EPA-2

Loss-of-function screening for regulators of melanogenesis: identification of role of mortalin in pigmentation

Ling LI[1,2], Nobuhiro ANDO[3], Christian MAHE[3], Sunil C. KAUL[1] and Renu WADHWA[1]

[1] DAILAB, AIST, Tsukuba
[2] University of Tsukuba
[3] KK Chanel Research & Technology Development Lab, Funabashi

Understanding the biology of skin color is an important aspect of functional cosmetics and treatment of moles, dark spots that appear on aging skin. In order to identify the cellular factors involved in human melanogenesis, we used shRNA-mediated loss-of-function screening in conjunction with induction of melanogenesis by OAG (diacylglycerol 1 -oleoyl-2-acetyl-sn-glycerol) in human melanoma G361 cells. Cells were transfected with shRNA library (2044 gene targets) and assayed for induction of melanogenesis by multidimensional approach, involving quantitative biochemical and visual determination of the melanin content and tyrosinase activity. Gene targets of the shRNAs that led to the loss of OAG-induced melanogenesis were considered as candidate cellular factors crucial for melanogenesis. By the four rounds of screenings, we identified 40 gene targets. Bioinformatics and pathway analyses revealed that these gene targets are involved in the regulation of cell proliferation, apoptosis, stress responses and mitochondrial functions. Based on these we investigated the role of mitochondrial stress chaperone, mortalin in melanogenesis and found that (i) it is an important regulator of melanogenesis (ii) it showed upregulation in clinical samples of keloids and (iii) it may serve as a molecular target for manipulation of melanogenesis suggesting its value for cosmetics and therapeutic manipulation of skin color and other characteristics regulating stress, tolerance and pathologies.

Ling LI (DAILAB, AIST, Tsukuba, Japan)
<e-mail: liling-li@aist.go.jp>