LabSolutions

DISCOVER® NIPT

Going to greater lengths *for the answers that matter most.*

LABSOLUTIONS.COM

The DISCOVER® prenatal test provides reliable, comprehensive answers about the health of a developing fetus.

The DISCOVER® test, from LabSolutions, represents a major advance in prenatal testing, providing accurate answers about fetal chromosomal health—without the risks associated with invasive procedures, such as amniocentesis or chorionic villus sampling (CVS).

Performed as early as 10 weeks gestation, the DISCOVER® test demonstrates superb sensitivity and specificity for the most prevalent trisomies.

Medical societies agree

that all pregnant women should be offered prenatal screening/diagnosis for fetal abnormalities and that NIPT is a major advance in screening methodologies.[1-5]

Test Performance In Most Common Chromosomal Aneuploides[6]

	N	Observed Sensitivity	95% CI	Observed Specificity	95% CI
T21 Down Syndrome	577	99.14%	98.0–99.7	99.94%	99.90–99.97
T18 Edwards Syndrome	175	98.31%	95.0–99.6	99.90%	99.86–99.93
T13 Patau Syndrome	53	98.15%	90.0–99.9	99.95%	99.91–99.97

The DISCOVER® test can also detect sex chromosome aneuploidies in singleton pregnancies—at no extra charge.

- Monosomy X (Turner syndrome)
- XXX (Triple X)
- XXY (Klinefelter syndrome)
- XYY (Jacobs syndrome)
- Fetal Sex (XX or XY) - aids in risk stratification of X-linked disorders such a hemophilia

*Sex chromosome mosaicism cannot be distinguished by this method (the occurrence of which is <0.3%). Patients with such mosaicism will have a sex chromosome result reported and will fall into one of the six categories (Monosomy X, XXX, XXY, XYY, XX, XY).

Test performance in most common sex aneuploides*[7]

	N	Sensitivity	95% CI	Specificity	95% CI	Accuracy	95% CI
MX	508	95.0% (19/20)	75.1–99.9	99.0% (483/488)	97.6–99.7	-	-
XX	508	97.6% (243/249)	94.8–99.1	99.2% (257/259)	97.2–99.9	98.4%	96.9–99.3
XY	508	99.1% (227/229)	96.9–99.9	98.9% (276/279)	96.9–99.8	99.0%	97.7–99.7

XXX, XXY, XYY: Limited data of these more rare aneuploides preclude performance calculations.

Intended Use In Singleton Pregnancies

This screening test is intended for patients at 10 weeks or greater gestation with singleton pregnancies who meet any of the following criteria:

- Advanced maternal age (≥35 years at delivery)
- Positive serum screen
- Abnormal ultrasound
- History suggestive of increased risk for T21, T18, or T13, or sex chromosome aneuploidy

Intended Use In Twin Pregnancies

This screening test is intended for patients at 10 weeks or greater gestation with twin pregnancies who meet any of the following criteria:

- Advanced maternal age (≥32 years at delivery)
- Positive serum screen
- Abnormal ultrasound
- History suggestive of increased risk for T21, T18, or T13

Expansion into twin pregnancies.

Recently, the DISCOVER® prenatal test has been expanded to include the option to test for T21, T18 and T13 in both monozygotic and dizygotic twin pregnancies. A test for the presence of the Y chromosome can be ordered for twins as well.

Committed to research.

With its superior technology, the DISCOVER® test provides clinical evidence showing across-the-genome analysis in a real-world population. The performance of the DISCOVER® prenatal test was evaluated in a major scientific study in which more than 60 leading US medical research and teaching institutions participated. The study findings were reviewed and published in the preeminent journal read by obstetricians and gynecologists. A second study, published subsequently, presented the test's performance under regular clinical conditions and found similar results.[8] LabSolutions continues to expand the technology with its commitment to sponsor and support continued clinical studies to advance the effectiveness of NIPT (non-invasive prenatal testing).

Taking a deeper look at the science of knowing.

The DISCOVER® Test Advantage: A more stringent and optimized approach to genetic sequencing.

