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生命科学

Loss of function-based screening for anti-pigmentation reagent: role of stress proteins, validation and identification of new natural compounds

■ はじめに

Environmental stresses have been established to determine skin coloration and characteristics. Whereas melanin is important for protection against UV-induced damage, its excessive production, accumulation, and abnormal distribution has been related to hyperpigmentation and other diseases of human skin. Pigmentation is mostly regulated by melanocytes in the epidermis. Molecular pathways of melanogenesis and impact of environmental stresses have been not well elucidated. With an aim to identify the cellular factors involved in skin pigmentation, we established cell based shRNA-mediated loss-of-function screening system.

■活動内容

OAG (diacylglycerol 1 -oleoyl-2-acetyl-sn-glycerol) was used to induce pigmentation in human melanoma (G361) cells. Among the shRNAs that abrogated OAG-induced pigmentation, we identified proteins involved in regulation of cell proliferation, apoptosis, stress response and mitochondrial functions. By molecular assays, we established the role of mitochondrial stress chaperone, mortalin in melanogenesis. We next recruited an established whitening reagent, TXC and investigated its impact on stress response proteins. We found that whereas treatment with OAG enhanced the expression of melanin and tyrosinase, treatment with non-toxic doses of TXC resulted in their reduction both in human melanoma and Caucasian skin-derived primary melanocytes. The OAG-induced melanin was associated with increase in mortalin, Reactive Oxygen Species (ROS) and decrease in mitochondrial membrane potential. TXC reverted these changes to a large extent. By recruiting mortalin expression as an indicator of pigmentation, we have identified five natural extracts with potential to reduce stress induced melanogenesis. These extracts could be recruited to study stress biology and its manipulation for health and cosmetic avenues.

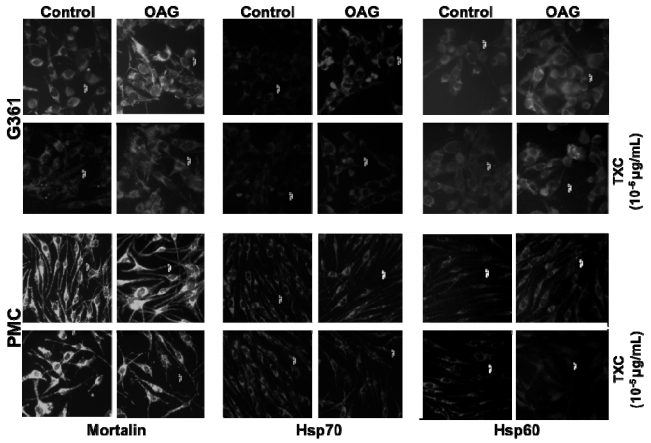

Fig. Effect of OAG and TXC on mortalin, HSP70 and HSP60 expressions in human melanoma (G361) and primary melanocytes from Caucasian skin (PMC) as determined by immunocytochemistry using specific antibodies .

■関連情報等（関連論文）

Wadhwa R, Priyandoko D, Gao R: Stress chaperone mortalin regulates human melanogenesis. Cell Stress Chaperones 2016, 21:631-644.

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