MedGenome Labs Ltd.
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CHROMOSOMAL MICROARRAY ANALYSIS REPORT – MEDGENOME LABORATORIES

Full Name / Ref No:	**B/o SULFANA C.P**	Order ID/Sample ID:	**835881/8308686**
DOB/Age/Gest. Age:	1 Month & 29 Days	Gender:	-
Parental Sample ID:	-	Sample Type:	Peripheral Blood in EDTA
Referring Clinician:	Dr. SHAMNAD M Baby Memorial Hospital - Calicut 673004	Date of Sample Collection:	15-01-2024, 21:17:00
		Date of Sample Receipt:	16-01-2024, 10:45:00
		Date of Report:	27-01-2024, 14:43:21
Test Requested:	**Chromosomal Microarray - Affymetrix Cytoscan Optima low resolution genechip [MGM514]**		

CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

This infant presented with dysmorphic features. Her sample is being evaluated for pathogenic Copy Number Variations (CNVs) by microarray analysis.

ARRAY TYPE

Affymetrix CytoScan™ Optima Array

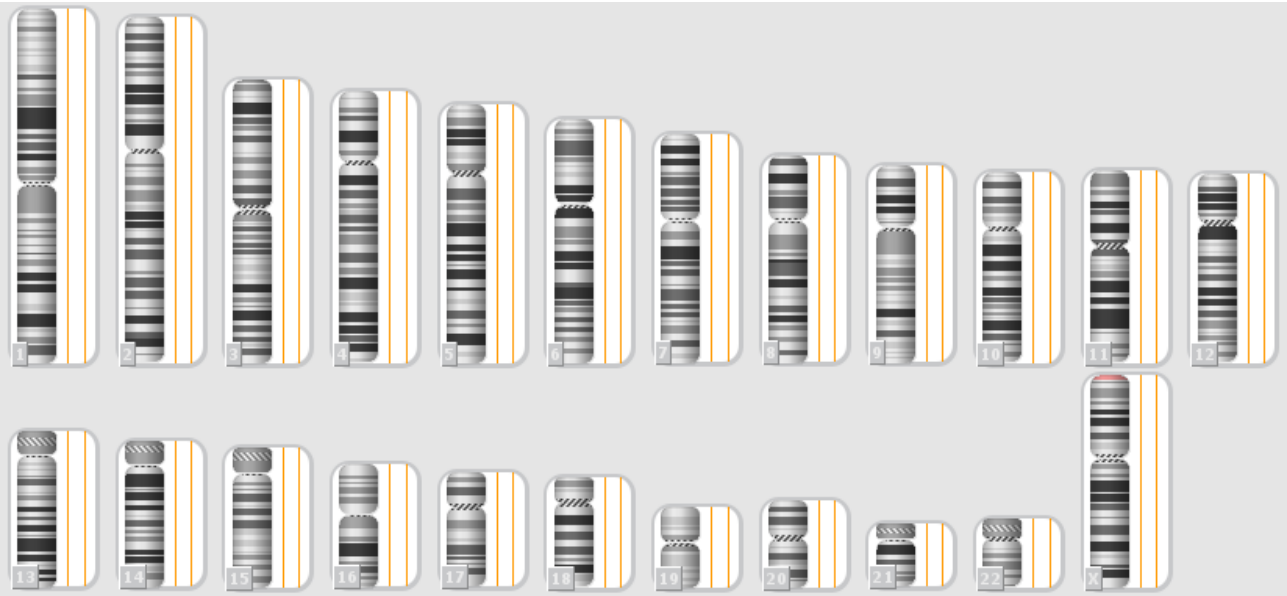
ISCN NOMENCLATURE

CNVs	**arr[GRCh38] (X,1-22)x2**
ROHs	arr[GRCh38] 6q22.33q24.1(127,067,041_139,479,755)x2 hmz

RESULTS

CNVs: NO SIGNIFICANT COPY NUMBER VARIATION DETECTED
ROHs : LONG CONTIGUOUS STRETCH OF HOMOZYGOSITY ON CHROMOSOME 6 - CLINICAL SIGNIFICANCE UNKNOWN

