CNGnome™ Report

Patient Name:
Date of Birth:
Gender:
Accession ID:
Cross Reference:

Specimen Type:
Receive Date:
Collection Date:
Report Date:

Client Name:
Hospital/Institution:
Mailing Address:
Phone Number:
Fax Number:

Test Performed: **CNGnome™**
Reason for Referral: **XXXXXXX**

Pathogenic Copy Number Variant (CNV) detected: Trisomy 13.

Correlation with clinical profile and family history is required.

Relevant Findings and Interpretation

CNGnome testing was performed to identify copy number variations in the clinical specimen from this individual. The whole genome was interrogated for copy number changes (gains/losses) and absence of heterozygosity (AOH). The following copy number changes were detected:

CNVs related to phenotype:

ISCN Nomenclature: seq[hg19] 13q11q34(19025440_115169878)x3

Event	Cytoband/Gene	Genomic Location	Size (bp)	Classification
CN Gain	Chromosome 13	chr13:19,025,440-115,169,878	96144439	Pathogenic

Chromosome 13 CN Gain - Pathogenic. Trisomy 13. A copy number gain of the entire chromosome 13 was identified in this assay. Approximately 80% of trisomy 13 arises from meiotic nondisjunction while chromosomal imbalance accounts for the remaining 20% (PMID: 17584770). Trisomy 13, also known as Patau syndrome, is characterized by life-threatening medical issues. Clinical features of trisomy 13 include severe intellectual disability and multiple congenital anomalies including brain and spinal cord abnormalities, microphthalmia, cardiac defects, cleft lip and palate, polydactyly, and hypotonia. The survival rate after one year of age ranges from 5-10% (https://ghr.nlm.nih.gov/condition/trisomy-13). Trisomy 13 is a well-documented pathogenic autosomal aneuploidy in recurrent miscarriages (PMID: 8116665, 23220825, 27458947, 16648416).

Recommendations

These results must be interpreted in the context of this individual's clinical profile and family history. Genetic counseling is recommended.

Parental karyotyping studies are recommended to determine if either parent is a carrier of a Robersonian translocation.

For more information, please contact the laboratory at 1-866-354-2910

Methods and Limitations

Direct sequencing of genomic DNA was performed using 2X150bp reads on Illumina next generation sequencing (NGS) systems at a mean coverage of 5X in the target region. Alignment to the human reference genome (hg19) was performed and copy number variant (CNV) calls made

using the NxClinical software v5.0 (BioDiscovery, Inc., El Segundo, CA). CNVs meeting internal quality assessment guidelines are confirmed by real time quantitative PCR (qPCR) for records after results are reported. Some CNVs are confirmed by qPCR before reporting at a director's discretion.

This assay cannot detect CNVs in regions of the genome that are not amenable to NGS and does not interrogate CNVs in mitochondrial DNA. This assay will not detect tandem repeats, balanced alterations (reciprocal translocations, Robertsonian translocations, inversions, and balanced insertions), point mutations, methylation abnormalities, genomic imbalances in segmentally duplicated regions and mosaicism; possible cases of mosaicism may be investigated at the discretion of the laboratory director. Small pathogenic CNVs within the exon, some small intragenic deletions or duplications, as well as complex rearrangements may not be detected. This assay has been validated to detect copy number variants >25 Kb and also has the ability to detect copy number changes such as homozygous deletions. For targeted CNV testing, smaller CNVs may be interrogated, analyzed, and reported per director discretion. This assay may not be able to discern between CNVs that are high copy number gains such as, duplication >=4X. CNVs involving genes with pseudogenes and pseudoexons may not be reliable detected or reported. Due to high similarity of certain regions on chromosome X and chromosome Y, CNVs in the following regions may not be detected for male patients (chrX: 60000-2699520; chrX:154930289-155260560; chrY:10000-2649520; chrY: :59033286-59363566).

NOTE: The interpretation of CNV changes is based on our current understanding of the genome. These interpretations may change over time as more information about this gene becomes available. Possible diagnostic errors include CNV call errors, sample misidentification, and other sources. Genomic coordinate numbering is based on GRCh37/hg19.

Possible sources of testing error include rare genetic variants that interfere with analysis, sample misidentification, and other sources. Pursuant to the requirements of CLIA '88, this technical component and the professional component was performed by PerkinElmer Genomics. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.

Director Signature(s)