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The association analysis between *HOTAIR* rs920778 single nucleotide polymorphism and ischemic stroke development in Ukrainian population

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Introduction. Ischemic stroke (IS) belongs to the diseases with hereditary predisposition and both environmental and genetic factors affect its development. Genome-wide association studies (GWAS) have established a vast *majority of single nucleotide* polymorphisms (SNPs) in protein-coding genes related to the emergence of IS. But nowadays non-coding genome is actively studied and long non-coding RNAs (lncRNAs) are under the close attention as potential biomarkers of different metabolic diseases. HOX transcript antisense RNA (HOTAIR) is a lncRNA, that binds and activates Polycomb repressive complex 2 (PRC2) and lysine-specific demethylase 1 (LSD1), contributing to Lysine-27 trimethylation and Lysine-4 demethylation in H3 histone, respectively. Thus HOTAIR occurs epigenetic regulation of different genes, particularly related to the cell cycle process. There are numerous researches devoted to the association between this lncRNA and oncological diseases, such as urogenital and digestive tumors. In contrast, the role of HOTAIR in IS emergence is just starting to be studied.

It was showed that HOTAIR induces IS through the increasing of NADPH oxidase 2 (NOX2) expression. Based on this data we decided to study the association between Cytosine (T) to Thymine (C) transition (rs920778) in *HOTAIR* gene and IS development in Ukrainian population using Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. Venous blood of 170 patients (mean age 64,68±9,52 year) with IS and 125 control subjects (mean age 76,95±9,05 year) were included for genotyping. All statistical calculations were done using SPSS 22.0 software and $P < 0.05$ was accepted as significant.

Results. It should be mentioned that genotypes frequencies in both control and IS group were in accordance with Hardy-Weinberg equilibrium (P_{HWE} = 0,699 and P_{HWE} = 0,458, respectively). The following genotypes distribution was found among IS patients and control group: TT – 35,3%, TC – 45,9%, CC – 18,8% and TT – 32,8%, TC – 50,4%, CC – 16,8%, respectively. There was no statistically significant differences between groups of comparison according to the χ^2-test (P = 0,74). There was no association between *HOTAIR* rs920778 and IS development in crude dominant, recessive, over-dominant and additive models of inheritance, as well as after the adjustment for age, body mass index, sex, arterial hypertension, type 2 diabetes mellitus and smoking in the regression analysis (P > 0,05).

Then we stratified the groups of comparison into subgroups according to the sex. The genotypes frequencies among IS (n = 98) and control (n = 80) males were following: TT – 33,7%, TC – 45,9%, CC – 20,4% and TT – 27,5%, TC – 56,2%, CC – 16,3%, respectively. The genotypes distribution among IS (n = 72) and control (n = 45) females was: TT – 37,5%, TC – 45,8%, CC – 16,7% and TT – 42,2%, TC – 40%, CC – 17,8%, respectively. No statistically significant differences in genotypes frequencies were found between compared groups (P > 0,05) and the results of logistic regression were insignificant (P > 0,05). It can be concluded that there is no association between *HOTAIR* rs920778 and IS development in Ukrainian population. This is the first research devoted to the analysis of the link between rs920778 locus and IS emergence.

Perspectives. In further studies we are going to explore the functional significance of this SNP and estimate the expression rate of *HOTAIR* depending on rs920778 genetic variant.