The DISCOVER® prenatal test leverages the power of Massively Parallel Sequencing (MPS) across the whole genome. The industry's ***deepest sequencing approach*** combined with a ***highly optimized algorithm*** provides a ***clearer, more reliable answer than other methods.***

The Science of Deeper Sequencing

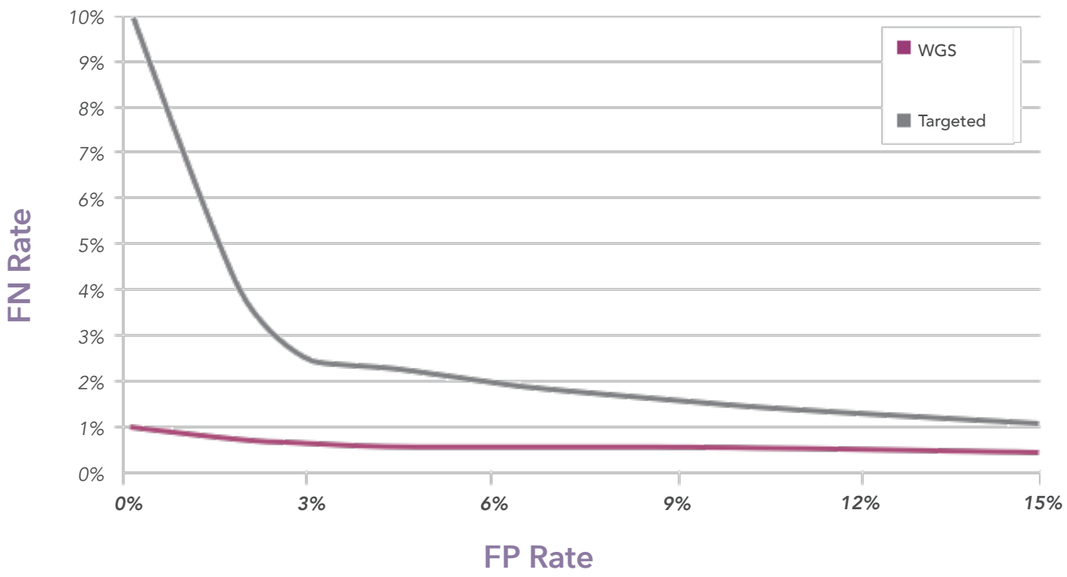
In the graph below, shallower sequencing necessitates using fetal fraction (ff) estimates as compensation for weaker sequencing power. Without using ff estimates, the incidence of false negatives would be clinically unacceptable and result in higher numbers of sample rejections and delayed result time.

Utilizing the power of deeper sequencing, the DISCOVER® test gives reassurance by:

- Eliminating unnecessary sample rejections
- Reducing the need for redraws
- Obviating requests for paternal samples
- Providing fast time to report (2–4 business days)[9]

Other Targeted Non-Invasive Prenatal Tests

DISCOVER® Prenatal Test: Whole Genome Sequencing



The proof is in the data.

Our excellent NPV and PPV results are achieved without relying on variable ff estimates or other correction factors.[6]

	Positive Predictive Value	Negative Predictive Value
T21	0.970	0.999

The DISCOVER® test with our enhanced SAFeR™ algorithm increases the specific signal of aneuploid chromosomes and hence improves the overall accuracy of classifying affected samples. The test output provides definitive results, not a risk score, and it is not dependent on maternal age, maternal weight, gestational age (after 10 weeks) or ethnicity.

DISCOVER® Test With SAFeR™	Available Targeted Sequencing Tests
Definite, informative results	Ambiguous risk scores similar to serum screens
Lowest test failure rate (0.1%)	High failure rates (5%-10% or greater)
Not constrained by patient factors or paternal sample	May reply on patient factors or require paternal samples to improve accuracy
Accepts egg donors	May exclude egg donors

Shedding needed light on fetal chromosomes *simply, safely, sooner.*

An easy, non-invasive blood test delivering the answers you seek in just days.

