Systemic lupus erythematosus (SLE) is an autoimmune disorder with B-cell hyper-reactivity, immune complex deposition, and organ damage. Its prevalence worldwide is ~40-150/100000. Exact epidemiologic data from Poland is lacking, however, the frequency of this autoimmune disorder appears to be increasing. 5-year and 10-year mortality is about 10% and 30% respectively. Kidney involvement develops in ~50-70% of SLE patients, representing the most frequent SLE organ damage-related cause of death. For diagnostic, prognostic and therapeutic purposes kidney biopsy is performed to evaluate glomerular lesions, which is mandatory to determine the stage of the disease according to the ISN/RPS classification system. However, kidney biopsy is an invasive method with broad number of side effects. Therefore it seems to be very important to look for a new diagnostic and prognostic markers, which can also elucidate patomechanism of the disease.

In autoimmune disorders B cells are considered as a pathogenic because of their capacity to secrete autoantibodies. The significance of self-reacting B-cells in the pathogenesis of lupus nephritis (LN) is supported by a strong causal link between autoantibodies against double stranded DNA (dsDNA) and kidney involvement. Moreover, rise in the titer of anti-dsDNA antibodies can occurs years before the clinical onset of proliferative LN.

The main aim of the current project is to elucidate the role of B regulatory (Breg) cells in LN. Despite several studies suggested potential role of CD19+$CD24_{high}CD38_{high}$ B-cell subset in SLE, there is a lack of a comprehensive analysis concerning their role in active and inactive LN. Establishing role of Il-10 produced by Breg cells seems to be crucial in order to understand its biological relevance in the pathogenesis of LN. In our research we will perform procedure combining magnetic cell sorting technology (negative selection of CD19+ cells) and superficial antigens staining (CD45, CD38, CD24, CD21, CD27 and IgD) to better distinguish B cell subsets. CD19+ cells (obtained through magnetic isolation) will be used to further analyze the repertoire of Breg cells (through superficial antigen staining; including their specific markers CD19+CD24+CD38+) and then to elucidate in vitro production of Il-10, their signature cytokine (intracellular staining). In the next part of the project we will also check serum cytokines level (i.e. Il-10). To better understand patomechanism of the disease we will analyze also frequency of T cell subsets. All of the immunological results will be correlated with clinical (SLEDAI-2K, renal-SLEADI) and laboratory (ex. proteinuria, lymphopenia) parameters. Results which will be obtained in proposed study will allow us to construct a whole model of immunological regulation in SLE.

Pathogenesis of lupus nephritis (LN) exacerbations remains elusive. Positive verification of the hypotheses mentioned above will allow us to better understand patomechanism of LN. Results which will be obtained in proposed study will allow us to elucidate impact of B regulatory cells on the course of LN. In addition, we will be able to find a novel immunological markers, which will be helpful in early diagnosis, monitor activity of the disease and also an useful parameter to predict severe complications (ex. end stage renal disease, death) in the course of the disease. It is so important to broaden knowledge about patomechanism of LN and on the bases to this to find a novel therapies (ex. biological drugs which can block one of the immunological pathway). However, at this step it is a basic research.