

## **Description for the general public**

Melanin is a natural pigment synthesized by specialized cells in different organisms including humans. Because of unique optical properties, electric semiconductivity, chemical reactivity and structure, melanin remains of considerable interest to researchers from different fields. Main biological function of melanin is protection of pigmented cells and tissues against harmful effects of solar radiation. Recently published papers describe some disturbing data suggesting that under certain conditions melanin could bring forth undesirable effects. This is connected with ability of melanin to photogenerate products that are harmful to normal cells and could even contribute to carcinogenesis. However, it is not known if cellular presence of melanin has any relationship with the pathogenesis of malignant melanoma, one of the most aggressive cancers with high mortality rate. Melanoma originates from transformed melanocytes, which in the human epidermis normally produce melanin. It is important to stress that investigation of melanin from the human skin is significantly hindered due to limited amount of the pigment that is practically available. A key question that remains to be answered is: which melanin pigment substantially increases the risk of melanomagenesis. There are two main types of skin melanin pigments: brown-black eumelanin and yellow-reddish pheomelanin. Epidemiological studies suggest that melanoma mostly occurs in individuals with the skin containing predominantly pheomelanin. Although pheomelanin is usually considered to be more photoreactive than eumelanin, there is a lack of systematic comparative studies, and even more so of a reliable analysis of the specific molecular and cellular mechanisms, which could explain the potential role of melanin in melanomagenesis. The proposed research projects concern these important issues. Taking advantage of unique methods to generate cells producing melanin in vitro through inducible pluripotent stem cells from blood cells of different donors, adequate amount of melanin will be obtained to carry out planned experiments. The investigation will comprise detailed characteristics of photoreactivity of the isolated melanin pigments and their phototoxicity in cells. Results of this project will extend the existing knowledge about key physicochemical properties of melanin pigments, and contribute to development of photochemistry, photobiology and photomedicine. Elucidation of the role of photoreactivity and phototoxicity of cellular melanin in the pathogenesis of malignant melanoma could have important impact on well-being of the society because such studies should contribute to development of successful preventive means against one of the most life-threatening types of cancer.