Biogenic amines (BA) are the classical neurotransmitters and include catecholamines (dopamine and it's derivatives), and serotonin playing a key role in the in brain homeostasis, the control of locomotion, mood, and behavior. The BA neurotransmitter disorders is a group of rare, inherited neurological syndromes, revealing mainly in childhood. Clinical symptoms are the result of catecholamine and serotonin deficiency in the central nervous system and are often very unspecific. Early diagnosis enables appropriate treatment, and thus significantly improves the prognosis in some patients.

The diagnosis of the BA disorder is based on the measurement of the concentration of neurotransmitters and their metabolites in cerebral spinal fluid (CSF) to delineate the metabolic defects, however, the molecular analysis is necessary to identify genetic cause (pathogenic variant on DNA level) and establish the final diagnosis which allows for implementation of specific treatments options. Interestingly, in some patients the levels of BA and their metabolites in CSF are abnormal, but the genetic basis has not been identified. Therefore, we hypothesized that, in such cases, unknown genetic variants may be responsible for the disturbances in the BA metabolism.

The aim of the project is to identify and characterize new genetic variants associated with the BA metabolism disturbances. The study group will consist of children and adolescents under the age of 18 with neurological symptoms and abnormal metabolism of the BA of unknown genetic cause. We plan to apply the next-generation sequencing (NGS) technique, which enables the simultaneous analysis of all coding regions of the human genome (exome). This will allow the identification of new variants in both known genes related to BA synthesis and metabolism, as well as candidate genes, not yet described in this context. The nature of the identified genetic variants (pathogenic or benign) will then be verified by *in vitro* experiments with the use of cell line

The results of the proposed project will enable expanding the knowledge on the pathogenesis of the inherited disorders of BA and the molecular aspects underlying the process of neurotransmission. In the future, the results could form the basis for the development of more effective personalized therapies depending on the type of identified genetic defect and molecular diagnostic algorithm for these patients. The latter is essential to ensure comprehensive genetic counselling and special medical, economic and social care for patients and their families.