Rheumatoid arthritis (RA) is a multifactorial autoimmune disease of unknown etiology. The basic symptoms of RA mainly affect the joints, but the complexity of the disease also indicates the occurrence of extra-articular symptoms. The main symptom of RA is a chronic inflammatory process that can damage many organs, including the heart, kidneys, lungs, digestive system, and nervous system.

In order to improve the clinical condition of patients with RA, reduce the degree of disease activity and prevent the occurrence of systemic complications, new research methods are constantly being evolved that are used in the development of new therapies modifying the course of the disease and eliminating the symptoms of inflammation.

The most promising anti-rheumatic therapies in RA are based on biological treatment with the use of genetically modified protein molecules with a diverse mechanism of action, e.g. directed against the one pro-inflammatory cytokine, anti-TNF-α. However, the latest therapeutic approach in RA (approved by the FDA and EMA) includes JAK inhibitors (JAKi) that inhibit signaling pathways (JAK/STAT) that target a wide spectrum of cytokines. JAKs are cytoplasmic proteins that connect signaling pathways in the cell of many cytokines and their membrane receptors, and through transcription factors and transcription activators (STATs) transmit signals necessary in the process of immune regulation.

The aim of the project is to study the population of γδ T lymphocytes, which may be important in searching for new biomarkers helpful in predicting response to JAKi treatment and ensuring optimal control of the inflammatory response.

Since γδ T cells play an important role in the immunoregulation process by performing essential functions of the immune system (they are able to stimulate, regulate and even suppress the immune response), it is important to determine the profile of cytokines and receptors involved in the JAK/STAT pathway, which play a significant role in the process proliferation, regulation and activation of γδ T lymphocytes.

A deeper understanding of the mechanism of the JAKi therapy in the context of γδ T cells will be enabled by the study of cells isolated from RA patients before and 6 months after therapy initiation. Also, studying the genetic variability of cytokines and γδ T cell receptors in the context of clinical parameters will be performed.

The research parameters used in this project will indicate the effectiveness of JAKi therapy and help to explain why some patients become less responsive to JAK inhibitor therapy.

Therefore, the overriding goal of the project is to identify those immunological and pharmacogenetic parameters related to the JAK/STAT pathway, which could bring researchers closer to answering the question of the role of γδ T lymphocytes in RA patients treated with JAKi. In the future, this may lead to an increase in the effectiveness of the therapies used, ensuring treatment without additional complications and associated with lower financial costs.