Although there are several recurrent molecular abnormalities present in CLL, none is specific for CLL and therefore immunophenotyping still plays a central role in the diagnosis of CLL. The current diagnostic criteria have some limitations affecting reproducibility, in particular relating to flexibility in the requirement for each marker to be present or absent as well as in the required expression level of each marker. In preliminary results we observed ca. 10-30 times higher level of 5-hydroxymethyluracil (5-hmUra) in DNA of peripheral blood nuclear cells of chronic lymphocytic leukemia (CLL) patients, comparing to non-CLL individuals. We hypothesise that in leukemic lymphocytes B 5-hydroxymethylcytosine, an intermediate of active DNA demethylation, could be deaminated by AID (or another enzyme from the APOBEC family) to yield 5-hmUra, as they are genetically programmed to deaminate cytosine in certain part of the genome at unprecedented level during antibodies diversification and, as cancerous cells, may have disturbed mechanisms controlling this process allowing also off-target reactions.

The main goal of the project is to investigate whether 5-hmUra may serve as a new, specific biomarker of leukemic cells in CLL.

The results of the research proposed by us should contribute to a better understanding of the relationship between the investigated DNA modification and the course of CLL, as well as provide a rationale for the development of relatively simple and cheap laboratory cytometric test to diagnose and monitor patients. If 5-hmUra will come out a biomarker specific for leukemic lymphocytes B, determination of 5-hydroxymethyluracil level by means of flow cytometry could become a standard diagnostic tool, particularly in the early disease stage, before clinically manifested lymphocytosis.