular and changes. Stem cell (SC) exhaustion is one of the hallmarks of aging. This literature review will describe the mechanism of human hair follicular aging and what happens in human hair follicular stem cells.

Keywords: Stem Cell, Human Hair Follicular Stem Cell, Hair Follicular Stem Cell, Hair Follicles Stem Cell, Hair Follicles Aging, Hair Follicular Aging

Introduction

Human hair follicles (HF) are essentially mini-organs in the skin comprised of multiple layers encapsulating and producing the hair shaft, which protrudes through the epidermis. The hair shaft is enclosed by the inner and outer root sheath (IRS, ORS), while the dermal papilla at the bottom of the hair follicle is surrounded by the matrix cells, which proliferate and differentiate to form the hair shaft. The hair bulge is located at the insertion site of the erector pili muscle to the hair follicle. Associated features of the hair follicle include the erector pili muscle, sebaceous glands, and sweat glands (Poblet et al., 2018).

The Hair Follicle is an epithelial organ consisting of two main parts: an epithelial cylinder composed of keratinocytes and the mesenchymal cells of dermal papilla (DP) and dermal sheath. HF represents independent, autonomous stem cell niches that cycle through multiple phases of growth (anagen), regression (catagen), and relative quiescence (telogen) during their lifespan (Poblet et al., 2018).

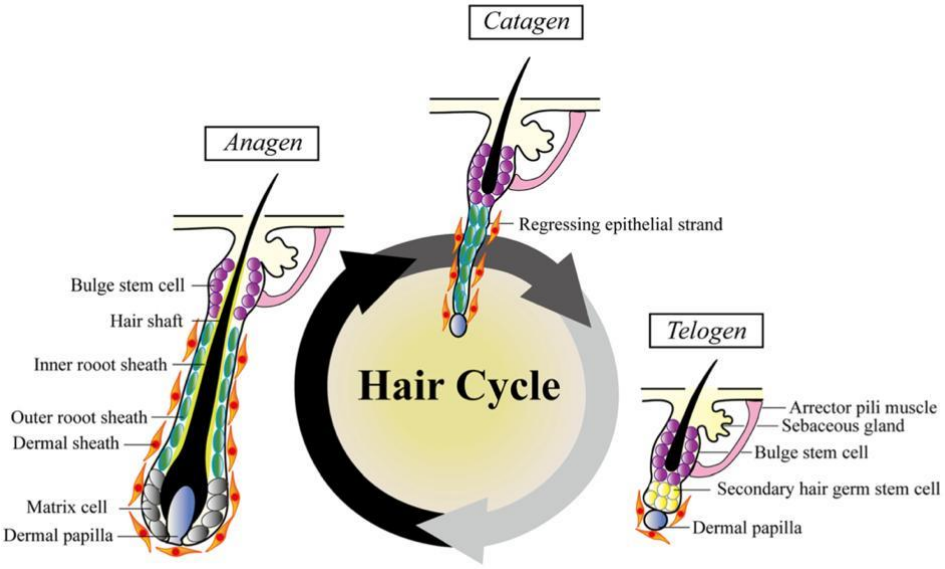

Figure 1
Hair follicle structure, hair follicle stem cell, and hair cycle (Chen et al., 2018)

Hair Follicle forms during embryonic skin development. Its functional and cycling activities rely on a coordinated communication between the different cell populations from epithelial, mesenchymal, and neural crest stem cell origin, which additionally regulates adult skin homeostasis and wound repair (Vandamme & Berx, 2019). During aging, cells undergo some detrimental changes, such as alterations in the microenvironment, a decline in the regenerative capacity, and loss of function (Sameri et al., 2020).

Method

Miniaturization of aging hair is defined as follicles containing hair shafts that are thinner than 30 μm in anagen. The depth of the hair root in a miniaturized hair is 0.646 ± 0.140 mm. In terminal hairs, the depth of the hair root is 3.8 to 4.6 mm in Caucasians and 4.0 to 5.0 mm in Asians. The shaft diameter of a terminal hair is over 60 μm, although it varies from 70 μm in Caucasians to 100 μm in East Asians. Hairs of diameter between 30 and 60 μm are considered intermediate. Intermediate hairs have a hair root depth of 2.59 ± 0.07 mm (Fernandez-Flores et al., 2019).

Result and Discussions

Human Hair Follicular Stem Cell (hHFSC) in Human Hair Follicular Aging Both extrinsic and intrinsic factors can contribute to hair aging. Environmental factors include exposure to sunlight, atmospheric pollutants, and cigarette smoking. Intrinsic factors such as DNA damage caused by reactive oxygen species (ROS) and free radicals are all detrimental to the maintenance of the stem cell population. Aged hair follicles typically display impaired ability to enter the hair growth phase (Fernandez-Flores et al., 2019).

