Name : **********

Lab No. : 111516723 **Age** **:** 28 Years **Gender:** Female

A/c Status : P **Ref by :** Dr. **********

Collected: 23-11-2015
Received: 24-11-2015 09:22:15
Reported: 03-12-2015

Report Status: Final

ChromoFic®, Chromosome SNP Microarray 750K, High Resolution

SPECIMEN

Peripheral blood

CLINICAL INDICATION

Failure to thrive, dysmorphism, triangular face, long philtrum, congenital heart disease, increased carrying angle (Suspected Turner syndrome)

RESULT SUMMARY

Following genetic abnormalities were detected in the sample submitted for analysis.

Sr. No.	Copy No. state	Type	Chromosome	Cytoband	Size (kbp)	Number of genes	ISCN nomenclature	Interpretation
1.	1	**Loss**	**5**	q15	7452.68	28	arr[hg19]5q15q21.1 (93,727,367-101,180,049)x1	Likely pathogenic
2.	1.35	**Mosaic loss**	**7**	q21.11	5195.01	27	arr[hg19] 7q21.11q21.2 (86,379,114-91,574,130)x1-2	Uncertain
3.	1	**Loss**	**7**	q21.12	3716.15	17	arr[hg19] 7q21.12q21.13(87,145,817-90,861,968)x1	Uncertain
4.	2.2	**Mosaic Gain**	**X**	q13.2	4644.54	30	arr[hg19] Xq13.2q21.1(72,634,004-77,278,543)x2-3	Likely Pathogenic
5.	2.21	**Mosaic Gain**	**X**	q26.2	2271.88	44	arr[hg19] Xq26.2q26.3(133,073,181-135,345,059)x2-3	Pathogenic
6.	1	**Gain**	**Y**	p11.2	957.92	4	arr[hg19] Yp11.2(5,156,574-6,114,495)x1	Uncertain

LOH (Loss of Heterozygosity) -- in a chromosomal region due to loss of one parental copy of that region

Gain – Gain of certain genes & / or surrounding chromosomal region
Loss – Loss of certain genes & / or surrounding chromosomal region.

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RESULT

Abnormal with apparent unbalanced t(5;7) derivative

INTERPRETATION

1. CMA test shows loss of about 7452 kbp in the 5q15 region of the proband. Microdeletions of the 5q14.3-q15 region have been described in patients with abnormal brain development, severe ID and epilepsy **[1].**
2. There is a loss of 3716 kbp in the 7q21.12 region. Some degree of mosaicsm was also observed in this region. No clinical correlation could be established with the indicated phenotype.
3. Mosaic gains were observed in two regions of the X chromosome; Xq13.2 and Xq26.2. Gains in the Xq13.2 have been associated with intellectual disability and dysmorphism. Important genes are: **SLC16A2, KIAA2022 and ATRX [2].**
4. Gains in Xp26.2 have been associated with X linked intellectual disability (XLID). Important genes are: **PHF6, HPRT1 and SLC9A6 [3]**
5. A 957 kbp single copy gain of Y chromosome material was observed. This finding appears to be a result of interchromosomal transposition of Yp11.2 / PCDH11Y to Xq21.3 region on the X chromosome. We could not find any direct correlation of this finding with the indicated phenotype.

GENES INVOLVED

Genes in Cytoband region 5q15: KIAA0825, **ANKRD32, MCTP1, FAM81B, TTC37,** ARSK, GPR150, RFESD, SPATA9, RHOBTB3, GLRX, C5orf27, ELL2, MIR583, PCSK1, CAST, ERAP1, ERAP2, LNPEP, LIX1, RIOK2, RGMB, RGMB-AS1, CHD1, LOC100289230, LOC100133050, FAM174A, ST8SIA4

Genes in Cytoband region 7q21.11: GRM3, KIAA1324L, DMTF1, TMEM243, TP53TG1, CROT, ABCB4, ABCB1, RUNDC3B, SLC25A40, DBF4, ADAM22, SRI, STEAP4, ZNF804B, C7orf62, DPY19L2P4, STEAP1, STEAP2, C7orf63, GTPBP10, LOC101409256, CLDN12, CDK14, FZD1, MTERF, AKAP9

Genes in Cytoband region 7q21.12: ABCB1, RUNDC3B, SLC25A40, DBF4, ADAM22, SRI, STEAP4, ZNF804B, C7orf62, DPY19L2P4, STEAP1, STEAP2, C7orf63, GTPBP10, LOC101409256, CLDN12, CDK14

