Above and Beyond the Autism of Today: Exploring a Retroelement Regulatory Hypothesis in Autism Spectrum Disorder

Walletzky, Leonard (School: Gymnazium Matyase Lercha)

Autism Spectrum Disorder (ASD) is a heterogeneous neurological disorder affecting approximately 1 in 100 children today. The diagnosis and treatment of ASD are complex, partly due to its obscure genetic basis. Transposable elements (TEs) are DNA sequences capable of changing their position in the genome. They comprise approximately 50% of the human genome. Although they have largely lost their ability to transpose, they acquired regulatory functions, such as host gene expression control, due to their enrichment with CpG sites and transcription factor binding sites. Notably, it has already been established that certain TE families are enriched near ASD-implicated genes, suggesting potential genomic and regulatory instability. This study utilized public RNA-seq data from post-mortem brain tissue of ASD and non-ASD control donors to investigate the impact of TE epigenetic modifications. We sought to identify common differentially expressed genes (DEGs) between the ASD and non-ASD groups and characterize their functional roles in ASD pathology through gene ontology and pathway enrichment analyses. Additionally, we aimed to identify TE families near these DEGs to explore their potential regulatory role in ASD gene expression. Our analyses revealed a consistent immune-related pattern among DEGs and identified specific TE families (e.g., L2a/b/c, MER4B, and MLT1J) enriched in proximity to DEGs. This suggests that TEs may contribute to immune dysregulation in ASD and potentially influence the autism phenotype. Our research proposes a functional hypothesis for ASD manifestation, identifying TEs as a novel therapeutic target to correct immune dysregulation, pending further experimental validation.

Awards Won: