UV-irradiation of human melanocytes and melanotic melanoma cells causes melanin-associated damage at high UV-intensity

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Epidemiology supports a role for UVA and melanoma in susceptible individuals [1] and melanoma induction has been demonstrated in the fish model Xiphophorus [2]. Melanin is a UV chromophore [3] and a hypothesis for the UVA induction of melanoma is photosensitised radical production via melanin within the melanocyte. Phaeomelanins photosensitise the superoxide radical during UV irradiation *in vitro* [4], and soluble synthetic eumelanins are biological photosensitisers at low concentration at solar UV fluence [5].

To investigate this hypothesis we have studied, using ESR and spin/trapping, the UV irradiation (solar intensity) of biological eumelanins, melanotic and amelanotic cells. UV-irradiation of Sepia, Chinese hair and black cat hair melanins with DMPO (pH 4.5 buffer) gave hydroperoxyl radical-adducts at melanin concentrations typical of Caucasian melanocytes. In the presence of a protein (BSA), protein-radical adducts could be detected. Irradiation of amelanotic cells resulted in the detection of hydroxyl-type radical-adducts (from DMPO photolysis or trapping of hydroxyl/superoxide radicals), that were not detected during comparable irradiation of melanotic cells. A different radical, however, could be detected in UV-irradiated cells containing melanin: this slowly tumbling species (also detected in the absence of DMPO) is still unidentified but is believed at this stage to be a product of phaeomelanin degradation. The formation of this species was marked at 2×10^8 cells/ml (where cells are likely to be closely, but not densely, packed and it is estimated that the UV-intensity/cell is maximal) and in cells containing low melanin. The results support the hypothesis that melanin may contribute to UV-associated damage and carcinogenesis when melanocytes with insufficient eumelanin are overwhelmed at high UV-intensity.

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