CMA ANALYSIS

Patient ID		Gender		Location	
Patient Name		Clinician Name		Sample Collected	
Patient DOB		GA/LMP Date		Sample Received	
Age		Hospital Name		Report Released	

Test Requested:- CMA 315K | Sample Type:- Amniotic Fluid | Sample Quality:- Acceptable

CLINICAL INDICATION

A 38 years old female with a gestational age of 17 weeks 5 days. Her anomaly scan report showed unossified nasal bone, a wave reversal in DV. Suspicion: High risk for Trisomy 21.

METHOD

Chromosome Microarray Analysis (CMA) based Cytogenetics Analysis by CytoScan315K on Affymetrix Platform.

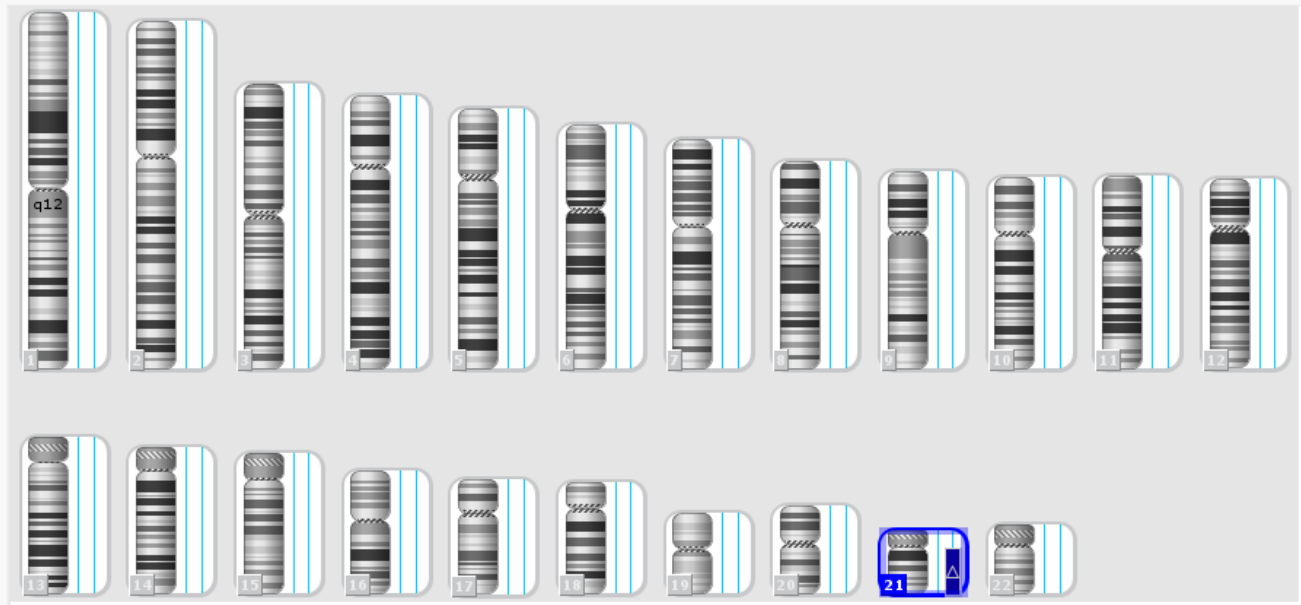
RESULT

Pathogenic variant is identified in the sample.

VARIANTS TABLE

CN state	Type	Chromosome	Cytoband	OMIM gene count	Size(kb)	Microarray nomenclature	Classification
3	Gain	21	q22.3	161	33,043	arr[GRCh38] 21q11.2q22.3(13,634,137_46,677,460)x3	Pathogenic

KARYOVIEW CNVs



898-898-0606 care@redcliffelabs.com www.redcliffelabs.com

Redcliffe Lifesciences Pvt. Ltd. H-55, 3rd Floor, Sec-63, Noida, UP-201301

CMA ANALYSIS

Patient ID		Gender		Location	
Patient Name		Clinician Name		Sample Collected	
Patient DOB		GA/LMP Date		Sample Received	
Age		Hospital Name		Report Released	

Test Requested:- CMA 315K	Sample Type:- Amniotic Fluid	Sample Quality:- Acceptable

INTERPRETATION

CMA analysis shows gain of 33,043 kbp on chromosome 21. This gain is consistent with trisomy 21 and it is caused by an extra copy of all or critical portion of chromosome 21. Genomic aneuploidy, defined as an abnormal number of copies of a genomic region, is a common caused of human genetic disorders.

