

Inflammatory Bowel Disease (IBD) are chronic, autoimmune disorders of digestive system which etiology is still unknown. Unfortunately, every year number of people who suffers from IBD in Poland and in the world is increasing. IBD manifest as a chronic and uncontrolled inflammation of mucosa. Patients lose the ability to suppress immune response resulting in maintaining of prolonged inflammation. It causes serious health consequences: abscesses, fistulas, narrowing of the intestinal lumen. Worsened physiological condition definitely affect patients' functioning, relations with environment in work and family and mental condition. IBD affect usually young persons in the second and third decade of life, however it may occur in later period of life. Lack of the possibility to complete recovery forcing patients to take the medicaments for a long period of time, in severe cases also surgery intervention is needed. IBD require long-term therapy, repeatedly for life, therefore personalization of the treatment is very important for IBD patients.

Generally used in IBD therapy drugs are glucocorticoids which are able to suppress inflammation state in a short period of time. However, it is assumed that 20% of patients are resistant and about 40% of patients show dependence of this medicaments. Thiopurine drugs are an alternative which enable to achieve long-time remission. Unfortunately, also this form of the therapy is not free of drawbacks. It was shown that about 30% of patients do not respond for thiopurine treatment, also adverse side effects occur. It is postulated that different patients' response for the therapy is caused by genetic variability in populations. This fact was confirmed by scientific studies of genes coding for thiopurine metabolism enzymes, however they were analyzed single factors. Without a doubt, organism response for the treatment is a complex process, therefore in our project we will analyze a large group of selected candidate genes, potentially involved in patients' response for thiopurine treatment. Using the newest achievements of molecular genetics, our studies will be based on modern, high-throughput next generation sequencing method (NGS). Selected genes will be analyzed for the presence of mutations and epigenetic changes and subsequently we will correlate results of genetic studies with a specific patients' response for thiopurine treatment.

Studies planned in the project are intended to identify and characterize genetic and epigenetic factors which may affect different patients' response for thiopurine treatment. In case we obtain results with a great importance or identify fundamental for whole process genes and their mutations or epigenetic factors, it will allow to adapt the results in clinical practice and choose the suitable form of the therapy with adapted dose, identify patients who do not response for treatment, avoid side effects and reduce costs of the therapy before it begins, finally contribute to patients' health improvement and save them from additional suffering which is a consequence of therapy failure.