CHROMOSOMAL MICRO ARRAY

Clinical History

Sneha Dhadekar is presented with bilateral club foot and severe gait difficulty and her husband, with high myopia and progressive vision loss. She was referred for chromosomal micro array for genetic evaluation of chromosomal abnormalities.

Array Type

Affymetrix Cyto scan 750K array

Test Result

NO SIGNIFICANT COPY NUMBER VARIATIONS(CNVs) IDENTIFIED.

Interpretations

The chromosomal microarray analysis showed a normal female karyoview. However, long continuous stretches of homozygosity (LCSH) are observed in chromosome 3 and 7 .Clinical Correlation is strongly recommended.

Gopi.P
Sr.Technical Officer Genomics

A. Radhika
Co-Head Genomics

Dr. NAUSHAD
CHIEF SCIENTIFIC OFFICER
Reg No.: 43432

Approved by

Dr. Kiran Kumar
Consultant Genomics

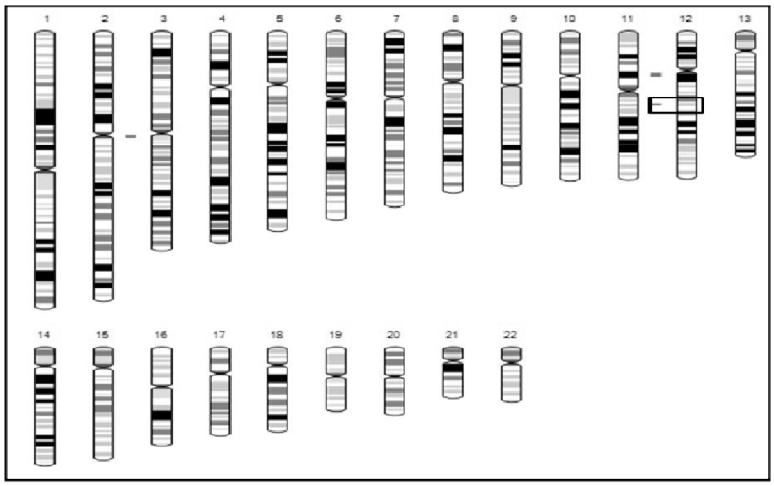

Fig. 1: Karyoview of the sample 10554049

LSCH : **L**ong **C**ontinuous **S**tretches of **H**omozygosity (LCSH) are observed in chromosome 3 and 7 which accounts for 0.25% of the genome (refer to appendix table).

Recommendations

- Genetic Counseling and clinical correlation are strongly recommended.
- Whole exome sequencing is recommended.

Test Method

Chromosomal microarray analysis (CMA) was performed using Affymetrix Cytoscan 750K array. This microarray consists of ~750,000 oligonucleotide probes across the genome, that include exonic, intronic, synonymous, missense, nonsense, mitochondrial, indels, andsex chromosome markers Genomic DNA (250ng) was digested with NSP1 enzyme and then ligated by NSP1 adapter. Cytoscan Taq amplified PCR products of size-selected 150bp to 2200bp were purified using AMP pure beads and fragmented to the product size of 25bp to 125bp, biotin labelled, hybridized on Cytoscan 750K gene chip and then scanned followed by washing the gene chip. Data was analyzed using chromosome Analysis Suite (ChAS) version 4.3. The analysis is based on the Human reference genome (GRCh38).

Gopi.P
Sr.Technical Officer Genomics

A. Radhika
Co-Head Genomics

Dr. NAUSHAD
CHIEF SCIENTIFIC OFFICER
Reg No.: 43432

Approved by

Dr. Kiran Kumar
Consultant Genomics

Limitations of Test and Other Test Notes

Chromosomal Microarray array is recommended for the sole purpose of identifying DNA copy number variations (CNVs) associated with chromosomal imbalances and for the detection of absence/loss of heterozygosity (AOH/LOH), regions/runs of homozygosity (ROH), or long contiguous stretches of homozygosity (LCSH).

CMA can detect only gross genomic copy number imbalances (aneuploidy, deletions and duplications) and AOH/LCSH in the nuclear genome. It cannot detect balanced chromosomal rearrangements such as inversions, balanced insertions, and reciprocal translocations.

The current reporting policy is as per recommendations from American College of Medical Genetics (ACMG)

CMA cannot detect

- Genomic copy number changes in the regions of the genome not represented on the microarray (including regions with repeat sequences such as segmental duplications, repeat sequences in the short arms of acrocentric chromosomes, and heterochromatic regions)
- low levels of mosaicism (<20-25%)
- point mutations and indels, Imbalances in the mitochondrial genome.
- complete uniparental heterodisomy for the entire chromosome. It can only detect uniparental isodisomy, and segmental heterodisomy.
  CMA cannot detect imbalances when mosaicism for reciprocal CNVs exist. Failure to detect an alteration at a specific locus does not rule out the diagnosis of a genetic disorder associated with that locus. Other abnormalities may be present that are undetectable by the microarray design. Failure to detect evidence of UPD/AOH does not exclude the clinical diagnosis of an imprinting or recessive disorder.

