The aim of the project is to identify genetic background of the reaction to glucocorticoid drugs in patient diagnosed with non-specific inflammatory bowel disease (IBD) and to select the factors that might be predictive for the patient's response to glucocorticoid therapy which is vital for optimal treatment planning.
Glucocorticoids (GKS) have been used as first-line treatment of exacerbations of IBD for many years, despite the fact that epidemiological studies suggest that about 15% of patients do not respond adequately to these medications.
An attempt to use the glucocorticoids in steroid resistant patients leads to the extended duration of exacerbations of IBD, and thus, increases the risk of the development of serious and life-threatening health complications such as abscesses, fistulas, intestinal perforation, toxicum megacolon. Prolonged use of GCs may contribute to the occurrence of severe side effects of therapy, among others: diabetes, hypertension, obesity, prolonged wound healing The occurrence of complications of the disease or side effects of GC therapy results in a more severe course of the disease, and therefore, deterioration of general health, reduced physical capacity, increased frequency of hospitalizations and surgical interventions. Due to possible toxic effects these drugs are not recommended to use in chronic therapy to maintenance remission of IBD. However, a large proportion of patients becoming dependent on Gcs as evidenced by the recurrence of the disease after discontinuation of these drugs or reduce their dose.
Problems of: resistance to glucocorticoids, glucocorticoids dependence and side effects induced by glucocorticoids, despite the long history of the use of drugs has not been resolved adequately, especially in patients with IBD. It has not been invented a tool for the physician, which could give the opportunity to plan treatment (choice of drug, dosage, form, etc.) depending on the expected individual response to drugs.
As evidenced by scientific data, inter-individual variability in response to Gcs depends strongly on genetic factors, and may depend on the variation of genes encoding proteins involved in the metabolism and action of Ccs such as: NR3C1 – gene encoding glucocorticoid receptor (GR), HSP90AA1 , HSPA4, STIP1 – genes encoding GR complex protein genes, ABCB1 - gene encoding the glycoprotein P170 involved in the transport of Gcs to the cytoplasm, IL1A, IL1B, IL2, IL4, IL8, IL10, TNF, MIF - genes encoding epithelial pro-inflammatory factors, CYP3A4 and CYP3A5 - encoding enzymes involved in Gcs metabolism, IPO13 - gene encoding protein responsible for the transport of Gcs to the cell nucleus

Characterization of genetic factors involved in the response to the GKS and understanding their impact on the course of therapy GKS might allow the identification of patients before starting steroid treatment, who will be able to opt out of glucocorticosteroid therapy shorten the period from the beginning of tightening the inclusion of appropriate therapy, and thus avoid complications NChZJ , surgical interventions, side effects of medications and sometimes even permanent disability. In patients with a predicted high sensitivity to steroids will be able to start treatment with lower doses of drugs - which will contribute to the reduction of side effects. NChZJ therapy planning based on research variants and mutations of genes is an innovative idea has not yet applied in practice.
Characterization of genetic factors involved in the response to the Gcs and understanding their impact on the course of Gcs therapy may enable the identification of steroid-resistant patients, before the start of treatment. In these patients it will be possible to dispense with glucocorticosteroid therapy, and hence shorten the period from the beginning of disease exacerbation to the inclusion of appropriate therapy, and thereby avoid the complications of IBD, surgical interventions, side effects of medications and sometimes even permanent disability. In patients with a predicted high sensitivity to steroids will be able to start treatment with lower doses of drugs - which will contribute to the reduction of side effects. IBD therapy planning based on testing of variants and mutations of genes is an innovative idea has not yet applied in practice.
The study will been help in understanding the molecular mechanisms by which glucocorticoids act and the basis of such inter-patient variability. So far no large complex cohort studies for many different factors involved in glucocorticoid resistance in inflammatory bowel disease have been reported.
Project implementation can contribute to a better understanding of the mechanisms of action of glucocorticoids. Perhaps the results of studies conducted in patients with inflammatory bowel diseases are used for therapy and diagnosis of other important civilization diseases such as asthma or multiple sclerosis and It is a breakthrough that wide opens the possibilities for further research in the field of pharmacogenetis and therapy of autoimmune diseases. This topic is an important scientific issue, not only for the Polish population, but also worldwide.