Trisomy 21 is a most common caused of genetic cause of physical growth delay, mild to moderate intellectual disability, and characteristic facial features. The average IQ of a young adult with Down syndrome is 50, equivalent to the mental ability of an eight- or nine-year-old child, but this can vary widely. They also typically have poor immune function, They have an increased risk of a number of other health problems, including congenital heart defect, epilepsy, leukemia, thyroid diseases, and mental disorders.

DISCLAIMER

As per joint CCMG-SOGC guidelines(2018) for the use of CMA analysis for prenatal diagnosis and assessment of fetal loss, variant of uncertain significance(VOUS) smaller than 1000Kb deletion or 2 Mb duplication will not be reported. Clinical interpretation of given result should be evaluated within the context of the pateint's medical history and diagnostic laboratory test results.

All investigations have their limitations which are imposed by the limit of sensitivity & specificity of individual assay procedure as well as the quality of specimen received by the laboratory. This is not a diagnostic test and so not to be considered as a purpose diagnosis of any disease. This test is meant for chromosomal aberrations and their clinical relevance, this test detects the chromosomal abnormalities only under its limit of resolution. This report must be given only in the presence of medical professional to explain the findings and implications. Company will not liable for any direct, indirect, consequential, special, exemplary or any other damages.

Note: No significant maternal cell contamination is detected. Maternal cell contamination(MCC) was ruled out using STR markers.

RECOMMENDATION

Clinical correlation is suggested and further genetic counselling is recommended.

TECHNOLOGY

Chromosomal Microarray Based Cytogenetic Analysis by Cytoscan 315K on Affymetrix (Thermo Fisher Scientific) Platform. The CytoScan™ 315K Array enables the detection of high resolution copy number across the genome as well as providing allelic imbalance information from single nucleotide polymorphisms(SNPs). This high density array contains greater than 3,15,000 markers for copy number and genotype-able SNPs which provide high resolution copy number, accurate breakpoint estimation, copy-neutral loss of heterozygosity (LOH) detection, uniparental isodisomy (UPD), and regions identical-by-descent. The SNPs on this array are from the public SNP database (dbSNP). They were chosen to maximize genomic coverage, genotyping accuracy, and optimized to enable detection of homo- zygosity. This microarray and associated software is designed by Affymetrix and used for the purpose of identifying DNA copy number gains and losses associated with chromosomal imbalances. DNA for the experiment is isolated from the provided sample using a commercial kit that works on silica-membrane-based DNA purification. Genome version used is Genome Reference Consortium Human Build 38 (GRCh38) – hg38. The following database are regularly used for interpretation calls- Database of Genomic Variants (DGV), Curated variants from NCBI-dbVAR database (formerly defined by International Standards for Cytogenomic Arrays -ISCA), Clinical Genome Resource (ClinGen), OMIM, DECIPHER, CLINVAR, UCSC. ACMG reporting guidelines are followed in making variant calls.

898-898-0606 care@redcliffelabs.com www.redcliffelabs.com

Redcliffe Lifesciences Pvt. Ltd. H-55, 3rd Floor, Sec-63, Noida, UP-201301

CMA ANALYSIS

Patient ID		Gender		Location	
Patient Name		Clinician Name		Sample Collected	
Patient DOB		GA/LMP Date		Sample Received	
Age		Hospital Name		Report Released	

Test Requested:- CMA 315K	Sample Type:- Amniotic Fluid	Sample Quality:- Acceptable

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 (VOUS)	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.

