

Leukemia is a cancer of the blood cells and begins when immature cells proliferate uncontrolled. The most common malignancy in children is acute lymphoblastic leukemia (ALL) derived from B-lymphocytes.

Treatment for leukemia depends on its subtype and risk factors both clinical and genetic. There are some strategies that can help to make treatment successful, especially when patient is precisely examined and molecular defect in his leukemic cells is well known. In some cases, no one knows why patient develop certain leukemic phenotype.

Newly identified subtype of acute lymphoblastic leukemia, namely BCR-ABL1-like or Ph-like ALL is a huge challenge for hemato-oncologists. This group is a high genetically heterogeneous and many of the described defects result in hyperactivity of signal transduction within the cell. Despite such patients have none of known risk factors, the relapses are very common and the chance for successful cure is weak. The crucial element in implementing effective therapy is accurate identification of BCR-ABL1-like patient at the onset of leukemia.

More recently have been identified susceptibility locus at the polymorphic site in GATA3 gene. This genetic change - SNP (single nucleotide polymorphism) could be carriers of risk allele, that is related to elevated level of GATA3 gene expression, which suggests a biological role of this polymorphism.

The main purpose of the research project is to evaluate association of GATA3 variation with the BCR-ABL1-like genetic profile and phenotype in pediatric patient.

Since, the molecular mechanisms of hyperactive intracellular signaling underlying the poor prognosis and bad outcome, they are that what have been observed in BCR-ABL1-like patients, therefore to assess the role of GATA3 in up-regulated pathways, functional in vitro analysis of GATA3 gene variation will be carried out in leukemic cells culture. Silencing of GATA3 gene expression in the cell lines, will help establish how exactly GATA3 variants contribute towards the BCR-ABL1-like phenotype. Confirmation of the susceptibility locus' importance and discovery of its biological role GATA3 will not only broaden the knowledge about itself, but will form the basis for the search for new applications as a marker. Determination of the polymorphic locus genotype as a diagnostic procedure enables more precise estimate the course of the disease and thus the identification of patients with BCR-ABL1-like subtype at the time of diagnosis, with a simple genetic test. Such a result referrals to further molecular diagnostics aimed at finding molecular targets for genetically-tailored therapies of ALL. Screening patients eligible for treatment intensification consequently may result in personalized therapy and improve the outcome of BCP-ALL.