Abstract

Pancreatic ductal adenocarcinoma (PDAC) is a serious oncological disease, which ranks among cancers with the worst prognosis and a three-year life expectancy of 10%. Ex-vivo organoid cultures derived from cancer tissue are popular and reliable research models, which reflect the morphology and histology of the original tissue. Genetic background leading to development PDAC confer typical alterations in genes KRAS, TP53, SMAD4 a CDKN2A. The aim of this thesis was to determine mutations present in organoid cultures derived from human PDAC. We used online genomic databases to estimate specific mutations typical for PDAC. Based on that research we designed protocols for the detection of PDAC genetic alterations and optimized those methods using cultured cells. We applied the approach on primary ex-vivo organoids derived from surgical cancer specimens and detected mutations in KRAS, TP53, SMAD4, or deletion of exons in CDKN2A. Alternatively, we proposed improvements for the analysis of genetic background in PDAC. The data obtained within this thesis will be used for the stratification of metabolomics and biochemical analyses further in the project.