Project 7.2 Role of the expression of steroidogenic factor 1 in somatotroph neuroendocrine pituitary tumors

Supervisor: Mateusz Bujko, PhD
Institute: Maria Skłodowska-Curie National Research Institute of Oncology
Unit: Department of Molecular and Translational Oncology
www: https://www.pib-nio.pl/

Background:

Acromegaly is a disease caused by somatotroph pituitary tumor secreting excessive amounts of growth hormone (GH). The results of our previous study on somatotroph tumors showed that they fall into 3 distinct biological subtypes. One of the subtypes is characterized by specific high expression of the NR5A1 gene (encoding the transcription factor, steroidogenic factor-1 (SF-1). Expression of SF-1 in a subtype of somatotroph tumors is surprising for two reasons:

1) according to the current WHO classification of pituitary neuroendocrine tumors (PitNETs), SF-1 factor is a diagnostic marker specific for gonadotroph tumors, and it should not be found in somatotroph pituitary tumors. Thus, our data to some extent challenge the assumptions of the current classification of PitNETs.

2) SF-1 is responsible for the activation of steroidogenesis pathway and it is expressed primarily in steroidogenic tissues as those of adrenal gland or gonads. We observed that tumors with high NR5A1 level have also high expression of key steroidogenesis-initiating genes STAR and CYP11A1. The role of steroidogenesis in pituitary somatotroph cells is unknown, however literature data indicate that specific steroid compounds (neurosteroids) have activity on somatotroph pituitary cells.

Aim:

The aim of the project is to determine the relevance of *NR5A1* (SF-1) expression in a specific subtype of somatotroph pituitary tumors including its diagnostic value in context of standard of classification of pituitary tumors as well as functional role of SF-1 of in somatotroph tumors and its putative role in tumorigenic process.
The particular aims are as follows:

- To verify high level of *NR5A1* and selected steroidogenesis- related genes including *STAR* and *CYP11A1* (and encoded proteins' expression) in a specific subset of somatotroph pituitary tumors.
- To verify whether difference in the expression of genes involved in steroid metabolism results in distinct metabolic profile of somatotroph pituitary tumors.
- To determine whether increased expression of SF-1 in model somatotroph cells contributes to change of cell phenotype and induction of steroid metabolism. The goal is also to identify which steroid metabolites have the effect on somatotroph tumor cell activity and potentially play a role in tumorigenesis.

Requirements:

- MSc in biology, chemistry, or related life science fields,
- familiarity with NGS technology, skills in NGS libraries preparations and data analyses will be an advantage
- in vitro cell culturing and experimenting skills
- experience in work with a light and fluorescence microscope
- skills in protein and gene expression evaluation

- involvement in data analyses and results dissemination
- English speaking (at least B2 level)