Results Male genomic profile with a variant of uncertain significance

**ISCN**
arr 18p11.32p11.23(2,839,614-8,299,575)x3

*INTERPRETATION:* An array profile consistent with a male sex chromosome complement was identified. No diagnostic copy number changes were observed, however, a variant of uncertain significance was identified: a heterozygous copy number gain of 5.5 Mb on 18p11.32-p11.2.

There is a paucity of reports regarding this particular duplication. Although this region spans 5.5 Mb, it contains only two OMIM disease-associated genes: LPIN2 and TGIF1. Homozygous missense mutations in LPIN2 have been reported in association with the autosomal recessive Majeed syndrome (OMIM 605519). Heterozygous missense mutations in TGIF1 have been associated with holoprosencephaly-4 (OMIM 142946). We did not identify any reports of whole gene duplications of LPIN2 or TGIF1 in association with any syndromes. Based on the available information, this duplication is best classified as a variant of uncertain clinical significance. Parental studies may be of assistance in further clarifying the nature of this duplication.

CONFIRMATION: Results for confirmatory FISH analysis are pending.
RECOMMENDATION: Clinical correlation, genetic counseling, and parental studies are recommended. For parental studies, please collect 4 mL blood in a green top (NaHep) tube and send along with a completed CombiMatrix Test Requisition Form. For assistance, please contact Client Services at (800) 710-0624.


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METHOD: CombiSNP™ Array for Prenatal Analysis analysis was performed using a custom-designed Illumina single nucleotide polymorphism (SNP) array. This array contains >845,000 SNP markers covering both coding and non-coding human genome sequences. The median spatial resolution between probes is 1 Kb within gene rich regions and 5 Kb outside of gene-rich regions. Extracted DNA was evaluated for copy number changes involving ≥16 probes, and for regions of homozygosity ≥10 Mb. Genomic imbalances are reported using UCSC Human Genome Build 19 (NCBI build 37, Feb 2009). Mosaicism for partial or whole chromosome aneuploidy is reported when present at or above the detection threshold of 15%. The CombiSNP™ Array for Prenatal Analysis lot number 9347028048 from Illumina was used. This test was performed by CombiMatrix Diagnostics (Irvine, CA; CLIA #05D1052995).

DISCLAIMER: The CombiSNP™ Array for Prenatal Analysis is designed to identify copy number changes genome-wide, covering regions of known clinical significance (recognized microduplication/microdeletion syndromes), pericentromeric and subtelomeric regions, and the genomic backbone. As with any microarray testing, the CombiSNP™ Array for Prenatal Analysis does not detect: point mutations; small intragenic deletions or duplications; balanced chromosomal aberrations such as Robertsonian or reciprocal translocations, inversions, and balanced insertions; or imbalances in genomic regions that are not represented on the microarray. Carrier status for recessive disorders due to a deletion/duplication of a single gene is typically not reported. Copy number gains and losses in the regions that contain no known or suspected clinical associations are not reported. The possibility of consanguinity will be reported if regions of homozygosity (ROH) comprise ≥10% of the entire genome. Uniparental disomy testing will be recommended for cases in which ROH on an imprinted chromosome is detected in the absence of other large ROH on other chromosomes. Although this test can detect uniparental isodisomy, it cannot detect uniparental heterodisomy. If an X-linked or autosomal recessive disorder is clinically suspected, please contact us for a complete list of the ROH that were detected. A list of the genes according to inheritance pattern can be obtained by visiting the University of Miami’s Online SNP Evaluation Tool at: http://www.ccs.miami.edu/cgi-bin/ROH/ROH_analysis_tool.cgi. Clinical assessment is required to determine if any of these genes may be implicated. The clinical implications of some of the reported findings may be unknown at this time. Normal microarray results do not rule out the possibility of a genetic disorder or syndrome that is due to a genetic alteration not detected or evaluated by this test. Consultation with a genetics professional is recommended for results interpretation. As a participant in the International Collaboration for Clinical Genomics (ICCG), this clinical cytogenetics laboratory contributes submitted clinical information and test results to a HIPAA compliant, de-identified public database as part of the NIH’s effort to improve understanding of the relationship between genetic changes and clinical symptoms. Confidentiality is maintained. Patients may request to opt out of this scientific effort by calling the laboratory at 800.710.0624 and asking to speak with a laboratory genetic counselor.

CombiSNP™ Array for Prenatal Analysis was developed and its performance characteristics determined by CombiMatrix Diagnostics. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. This test is intended for clinical use. It should not be regarded as investigational or for research use only. CombiMatrix Diagnostics laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA ‘88) as qualified to perform high complexity clinical laboratory testing.