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皮膚メラニン制御機構としての自然免疫機構分子の作用

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Innate Immune Molecules as Regulators of Melanogenesis

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Abstract

The epidermis is the outermost layer of the living organism and the first site of contact with external stimuli such as ultraviolet light and microorganisms. Among the cells that make up the epidermis, melanocytes play a wide range of roles besides producing melanin pigment, including absorption of UV light, regulation of body temperature, and protection from foreign enemies through camouflage. Melanocytes also function as antigen-presenting cells that modulate immune responses, and pigmented lesions have been observed in diseases related to immunodeficiency such as Hermansky-Pudlak syndrome, indicating a common molecular action between the endosomal formation of immune system cells and the melanosomal mechanism of pigmented cells. The melanin-producing action of melanocytes requires the maturation of melanosomes, which are endoplasmic reticulum structures, and the control of transporters and endoplasmic reticulum transport associated with melanosome maturation requires regulation in response to external stimuli.

My group has studied how skin pigmentation is affected by genetic background and skin microenvironment. For the genetic approach, we conducted a genome-wide association study (GWAS) of Japanese skin types using data from the Tohoku Medical Megabank Cohort Study and identified OCA2 and other genes as Japanese skin type-related genes. To investigate the effects of skin microenvironment on skin pigmentation, we also examined whether innate immune stimulation *via* toll-like receptors (TLRs) affects melanin synthesis and melanosome trafficking. We identified TLR3-RAB27A axis and TLR2-RAB11A axis, which enhance melanosome release from melanocytes. In this paper, we summarize these results and describe the impact of innate immune machinery molecules on melanin production mechanisms.

Key words: skin type, GWAS, melanosome, TLR, RAB.