Whole Exome Sequencing Test Report

Personal Information
Name: Jason Doe
Relation: -
Sex/Birth: F / 2023-02-15

Specimen Information
Sample ID: 20230405-971-0000
Medical record No: -
Date received: 2023-04-05

Test Information
Test reported: 2023-05-15
Ordering physician: Dr Smith
Institution: Hospital A

TEST PERFORMED

WES(Sequence analysis of whole exome of human genes)

REASON FOR REFERRAL

clinical patient information: epilepsy, seizures
clinical diagnosis: please see the attached word file
The patient presented seizures since day 2 of life with phenotype: jerking of eyelid, asymmetrical focal tonic on both hands, cyanosis and apnea about 20s-40 seconds.

RESULT

POSITIVE

A pathogenic variant was identified in the GNAO1 gene, related to the patient's clinical phenotype.

Gene	DNA change	Predicted AA change	Zygosity	OMIM Disease	Inherit	Class
GNAO1	c.118G>T	p.Gly40Trp	Het	DAEE17, NDWIM	AD	PV

Reference sequence: NM_020988.3(GNAO1)
OMIM disease: DAEE17, Developmental and epileptic encephalopathy 17; NDWIM, Neurodevelopmental disorder with involuntary movements
Abbreviation: AD, Autosomal dominant; Het, Heterozygous; PV, Pathogenic Variant

INTERPRETATION

[2023.05.15]
GNAO1, NM_020988.3:c.118G>T (p.Gly40Trp)
This sequence change replaces 40th amino acid Glycine with Tryptophan of the GNAO1 protein. This variant is not present in population databases. This variant has been reported in individuals affected with Infantile spasms (PMID: 32695065, 30682224, 31440721, 29390993). ClinVar contains an entry for this variant as Pathogenic (Variation ID: 280526). In silico analyses, which predict the effect of the effect of missense changes on protein structure and function output, are as the following: SIFT: deleterious, PolyPhen: probably damaging. For these reasons, this variant has been classified as Pathogenic.
Pathogenic GNAO1 variants are associated with Developmental and epileptic encephalopathy 17, Neurodevelopmental disorder with involuntary movements. Developmental and epileptic encephalopathy 17 is a severe neurologic disorder characterized by onset of intractable seizures in the first weeks or months of life. EEG often shows a burst-suppression pattern consistent with a clinical diagnosis of Ohtahara syndrome. Affected infants have very poor psychomotor development and may have brain abnormalities, such as cerebral atrophy or thin corpus callosum. Some patients may show involuntary movements.

Clinical correlation and, if necessary, family testing are recommended.

Tested by: M-K Lee M.T(20058) Confirmed by: Sae-Mi Lee M.D(1067) Chang-ahn Seol M.D(1037)

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INCIDENTAL FINDINGS

No (Likely) Pathogenic Variant was identified in the 78 genes recommended by ACMG
* Investigation of 78 genes recommended by ACMG SF v3.1 (Genet Med.2022 June 17.)

METHODS

Genomic DNA was extracted from EDTA whole blood and we captured all the exons of human genes using MGIEasy Exome Capture V5 (MGI). Sequencing was performed on DNBSEQ-G400 (MGI) or DNBSEQ-T7 (MGI) platform generating 2 × 100 bp paired-end reads. The DNA sequence reads were aligned to reference sequence based on public human genome build GRCh37/UCSC hg19. Using a in-house bioinformatics pipeline, data were filtered and analysed to identify sequence variants.

Sequence variants were classified based on the ACMG/AMP guidelines (Richards et al., 2015). Reported results are focused on pathogenic and likely pathogenic variants in genes related to the phenotype of proband, while variants of uncertain significance are only rarely reported at our discretion. Depending on the results of additional studies in the literature and databases, the classification of the variant may change. Variants that pass internal QC criteria are not validated by Sanger sequencing.

ANALYSIS STATISTIC

Mean depth of coverage	163.25X
% of > 10x	98.2%

LIMITATIONS

The absence of definitive pathogenic findings does not rule out the diagnosis of a genetic disorder as some genetic abnormalities may be undetectable with this test. It is possible that the genomic region where a disease-causing variant exists in the proband was not captured or sufficiently sequenced with low quality. Additionally, multifactorial disorders and some types of genetic disorders due to nucleotide repeat expansion/contraction, abnormal DNA methylation, and other mechanisms may not be detectable with this test. This test also cannot reliably detect mosaicism, chromosomal aberrations, and deletions/insertions of 20 bp or more. Some genes have inherent sequence properties (for example: repeats, homology, high GC content, rare polymorphisms) that may result in suboptimal data, and variants in those regions may not be reliably identified.

※ This test was developed and its performance characteristics determined by GC Genome. It has not been cleared or approved by the Korean Ministry of Food and Drug Safety (MFDS).

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