innatal®
PRENATAL SCREEN

An upgraded cell-free DNA prenatal screening platform

Screen for chromosomal disorders using advanced noninvasive cell-free DNA technology.

Highlights

High Quality
Proven to produce precise and accurate results

Exceptional Performance
>99% sensitivity and specificity across tested disorders

Fetal Fraction
Routinely reported quality metric

Low Rates of Failed Results
<1% failure rate

Background

ACOG recommends that all women be offered aneuploidy screening or diagnostic testing during pregnancy.[1] Conventional screening for fetal aneuploidy is typically done using ultrasound and analysis of various biomarkers in maternal serum. Detection rates for these methods can be as high as 96%, but false positives can approach 10%.[2] Screening using cell-free DNA (cfDNA) testing has both higher sensitivities and specificities compared to serum screening, which leads to significantly higher positive predictive values (PPV).[3,4]

PPV is based on test sensitivity, specificity and the prevalence of the disorder in the population. For aneuploidies, both maternal age and gestational age determine the prevalence, which greatly influences the PPV for cfDNA screening results. ACMG recommends that a patient-specific PPV be included on all cfDNA screening results.[5] It is important information used by patients and providers to interpret test results.

Updated Technology

The Innatal® Prenatal Screen utilizes massively parallel sequencing (MPS) across the whole genome. This method sequences short fragments of DNA, creating millions of reads that are then mapped to the reference genome. The reads are counted to determine whether the sample has extra or missing reads from a particular chromosome. Abnormal dosage indicating aneuploidy is presumed to be fetal in origin. In rare circumstances, there is an alternative explanation.

Progenity has upgraded the Innatal Prenatal screen with the latest sequencing technology and improved chemistry, demonstrating **higher sensitivities than previous versions** of the test. Fetal fraction is determined for each sample using a proprietary algorithm. Previous performance strengths have been maintained, including low failure rates and quick results.

> “THE LATEST SEQUENCING TECHNOLOGY AND IMPROVED CHEMISTRY

Performance

In-depth verification and validation testing of the Innatal assay, using >1000 samples, was conducted as prescribed by multiple peer-reviewed guidelines.[6,7,8] Verification and validation reports are on file at Progenity, Inc. in accordance with CAP and CLIA regulations, and the test has been submitted to NY State for approval as well.

PERFORMANCE DATA[9]

Disorder	Sensitivity	Specificity	Accuracy
Trisomy 21	99.2%	>99.9%	-
Trisomy 18	> 99.9%	99.7%	-
Trisomy 13	> 99.9%	>99.9%	-
Monosomy X	> 99.9%	99.8%	-
XX	99.0%	99.9%	99.4%
XY	99.9%	99.0%	99.4%
XXX, XXY, XYY	Aneuploidies will be reported if detected. Limited data on these less common aneuploidies preclude performance calculations.		

Improved PPVs

With increased sensitivities and similar specificities, the upgraded Innatal platform provides increased PPVs for most patients. Patient-specific PPV is included on most positive results.

Reliable fetal fraction

Fetal fraction (FF) is reported for each resulted sample. The mean fetal fraction in the validation cohort was 8.6%. Repeat samples showed consistent fetal fraction values, with an average ΔFF of <1% between repeat analyses (n=304 samples).[9]

Low failure rate

Based on aggregate runs our failure rate is maintained at <1%.[10] Failure rates are an important and often overlooked performance metric, as the impact of test failures on both providers and patients is significant. Test failures are treated as high-risk results, and thus invasive diagnostic testing is recommended for patients.[11] Low test failures keep the specificity of the test high.

Conclusion

Progenity is dedicated to continuous product improvement and has validated an upgraded version of the Innatal Prenatal Screen in accordance with well-accepted practices for laboratory-developed tests. Updated performance metrics reflect high sensitivities and specificities and maintenance of a low failure rate. Fetal fraction assessment has been added to the proprietary algorithm and will be routinely reported with results. Test improvements demonstrate a commitment to excellence - promising high-quality results that help guide prenatal care.

PRECISE

Proven reproducible and repeatable. There was almost perfect agreement (>99%) for repeatability and reproducibility across multiple lots, manufacture builds, instruments, and operators.

ACCURATE

Proven to match known outcomes. Methods of comparison against samples with previously determined clinical outcomes showed high concordance calls for chromosomes 21, 18, 13, X and Y.

SENSITIVE

Proven to identify affected fetuses. Sensitivity is >99% for the core trisomies and fetal sex aneuploidies, meaning false negatives are very rare.

SPECIFIC

Proven to rule-out unaffected fetuses. Specificity is >99% for the core trisomies and fetal sex aneuploidies, meaning false positives are very rare.

References

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8. Rehm et al. ACMG clinical laboratory standards for next-generation sequencing. Genet Med. 2013;15(9):733-47.
9. Progenity, Inc. Validation data on file.
10. Progenity, Inc. Aggregate data on file.
11. American College of Obstetricians and Gynecologists Committee Opinion No. 640. Cell-free DNA screening for fetal aneuploidy. Obstet Gynecol. 2015;126:e31-7.

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