Although some genetic disorders are rare, they are a serious global issue. Nearly 30 million people suffer from rare inherited diseases in Europe. Medicine can treat some of them but in most cases patients remain helpless. One of the groups of genetic disorders are congenital disorders of metabolism, among which, Niemann-Pick type C disease (NPC) can be mentioned. This disease is caused by mutations in one of the two genes, *NPC1* or *NPC2*. Due to mutations, the proteins encoded by these genes are not functional. Consequently, this causes disturbances in the distribution of intracellular cholesterol and its accumulation in lysosomes or late endosomes. Niemann-Pick type C disease is a very rare disease. It occurs with a frequency of 1: 120,000 live births and is inherited in an autosomal recessive manner. Diagnosis of this disease is very difficult and long-lasting. Research on the selection of the right biomarker that would allow faster and more accurate diagnostics is still ongoing.

The clinical picture of the disease is very heterogeneous. Symptoms can occur at various age, from perinatal period to adulthood. Depending on the age of onsett of the first symptoms and the dynamics of the disease, there are several types of this disorder. Apart from a small number of patients who die at birth or in the first months of life due to liver or respiratory malfunction, all other patients will eventually develop a progressive and fatal neurological disease. Patients' lifespan can vary from a few days to 60 years, but most patients die between 10 and 25 years of age. The earlier the neurological symptoms appear, the more severe the course of the disease will be.

The main goal of the project is to identify genetic modifiers in Niemann-Pick type C disease. The proposed research will answer the following questions: are there additional genetic factors (beside the mutations in the *NPC1* or *NPC2* genes) influencing the phenotype of the disease, and whether there are molecular variants that result in delayed onset of symptoms. In the first step of the proposed project, cell cultures of skin fibroblasts will be set up. Fibroblasts will be taken from 20 patients and 20 controls. Next, DNA isolated from the cultured cells will be used to the whole exome sequencing (coding parts of the human genes). On the basis of bioinformatic analysis, a selection of molecular variants will be carried out that can affect the phenotype of patients suffering from NPC. These studies will allow a deeper understanding of the pathomechanism of the disease and also contribute to the direction of subsequent research related to the searching of potential treatment.