## Description for the general public

### The role of insulin signaling in melanoma maintenance and response to targeted therapies

Melanoma is largely refractory to currently available anti-cancer agents. Despite the introduction of targeted therapeutics that inhibit the major signaling pathway in melanoma (RAF/RAF/MEK/ERK), cancer cells often exhibit a high initial tolerance of the drugs. Tumor response to anti-cancer therapy is dependent on signals from its microenvironment. In spite of a large body of epidemiological evidence pointing to a relationship between high levels of blood insulin levels and cancer incidence, insulin's role in melanoma progression and drug resistance remains unclear. This project aims to investigate insulin's influence on the effectiveness of vemurafenib and trametinib – currently available targeted therapeutics. Research will be carried out on patient-derived melanoma cell lines. Our preliminary results indicate that melanoma cells grown in presence of insulin comprise a higher percent of cells that exhibit features typical for stem cells. In this study, the influence of insulin on melanoma cell primitive phenotype will be analyzed. Moreover, since inefficient therapy often results in a selection of less sensitive cancer stem-like cells, the cooperation of insulin and targeted therapeutics in the selection process will be studied.