USING WHOLE-GENOME NANOPORE LONG-READ DATA TO EXAMINE AUTOSOMAL DNA METHYLATION IN INDIVIDUALS WITH SEX CHROMOSOME ANEUPLOIDIES

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ABSTRACT

Although sex chromosome aneuploidies (SCA) are the most common type of aneuploidy, there are still many unanswered questions about these conditions. Specifically, how the change in sex chromosome counts affects the individual genetically and phenotypically, and why there is so much variability in the severity of their outcome. In this study, we used whole-genome Nanopore sequencing of blood samples from a cohort of Klinefelter males, Turner females and control males and females to extract data about the control and SCA autosomal methylome. Two tools were developed to process the methylation data to segment the genome into regions of different methylation states, and to identity differentially methylated regions (DMRs) and associated differentially expressed gene transcripts (DEGs). The result of the study was the rediscovery of previously identified candidate genes showing differential methylation and/or differential expression, and the discovery of new candidate genes on the autosomes. With the methylation data, we also found evidence of genome-wide effects of sex chromosome count on autosomal methylation and expression.

ABBREVIATIONS

CGI – CpG island

CpG – A cytosine and guanine connected by a phosphate

DEG – Differentially expressed gene or gene transcript

DMR – Differentially methylated region

GI – Genomic imprinting

KS – Klinefelter syndrome

TS – Turner syndrome

ONT – Oxford Nanopore Technologies

PAR – Pseudoautosomal region.

SCA – Sex chromosome aneuploidy