**Epigenetics: The New Frontier of Autism Research**

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**Epigenetic modifications occur constantly based on the organism’s needs and current state. These modifications mandate which genes are replicated and/or translated into proteins. The role of epigenetics in the etiology of diseases is an area of research that is largely uncharted, but shows great potential. Autism Spectrum Disorder is classified as a multifactorial disorder, and those affected exhibit large amounts of both genetic and environmental variation. Current research suggests epigenetic modifications may play a significant role in the development of Autism Spectrum Disorder. Several thousand epigenetic modifications unique to affected individuals have been discovered (Sun et al., 2016). Though the exact causes are not yet fully understood, researchers are optimistic they will be brought to light with the help of epigenetic testing.**

**Introduction**

Epigenetics is the study of reversible changes in gene expression that do not involve the underlying DNA, or a change in the phenotype without change in the genotype ("Epigenetics: Fundamentals", 2019). Epigenetic changes are the body’s way of adapting based on its environment, age, nutrition, lifestyle, and state of disease. Histone modifications are post-translational modifications to histone proteins, a type of protein that wraps around DNA (Histone Modifications, 2019). These modifications control gene expression. Histone modifications can alter multiple bodily processes, including chromosome packaging, activation/inactivation of gene transcription, and damage/repair of DNA. Essentially, genes are turned “on” or “off” depending on what the body needs at a particular moment. A specific type of histone modification, acetylation, is the addition or removal of an acetyl group to the histone. Addition of an acetyl group to a histone partially unravels it, which allows the DNA inside to be transcribed.

Autism Spectrum Disorder (ASD) is defined as a collection of multifactorial neuro-developmental disorders that adversely affect an individual’s communication and social interaction abilities (Sun et al., 2016). ASD is a complex disorder with many determinants contributing factors. Several hundred genetic mutations have been found so far that contribute to autistic behaviors to varying degrees. It is also believed that environmental factors that contribute to the disorders. Like most multifactorial diseases, Autism Spectrum Disorder is very complex and likely has many contributing factors involved in its etiology. The mechanisms that contribute to its development are not yet well-understood, and there is a vast amount of research still to be done. Genome sequencing and analysis has been performed on ASD patients and DNA has shown to affect the etiology of ASD at various levels of significance. However, there has not been a consistent gene or group of genes whose mutations clearly lead to Autism. The combination of possible environmental and genetic factors has led researchers to question the role that epigenetic modifications play in the development of ASD.

**Recent Progress**

Sun et al. conducted a study to test for epigenetic differences in ASD and non-ASD patients’ brain tissue. Previous research had shown a possible relation common molecular pathways, including transcriptional regulation, and development of Autism Spectrum Disorder. However, this research only focused on the epigenetic and genetic variations of coding regions of DNA. The variations that had been found in these studies are rare and not consistently observed across large groups of ASD-affected individuals. Previous research mainly focused on histone methylation, a different type of epigenetic change, but changes due to acetylation were not yet examined. The researchers conducting this study hypothesized that histone acetylations in the non-coding regions of DNA may contribute to the occurrence of ASD. Despite ASD samples showing little genetic variation, they predicted a there would be translational differences in a number of downstream pathways that may account for some of the symptoms of ASD.

“Histone Acetylome-wide Association Study of Autism Spectrum Disorder” (Sun et al., 2016) was considered a histone acetylome-wide association study, or a study of the entirety of histone acetylations in an organism. They obtained 257 postmortem brains of humans diagnosed with ASD and cross-compared them to control postmortem brains of unaffected individuals. They took samples from three regions of the brain – the prefrontal cortex (PFC), the temporal cortex (TC), and the cerebellum (CB). The researchers performed three different tests on the samples to identify epigenetic differences. First, they were tested for the acetylation marker H3K27ac. This is a well-suited marker because its presence represents active enhancers and promoters, and it is associated with transcription factor binding and gene expression (Kumar et al., 2013). They also used a test called chromatin immunoprecipitation sequencing (ChIP-seq), which detected single-nucleotide polymorphisms within active enhancers and promoters. Lastly, a genotype-independent signal correlation and imbalance (G-SCI) test was done to identify histone acetylation in loci that are linked to psychiatric diseases.

This study’s test results exhibited a large number of cerebral cortex histone acetylation abnormalities in Autism Spectrum Disorder patients. They identified over 5,000 enhancer or promoter loci that were abnormally up- or down-regulated. The most significant differences occurred in the cerebral cortex samples (TC and PFC). The article states, “acetylation changes in ASD cerebral cortex were significantly correlated with differential gene expression, consistent with the known functional consequences of these alterations in chromatin structure” (Sun et al., 2016). There was a positive correlative relationship between increased H3K27ac within loci and activation of genes associated with ion channels, neuronal excitability, and synaptic function. Dysregulation of these downstream pathways are linked to ASD behaviors and traits.

**Discussion**

The study performed by Sun et al. brought new information to light, and because of the study researchers are one step closer to fully understanding the development of ASD. In future studies, these five thousand differences found between control brains and ASD brains can used as a reference set to aid in learning more about ASD development. The information they found is also not limited to Autism studies, as epigenetic changes are likely involved in multiple diseases and disorders. Genome sequencing and analysis is becoming more prevalent in research, and epigenetic research will likely soon follow.

 This study did produce some valuable information, most notably the observed difference in the translational regulation of heterogeneous loci that affected downstream pathways involved in ASD characteristics. There is great potential for further research, involving ASD and any number of other multifactorial diseases. If the specific causes of ASD are eventually determined, the opportunity for developing treatment and/or preventative measures could prevent many individuals from the effects of ASD.

**References**

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