REPORTING & LIMITATIONS

1. This is an investigational assay and should be followed up with appropriate tests as advised by the physician.
2. The assay detects chromosomal copy number changes in the form of duplications, deletions, mosaic duplications and deletions, Trisomy, Triploidy, Uniparental Disomy, Loss of heterozygosity, within the limits of its sensitivity, specificity, and resolution.
3. The assay is impacted by Tissue/DNA quality and in absence of resampling possibility, results are aligned to make most confident calls.
4. Regions having copy-neutral Loss of Heterozygosity, lesser than 10000kb in size, are not reported.
5. Smaller aberrations are reported. However, higher confidence is associated with > 1000kb change.
6. This technique will not confidently detect mosaicism at lesser than 20%, balanced translocations, inversions and point mutations.
7. The assays detection is limited to regions with adequate probe representation on the array.

REFERENCES

1. Firth, Helen V., Shola M. Richards, A. Paul Bevan, Stephen Clayton, Manuel Corpas, Diana Rajan, Steven Van Vooren, Yves Moreau, Roger M. Pettett, and Nigel P. Carter. "DECIPHER: database of chromosomal imbalance and phenotype in humans using ensembl resources." The American Journal of Human Genetics 84, no. 4 (2009): 524-533.
2. Hamosh, Ada, Alan F. Scott, Joanna S. Amberger, Carol A. Bocchini, and Victor A. McKusick. "Online Mendelian Inheritance in Man (OMIM), a knowledgebase of human genes and genetic disorders." Nucleic acids research 33, no. suppl_1 (2005): D514-D517.
3. Landrum, Melissa J., Jennifer M. Lee, Mark Benson, Garth Brown, Chen Chao, Shanmuga Chitipiralla, Baoshan Gu et al. "ClinVar: public archive of interpretations of clinically relevant variants." Nucleic acids research 44, no. D1 (2016): D862-D868.
4. Ljunger, Elisabeth, Sven Cnattingius, Catarina Lundin, and Göran Annerén. "Chromosomal anomalies in first trimester miscarriages." Acta obstetricia et gynecologica Scandinavica 84, no. 11 (2005): 1103-1107.
5. "Clinical practice. The care of children with Down syndrome". European Journal of Pediatrics. 169 (12): 1445–52 doi:10.1007/s00431-010-1253-0. PMC 2962780. PMID 20632187:
6. National Academies of Sciences, Engineering, and Medicine. 2015. Improving Diagnosis in Health Care. Washington, DC: The National Academies Press.

END OF REPORT

Mr. Nakul Mohan
Senior Executive
MSc biotechnology

Reviewed by
Dr. Prabhaker Yadav
Postdoc-Molecular Genetics
Section Head-NGS

Dr. Himani Pandey
Lab Head - Genomics
Post-Doc.Fellowship
(Medical Genetics),SGPGIMS

898-898-0606 care@redcliffelabs.com www.redcliffelabs.com
Redcliffe Lifesciences Pvt. Ltd. H-55, 3rd Floor, Sec-63, Noida, UP-201301

Terms and Conditions of Reporting

1. The presented findings in the Reports are intended solely for informational and interpretational purposes by the referring physician or other qualified medical professionals possessing a comprehensive understanding of reporting units, reference ranges, and technological limitations. The laboratory shall not be held liable for any interpretation or misinterpretation of the results, nor for any consequential or incidental damages arising from such interpretation.

2. It is to be presumed that the tests performed pertain to the specimen/sample attributed to the Customer's name or identification. It is presumed that the verification particulars have been cleared out by the customer or his/her representation at the point of generation of said specimen / sample. It is hereby clarified that the reports furnished are restricted solely to the given specimen only.

3. It is to be noted that variations in results may occur between different laboratories and over time, even for the same parameter for the same Customer. The assays are performed and conducted in accordance with standard procedures, and the reported outcomes are contingent on the specific individual assay methods and equipment(s) used, as well as the quality of the received specimen.

4. This report shall not be deemed valid or admissible for any medico-legal purposes.

5. The Customers assume full responsibility for apprising the Company of any factors that may impact the test finding. These factors, among others, includes dietary intake, alcohol, or medication / drug(s) consumption, or fasting. This list of factors is only representative and not exhaustive.