

Changes in the expression of lncRNAs RGD1564482 and RT1-CE6 in the adrenal glands may be associated with the development of a stress-sensitive form of hypertension in ISIAH rats

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The functional role of the adrenal glands in the regulation of blood pressure and the development of arterial hypertension is well known. The ISIAH rat strain is a model of stress-sensitive arterial hypertension. Previously, we have shown that the manifestation of increased activity of the neuroendocrine hypothalamic-pituitary-adrenal (HPA) and sympathetic-adrenal systems (SAS) in these rats is accompanied by differences in the level of transcription of numerous genes, both in brain structures (brain stem, hypothalamus) and in peripheral target organs (adrenals, kidneys). The aim of this work was to identify lncRNAs that may be involved in the manifestation of the hypertensive phenotype in ISIAH rats. The study was performed using adrenal transcriptome sequencing data from 3-month-old hypertensive ISIAH and normotensive WAG rats. Three animals were analyzed in each group. The Cufflinks/Cuffdiff software packages were used to identify interstrain differences in transcription levels. Genes were considered differentially expressed at a false discovery rate (q value) < 5 %. Pearson's correlation coefficients were calculated to identify correlations between the level of lncRNA transcription and the level of transcription of genes differentially expressed in the adrenal glands of ISIAH and WAG rats. A 99 and 99.9 % (df = 4; $P < 0.01$ (0.917); $P < 0.001$ (0.974)) two-tailed confidence intervals were recognized as significant for the identification of the lncRNA-DEGs coexpression. Functional analysis of DEGs whose expression correlates with lncRNA levels was performed in DAVID (Database for Annotation, Visualization and Integrated Discovery) gene annotation tool (<https://david.ncifcrf.gov/tools.jsp>). A total of 25 expressed lncRNAs were identified, five of which demonstrated differential levels of transcription in the adrenal glands of ISIAH and WAG rats. Correlation analysis showed that the expression of three of them correlated with the expression of a large number of DEGs: Aoc2-ps1 (244 DEGs), RGD1564482 (439 DEGs), RT1-CE6 (406 DEGs). Expression of these lncRNAs has not previously been studied in rat adrenal glands, and they have not been functionally characterized to date. Correlation analysis showed that the expression of lncRNAs RGD1564482 and RT1-CE6 correlates with each other ($r = 0.985$) and with the expression of 10 DEGs associated with hypertension and making the most significant contribution to interstrain differences, which were previously identified when comparing gene transcription profiles in the adrenal glands of ISIAH and WAG rats [1]. The expression of lncRNAs RGD1564482 and RT1-CE6 correlates with the expression of DEGs that, according to the functional annotation, are associated with various biological processes, including neurogenesis, cell adhesion, inflammatory response, response to

oxidative stress, response to insulin, regulation of signaling. In addition, many terms associated with processes that contribute to the regulation of blood pressure levels and the development of hypertension have been identified – vasculature development, regulation of smooth muscle cell proliferation, regulation of calcium ion transport, regulation of catecholamine secretion, as well as blood circulation, blood coagulation, regulation of blood pressure. The results of our study suggest that the downregulation of lncRNAs RGD1564482 and RT1-CE6 in the adrenal glands of ISIAH rats may be associated with the development of a stress-sensitive form of hypertension in this strain of rats.

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References

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