Presenting Author Name
Anha Afrin Shefa

Presenting Author Category
Masters Student

Research Category
Basic Science

Abstract Title
Cell-Type-Specific Analysis of the Genetic and Environmental Contributions to Autism Spectrum Disorder

Background
Being highly heritable, DNA and/or chromosomal alterations may lead to Autism Spectrum Disorder (ASD). ASD is a neurodevelopmental disorder characterized by restricted and/or repetitive behaviors. Treatment is limited to therapies such as speech, occupational, physical, and applied behavior therapy. There is still a large gap in understanding how ASD alters neurodevelopment at the cellular level. 16p11.2 deletion syndrome is among the most frequent Copy Number Variations in human. There is still a large gap in understanding how ASD alters neurodevelopment at the cellular level.

Objective
Our working hypothesis is that 16p11.2 gene dosing and environmental factors can contribute to overcome 16p11.2 deletion's effect.

Methods
This study measures the dosage-dependent requirements of 16p11.2 by applying Mosaic Analysis with Double Markers (MADM). MADM is a lineage tracing approach that allows cells with two different genotypes (wild-type and knockout) to be generated within the same tissue and for cells of each genotype to be identified with a different fluorescent marker (Red, Green and Yellow). Green cells will represent wild type cells, green cells will have homozygous 16p11.2 gene deletion and yellow cells will represent cells with heterozygous 16p11.2 deletion. So, cells with different genotypes were generated within the same tissue and each genotype was identified with a different fluorescent marker.

Results
To test the hypothesis that 16p11.2 is required in a cell-type-specific manner, MADM-based mouse models were combined with tissue-specific Cre drivers (targeting interneurons/excitatory neurons) as well as 16p11.2 deletion allele. . Thus, 16p11-MADM mosaic mice were successfully generated, and analysis is ongoing. Brains were dissected on postnatal day 1 and 21 followed by immunohistochemistry to identify cortical structures and cell types. To identify populations of cells requiring 16p11.2, we compared the ratio of green/red cells, yellow/red cells and number of cells per unit volume. Some changes in cellular phenotypes depending on 16p11.2 gene dosing was found.

Conclusion
Gaining deeper insights into ASD neurobiology is crucial for improving diagnosis and developing targeted treatments. MADM technology permits the identification of key molecular changes in each brain cell type as ASD progresses. This understanding is vital for validating future therapies before clinical trials.

Authors

Name	Role	Profession
Anha Afrin Shefa	Presenting Author	Graduate
Paul Houston	Co Author	Graduate
Robert Beattie	Co Author	Assistant Professor