The aging process of melanocytes as it is for HFSC, and may directly cause melanocyte apoptosis. The generation of melanin itself is an oxidative reaction, resulting in ROS production in melanocytes (Nishimura et al., 2011). MSCs are intermingled with HFSC in the bulge and the hair germ. The MSC generates mature melanocytes that produce melanin, which absorbs UV light to prevent DNA damage and gives skin and hairs their distinctive colors (Ji et al., 2017). Hair follicles experience several changes with aging, the most noticeable of which is graying of the hair shaft due to loss of melanin. Additional changes in the diameter and length of the hair have contributed to the concept of senescent alopecia, which differs from androgenetic alopecia. Miniaturization of aging hair is defined as follicles containing hair shafts thinner than 30 µm in anagen.

Moreover, the depth of the hair root in a miniaturized hair is 0.646 ± 0.140 mm. In terminal hairs, the depth of the hair root is 3.8 to 4.6 mm in Caucasians and 4.0 to 5.0 mm in Asians. The shaft diameter of a terminal hair is over 60 µm, although it varies from 70 µm in Caucasians to 100 µm in East Asians. Hairs of diameter between 30 and 60 µm are considered intermediate. Intermediate hairs have a hair root depth of 2.59 ± 0.07 mm (Fernandez-Flores et al., 2019).

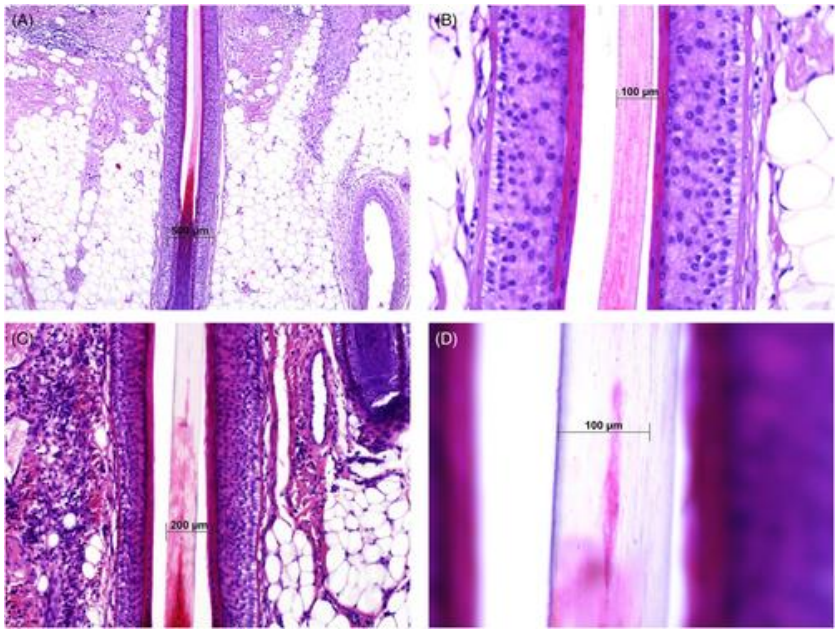

Figure 2

A and B, Hair follicle from the scalp of a 52-year-old woman with a hair shaft diameter over 70 µm (hematoxylin and eosin (H&E)×40 and H&E ×200). C and D, White hair with a shaft diameter over 70 µm (H&E ×100 and H&E ×400) (Flores et al., 2019). Hair graying in Caucasians, the age of onset is commonly 34 ± 9.6 years, while in Africans with, the age of onset is 43.9 ± 10.3 years. By 60, all individuals will have at least some gray hair independently of their phototype and ethnicity. MelSCs form a stem cell system within individual hair follicles and provide a 'hair pigmentary unit' for

each cycle of hair pigmentation (Seleit et al., 2015). Hair graying is also influenced by genetic as well as environmental factors that act on the hair follicle stem cells, as well as on the hair melanocytes. The Melanocytes Stem Cell (MelSC) directly adhere to HFSC and reside in the hair follicle bulge-subbulge area (the lower permanent portion of the hair follicle) to serve as a melanocyte reservoir for skin and hair pigmentation (Flores et al., 2019).

