Genome-Wide DNA Methylation Analysis in Autism

Xi-Yu Jia, Xueguang Sun, Eliza Bacon, Adam Peterson, TzuHung Chung

Zymo Research Corporation, Irvine, CA

ZYMO RESEARCH
The Beauty of Science is to Make Things Simple

Abstract

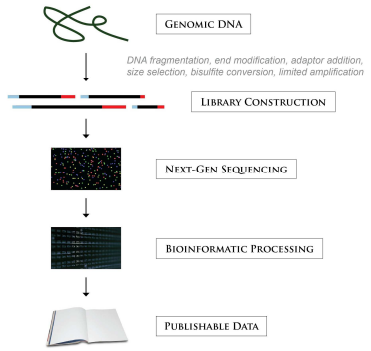
Lacking consistent genetic mutation data in autism and increased risk of prenatal /maternal factors for disease development suggest a possible epigenetic mechanism for the disease development. DNA methylation is one of the major epigenetic regulators and its importance in development and disease is well established. Using next generation sequencing in combination with bisulfite-based DNA methylation detection, genome-wide 5-methylcytosine (5-mC) were investigated in autism blood samples from monozygotic twins. Our results indicate that "epimutations" are present in the affected children's blood DNA and these epigenetic changes were in agreement with other published biochemical data implicating epigenetics as a key element in the development of the disease.

Introduction

Autism and Autism Spectrum Disorder (ASD) are both general terms for a group of complex disorders of brain development. On average, 1 in 110 American 8-year-old children in the United States is diagnosed to have an ASD. Because ASD is a wide-spectrum disorder, professional assessment is required. However, in the future epigenetic biomarkers could aid professionals and help to optimize and validate the diagnoses of Autism and ASD.

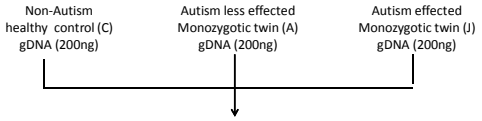
Here, we present preliminary data showing the genome-wide 5-methylcytosine (5-mC) profiles from autism blood samples of monozygotic twins compared to a healthy control. The results show that in addition to significant differences in DNA methylation. These findings indicate that specific detection of 5-mC could be an additional layer of information that could be a promising source for future biomarker candidates in autism and ASD.

Workflow

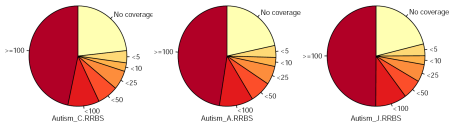


www.zymoresearch.com/services
services@zymoresearch.com

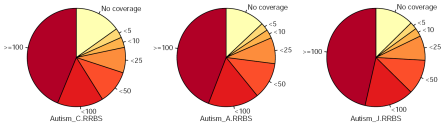
Genomic 5-mC Profiling in Autism



➢ **Genome Coverage :**



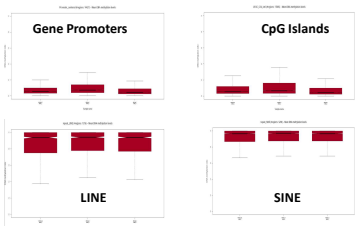
Gene Promoters



CpG Islands

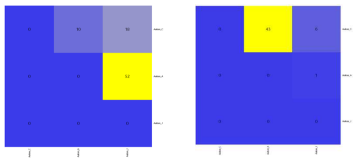
Graph show the overall distribution of sequencing reads and coverage at gene promoters. CpG island.

➢ **Methylation Index**



There is no obvious global DNA methylation changes in gene promoters CpG Islands and DNA repeats from global DNA methylation level calculated for specific regions.

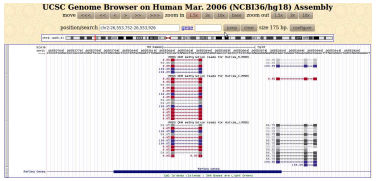
➢ **Number of Different Methylated Regions**



Hypermethylation **Hypomethylation**

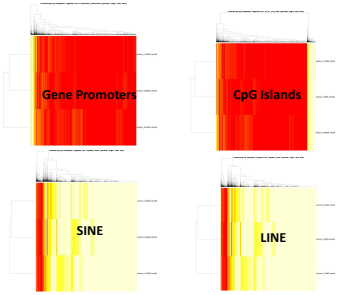
Pairwise comparison of gene loci displaying strong hypermethylation and hypomethylaiton (> 30% meth ratio difference) .

➢ **UCSC Genome Browser Tracks**



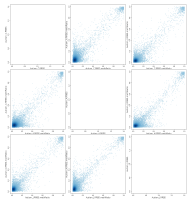
UCSC genome browser track shows the sequencing reads and DNA methylation values for the samples. Blocks indicate individual CpG sites. The adjacent numbers indicate the average DNA methylation value for a particular read. The methylation value is calculated by averaging the reads within a 2 kb window.

➢ **Hierarchical Clustering:**



Heat map showing the hierarchical clustering by region (Gene promoter , CpG Islands, SINE and LINE) and sample. (Autism_C, Autism _A and Autism_J)

➢ **Correlation Analysis**



Pearson correlation between samples

Conclusions

- autism samples have a very similar global methylaton level as healthy control
- Over a hundred different methylated regions were identified through pairwise comparison between autism samples and control
- Methylation levels from DNA repeats are better in clustering autism sample from control.