KARYOVIEW_CNVs



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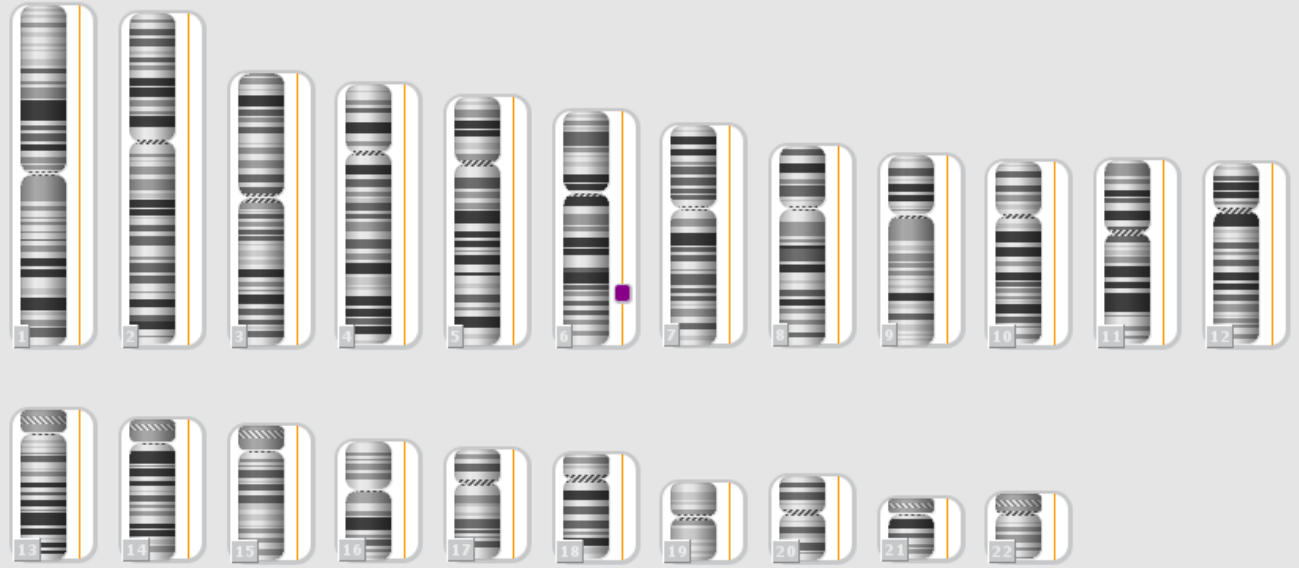
KARYOVIEW_ROHs



INTERPRETATION

The cytogenomic microarray analysis indicated no clinically significant abnormalities and is consistent with a female chromosome complement.

REGIONS OF HOMOZYGOSITY (ROHs)

Homozygosity for contiguous SNP alleles was detected on chromosome 6 as tabulated below. While this finding increases the suspicion for a recessive genetic condition mapping to this interval, it is important to stress that this finding is not diagnostic of a recessive condition. Clinical correlation and consideration of these possibilities is recommended. However, please consider the smaller stretches of homozygosity may only represent haplotype structure whereas the larger stretches are more likely to be identical by descent.

OMIM genes mapping to stretches of homozygosity are listed below (hg38):

