SAMPLE REPORT

DGS (Diagnostic Genome Sequencing) Report

Personal Information	Specimen Information	Test Information
Name: Jane Doe	Sample ID: 20200901-971-2105	Test reported: 2020-01-01
Date of Birth: 1984.01.01	Medical record No:	Ordering physician: Dr. Smith
Sex: Female	Date received: 2020-01-01	Institution: Hospital A

TEST PERFORMED

DGS (Diagnostic Genome Sequence)

CLINICAL INFORMATION

Muscle weakness, r/o periodic paralysis

RESULT: POSITIVE

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

Gene	DNA change	Predicted AA change	Zygosity	Disease	Inherit	Class
KCNJ2	c.199C>T	p.(Arg67Trp)	Het	Andersen syndrome	AD	PV

Reference sequence: NM_000891.3(KCNJ2)
Abbreviation: AD= Autosomal dominant; Het= Heterozygote; PV= Pathogenic variant

Medical Technologist:
Sung-Hee Bang M.T.(33995)

Lab Director(medical doctor):
Sae-Mi Lee M.D.(1067)

Chang-Ahn Seol M.D.(1037)

GC Genome

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

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INTERPRETATION

[2020.10.22]

KCNJ2, c.199C>T p.(Arg67Trp)

This sequence change replaces arginine with tryptophan at codon 67 of the KCNJ2 protein (p.Arg67Trp). The arginine residue is highly conserved and there is a moderate physicochemical difference between arginine and tryptophan. This variant is not present in population databases (gnomAD). This variant has been reported in individual affected with Andersen-Tawil syndrome (PMID: 12796536, 12148092, 17221872, 22806368, 23867365, 22589293). This variant is reported as pathogenic by multiple laboratories in ClinVar (Variation ID: 8923). Functional studies have shown that this missense change results in a complete loss of channel function (PMID: 12148092, 20713726). For these reasons, this variant has been classified as Pathogenic.

Pathogenic KCNJ2 variants are associated with autosomal dominant Andersen-Tawil syndrome, Short QT syndrome, Familial atrial fibrillation. Andersen-Tawil syndrome (ATS) is characterized by a triad of: episodic flaccid muscle weakness (i.e., periodic paralysis); ventricular arrhythmias and prolonged QT interval; and anomalies including low-set ears, widely spaced eyes, small mandible, fifth-digit clinodactyly, syndactyly, short stature, and scoliosis. Affected individuals present in the first or second decade with either cardiac symptoms (palpitations and/or syncope) or weakness that occurs spontaneously following prolonged rest or following rest after exertion. Mild permanent weakness is common. Mild learning difficulties and a distinct neurocognitive phenotype (i.e., deficits in executive function and abstract reasoning) have been described. (Reference: OMIM, GeneReviews)

RECOMMENDATIONS

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

INCIDENTAL FINDINGS Examination of 59 genes recommended by ACMG SF v2.0 (Kalia et al., 2017)

No reportable incidental findings were identified in coding regions covered by this test.

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METHODS

Genomic DNA was extracted from EDTA whole blood and sequenced with paired-end reads on BGI G400 platform. 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 analyzed to identify sequence variants. CNV calling is based on parliament2 pipeline. Evaluation is focused on coding exons along with flanking +/-20 intronic bases, however extended to the complete gene region for candidate genes or in search for a second previously described variant in AR inheritance pattern. 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. Variants that pass internal QC criteria are not validated by Sanger sequencing.

ANALYSIS STATISTICS WGS

MEAN DEPTH OF COVERAGE	33X
% of > 10x	98.5

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.

ADDITIONAL INFORMATION

This test was developed and its performance validated by GC Genome. This test has been developed for clinical purposes. The laboratory is certified by the CAP (College of American Pathologists). All test results are reviewed, interpreted and reported by our medical experts.

The classification of variants can change over the time. Please feel free to contact GC Genome (info.gcgenome@gccorp.com) in the future to determine if there have been any changes in classification of any reported variants.

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