Kinases constitute one of the main protein groups regulating various biological cell processes. Due to their binding with other proteins, they are capable of augmenting or diminishing their activity, what results in changes in cells' functioning.

PIM family of proteins also falls under the definition of kinases. Three members are distinguished e.g. PIM-1, PIM-2 and PIM-3. These proteins belong the group of serine-threonine kinases, what means that they are capable of activating or blocking the activity of other particles by phosphorylating their serine and threonine residues. PIM kinases participate in regulation of several cellular processes such as cell growth, programmed cell death (apoptosis), movement and response to stress induced for example by chemotherapy agents. Interestingly, PIM kinases posses a short half-life time, are in a constant activation state and do not undergo any major structural changes once they are produced. Numerous research noted their high levels in cancer cells of lymphomas and leukemias. Furthermore, their high level in the abovementioned diseases was associated with patient's poor outcome and resistance towards anti-tumor medications. It was shown, that blockade of PIM kinases activity resulted in cancer cells' death.

One of characteristic features of cancer is the instability of its genetic material, what may lead to generation of various gene mutations resulting in structural protein changes and poor impact on the clinical course of disease. This phenomenon also occurs within PIM-1. Earlier studies indicate, that PIM-1 mutations occur in aggressive forms of lymphomas. However these results are derived from experiments performed on small patients groups and did not analyze the biological properties of the mutated forms. Nevertheless, it was shown that these mutations may lead to changes in the proteins activity and may therefore be associated with ineffectiveness of the treatment. Based on the abovementioned facts, the aim of the proposed project is to analyze the frequency of PIM-1 mutations in chronic lymphocytic leukemia (CLL). There are estimated 15 000 new CLL diagnoses annually in the US, with an estimated prevalence of over 172 000 cases in the developed countries. CLL can be effectively controlled with the initial treatment, but progressed disease is usually less responsive to subsequent therapies.

Within the scope of the project using sequencing and polymerase chain reaction techniques, the frequency of PIM-1 mutations in cells sampled from patients with CLL will be determined. Thereafter, the obtained results will be compared with the clinical course of the disease, particularly with response to chemotherapy, what will allow establishing the impact of PIM-1 mutations on patients' prognosis. Simultaneously with the abovementioned research, experiments aiming at generation of cell lines bearing mutated forms of PIM-1 will be conducted. The obtained CLL cell lines will be utilized to characterize the biological role of the mutants, especially in the processes of cell division, programmed cell death, movement and response to cytostatic drugs widely used in the treatment of CLL.

Accomplishment of this project might allow for detailed insight into the pathogenesis of tumors of the lymphoid origin, as well as establish new effective and safe anti-tumor treatment combinations. Currently widely applied in the clinical practice cytostatic drugs are characterized by frequent occurrence of side effects leading often to premature treatment ending.