Acute lymphoblastic leukemia B-cell (B-ALL) is a heterogeneous group of diseases caused by specific genetic lesions which cause abnormal differentiation and proliferation of hematopoietic cells. However, in adult with B-ALL the therapeutic results are still lagging behind the excellent cure rates obtained in pediatric B-ALL. One of the reasons responsible for this is high incidents of genetic subtypes with poor outcome – *BCR-ABL1*-positive and *BCR-ABL1-like* B-ALL in adults. In recent years the great progress has been made in the treatment of B-ALL, particular in children. Nearly half of adults with B-ALL having either *BCR-ABL1*-positive or *BCR-ABL1-like* disease. Although genetic aberrations underlying in *BCR-ABL1*-positive and *BCR-ABL1-like* leukemias, affecting different molecules, have a similar gene expression profile and lead to activation of the same JAK-STAT pathway and cytokine-independent growth of hematopoietic progenitor cells.

Recent reports indicate that both subtypes of B-ALL also might have similar mechanism responsible for the progression of the disease, which is associated with poor prognosis. It has been shown that *BCR-ABL1*-positive as well as *BCR-ABL1-like* characterized by a high percentage of specific genetic mutations (*copy number alterations*, CNAs), mainly deletions. Sequencing of the surrounding breakpoints of CNAs indicate that it may be resulting from the abnormal activity of some cellular enzymes. The recombinase complex – RAG and APOBEC enzymes including cytidine deaminase – AID are enzymes involved in important physiological process, like production of functional antibodies and their diversity in contact with the pathogens.

The activity of both enzymes is specific for the lymphoid tissue which B-ALL derive. But it is a double-edged sword, on the one hand allows the to a production of antibodies that protect us from the threat of microorganisms, on the other hand causing genetic changes and lead to initiation and progression of tumors. Thus, the attention will be focused on endogenous genome mutators – RAG and AID. To achieve the objective different molecular biology methods will be used, in including DNA sequencing and gene expression analysis.

The purpose of above project is to clarify the molecular basis leading to such a poor prognosis in adults with B-ALL. More specifically, the phenomenon of genetic instability mediated by RAGs and APOBEC enzymes. It contributes to the formation of cancer subclones and to intrinsic heterogeneity of the malignancy. Then newly formed subclones might undergo clonal selection, evolve and subsequently be responsible for leukemia progression. However, despite the great progress in this field of science is still too little knowledge. These studies can also be translated into other areas of oncology, provide a starting point and inspiration to repeat similar studies in other disease entities.