The DISCOVER® prenatal test is easy to order and needs only 1 tube of blood (just a 7mL sample). Simply ship the blood sample in its proprietary packaging to our CAP- accredited† clinical lab. Our easy-to-read reports are available to the ordering physician via online portal, fax or mail, within just 2–4 business days.

The DISCOVER® test report is well organized and easy to read.

Basic reports contain results for chromosomes 21, 18 and 13. Test reports include one of three possible results for chromosomes 21, 18, and 13: No Aneuploidy Detected, Aneuploidy Detected, or Aneuploidy Suspected (Borderline Value). If the sex chromosomes option is selected, results for Monosomy X, XXX, XXY and XYY will be included. (If no aneuploidies are detected, fetal sex will be reported.) Sex chromosomes will be reported as No Aneuploidy Detected or Aneuploidy Detected.

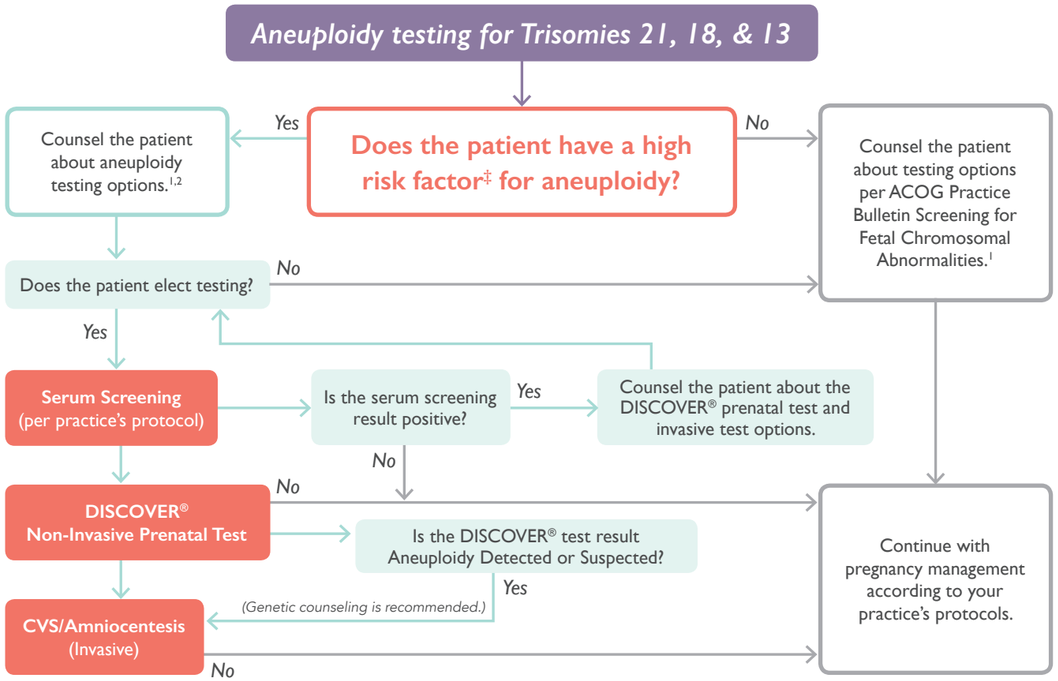
Know what a DISCOVER® test case looks like.

High-Risk Patient Considering An Invasive Procedure

38-Year-Old Woman With History of Infertility Who Conceived Via In Vitro Fertilization (IVF)	
Genetic Counseling To Discuss Testing Options	• Screening • Invasive test—fearful of procedural loss • DISCOVER® prenatal test • Ultrasound
Patient Elects The DISCOVER® Prenatal Test	• Chromosome 21—No Aneuploidy Detected • Chromosome 18—No Aneuploidy Detected • Chromosome 13—No Aneuploidy Detected • Normal ultrasound

Patient comfortable declining invasive testing due to high sensitivity of DISCOVER® prenatal test and normal ultrasound result. ***Procedural risks avoided.***

