Melanoma represents about 5% of all skin cancers, and its rapid growth, numerous metastases generated within a short period of time and low susceptibility to treatment of advanced stages of cancer, making melanoma the leading cause of death among all cases of skin cancer. The main environmental factor which contributes to development of melanoma is ultraviolet (UV) radiation, particularly UVB radiation. Although human skin is constantly exposed to the effects of compounds that can affect aromatic hydrocarbons receptor (AhR), its role in cancerogenesis has not been fully studied. Recently, it has been found that some derivatives of tryptophan, an essential amino acid, including L-kynurenine acid, kynurenine, and 6-formyl-indole[3,2-b]carbazole (FICZ), interact with AhR. They are produced in skin cells through enzymatic reactions (L-kynurenine, kynurenic acid), or formed after UV exposure (FICZ). However, previous studies shown that they are also present in many daily care products (i.e. face creams, shampoos, ect.), as well as herbs and honey-bee products (honey, propolis) applied in beauty treatments. Importantly, these substances may be involved in cancer initiation and progression. Kynurenic acid inhibits growth and migration of various cancer cells including colon cancer, renal cancer and glioblastoma. L-kynurenine may modify the immunological response of the body to cancer cells, whereas FICZ interacts with signaling pathways, disturbances of which may lead to cancer promotion.

The key objective of this project is the investigation of tryptophan-derived AhR ligands activity on UVB-induced melanocyte-to-melanoma transition and melanoma progression in vitro and in vivo.

The studies will be conducted on melanocytes, melanoma cell lines representing subsequent stages of melanoma development and on the animal model of zebrafish (Danio rerio). Zebrafish are able to develop benign and malignant cancers, with similar features to human cancers. We will investigate the effect of L-kynurenine, kynurenic acid and FICZ on selected cellular processes, expression of selected proteins and genes considered as markers of melanoma induction and aggressiveness. We will also verify whether AhR receptor is crucial for the observed cellular changes.