Extrinsic signaling is proposed to regulate hHFSC homeostasis (comprising both self-renewal, and differentiation) via molecules of opposing force: the activators and inhibitors that regulate quiescence or induction of the hair growth phase. In mice, the Wnt signaling pathway and its antagonist pair, bone morphogenetic proteins (BMP), and members of the transforming growth factor (TGF)-b superfamily are essential for bulge stem cell homeostasis. Transcription factor nuclear factor of activated T-cell c1(Nfatc1), a downstream regulator of the Bone Morphogenetic Protein (BMP) signaling pathway, is likely to be important in follicular aging process. The failure of aged follicles to downregulate Nfatc1 impaired stem cell proliferation, which was reversed by administering of Nfatc1 inhibitor (Keyes et al., 2013). Following the identification of Nfatc1 as a mediator of HFSC activation, a recent study has further highlighted the importance of the fork-head box C1 (Foxc1) gene. It is a transcription factor upstream of Nfatc1, which regulates stem cell homeostasis. Reduced Foxc1 expression in the basal hair follicle layer, where stem cells are located, results in a shortened telogen phase and loss of the old hair. The deletion of Foxc1 also leads to elevated expression of genes regulating the cell cycle and enhanced HFSC activity (Ji et al., 2017).

hHFSC aging results from proteolysis of type XVII Collagen (COL17A1/BP180) by neutrophil elastase in response to DNA damage in HFSC and the commitment of stem cells to epidermal differentiation. Terminal differentiation of HFSC into epidermal keratinocytes drives HF miniaturization and enables the elimination of damaged stem cells. The fate of aged HFSC abrogates their commitment to follicular differentiation to grow hair. HF aging can be recapitulated by Col17a1 deficiency and prevented by the forced maintenance of COL17A1 in HFSCs. This demonstrates that COL17A1 in HFSC orchestrates the stem cell–aging centric program of the mini epithelial organ (Matsumura et al., 2016).

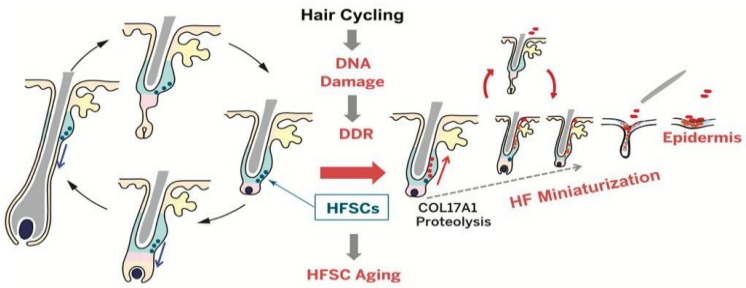

Figure 3

The mechanism of HF aging and associated hair loss (Shin et al., 2020). Senescent alopecia due to HF aging is characterized by progressive HF atrophy with hair shaft miniaturization, prolonged telogen, and even loss of the entire HFs, resulting in diminished hair amount (Huang et al., 2017). An aging process that affects the hHFSC, the telogen phase of the hair cycle becomes dominant, and as each hair cycle progresses with a shorter growth phase, the hair miniaturization occurs and results in baldness (Ji et al., 2017).

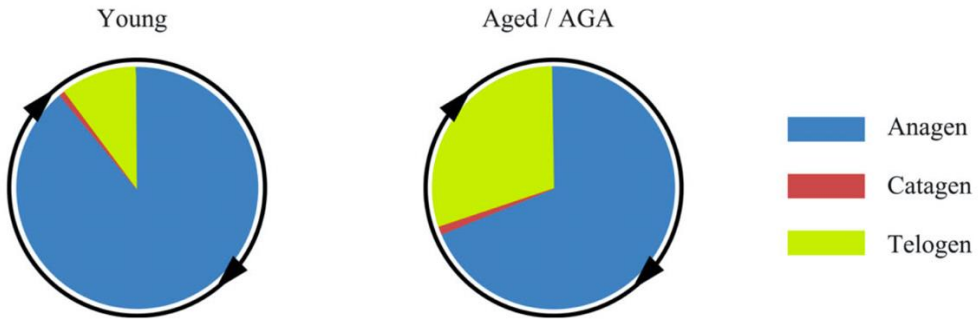

Figure 4

Most human scalp hair follicles are under the growth phase (anagen), lasting on average 2–8 years, while approximately 1% of hair follicles are in the catagen phase lasting 2–3 weeks, and the telogen phase typically lasts approximately three months. In aging or androgenetic alopecia, intrinsic and extrinsic factors affect the HFSC, the telogen phase of the hair cycle becomes dominant, and as each hair cycle progresses with a shorter growth phase, the hair miniaturization occurs and results in baldness (Ji et al., 2017).

Conclusion

Hair follicular aging is a type of tissue-specific aging and characterized by reduced regenerative and homeostatic capacities. Aged hair follicles typically display an impaired ability to enter the hair growth phase. HFSC revealed the critical role of HFSC in the induction of aging. The aging program driven by transepidermal elimination of aged HFSC through their depletion of COL17A1. The aging process of melanocytes may directly cause melanocyte apoptosis.

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