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メラノソームの生合成と輸送の仕組み

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Mechanisms of Melanosome Biogenesis and Transport

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Abstract

Melanocytes contain specialized membranous organelles that synthesize and store melanin pigments. Melanosomes mature through four morphologically distinct stages (I–IV), and they are largely divided into two processes: formation of premelanosome limiting membrane and transport of proteins required for melanin synthesis to premelanosomes by membrane traffic. After the stage I melanosome is formed from an early endosome, PMEL is first transported to the stage I melanosome and forms amyloid-like fibrils, where melanin is deposited at later stages. The resulting fibril-containing melanosome is called as the stage II melanosome, but because of the absence of melanin at this stage it is still transparent. To achieve melanin synthesis and to form black melanosomes (stages III and IV), a variety of membrane proteins, including melanogenic enzyme tyrosinase, cupper transporter ATP7A, and ion channels involved in luminal pH regulation, must be transported to the stage II melanosome by membrane traffic (mainly through endosomal traffic). BLOC-1–3, adaptor proteins, and RAB small GTPases are known to be involved in these membrane trafficking events, and their dysfunctions often cause hereditary oculocutaneous albinism such as Hermansky-Pudlak syndrome. The mature stage IV melanosome is transported from the perinucleus to the tips of dendrites along the cytoskeleton (microtubules and actin filaments) and then transferred from melanocytes to adjacent keratinocytes. The transferred melanosome in keratinocytes is finally transported to the upper side of the nucleus to form the supranuclear melanin cap for protection of DNA from UV irradiation. These melanosome transport processes are regulated by motor protein complexes, and one representative example is the RAB27A–MLPH/SLAC2-A–MYO5A complex in actin-based melanosome transport in melanocytes. Dysfunction of the complex results in impaired melanosome transport, and thereby the complex would be an ideal target for development of cosmetics to prevent skin darkening or gray hair at the melanosome transport level.

Key words:　endosome, melanosome, membrane traffic, tyrosinase, RAB small GTPases.