【Grant-in-Aid for Scientific Research (S)】

Biological Sciences (Medicine, Dentistry, and Pharmacy)

Title of Project : Stem Cell Regulation and Dynamics in Hair Follicle Regeneration and Aging

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Research Project Number : 26221303　Researcher Number : 70396331
Research Area : Stem cell biology, dermatology, experimental pathology
Keywords: regeneration, aging, hair loss, tissue stem cells, self-renewal

【Purpose and Background of the Research】

In rapidly aging societies, it is urgent to address aging-associated diseases by understanding the underlying mechanisms of aging-associated tissue declines.

Hair loss and hair graying are typical aging phenotypes in mammals, but the underlying mechanisms of aging are still largely elusive in most tissues. Aging-associated somatic stem cell changes have also been reported in different tissues, but the exact mechanisms underlying the expression of aging phenotypes and whether tissue aging programs exist is still largely unknown. We have studied the mechanisms of aging-associated hair graying and hair loss by focusing on adult stem cells. We previously identified melanocyte stem cells (McSCs) within the bulge-subbulge area of mouse hair follicles. That population is cyclically activated to self-renew and to provide mature melanocytes for hair pigmentation (Nishimura EK et al. 2002). Our chronological analysis of McSCs and hair follicle stem cells (HFSCs), which function as niche cells for McSCs (Tanimura S et al. 2011), demonstrated that mouse hair follicles age through the defective renewal of McSCs. McSCs differentiate into pigment-producing melanocytes in the niche without renewing themselves under excessive genomic stress or with aging (Nishimura EK et al. 2005, Inomata K et al. 2009). As the niche plays a dominant role in McSC fate determination (Nishimura EK, 2005), aging-associated tissue changes in hair follicles may primarily originate from the aging of HFSCs.

In this study, we will characterize the underlying mechanisms of stem cell regulation and dynamics in hair follicle regeneration and aging especially by analyzing the signatures of aging HFSCs and aging-specific tissue changes in mouse and human hair follicles.

【Research Methods】

1) Analysis of HFSC aging signatures.
2) Analysis of hair follicle dynamics during aging by fate-tracing of HFSCs and other cell populations.
3) Clarification of key stem cell regulators in hair follicle regeneration and aging.
4) Clarification of the mechanisms of stem cell renewal and aging.
5) Development of methods to promote stem cell regulation and rejuvenation.

【Expected Research Achievements and Scientific Significance】

We aim to elucidate tissue aging mechanisms by focusing on stem cell aging in hair follicles. Our approach will enable us to determine whether tissue aging is programmed or not and also whether the changes originate from stem cells or other cell populations. Application of the key stem cell regulators which govern tissue aging will be beneficial for regenerative medicine and the prevention of aging-associated diseases.

【Publications Relevant to the Project】

・Tanimura S et al. Hair follicle stem cells provide a functional niche for melanocyte stem cells. **Cell Stem Cell**, 8, 177-187, **2011.**
・Inomata K et al. Genotoxic stress abrogates renewal of melanocyte stem cells by triggering their differentiation. **Cell.** 137(6):1088-99, **2009**.
・Nishimura EK et al. Mechanisms of hair graying: incomplete melanocyte stem cell maintenance in the niche **Science.** 307(5710):720-724. **2005.**
・Nishimura EK et al. Dominant role of the niche in melanocyte stem cell rate determination. **Nature.** 416(6883):854-60, **2002.**

【Term of Project】

FY2014-2018

【Budget Allocation】

150,000 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.tmd.ac.jp/mri/scm/