Epilepsy is a common group of disorders characterized by clinical variability, affecting about 1% of any population worldwide. This is a disorder of the developmental period and nearly 80% of epilepsy patients are children and adolescents. Epilepsy has many possible causes, it is supposed that 40-60% has a genetic background. Until now a variety of genes causative for different types of epileptic syndromes have been identified. One of the most important is a *SCN1A* gene, that encodes the protein called $Na_v1.1$. This protein it the most important functional element (subunit α) of the voltage-gated $Na^+$ channels, located in cellular membranes of central and peripheral nervous system neurons. These channels are responsible for the action potential generation. Mutations of the *SCN1A* gene are causative for several epilepsies manifesting with different symptoms and severity, therein drug-resistant, catastrophic epilepsy – Dravet Syndrome. Until now there is no clear relationship between the type of mutation, its localization in the *SCN1A* gene and clinical course of the disease. In the most cases there is also missing data about the type of the $Na_v1.1$ protein dysfunction. However it has been observed, that among the relatives, the same mutation may be responsible for different clinical pictures of the disease. This led us to hypothesize that other genetic factors may contribute to the final disease course – genetic modifiers, variants in the other genes (e.q. genes encoding other ion channels), what we can call as personal genetic variability.

The aim of the project is to investigate the relationship between the type of the *SCN1A* gene mutation, $Na_v1.1$ dysfunction and clinical presentation of the disease. Additionally for the carriers of these same mutations, analysis of the variability of the genes, coding another ion channels, in correlation with clinical variability will be performed.

The analysis of the $Na_v1.1$ dysfunction will be performed with use of the methods in vitro (voltage-clamp methodology in model cells system), but also with novel clinical neurophysiology technique - nerve excitability study (NES) performed in patients with $Na_v1.1$ mutation. Comparison of both types of experiments results will allow to investigate the usefulness of the NES technique as a tool to describe the pathogenicity of the *SCN1A* gene mutations in vivo. Analysis of the genetic variability of the genes – modifiers of the clinical picture will be performed with whole-exome next generation sequencing.

This research project will improve our knowledge about the molecular and functional background of the genetic epilepsies, especially severe epileptic encephalopaties, and will help us to understand the relationships between dysfunction of the $Na^+$ channel caused by genetic factors and the clinical presentation of the disease.