Genes in Cytoband region Xq13.2: CDX4, MAP2K4P1, CHIC1, TSIX, XIST, JPX, FTX, MIR421, MIR374B, MIR374C, MIR545, MIR374A, ZCCHC13, **SLC16A2**, RLIM, **KIAA2022**, ABCB7, UPRT, ZDHHC15, TTC3P1, MAGEE2, PBDC1, MAGEE1, MIR384, FGF16, **ATRX**, MAGT1, COX7B, ATP7A, PGAM4

Genes in Cytoband region Xq26.2: GPC3, MIR363, MIR92A2, MIR19B2, MIR20B, MIR18B, MIR106A, CCDC160, **PHF6, HPRT1**, MIR450B, MIR450A1, MIR450A2, MIR542, MIR503HG, MIR503, MIR424, LINC00629, PLAC1, FAM122B, FAM122C, MOSPD1, SMIM10, FAM127C, FAM127A, FAM127B, LINC00087, LINC00633, CXorf48, ZNF75D, ZNF449, LINC00086, DDX26B, CT45A1, CT45A2, CT45A4, CT45A3, CT45A5, CT45A6, SAGE1, MMGT1, **SLC9A6**, FHL1, MAP7D

Genes in Cytoband region Yp11.2: PCDH11Y, TTTY23, TTTY23B, TSPY2

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METHODOLOGY

SNP microarray analysis was performed using the Affymetrix Cytoscan 750K platform which uses over 550,000 non-polymorphic probes and 200,000 SNP probes. 250 ng of total genomic DNA extracted from peripheral blood was digested and amplified. Purified DNA products were fragmented and biotin labeled and hybridized to the Affymetrix Cytoscan 750K GeneChip. All data was analyzed and reported using the February 2009 NCBI human genome build 37.1 (hg19). Deletions larger than 200 kilobases, duplications larger than 500 kilobases, regions with interstitial absence of heterozygosity (AOH) larger than 10.0 megabases and regions with terminal AOH larger than 5.0 megabases are generally reported.

KARYOVIEW

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RECOMMENDATIONS

1. Parental karyotype is recommended to rule out balance translocation
2. Genetic counselling is also recommended

COMMENTS

This array detects copy number changes and absence of heterozygosity (AOH), which may be due uniparentaldisomy (UPD) or identity by descent (IBD). The array detects gains and losses at a minimum of 400kb and 200kb, respectively, across the genome, or smaller (≥50Kb) for clinically relevant deletion/duplication syndromes, subtelomere, and pericentromere region or targeted genes. Significant AOH is reported for stretches of DNA > 15Mb on a single chromosome, suggestive of UPD or >10Mb on multiple chromosomes, suggestive of IBD. Benign copy number changes present in >1% of the population are not reported. This test detects gain or loss of entire chromosomes, deletions and duplications of the loci represented on this array. Balanced rearrangements such as Robertsonian translocations, reciprocal translocations & inversions and balanced insertions will not be detected by this test. It will also not detect DNA mutations, deletions or duplications below the resolution of this array or disease associations based on linkage analysis. SNP analysis can detect uniparentalisodisomy and some cases of heterodisomy, but this test cannot rule out the presence of UPD caused by heterodisomy. The detection of mosaicism by this array is variable and is dependent on the size of the chromosomal imbalance, type of the array used and the quality of array results. Results of this test are for investigational purposes only as per the assay's manufacturer. The assay has not been cleared or approved for specific uses by FDA.

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LIMITATIONS

This test does not detect:

- Base pair mutations
- Balanced rearrangements (translocations, inversions and balanced insertions)
- Imbalances of mitochondrial genome

This test may not report:

- CNVs devoid of relevant gene content or reported as common findings in the general population
- Duplications <400 kb and deletions <50 kb, depending on genomic content of the imbalance
- LCSH <8 Mb (telomeric) or <15 Mb (interstitial) on imprinted chromosomes
- LCSH <10 Mb (telomeric) or <15 Mb (interstitial) on non-imprinted chromosomes
- LCSH <3% of the autosomal genome

LCSH- Long Contiguous Stretches of Heterozygosity; CNV-Copy Number Variants

Note:

1. *This report is solely based on genetic makeup of the individual and mutation detected at the time of sample collection.*
2. *Individuals can show new mutations based on environmental changes that can alter the risk for different diseases.*
3. *All results must be clinically correlated.*

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