Disclaimer

This CMA test has been developed and validated but has not been approved by the US FDA for diagnostic purposes. Thus, this test is recommended for research use only but not a diagnostic test and hence not to be considered as a purpose of diagnosis of any diseases. This test is meant for only understanding chromosomal aberrations and their clinical relevance. The company will not be liable for any direct, indirect, consequential, special, exemplary, or any other damages. This test detects chromosomal abnormalities only under its limit of resolution.

In some instances, the classification and interpretation of variants (VUS) may change as new scientific information comes to light. We recommend re-analysis of this report yearly. Please contact laboratory in case re-analysis of the report is desired. It is the lab's policy to perform re-analysis once on a complimentary basis. However, this re-analysis is performed only when requested.

Gopi.P
Sr.Technical Officer Genomics

A. Radhika
Co-Head Genomics

Dr. NAUSHAD
CHIEF SCIENTIFIC OFFICER
Reg No.: 43432

Approved by

Dr. Kiran Kumar
Consultant Genomics

References

1. https://bmcmedgenomics.biomedcentral.com/articles/10.1186/s12920-019-0496-5
2. Detection and Reporting of Homozygosity Associated with Consanguinity in the Clinical Laboratory https://www.karger.com/article/pdf/362448
3. Uniparental disomy: Origin, frequency, and clinical significance https://obgyn.onlinelibrary.wiley.com/doi/10.1002/pd.5837
4. Chromosomal mosaicism: Origins and clinical implications in preimplantation and prenatal diagnosis
5. Brynn Levy,Eva R. Hoffmann,Rajiv C. McCoy,Francesca R. Grati https://www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/Practice-Guidelines.aspx
6. https://www.deciphergenomics.org/

APPENDIX

Gopi.P
Sr.Technical Officer Genomics

A. Radhika
Co-Head Genomics

Dr. NAUSHAD
CHIEF SCIENTIFIC OFFICER
Reg No.: 43432

Approved by

Dr. Kiran Kumar
Consultant Genomics

LCSH regions in index patient, Size & [Genomic coordinates]	Genes
chr3q22.2q22.3q23q24;9.2MB(134025422-143260054)	AMOTL2; ANAPC13; CEP63; CEP63; CEP63; KY; EPHB1; PPP2R3A; PPP2R3A; MSL2; PCCB; STAG1; TMEM22; NCK1; IL20RB; SOX14; CLDN18; CLDN18; DZIP1L; DZIP1L; A4GNT; DBR1; ARMC8; TXNDC6; MRAS; MRAS; ESYT3; CEP70; FAIM; FAIM; PIK3CB; FOXL2; C3orf72; PRR23A; PRR23B; PRR23C; BPESC1; PISRT1; MRPS22; COPB2; RBP2; RBP1; RBP1; RBP1; NMNAT3; CLSTN2; TRIM42; SLC25A36; SPSB4; ACPL2; ZBTB38; RASA2; RNF7; GRK7; ATP1B3; TFDP2; GK5; XRN1; ATR; PLS1; PLS1; TRPC1; PCOLCE2; PAQR9; SR140; CHST2; SLC9A9;
chr7q11.22q11.23;6.5MB(68910326-75457127)	AUTS2; AUTS2; WBSCR17; CALN1; TYW1B; TYW1B; SBDSP; SPDYE7P; POM121; NSUN5C; LOC541473; STAG3L3; PMS2L14; SPDYE3; GTF2IP1; GTF2IP1; NCF1B; GTF2IRD2B; NSUN5; TRIM50; FKBP6; FKBP6; FZD9; BAZ1B; BCL7B; TBL2; MLXIPL; VPS37D; DNAJC30; WBSCR22; STX1A; WBSCR26; ABHD11; ABHD11; ABHD11; CLDN3; CLDN4; WBSCR27; WBSCR28; ELN; LIMK1; EIF4H; MIR590; LAT2; RFC2; CLIP2; GTF2IRD1; GTF2IRD1; GTF2I; NCF1; GTF2IRD2; STAG3L2; LOC401379; GATSL1; WBSCR16; GTF2IRD2B; NCF1C; GTF2IP1; GATSL2; SPDYE3; SPDYE3; PMS2L14; STAG3L1; TRIM73; NSUN5B; POM121C; SPDYE5; PMS2L3; HIP1; CCL26; CCL24;

***** End Of Report *****

Suggested clinical correlation & follow up

Gopi.P
Sr.Technical Officer Genomics

A. Radhika
Co-Head Genomics

Dr. NAUSHAD
CHIEF SCIENTIFIC OFFICER
Reg No.: 43432

Approved by

Dr. Kiran Kumar
Consultant Genomics