Identification of Novel Biomarkers in Altered Neurogenesis

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Epigenetics is the study of how environmental stimuli affect gene expression without altering the DNA sequence. DNA methylation is an epigenetic mechanism in which a 5-methyl group binds to the DNA, impacting gene expression. DNA methylation in the mouse hippocampus significantly alters the ability to learn, process, and respond. Neurogenesis is the process by which new neurons are generated in the brain. Environmental stimuli such as early-life stress and exercise are known to alter neurogenesis. However, the genetic mechanism leading to altered neurogenesis is unknown. My project aims to identify neurogenesis-regulating genes impacted by early-life stress and a sedentary lifestyle. My hypothesis is, if DNA methylation occurs from early-life stress and a sedentary lifestyle, then neurogenesis-regulating gene expression will be altered, with hypermethylation having lower gene expression and hypomethylation having higher gene expression. To test this hypothesis, I performed bioinformatics on DNA methylation data from the mouse hippocampus to identify potentially altered genes, then I performed real-time PCR to measure the expression of genes identified from bioinformatics. I found four novel biomarkers for altered neurogenesis: Disc1, Ror1, Atp1a3, and Hspg2. Atp1a3 and Hspg2 had an interaction effect with exercise, causing a decreased expression in naïve female mice and an increased expression in stressed female mice. In Ror1, stress leads to a decreased expression in female mice. Exercise has the opposite effect on Disc1 expression in males and females, increasing and decreasing, respectively. In conclusion, I identified four novel biomarkers for altered neurogenesis from early-life stress and a sedentary lifestyle.

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