Report Date:	3/8/2024
Case File ID:	11393572
Secondary Kit ID:	B033375
Test Methodology:	Next Generation Sequencing (NGS)

natera | Spectrum® Preimplantation genetics

About this test: Spectrum preimplantation genetic testing (PGT) for aneuploidy evaluates embryos for extra or missing chromosomes, or pieces of chromosomes, improving the chances of a healthy pregnancy.

PREIMPLANTATION GENETIC TESTING (PGT) FOR ANEUPLOIDY WITH MOSAICISM

Patient:	Partner:	Attending Physician:	Clinic:	Samples Collected:
Megan Thielman	Kaan Divringi	Temeka Zore, REI	Spring Fertility	02/27/2024
Date of Birth:	**Date of Birth:**			**Samples Received:**
12/07/1984	11/10/1982			02/28/2024
Egg donor:	**Sperm donor:**			**Sample Type:**
-	-			Embryo trophectoderm (TE) biopsy

*If the ordering provider has questions about these results, please call **844-778-4700** and ask for the genetic counselor on call or e-mail **gc@natera.com**.*

Case Specific Notes:N/A

Euploid

Sample	Result Details	Sex
1 26894377.A-2	Euploid	XX
4 26894377.D-2	Euploid	XX

Segmental and/or Mosaic

Sample	Result Details	Sex
2 26894377.C-2	HMT 19	XX

Aneuploid

Sample	Result Details	Sex
9 26894377.B-2	Trisomy 15, 16	XX

Report Date: 3/8/2024
Case File ID: 11393572
Secondary Kit ID: B033375
Test Methodology: Next Generation Sequencing (NGS)

natera | Spectrum® Preimplantation genetics

Detailed Information on Chromosome Copy Number

Data from each sample is presented in one column. Each row corresponds to a particular chromosome. Each cell in the table represents the number of copies for that chromosome (or the type in case of sex chromosomes). HM: High Mosaic, LM: Low Mosaic, T: Trisomy, M: Monosomy. Del represents a deletion and Dup represents a duplication of the short (p) or long (q) arm.

	1	9	2	4
	26894377.A-2	26894377.B-2	26894377.C-2	26894377.D-2
Chr-1	2	2	2	2
Chr-2	2	2	2	2
Chr-3	2	2	2	2
Chr-4	2	2	2	2
Chr-5	2	2	2	2
Chr-6	2	2	2	2
Chr-7	2	2	2	2
Chr-8	2	2	2	2
Chr-9	2	2	2	2
Chr-10	2	2	2	2
Chr-11	2	2	2	2
Chr-12	2	2	2	2
Chr-13	2	2	2	2
Chr-14	2	2	2	2
Chr-15	2	3	2	2
Chr-16	2	3	2	2
Chr-17	2	2	2	2
Chr-18	2	2	2	2
Chr-19	2	2	HMT	2
Chr-20	2	2	2	2
Chr-21	2	2	2	2
Chr-22	2	2	2	2
sex-chr	XX	XX	XX	XX

Report Date:	3/8/2024
Case File ID:	11393572
Secondary Kit ID:	B033375
Test Methodology:	Next Generation Sequencing (NGS)

natera | Spectrum® Preimplantation genetics

Result Nomenclature		
Embryo Result	**Spectrum Report Result**	**ISCN / HGVS Nomenclature**
Euploid Female	Euploid	46,XX
Euploid Male	Euploid	46,XY
Mosaic Monosomy	LMM or HMM chromosome number	45,XX,-chromosome number (LMM/HMM)/46,XX or 45,XY, -chromosome number (LMM/HMM)/46,XY
Mosaic Trisomy	LMT or HMT chromosome number	47,XX,+chromosome number (LMT/HMT)/46,XX or 47,XY, +chromosome number (LMT/HMT)/46,XY
Mosaic Deletion	LMDel or HMDel chromosome number	seq[GRCh37] mos del(chromosome number)(p) or seq[GRCh37] mos del(chromosome number)(q)
Mosaic Duplication	LMDup or HMDup chromosome number	seq[GRCh37] mos dup(chromosome number)(p) or seq[GRCh37] mos dup(chromosome number)(q)
Partial Deletion	Del (chromosome number) (q) or (p) (size in Mb)	seq[GRCh37] del(chromosome number)(p) or seq[GRCh37] del(chromosome number)(q)
Partial Duplication	Dup (chromosome number) (q) or (p) (size in Mb)	seq[GRCh37] dup(chromosome number)(p) or seq[GRCh37] dup(chromosome number)(q)
Monosomy	Monosomy,chromosome number	45,XY,-chromosome number or 45,XY,-chromosome number
Trisomy	Trisomy,chromosome number	47,XX,+chromosome number or 47,XY,+chromosome number
Triploidy	Triploid	69,XXY or 69,XYY

Euploid
Results reported as euploid indicate that two copies of each chromosome are detected. Two copies of a particular chromosome is referred to as “disomy” and two copies of every chromosome (1-22, and the sex chromosomes, XX or XY) is referred to as “euploid”. This represents the normal or balanced number of chromosomes in a sample.

Low-level Mosaic Aneuploidy
A mosaic result indicates the presence of one or more chromosomally abnormal cell lines mixed with a normal cell line . The level of mosaicism detected may not represent the chromosomal aneuploidy of the embryo or a subsequent re-biopsy sample. Mosaicism estimated to be between 30% and <50% is reported as low-level mosaicism. Low level mosaicism estimated <30%, if detected, is reported as Euploid.

