Synopsis of Original Research Paper

Melanocyte-derived lipocalin-type prostaglandin D synthase as a regulator for skin homeostasis

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Microphthalmia-associated transcription factor (Mitf) is responsible for differentiation of melanocytes. The Mitf gene contains many promoters that generate multiple Mitf isoforms with distinct amino-termini, such as a melanocyte-specific Mitf-M. We have been interested in a Mitf mutant mouse, black-eyed white (bw), which is characterized by the white coat color and inner ear deafness due to the lack of melanocytes and by normally pigmented eyes. By cDNA microarray analysis between wild type and bw mouse skin, we have identified lipocalin-type prostaglandin D synthase (L-PGDS) as a new melanocyte marker. L-PGDS is a unique bifunctional protein; it functions as an enzyme that catalyzes the conversion of prostaglandin H_2 (PGH_2) to prostaglandin D_2 (PGD_2) and as an extra-cellular carrier protein that specifically binds small lipophilic molecules, such as retinoic acid and bilirubin. Mitf appears to be involved in transcription of the L-PGDS gene in melanocytes. Importantly, L-PGDS is expressed in normal human epidermal melanocytes, but not in human melanoma cell lines, as judged by northern blot and RT-PCR analyses. We also showed the inhibitory effect of PGD_2 on the growth of human melanocytes and melanoma cell lines, HMV-II, SK-MEL-28, 624mel, and G361. These results suggest that L-PGDS may modulate the growth potential of melanocytes through PGD_2, thereby maintaining the skin homeostasis.