

Report date:  
Case file ID:  
Patient:

**Microarray Chromosome Analysis with Parental Support**<sup>TM</sup>

|                            |                             |   |   |
|----------------------------|-----------------------------|---|---|
| Patient:<br>Date of birth: | Attending physician:<br>N/A | Clinic:<br>Prom-Test LLC<br>Komitas Ave 58/12<br>Yerevan 0014<br>+37495155858 | Samples collected:<br>05/13/2022<br>Samples received:<br>05/23/2022 15:48 PDT<br>Sample type: Products of<br>Conception (POC) |
|----------------------------|-----------------------------|---|---|

| Sample                                | Result Details  | Parental Origin of Abnormality |
|---------------------------------------|---|--------------------------------|
| <b>9181714.2-2-P</b><br>POC125588-DNA | <b>RESULT: Abnormal Male</b><br><b>MICROARRAY RESULT: arr(16)x3</b><br><b>Clinical Interpretation:</b> Abnormal result. Trisomy 16 detected. Trisomy 16 is generally incompatible with fetal survival. Overall, trisomy is found in approximately 45% of miscarriages. Genetic counseling is recommended to discuss the significance of this result. Referral to a local genetic counselor may be considered. | Maternal                       |

## REPORT TERMINOLOGY DEFINITIONS

### Clinical Significance

Results listed as 'Abnormal' are generally associated with an abnormal phenotype which could result in miscarriage or an affected livebirth.

### Parental Origin of Abnormality

If a biologic parental sample is submitted, parental origin of an abnormality may be reported except in cases with mosaicism. Reporting will fall into one of three categories: "Maternal" indicates that all abnormalities in the sample tested are due to loss or gain of the maternal copy of the chromosome and/or segment; "Paternal" indicates that all abnormalities in the sample tested are due to loss or gain of the paternal copy of the chromosome and/or segment; "Mixed" indicates that abnormalities in the sample tested are a combination of maternal loss/gain and paternal loss/gain.

### UPD

Uniparental Disomy (UPD) is defined as having two copies of a given chromosome from one parent and none from the other. This testing can detect UPD due to heterodisomy (two homologous or 'unmatched' chromosomes from one parent) and UPD of a single chromosome due to isodisomy (two identical or 'matched' chromosomes from one parent). UPD of every chromosome due to isodisomy will be reported as full UPD. UPD detection is based on a statistical model validated on single cells from a UPD cell line.

### Gains/Losses

Gains and losses occur when a segment of a chromosome is missing (loss) or repeated (gain). Losses are indicative of a deletion and gains are indicative of a duplication. Gains and losses can occur as isolated de novo events or through inheritance of unbalanced rearrangements. Gains (duplications) and losses (deletions) diagnosed in a fetus or livebirth are generally associated with an abnormal phenotype. The criteria for a reportable gain and/or loss include: (a) Gain or loss greater than 5 MB in size, (b) One of the known deletion/duplication syndromes, (c) Terminal gain or loss greater than 1 MB in size, (d) All interstitial gains and losses < 5Mb in size and > 1 MB in size are reviewed and will be reported based on clinical relevance. The cytogenetic band breakpoints reported are based on microarray probe location using Human Genome Build hg18 and are the minimally deleted and/or duplicated regions. Databases used for clinical interpretation of gains/losses include PubMed, OMIM, Decipher, UCSC Genome Browser, and Database of Genomic Variants.

### Regions of Homozygosity

Regions of homozygosity will be reported if two or more tracks of homozygosity >8 Mb in size are detected. This is likely consistent with identity by descent. Details of the regions of homozygosity can be provided by Natera upon request.

### Testing methodology

Samples are analyzed using Illumina HumanCytoSNP-12 v 2.1 DNA BeadChips which include ~300,000 SNPs genome-wide and targeting regions shown to be important for cytogenetic analysis. The mean spacing of the SNPs is 9.7 kb resulting in dense coverage of ~250 disease regions, including subtelomeric regions, pericentromeric regions, and sex chromosomes, commonly screened in cytogenetics labs. Analysis includes an informatics-based algorithm (Parental Support<sup>TM</sup>) that references parental genotype data to rule out maternal cell contamination and determine parental origin of chromosome abnormalities. This testing platform uses Human Genome Build hg18.

### Limitations

There remain certain chromosome abnormalities that this analysis will not detect. These include:

- Balanced chromosome rearrangements (balanced translocations or inversions).
- Some gains or losses of chromosome material less than 5 MB.
- Specific genes and conditions caused by single gene mutations.
- Copy number variants (CNVs).
- Tetraploidy (four copies of the complete set of chromosomes) if maternal and paternal chromosome contributions are equal.
- Low levels of chromosome mosaicism.
- Full trisomy cannot be distinguished from trisomy due to a Robertsonian translocation (involves chromosomes 13, 14, 15, 21, or 22) or isochromosome. Depending on patient history, parental chromosomes may be considered to rule out a Robertsonian translocation or isochromosome in one of the parents.

This analysis does not test specific genes and will not detect conditions caused by single gene mutations.

Reporting of certain chromosome abnormalities will be as follows:

- Two copies of the Y chromosome will always be reported as a single Y.

### Genetic Counseling

Genetic counseling may be considered for discussion of these results. Natera genetic counselors only offer information about Natera's tests and do not provide comprehensive genetic counseling based on a complete review of family and personal medical history. If a patient has questions or issues beyond the specific details of Natera's tests and test results, the patient's physician should consider referring the patient to a local genetic counselor or clinical geneticist for comprehensive genetic counseling. Genetic counselors in the patient's community may be found through [www.nsgc.org](http://www.nsgc.org).

### References

- Genomic Imbalance in Products of Conception Single-Nucleotide Polymorphism Chromosomal Microarray Analysis. Levy B, et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):202-9.
- Informatics enhanced SNP microarray analysis of 30 miscarriage samples compared to routine cytogenetics. Lathi RB, et al. PLoS One. 2012;7(3):e31282.
- Preclinical validation of a microarray method for full molecular karyotyping of blastomeres in a 24-h protocol. Johnson DS, et al. Hum Reprod. 2010 Apr;25(4):1066-75.

Non-paternity may produce inconclusive test results and may be reported out as no results. Natera has a policy of non-disclosure for non-paternity.

Natera's POC testing can also be performed on prior losses preserved in paraffin. If there is interest in testing a previous loss, please contact Natera for details.

These results should always be interpreted by a clinician in the context of clinical and familial data.

Approved by:



J. Dianne Keen-Kim, Ph.D., FACMGG  
Senior Laboratory Director

This test was developed by Natera, Inc. a laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA). This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). Although FDA does not currently clear or approve laboratory-developed tests in the U.S., certification of the laboratory is required under CLIA to ensure the quality and validity of the tests. ©2020 Natera, Inc.