Title: The Role of Long Non-Coding RNA in Major Depressive Disorder: A Mouse Model, with Special Emphasis on the Prefrontal Cortex
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Scientific Discipline: Neuroscience

Objectives: After many years of research, the understanding of the pathophysiology of major depressive disorder (MDD) is still incomplete. Due to the fact that only a subset of patients respond to the available drugs for depression, there is a need for a better understanding of the molecular mechanisms of depression to find new drug targets. The overexpression of certain genes and further research regarding the implications of different forms of RNA, specifically long non-coding RNA, may be the key to combatting depression in the future.

Methods: Molecular cloning was performed to make viruses in order to overexpress four lncRNAs in the prefrontal cortex of mice. The mice underwent surgeries to insert the lncRNAs into their brains and multiple behavioral tests were conducted. Following sacrificing of the mice, brain punches were taken, neuronal nuclei were isolated through fluorescence-activated cell sorting (FACS), and the RNA was purified. Promoter prediction was then done to determine transcription factors that regulate the lncRNAs and fluorescence in situ hybridization (FISH) was conducted.

Results: Large subsets of lncRNA were differentially expressed in depressed brains compared to controls. In addition, three lncRNAs had a significant effect on depression-like behaviors of female mice. However, there were no significant results indicating a connection between these three lncRNAs and depression in male mice. As shown by these results, differential regulation of these lncRNAs is sex specific, whether in female and male mice or humans. Through promoter prediction, two transcription factors, Npas2 and Egr1, were identified as potential regulators of these lncRNAs.

Discussion: Specific lncRNAs are potential key regulators in depression and further research could potentially uncover more. Additional bioinformatics will be necessary as well as RNAseq of the brain punches to reveal the amount of RNA present in each sample. Npas2 and Egr1 will need to be tested in cell lines to confirm whether or not they regulate the lncRNAs. Future research would involve overexpressing these lncRNAs in mice in different brain regions of the reward pathway and testing their behavior to find similar correlations between lncRNAs, sex, and depression-like behaviors.