

A reappraisal of the biological functions of melanins and melanogens: the role of 5,6-dihydroxyindole-2-carboxylic acid (DHICA) in skin (photo)protection

Solar ultraviolet rays (UVR) play an important role in melanoma and non-melanoma skin cancer development while melanins, produced by melanocytes, are involved in photoprotection, control of oxidative stress, regulation of skin homeostasis and immunity. The ratio between the two main groups of melanin, eumelanins and pheomelanins, is regulated by the *mc1r* gene encoding for melanocortin-1-receptor (MC1R), whose inactivation causes a switch from eumelanin to pheomelanin production. While eumelanins are considered to be photoprotective, pheomelanins are known to be (photo)toxic as they lead to the production of reactive oxygen species in the presence and in the absence of UV radiation. It seems that not only eumelanins but even their precursors can contribute to the (photo)protective action. In particular, 5,6-dihydroxyindole-2-carboxylic acid (DHICA) and its main metabolite 6-hydroxy-5-methoxyindole-2-carboxylic acid (6H5MICA) have antioxidant properties so they could play a critical role in the responses of the melanocyte to oxidative stress and inflammation.

Moreover, it has been shown that DHICA is able to act as a chemical messenger inducing antioxidant defense systems and cell differentiation in keratinocytes. On these basis, DHICA and its methylated metabolite could play an important role in chemopreventive strategies of melanoma skin cancer