Malignant melanoma is one of the most invasive and aggressive cancers, constituting the most common cause of death among all skin cancers. Due to the high resistance to conventional chemotherapy regimens, the advanced stage of melanoma is practically incurable disease associated with very poor prognosis and short survival time. Although, except Australia and New Zealand, the incidence of melanoma is not high, the systematic increase in the number of cases has been observed over past decades. Among the main causes of malignant transformation there are mutations in genes encoding proteins that regulate melanocyte proliferation, growth, cell cycle, and apoptosis induction. In melanoma patients, several genes have been identified, the mutation of which promotes the disease occurrence. One of the most common mutations found in approximately 50-70% of skin melanomas is the mutation in BRAF proto-oncogene. Treatment of advanced melanoma containing BRAF mutation involves application of agents from the tyrosine kinase inhibitors group. All phase I-III clinical trials conducted on patients with advanced BRAF melanomas, demonstrated high efficacy of BRAF-inhibitors, which was manifested by a high rate response to treatment and prolonged disease-free survival. Unfortunately, after promising initial responses within 6-8 months the majority of patients no longer respond to BRAF inhibitor (BRAFi) treatment and relapse. Importantly, literature data indicate that targeting the glycolysis can overcome the resistance to BRAF inhibitors in melanoma patients.

The glycolytic enzyme which expression seems to alter in carcinogenesis is phosphofructokinase II (PFK-2). In cancer cells the expression of PFK-2 isoenzymes encoded by *PFKFB3* and *PFKFB4* genes is commonly observed. What is more, a number of reports in literature indicate a correlation between expression of PFK-2 and tumor aggressiveness, suggesting that this enzyme may significantly contribute to tumor development.

Thus, the research hypothesis of this project assumes that cancer specific isoenzymes of PFKFB3/4 playing important role in enhancing the glycolytic rate and the same growth, survival and therapy resistance of melanoma cells, constitute the novel target for anti-melanoma therapy. In order to validate the research hypothesis, initially, we plan to verify the expression of cancer specific isoenzymes PFKFB3/PFKFB4 in melanoma patients with subsequent analysis of their importance using the melanoma cell lines as a model. Based on the data obtained, we will verify if targeting the cancer specific isoenzymes of PFK-2 results in inhibition of glycolysis rate and in consequence attenuation of growth and overcoming therapy resistance to BRAFi. Characteristic of PFKFB3/4 expression in melanoma patients and understanding the role of co-expression of these isoenzymes in malignant melanoma biology may significantly contribute to development of novel anti-melanoma strategies specifically targeting the glucose metabolism and most probably as a consequence decreasing the progression of this highly lethal cancer.