Cell death is a key cellular process responsible for maintaining homeostasis and ensuring a relatively constant number of cells in the human body. Disturbances in the mechanisms of cell death regulation accompany the development of many diseases, including cancer. Melanoma is one of the most malignant tumors that is highly resistant to anti-cancer drugs, including targeted therapies that inhibit the activity of the RAF/MEK/ERK signaling pathway, which is important for the survival of melanoma cells. One of the reasons for the insensitivity of this cancer to available therapies is the high level of anti-apoptotic proteins from the BCL-2 family. For this reason, my research focuses on this group of cell death regulators. An interesting aspect of the regulation of BCL-2 gene expression is the contribution of the melanocyte- and melanoma-specific transcription factor MITF (*Hartman & Czyz, 2015 J Invest Dermatol*). Our research demonstrates that changes in the phenotype of melanoma cells in response to microenvironmental factors are accompanied by transient changes in the level of some anti-apoptotic proteins, and inhibiting their activity may be of key importance in limiting the adaptive capabilities of melanoma cells (*Hartman et al., 2015 PloS One*). Melanoma cells differ in the expression profile of BCL-2 family genes, depending on the stage of cancer development and progression (*Hartman & Czyz, 2014 Cancer Lett*). Moreover, these proteins regulate types of cell death other than apoptosis (*Hartman & Czyz, 2020 Cell Death Dis; Hartman, 2020 Int J Mol Sci; Hartman & Czyz, 2023 Cell Death Differ*). An important clinical aspect is the inducing a specific type of death selectively in melanoma cells. Physiological inhibitors of BCL-2 anti-apoptotic proteins are proteins containing only the BH3 domain (BH3-only proteins). Compounds that mimic the activity of BH3-only proteins (so-called BH3 mimetics) have anti-cancer properties (*Hartman & Czyz, 2012 Anticancer Agents Med Chem*). Previous research indicates that the response of melanoma cells to mutant BRAF kinase inhibitors depends on the baseline BCL-2 protein level. The combination of BH3 mimetics and inhibitors of the RAF/MEK/ERK signaling pathway is therefore an interesting therapeutic approach. In the SONATA project, financed by the National Science Centre, we showed that inhibition of MCL-1, BCL-XL, and BCL-2 activity in some cell lines by selective BH3 mimetics resulted in the enhancement of the pro-apoptotic activity of encorafenib, a new generation $BRAF^{V600E}$ kinase inhibitor (*Hartman et al., 2021 Cancer Lett*). The use of a unique *in vitro* melanoma model in research, in which heterogeneous cell populations with the $BRAF^{V600E}$ mutation derived from tumors obtained from patients are characterized by different levels of BCL-2 family proteins, including MCL-1 protein (*Hartman et al., 2016 Oncotarget*), allowed for the assessment of the degree of sensitization (mitochondrial priming) of melanoma cells to encorafenib, taking into account the molecular characteristics of each cell line. For this purpose, the relatively recently described Dynamic BH3 Profiling was used, which was an innovative approach to studying the apoptosis process in melanoma cells (*Hartman et al., 2021 Cancer Lett*). We have also shown that trametinib-resistant cells show different sensitivity to the MCL-1 inhibitor depending on their phenotype (*Hartman et al., 2023 Cancers*). The obtained conclusions allowed us to expand our knowledge about the personalization of therapy for melanoma patients. My current research interests include mechanisms of resistance to molecularly targeted drugs in melanoma cells with particular emphasis on types of cell death other than apoptosis, especially cuproptosis. The research on this type of cell death will be performed in the OPUS project '*Cuproptosis, a novel pathway of regulated cell death as a therapeutic target in treatment-naïve and targeted therapy-resistant melanomas'* financed by the National Science Centre.