High-level Mosaic Aneuploidy
A mosaic result indicates the presence of one or more chromosomally abnormal cell lines mixed with a normal cell line . The level of mosaicism detected may not represent the chromosomal aneuploidy of the embryo or a subsequent re-biopsy sample. Mosaicism estimated to be between 50% and <70% is reported as high-level mosaicism. Mosaicism estimated ≥70%, if detected, is reported as Aneuploid.

Deletion/Duplication (del/dup)
Deletions and duplications occur when a segment of a chromosome is missing (deletion) or added (duplication). Deletions and duplications can occur as isolated *de novo* events or through inheritance of unbalanced translocations from a parent with balanced translocations. Deletions and duplications diagnosed in a fetus or livebirth are generally associated with an abnormal phenotype. The report will indicate a del (chromosome number) (band) (size in megabase; Mb) if there is a deletion and dup (chromosome number) (band) (size in megabase; Mb) if there is a duplication. The band designation specifies whether the abnormality is on the short arm (p) or the long arm (q) of the chromosome. Deletions or duplications smaller than 10 Mb of DNA will not be identified with this technology when PGT-A is performed, and smaller than 7 Mb of DNA will not be identified when PGT-SR is performed. The size of the reported deletion or duplication (in Mb) is approximate and based on molecular karyotyping with next generation sequencing technology.

Monosomy
Results reported as monosomy indicate that one copy of the specified chromosome is detected.

Trisomy
Results reported as trisomy indicate that three copies of the specified chromosome are detected.

Triploid
Results reported as triploid indicate that three copies of the complete set of chromosomes are present, for a total of 69 chromosomes. Triploid with sex chromosome complement of XXY or XYY can be detected by this technology .

Complex Abnormal
An embryo sample will be reported as “complex abnormal” if there is a combination of five or more abnormal findings.

Inconclusive Results or Insufficient DNA Results
Common reasons for inconclusive results or insufficient DNA results in a sample include : 1) anucleated blastomere, a situation which occurs most often with embryos of poor morphology when the cell or cells biopsied have no DNA; 2) displacement or disruption of the sample during the washing procedure or shipment resulting in loss of DNA from the sample enclosed in the microfuge tube ; 3) delay or improper freezing during shipment; or 4) insufficient amount or poor quality DNA in the microfuge tube resulting in suboptimal amplification or inconclusive results . There is also a rare chance of failure of lab equipment and/or reagents resulting in suboptimal DNA amplification or inconclusive results . In most cases it is not possible to determine the exact cause of DNA loss from a specific sample .

Report Date:	3/8/2024
Case File ID:	11393572
Secondary Kit ID:	B033375
Test Methodology:	Next Generation Sequencing (NGS)

natera | Spectrum® Preimplantation genetics

Testing Methodology

Samples are analyzed using the Ion ReproSeq™ Assay, Ion Gene Studio S5 System PGT-A Assay, and IC™ (Ion Chef) PGT-A Assay which includes genome-wide coverage shown to be important for molecular cytogenetic analysis. The mean spacing of sequencing reads is 15 kb resulting in dense coverage, including subtelomeric regions, pericentromeric regions, and sex chromosomes, commonly screened in molecular cytogenetics labs. Analysis includes a proprietary bioinformatic algorithm (NextGen Genetics Laboratories mosaic algorithm) to detect mosaicism within an embryo sample. This testing is analyzed using Ion Reporter™ Software and the platform uses Human Genome Build hg19. Embryo result interpretation is summarized on page 1 of the report in groups of euploid, segmental and/or mosaic, aneuploid, inconclusive results or insufficient DNA. The embryo biopsy samples are collected and processed using the Ion SingleSeq Kit™ which includes a proprietary lysis buffer, whole genome amplification (library preparation), and barcoding.

Limitations

Due to the risk of mosaicism, aneuploidy screening results may not be representative of the chromosome make-up of the embryo. Mosaicism is defined as more than one chromosomally distinct cell line in the same embryo. Mosaicism occurs by chance during embryonic development and can cause a misdiagnosis if the cell(s) that are biopsied and tested are not representative of the remainder of the embryo. This test does not detect uniparental disomy (UPD), haploidy, or triploid with XXX sex chromosome complement (69,XXX). PGT-A and PGT-SR cannot detect structural rearrangements in which genetic material is balanced (euploid). Full trisomy cannot be distinguished from trisomy due to a Robertsonian translocation (involves chromosomes 13, 14, 15, 21, or 22) or isochromosome. There remain multiple rare chromosomal problems, including but not limited to certain types of aneuploidy, such as tetraploidy (four copies of the complete set of chromosomes) and polysomy beyond three total copies of a chromosome, which could arise and that this test does not or cannot test for. This test does not analyze specific genes and will not detect conditions caused by single gene mutations, such as cystic fibrosis or Tay-Sachs disease. There is a 3-5% background population risk for birth defects or genetic conditions in any pregnancy. This test only detects the portion of birth defects caused by aneuploidy.

Further Testing Recommendations

PGT cannot detect all chromosome abnormalities and does not guarantee the birth of a chromosomally normal child . Since PGT is a screening test and cannot rule out mosaicism, women who become pregnant following IVF with PGT should be offered prenatal testing during pregnancy . Only diagnostic testing options including chorionic villus sampling (CVS) or amniocentesis can confirm normal chromosome number in an ongoing pregnancy. Some patients may choose to pursue prenatal screening, but these tests are not as accurate as diagnostic testing. We suggest that patients review the various prenatal diagnostic testing and screening options with their healthcare provider after a pregnancy is achieved.

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.

These results should always be interpreted by a clinician in the context of clinical and familial data. For assistance in interpretation call 844-778-4700.

Approved by:

Youbao Sha, Ph.D.,FACMG
Laboratory Director, Natera

Reviewed by: Susan Zneimer Ph.D., FACMG
Laboratory Director: NextGen Genetics