Incorporating the DISCOVER® Prenatal Test Into Practice



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4. *Benn P, Borell A, Chiu R, et al. Position Statement from the Aneuploidy Screening Committee on Behalf of the Board of the International Society for Prenatal Diagnosis. Prenat Diagn. 2013;33:622–629.*
5. *Devers PL, Cronister A, Ormond KE, Facio F, Brasington CK, Flodman P. Noninvasive prenatal testing/noninvasive prenatal diagnosis: the position of the National Society of Genetic Counselors. J Genet Couns. 2013:22:291–295.*
6. *Bhatt S, Parsa S, Snyder H, Taneja P, Halks-Miller M, Seltzer W, DeFeo E. Clinical Laboratory Experience with Noninvasive Prenatal Testing: Update on Clinically Relevant Metrics. ISPD 2014 poster.*
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8. *Futch T, Spinosa J, Bhatt S, de Feo E, Rava RP, Sehnert AJ. Initial clinical laboratory experience in noninvasive prenatal testing for fetal aneuploidy from maternal plasma DNA samples. Prenat Diagn. 2013:33:569–574.*
9. *Data on file: Internal data from lab metric updates.*

ADDITIONAL STUDIES

Bianchi DW, Platt LD, Goldberg JD, et al. Genome-wide fetal aneuploidy detection by maternal plasma DNA sequencing. *Obstet Gynecol.* 2012;119:890–901.

Rava PP, Srinivasan A, Sehnert AJ, Bianchi DW. Circulating fetal cell-free DNA fractions differ in autosomal aneuploidies and monosomy X. *Clin Chem.* 2014;60:243–250.

Sehnert AJ, Rhees B, Comstock D, et al. Optimal detection of fetal chromosomal abnormalities by massively parallel DNA sequencing of cell-free fetal DNA from maternal blood. *Clin Chem.* 2011;57:1042–1049.

†College of American Pathologists, ‡This workflow was developed in adherence to the current ACOG/SMFM Committee Opinion No. 545, December 2012. Patient can choose/decline options based on clinical discussion with her provider.

DISCLAIMER

The manner in which this information is used to guide patient care is the responsibility of the healthcare provider, including advising for the need for genetic counseling or additional diagnostic testing. Any diagnostic testing should be interpreted in the context of all available clinical findings.

This test was developed by Illumina, and its performance characteristics were determined by Illumina. It has not been cleared or approved by the U. S. Food and Drug Administration. Although laboratory-developed tests to date have not been subject to U.S. FDA regulation, certification of the laboratory is required under the Clinical Laboratory Improvement Amendments (CLIA) to ensure the quality and validity of the tests. Our laboratory is CAP-accredited and certified under CLIA as qualified to perform high-complexity clinical laboratory testing.

LIMITATIONS OF TEST

The DISCOVER® prenatal test is a highly accurate advanced screening test that is non-invasive. This test is designed to detect chromosome aneuploidies and is validated for chromosomes 21, 18, and 13, X and Y. The test is validated for singleton and twin pregnancies with gestational age of at least 10 weeks. Genetic counseling before and after testing is recommended. These results do not eliminate the possibility that this pregnancy may be associated with other chromosomal abnormalities, birth defects, or other complications. A negative test result does not preclude the presence of Trisomy 21, Trisomy 18, or Trisomy 13, Monosomy X, XXX, XXY, and XYY. When an aneuploidy detected result is reported in a twin pregnancy, the status of each individual fetus cannot be determined. The presence or absence of Y chromosome material can be reported in a twin pregnancy; however, the occurrence of sex chromosome aneuploidies such as MX, XXX, XXY, and XYY, cannot be evaluated in twin pregnancies. There is a small possibility that the test results might not reflect the chromosomes of the fetus, but may reflect the chromosomal changes of the placenta (confined placental mosaicism), or of the mother (chromosomal mosaicism).

Results of "Aneuploidy Detected" or "Aneuploidy Suspected" are considered positive, and patients should be offered invasive prenatal procedures for confirmation. Chorionic villus sampling and amniocentesis provide diagnostic information.

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