IL15 GENE POLYMORPHISMS MODIFY SUSCEPTIBILITY TO ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN

Author: Dmitrijs Rots[1]
Scientific research supervisor: Madara Kreile MD[1]
[1]Riga Stradins university, Scientific laboratory of molecular genetics, Latvia

Introduction. Acute lymphoblastic leukemia (ALL) is the most common pediatric cancer. It is generally considered that the development of ALL is a

comprehensive result of environmental and genetic risk factors, and gene-environment interactions.

IL-15 is a pleiotropic proinflamatory cytokine. IL-15 influences proliferation and differentiation of normal B-lymphocytes and increases pre-B ALL cell growth in vitro.

Previous studies have shown that single nucleotide polymorphisms (SNP) rs10519612, rs10519613 and rs17007695 in *IL-15* gene that we observed is associated with risk of the developing adult ALL (Lin et al., 2010).

Materials and Methods. In the study were included 77 children DNA with pre-B cell ALL in complete remission as well as in 50 cases DNA of both biological parents were available. Control group consisted of 122 unaffected, age and sex matched subject DNA.

DNA was extracted from peripheral blood using standart phenol-chloroform method. For SNP's genotyping polymerase chain reaction - restriction fragment-length polymorphism (PCR-RFLP) assay were used.
Statistical analyses were carried out using the *PLINK* and R software.

Aim. To evaluate the impact of the *IL-15* gene polymorphisms on the susceptibility of developing childhood pre-B ALL.

Results. Combining case – control and case parent trio data with hybrid analysis method there were no statistical significant association betweeen risk of the developing childhood ALL and individual contribution of SNPs rs10519612, rs10519613 and rs17007695. As well no statistically significant association was found analyzing separately case-parent trios.

Analyzing possible SNP haplotypes in cases-controls and trios no significant association were found. But haplotype analysis with hybrid analysis method with sliding window two: rs10519613/rs17007695 a-c in heterozygous state is statistically significant associated with increased risk of ALL (p=0.04; RR=5.28; 95%CI 1.06-26). At the same time haplotype C-T in heterozygous and homozygous state found to be protective (p=0.02; RR=0.21; 95%CI 0.06-0.81 and p=0.03; RR=0.22; 95%CI 0.06-0.88, respectively). Rs10519612/rs17007695 haplotype A-T also is protective in heterozygous and homozygous state (p=0.02; RR=0.23; 95%CI 0.06-0.83 and p=0.02; RR=0.21; 95%CI 0.06-0.83, respectively). SNPs rs10519612 and rs10519613 are in linkage disequilibrium (D=1, r^2=0.95). Haplotype analysis with sliding window three: rs10519612/ rs10519613/rs17007695 - AA-CC-TT has protective role in risk of developing ALL (p=0.0046; RR=0.13; 95%CI 0.03-0.52).

Conclusions.

1. A-c haplotype (rs10519613 and rs17007659) in heterozygous state

could be probable risk haplotype for childhood pre-B cell ALL.

2. C-T (rs10519613 and rs17007659), A-T (rs10519612 and rs17007659) haplotypes in heterozygous and homozygous state and AA-CC-TT (rs10519612/rs10519613/rs17007695) haplotype could have protective effect for developing childhood ALL.

3. Haplin software for hybrid analysis is very important to use in small populations/rare diseases, because it is more powerfull than family-based and case-control studies.

4. Single SNP might have a small effect on the risk of developing ALL, several SNPs interaction is needed to increase susceptibility to childhood ALL.