Unveiling the LncRNA-miRNA-mRNA Regulatory Network in Arsenic-Induced Nerve Injury in Rats through High-Throughput Sequencing

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Introduction: Arsenic is a natural toxin which is widely distributed in the environment, incurring diverse toxicities and health problems. Previous studies have shown that long non-coding RNAs (LncRNAs) are also reported to contribute to As-induced adverse effects. LncRNAs are involved in the development of nerve injury, generally acting as sponges for microRNAs (miRNAs). This study aimed to investigate the competitive endogenous RNA (ceRNA) regulatory networks associated with arsenic-induced nerve damage.

Methods: A total of 40 male Wistar rats were exposed to different doses of arsenic for 12 weeks, and samples were collected for pathological observation and high-throughput sequencing. The ceRNA network was constructed using Cytoscape, and key genes were identified through the PPI network and CytoHubba methods. A real-time quantitative PCR assay was performed to validate gene expression levels.

Results: The results showed subchronic exposure to arsenic in drinking water resulted in pathological and ultrastructural damage to the hippocampal tissue, including changes in neuron morphology, mitochondria, and synapses. Exposure to arsenic results in the dysregulation of LncRNA and mRNA expression in the hippocampal tissues of rats. These molecules participated in multiple ceRNA axes and formed a network of ceRNAs associated with nerve injury. This study also verified key molecules within the ceRNA network and provided preliminary evidence implicating the ENRNOT-00000022622-miR-206-3p-Bdnf axis in the mechanism of neural damage induced by arsenic in rats.

Conclusions: Subchronic exposure to arsenic in drinking water can cause pathological damage in hippocampal tissue, resulting in ultrastructural changes in hippocampal mitochondria and synapses. Subchronic arsenic exposure leads to altered expression of multiple LncRNA and mRNA molecules in the rat hippocampus, involved in multiple ceRNA axes forming a network associated with nerve damage. Additionally, our study preliminarily verified arsenic may be involved in the mechanism of nerve injury in rats through the ENSRNOT00000022622-miR-206-3p-Bdnf axis.

Keywords: arsenic; nerve; high-throughput sequencing; ceRNA; lncRNA