LABORATORY REPORT

Redcliffe labs

MC-5280

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 750K	Sample Type:- Blood	Sample Quality:- Adequate

CLINICAL INDICATION

Whole exome sequencing revealed a heterozygous likely pathogenic variant in FBN1 (c.763G>A). The affected sibling carries the same variant. The proband presents with additional phenotypic features, including lens dislocation (explained by FBN1) along with polycoria and glaucoma.

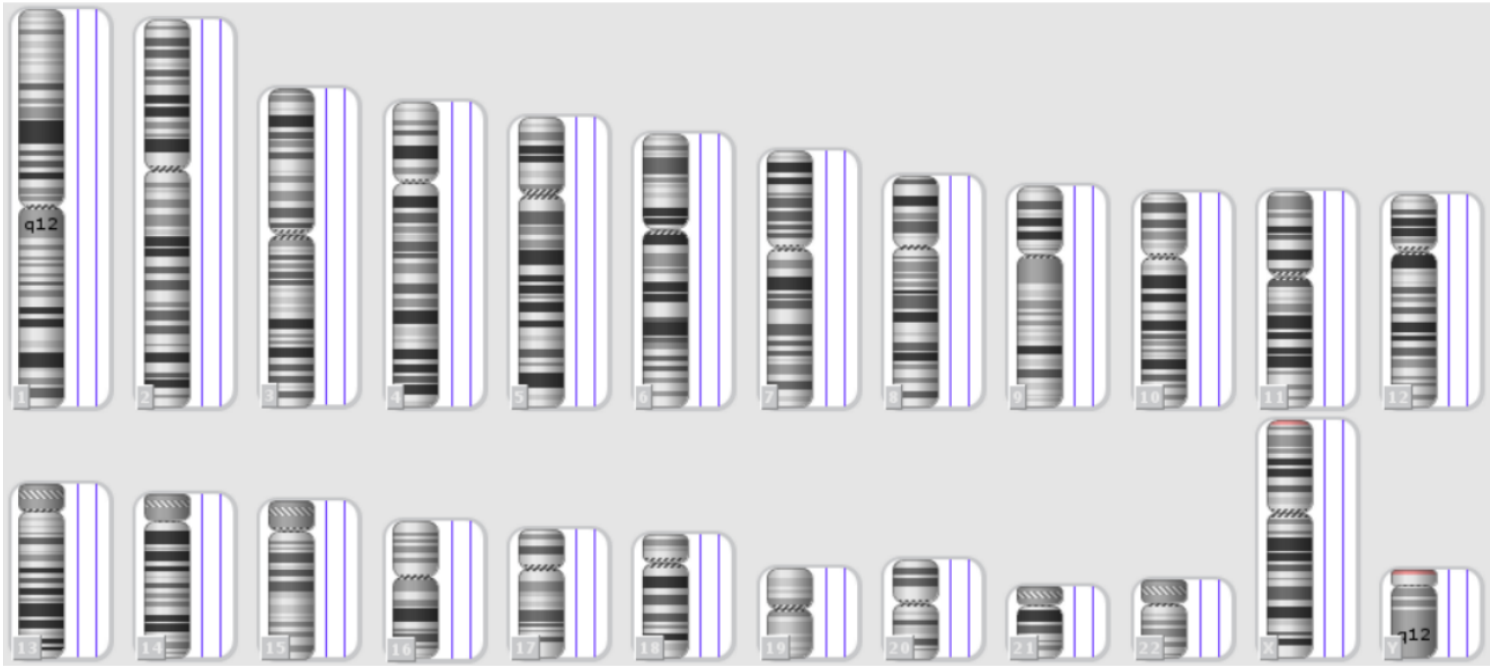
METHOD

Chromosome Microarray Analysis (CMA) based Cytogenetics Analysis by CytoScan 750K on Affymetrix Platform.

RESULT

No aneuploidy is detected for the requested sample.

KARYOVIEW CNVs



INTERPRETATION

No full chromosomal trisomy, monosomy or polyploidy was detected in the sample.
No significant single nucleotide polymorphism or copy number variations were detected during the analysis of the sample.

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RECOMMENDATION

Clinical correlation is suggested, and further genetic counselling is recommended.

TECHNOLOGY

Chromosomal Microarray Based Cytogenetic Analysis by Cytoscan 750K on Affymetrix (Thermo Fisher Scientific) Platform. The CytoScan™ 750K 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 750,000 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 homozygosity. 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.

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.

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 200Kb deletion or 400 kb 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: This report pertains solely to the blood sample provided in response to the clinician's request.

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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 10MB in size, are not reported.
5. Smaller aberrations are reported. However, higher confidence is associated with > 100kb 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. Lu, Xinyan, Chad A. Shaw, Ankita Patel, Jiangzhen Li, M. Lance Cooper, William R. Wells, Cathy M. Sullivan et al. "Clinical Implementation of Chromosomal Microarray Analysis: Summary of 2513 Postnatal Cases." PLoS One 2, no. 3 (2007): e327.
2. South, Sarah T., Charles Lee, Allen N. Lamb, Anne W. Higgins, and Hutton M. Kearney. "ACMG Standards and Guidelines for Constitutional Cytogenomic Microarray Analysis, Including Postnatal and Prenatal Applications: revision 2013." Genetics in Medicine 15, no. 11 (2013): 901.
3. Armour, Christine M., Shelley Danielle Dougan, Jo-Ann Brock, Radha Chari, Bernie N. Chodirker, Isabelle DeBie, Jane A. Evans et al. "Practice guideline: joint CCMG-SOGC recommendations for the use of chromosomal microarray analysis for prenatal diagnosis and assessment of fetal loss in Canada." Journal of medical genetics 55, no. 4 (2018): 215-221.

END OF REPORT

Note: This is a sample report for illustrative purpose only. Actual report may vary

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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.