**Diagnostic exome sequencing identifies a homozygous whole-gene deletion of *DPY19L2* that was not detected by a high-density single nucleotide polymorphism (SNP) array**

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While both exome sequencing and high-density single nucleotide polymorphism (SNP) arrays are capable of detecting copy number variants (CNVs), neither methodology is comprehensive and each can miss certain regions of the genome. In a clinical setting, SNP array testing usually precedes exome sequencing primarily due to its lower cost and ability to reliably detect large CNVs that are at least 100 kilobases (kb) in length. It is therefore important for SNP arrays to be able to detect, at the very least, known clinically relevant CNVs that meet the length cutoff so as to minimize additional unnecessary investigations towards a genetic diagnosis. We present a case example of an adult male with globozoospermia, a spermatogenic defect that can cause male infertility, who pursued diagnostic exome sequencing at our clinical genetic testing laboratory after having a negative CytoscanHD Array (Affymetrix) result. His exome data showed complete or almost-complete absence of coverage in all coding exons of *DPY19L2*, a gene known to cause globozoospermia when homozygously deleted. Homozygous deletions of this gene, which are approximately 200kb, are a common cause of this condition due to nearly-identical low copy repeats on either side of this gene that facilitate non-allelic homologous recombination. We confirmed the deletion in the patient by polymerase chain reaction-based amplification of three of the 22 coding exons (3, 11, and 22) of this gene, which showed no amplification. In contrast, two of six coding exons of the nearest gene *TMEM5* located 111kb away amplified successfully. Due to the presence of four pseudogenes in the genome, probe coverage of *DPY19L2* on the CytoscanHD array is poor, with only three intragenic SNPs in the entire 110kb length of the gene. However, homozygous deletions of *DPY19L2* have previously been detected by array comparative genomic hybridization (aCGH). This case illustrates the utility of exome sequence data in revealing CNVs previously missed by a high-density SNP array and suggests that a clinical high-density aCGH may be a favorable alternative for cases where discovering pathogenic CNVs is the primary intent before pursuing other genetic diagnostic tests.