

The main objective of this research project is to elucidate molecular and cellular processes responsible for transformation of the skin pigment melanin from an efficient photoprotectant and antioxidant into a photosensitizing and prooxidant agent. It is postulated that these dramatic changes of physicochemical properties of the skin melanin are induced by excessive exposure of the skin to intense solar radiation, leading to oxidative degradation of the melanin. Such photomodified melanin has the ability to photogenerate singlet oxygen, to induce damage to cellular DNA, proteins or lipid components of membranes and exert phototoxic reactions.

To achieve the intended objective, detailed studies are planned using systems of different complexity – from well-defined models to skin cells *in vitro*, in which advanced spectroscopic and analytical methods will be employed. We want to identify key photochemical processes responsible for critical modifications of the structure and physicochemical properties of melanins, which lead to enhanced photoreactivity of the pigment and its phototoxicity in cells. Therefore, the investigations will be carried out on synthetic melanins – models of natural pigments responsible for black or red pigmentation of the human hair, pigment granules isolated from hair of different color and on cultured keratinocytes, with melanin granules introduced into the cells by phagocytosis. Synthetic melanins and natural pigments, isolated from hair, will be subjected to irradiation from a solar simulator, and the degree of their photochemical modifications will be determined by optical and electron paramagnetic resonance spectroscopies and special degradation analysis. Photoreactivity of control and photomodified melanins will be determined by measuring the efficiency of photogeneration of reactive oxygen species, including singlet oxygen, and the ability of melanins to photoinduce oxidation of proteins, unsaturated lipids and photogenerate specific DNA lesions. Phototoxicity of the studied melanins will be analyzed in keratinocytes *in vitro* using standard cell biology methods as well as employing advanced imaging methods such as atomic force microscopy and laser scanning confocal microscopy. The study will also include a thorough analysis of the efficacy of selected antioxidants to protect against phototoxicity mediated by photomodified melanins.

Numerous epidemiological studies indicate the increasing hazard of phototoxic action induced by solar radiation, which in people is responsible for an alarming rise in the incident of skin cancer, including the particularly aggressive malignant melanoma, photoallergies and disorder of immunological responses, and premature skin aging. That is why our project, in which the role of the natural skin pigment melanin in photochemical reactions leading to an increased formation of reactive oxygen species, subcellular organelle damage and cytotoxicity will be analyzed, as well as the potential protective action of selected antioxidants will be analyzed, is viewed as timely and important. The project research is innovative for it is based on an original hypothesis and postulates that are result of long-term studies of biophysical properties of melanin pigments, in which the project leader contributed substantially.