The main aim of the proposal is the identification of the interdependence between the machinery controlling gene expression, metabolic disorders and RNA modification in order to select genes i/or their protein products as molecular targets serving as the basis for establishment of new anticancer therapy against salivary gland adenoid cystic carcinoma.

Adenoid cystic carcinomas of the head and neck area, including adenoid cystic salivary gland cancers (SACC, ACC - adenoid cystic carcinoma) are relatively rare slow-growing cancers. For the first time this type of cancer was described by Billorth in 1859 as 'cylindrical' due to the formation of specific structures. This tumor has a different clinical course, has a long period of time with no symptoms, tends to form late metastases, and is resistant to classic chemotherapy. Current medicine unfortunately can't offer too much to patients suffering from ACC. Surgery and radiotherapy therapy are the only methods of treating this type of cancer, and metastasis treatment is an extremely difficult challenge for clinicians. ACC have a high tendency to spread through nerves, and is also characterized by atypical metabolic disorders. Due to the fact that most of the papers considering ACC cell lines are of dubious quality, since these lines do not actually correspond to the ACC picture, the molecular mechanisms responsible for the formation and progression of this cancer are not thoroughly understood. Recently, ACC lines have been verified, and new cell lines corresponding to ACC have been introduced, on which it will be possible to conduct scientific research.

Our research shows that ACC is characterized by overexpression of proteins that are components of the multi-protein SWI/SNF complex responsible for triggering the expression of many genes. It is interesting that in the most of cancers these proteins are significantly less abundant, which causes disorders in the number of complexes and dysregulation of expression of various genes. Interestingly, in these tumors, in addition to dysregulation of SWI/SNF complexes, we also observe disorders in alternative mRNA splicing. Our molecular studies have shown that the proteins responsible for splicing interact directly with the SWI/SNF complex. In addition, we have observed that this complex also interacts with proteins that impose m6A modification on RNA, so called 'writers'. **Therefore, planned in this proposal study of the interactions and interdependences between the SWI/SNF complex, metabolism, alternative splicing and RNA modifying complex will allow to learn about molecular mechanisms of regulation of gene expression at various levels in ACC and select potential targets for innovative combined therapy including use of so called epidrugs-compounds inactivating such protein machineries as i.e. SWI/SNF complex.**

In this project we will use a broad repertoire of most modern and highly advanced molecular biology and oncology techniques e.g. next-generation deep sequencing, as well as advanced metabolome profiling and immunocytochemistry, and immunohistochemistry methods, etc.

The expected results will be of great interest for broad scientific and non-scientific audience including oncologists, patients and their families.