

Tumors of the central nervous system (CNS) are the most common solid tumors in pediatric population and the second neoplasms occurred in children after leukemias. They account for about 25% of all tumors in this age group. Peak morbidity is between 3 and 10 years of old, although they may occur also in infants and teens. Despite the progress which was made in diagnostics and therapeutic achievements CNS tumors are still in third place due to the causes of death in this age group and the first among cancer disease. Brain tumors that occur in children differ significantly from the common CNS tumors in adults. The observed differences relate to their histopathology, location, and the original nature of the tumor molecular background.

The WHO grading system of the central nervous system tumors is based on clinical and histological criteria and is used to make precise diagnosis, estimate prognosis and in some cases to choose the tailored therapy. Increasingly, such guidelines are described as insufficient to make the right decision during diagnosis and treatment. In such case genetic and epigenetic features of the tumor could be helpful to make precise diagnosis and choose optimal care for patients.

In recent years, a breakthrough has been made in the field of modern understanding of oncogenesis. An example of such progress is the discovery of the microRNA (miRNA). MiRNAs are a class of endogenous, non-coding single stranded RNAs of approximately 19-25 nucleotides that may play an important role in gene regulation in physiological and pathological processes.

The objective of the project is to evaluate the contribution of microRNA molecules in the pathogenesis of the most common types of the central nervous system tumors occurring in the pediatric population: pilocytic astrocytomas, medulloblastomas, and ependymomas. Research will be focused on analysis of the expression level of miRNA molecules belonging to the relevant in oncogenesis the miR-17-92 cluster called also Oncomir-1. In order to fully assess the biological significance of its expression alterations, the analyses will also include its molecular paralogous, the miR-106a-363 and the miR-106b-25 cluster. The project envisages verifying the hypothesis that miRNAs from miR-17-92, miR-106a-363 and miR-106b-25 clusters are associated with the development and malignancy of childhood brain tumors, and whether there is association between the activity of the miRNA fractions analyzed and the genes belonging the *MYC* and *E2F* families.

Previous data indicate the importance of those molecules in oncogenesis, but there is no sufficient information available to evaluate it in childhood brain tumors. The studies conducted so far have been limited to the analysis of individual types of cancer, and usually do not cover all of interrelated and mutually interacting miRNAs of Oncomir-1 and its paralogs. The project will be able to make an important contribution to explaining the mechanisms underlying the development of brain tumors, particularly with regard to genomic regulatory mechanisms.