

ISIAH rat genotype-specific SNPs located at microRNA-binding sites in the 3'UTRs of genes associated with behavior and arterial hypertension

Redina O.E.*, Babenko R.O., Ershov N.I., Smolenskaya S.E., Markel A.L.

Institute of Cytology and Genetics, SB RAS, Novosibirsk, Russia

* *oredina@bionet.nsc.ru*

A model of a stress-sensitive arterial hypertension – the ISIAH rat strain is characterized by an increased reactivity of the hypothalamic-pituitary-adrenocortical and sympathetic adrenal systems compared to the control normotensive rats. In addition, ISIAH rats demonstrate enhanced reactivity of locomotion responses and exploratory behavior in various behavioral tests, as well as an increased level of anxiety (emotionality) in an unfamiliar environment. Numerous studies have confirmed the role of miRNAs in various biological processes, including cardiovascular complications. Binding of a mature microRNA integrated into the RNA-induced silencing complex (RISC) to the 3'-untranslated region of the mRNA leads to mRNA degradation or translation inhibition. The aim of this study was to identify SNPs located at microRNA binding sites in the 3'UTR of genes that may contribute to the manifestation of specific phenotypic features of ISIAH rats. Transcriptome sequencing of several organs/tissues of hypertensive ISIAH and normotensive WAG rats revealed 2773 SNPs that are specific for the ISIAH genotype and are located in the 3'UTRs of 1384 genes. According to the Rat Genome Database (<https://rgd.mcw.edu/>), among them, 177 SNPs were assigned to 71 genes associated with hypertension, and 645 SNPs were assigned to 306 genes associated with behavior/neurological phenotype. The miRDB database (<http://mirdb.org/>) was used to identify SNPs that disrupt microRNA binding sites. 11 SNPs were identified at microRNA binding sites in the 3'UTRs of 11 genes associated with hypertension. 59 SNPs were identified at microRNA binding sites in the 3'UTRs of 50 genes associated with behavior/neurological phenotype. According to the Gene Ontology functional annotation, 21 of these genes are associated with neurogenesis (FDR 1.44E-04). Conclusion: In the genotype of hypertensive ISIAH rats, 61 SNPs were identified that can disrupt microRNA binding to 3'UTRs of genes associated with behavior/neurological phenotype and/or arterial hypertension, which may contribute to the regulation of the expression of a number of genes and the manifestation of specific phenotypic features of hypertensive ISIAH rats.

Acknowledgements: The work was supported by RFBR grant 20-04-00119a and Budget project FWNR-2022-0019.