Despite enormous progress in the diagnosis and therapy of malignant tumors treatment results, especially in advanced stages remain disappointing. New molecular targeted drugs like BRAF inhibitors (vemurafenib, dabrafenib) combined with MEK inhibitors (cobimetinib, trametinib) or immunotherapy (pembrolizumab, nivolumab) significantly prolong survival of patients with metastatic melanoma. However, in some patients these drugs are ineffective or rapid acquired resistance to the applied therapy is observed (progression of the disease, despite earlier response to therapy). Therefore, it is important to identify the molecular factors of treatment failure. The efficacy of therapy with BRAF and MEK inhibitor in patients with advanced melanoma harbouring *BRAF* mutation might be linked with the lncRNA expression level in the tumors or in the blood. LncRNA are small molecules involved in the regulation of development and tumor growth. Many studies demonstrated dysregulation of lncRNA in malignant tumors. However, their function is poorly understood.

The main objective of the project is to determine the function and mode of action of long non-coding RNA (lncRNA) in skin melanoma. We expect to find such an lncRNA which presence or the adequate concentration in the tumor and/or blood will be linked with effective therapy. The study will be conducted in patients with advanced inoperable melanoma with *BRAF* mutation receiving BRAF inhibitor with or without MEK inhibitor. *BRAF* mutation is observed in about 50% of melanoma patients and is evaluated in the tumor. LncRNA will be assessed to select patients that will benefit from the treatment. Expression of 90 lncRNA will be evaluated in cancer tissue and blood (serum) for the selection of a group of patients responding to the treatment. The expression level of various lncRNA will be correlated with treatment efficacy. Moreover, it is planned to evaluate lncRNA expression in melanoma tumors without *BRAF* mutation, as well as in the serum of healthy volunteers and pigmented nevi (non-malignant lesions).

Implementation of the project will have a significant impact on the development of oncology. Finding the factors for patients selection who will benefit from the treatment will lead to the validation of these molecules in a randomized clinical study conducted in a large group of patients. Finally, it may lead to changes in the standard of melanoma treatment. Results of the planned research will help to better understand the biology of skin melanoma and can contribute to the development of combination therapies involving the use of targeted therapy in combination with the silencing of genes regulating the expression of some lncRNA, in order to overcome resistance to the treatment.

.