Molecular Karyotype	Size (Kb)	Primary Genes (OMIM)
arr[GRCh38] 6q22.33q24.1(127,067,041_139,479,755)x2 hmz	12412.715	*RSPO3 (610574), RNF146 (612137), ECHDC1 (612136), KIAA0408 (619236), THEMIS (613607), PTPRK (602545), LAMA2 (156225), ARHGAP18 (613351), L3MBTL3 (618844), EPB41L2 (603237), AKAP7 (604693), ARG1 (608313), MED23 (605042), ENPP3 (602182), ENPP1 (173335), CCN2 (121009), MOXD1 (609000), STX7 (603217), TAAR9 (608282), TAAR8 (606927), TAAR6 (608923), TAAR5 (607405), TAAR2 (604849), TAAR1 (609333), VNN1 (603570), VNN3P (606592), VNN2 (603571), SLC18B1 (613361), RPS12 (603660), EYA4 (603550), TARID (616058), TCF21 (603306), TBPL1 (605521), SLC2A12 (610372), SGK1 (602958), ALDH8A1 (606467), HBS1L (612450), MYB (189990), AHI1 (608894), PDE7B (604645), BCLAF1 (612588), MAP7 (604108), MAP3K5 (602448), PEX7 (601757), SLC35D3 (612519), IL20RA (605620), IL22RA2 (606648), IFNGR1 (107470), OLIG3 (609323), WAKMAR2 (618508), TNFAIP3 (191163), PERP (609301), ARFGEF3 (617411), PBOV1 (605669), HEBP2 (605825), NHSL1 (620171), CCDC28A (615353), REPS1 (614825), HECA (607977), TXLNB (611438), CITED2 (602937)*

RECOMMENDATIONS

Genetic counselling and additional testing may be warranted based on specific phenotypic indications.

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TEST METHODOLOGY

Chromosomal microarray analysis (CMA) was performed using an Affymetrix CytoScan™ Optima array. This microarray consists of 315K oligonucleotide probes across the genome, including 18K unique non-polymorphic probes, and 148K bi-allelic SNP (single nucleotide polymorphism) probes. Genomic DNA (250 ng) was digested with Nsp1 and then ligated by Nsp1 adapter. Cytoscan Taq amplified PCR products of size 150 to 2200bp were purified using AMP pure beads and fragmented to the product size of 25bp to 125bp, biotin labelled, hybridized on CytoScan™ Optima gene chip, and then scanned. Data was analyzed using Chromosome Analysis Suite (ChAS) version 4.3.0.71. The analysis is based on the Human reference genome (GRCh38/hg38).

POSITIVE EVALUATION CRITERIA

Deletions smaller than 200 kb and duplications smaller than 500 kb may not be reviewed. Detected copy number variations (CNVs) are reported when found to have clear or suspected clinical relevance; CNVs devoid of relevant gene content or reported as common findings in the general population may not be reported. Regions of homozygosity are reported when a single LCSH is greater than 8-15 Mb (dependent upon chromosomal location and likelihood of imprinting disorder), or when the total autosomal LCSH proportion is greater than 3% (only autosomal LCSH greater than 3 Mb are considered for this estimate). Genomic linear positions are given relative to NCBI build 38 (hg38).

Test results are interpreted based on the recommendations and guidelines of International Standard of Cytogenomics Arrays (ISCA) as described below

Copy Number Change	A change in a segment of DNA at least 1kb in size that differ in copy number compared to reference genome. This could be either increase (Gain) or decrease (Loss) in chromosome number.
Pathogenic	This category includes CNVs, which overlaps with clearly established clinical significance. This usually means that a suspected disorder for which testing had been requested has been confirmed.
Likely Pathogenic	This category includes CNVs, that overlaps with a genomic region consistent with a syndrome containing OMIM morbid genes as well as deletions that overlap autosomal recessive genes (which may unmask a recessive allele associated with a syndrome/disorder).
Variants of unknown significance	This category includes CNVs, within a region which is not associated with genetic syndromes or symptoms of disease, deletions that overlap autosomal recessive genes (which may unmask a recessive allele but is not associated with a syndrome/disorder), *de novo* CNVs with no OMIM genes or genes associated with diseases
Likely Benign	The CNVs overlaps with the genome listed as benign in ISCA or other database based on large patient samples. Heterozygous duplication with no known OMIM morbid genes.
Benign	This category includes CNVs which are known not to be responsible for disease. Generally, no further action is warranted on such detections.

DISCLAIMER

- This technique only identifies copy number variations viz., gain and losses along with regions of heterozygosity.
- Copy Number Variations that are benign, likely benign and variants of uncertain significance with no clinical evidence may not be reported.
- Any other forms of polyploidy, truly balanced chromosome rearrangements (e.g., Inversions and balanced chromosomal imbalances), point mutation, small deletions and some mosaic conditions will not be detected.

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REFERENCES

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