Title of the project: Identification of new genetic alterations in high grade paediatric brain tumours using next generation sequencing and evaluation of their usefulness for clinical purposes.

Tumours of the central nervous system (CNS) are among the most frequent childhood solid tumours. Every year in Poland brain tumours are diagnosed in about 300 children, what makes up for about 20 % of all childhood tumours. Brain tumours in children are characterised by a high mortality. Average survival of patients with some tumour types is as low as even only a dozen of months. Currently used treatments have many side effects, which utterly decreases life quality of patients having undergone the treatment. At the same time it is recognised that including the evaluation of molecular markers in standard diagnostic and therapeutic procedures may significantly increase the efficiency of the treatment.
Despite the fact that during the last decade an important progress has been made in identification of clinically important genetic changes which have been introduced as a criterion into the most recent WHO (2016) classification of CNS tumours, for many of the remaining tumours underlying changes are not recognized. Therefore, it is necessary to further broaden our knowledge about the molecular mechanisms responsible for tumours development. In the proposed project, we are planning to identify such hereditary (called germinal) and non-hereditary (called somatic) genetic changes which contribute to the development of highly malignant brain tumours in children.

We expect that our results based on analysis of rare childhood brain tumours, together with the data from studies conducted by other research teams will significantly contribute to:

1/ identification of new genetic changes characteristic for different tumour types, including alterations which will allow for differentiation of tumours with similar morphological features,

2/ determination of the usefulness of the identified changes as markers which allow for prediction of the disease course and patient prognosis, as well as to choose the appropriate treatment,

3/ identification of markers contributing to development of this type of tumours,

4/ possible identification of therapeutic targets for particular groups of malignant brain tumours.

The analyses will be done on a group of 120 children who had been diagnosed with malignant brain tumours, including rare tumours. Moreover, we will analyse molecular profiles of tumours for which the diagnosis is unclear. We will use modern technology which has been proven as highly effective in previous studies aiming to identify molecular markers, namely whole exome and total RNA sequencing, as well as DNA methylation profiling. We will also evaluate clinical importance of the identified markers by analysing associations between the genetic profiles of tumours and the other characteristics.
Application of molecular markers responsible for the development of malignant brain tumours in children will contribute to our knowledge and may be beneficial for treatment decision making.