

## **DESCRIPTION FOR THE GENERAL PUBLIC**

Rheumatoid arthritis (RA) is a complex, chronic autoimmune disease (AID) that is characterized by inflammation and progressive destruction of the synovial joints leading to pain, long term disability, and reduced quality of life in many patients. Both variant of autoimmune susceptibility, genes and environment, are involved in the generation of aberrant epigenetic profiles in a cell-specific manner, which ultimately results in dysregulation of expression. In addition, in patients with RA, we observed an abnormal regulatory T cell (Treg) response with a shift towards a Th17 cell response; however the mechanism behind this phenomenon remains unclear. Over the past several years, it has become clear that alternations in the expression level of different microRNA (miRNA) may contribute in the pathogenesis of RA. The identification of disease-associated miRNAs will guide us into the post-genomic era, providing the real likelihood of manipulating the genetic influence on autoimmune diseases. miRNAs, represent a large family of small, evolutionary conserved endogenous noncoding RNAs that comprise a fundamental layer of post-transcriptional regulation of gene expression, are essential regulators of the immune responses. In addition, miRNAs can regulate the plasticity and the effector functions of differentiated Th cell subsets. It is also now evident that aberrant miRNA expression in the immune system is sufficient to cause disease, and so proper regulation of miRNA expression seems to be crucial for disease prevention. The earlier investigations confirmed the pivotal role of miRNAs in the Treg/Th17 cell differentiation and function but did not identify the individual miRNAs that are relevant to these processes. Moreover, the current state of our knowledge in this area is far from being complete and continued investigations will be needed to reveal a better understanding of the miRNA network that is involved in gene regulation in Treg/Th17 cells. The aim of this study will be understand the possible impact of selected miRNAs on Treg and Th17 cells frequency and function as well as identify cell free circulating miRNAs that are expressed similarly for intracellular miRNAs of RA patients, which could be a marker for monitoring of the disease process, and other clinical application. Using this approach, we hope to identify potential tools involved in Treg/Th17 imbalance, markers of clinical activity or predictors of disease outcome. In order to verify our hypothesis we use different clinical materials from one patient after receiving informed consent. The studies will be conducted on a group of about 40-50 patients with rheumatoid arthritis are under the care of the National Institute of Geriatrics, Rheumatology and Rehabilitation in Warsaw. In the first step we plan to conduct an analysis of selected miRNAs in plasma and in Treg and Th17 cells derived from various clinical materials (peripheral blood, synovial fluid) from the one patient with RA. This study will be extended by the analysis of transcription factors, involved in Treg/Th17 cells differentiation and/or function, mRNA expression and by the analysis cytokines, produced by Treg and Th17 cells, expression levels in plasma from patients with RA. Complements our research will be determine the number of Treg and Th17 cells in the peripheral blood and synovial fluid. The analysis will also be considered accurate clinical data of patients, in order to give an accurate assessment of the severity of the disease. As miRNAs are stably present in cell free form in body fluids and circulating miRNAs, they are becoming new candidate biomarkers for diagnosis and prognosis in autoimmune/inflammatory diseases. Identifying specific miRNAs with their key nodes and networks that are involved in regulating Treg and Th17 cells and delineating their balance and function are of great interest for not only RA but also various inflammatory and autoimmune diseases. Additionally, the specific circulating miRNA species may also be useful for the diagnosis, classification, prognosis of diseases and prediction of the therapeutic response. Moreover, the expected results will gain knowledge, which in the future will be used in clinical trials.