Myriad genetics

Fetal-fraction amplification increases analytical performance of noninvasive prenatal screening

History

Noninvasive Prenatal Screening (NIPS) via cell-free DNA analysis (cfDNA) has been rapidly incorporated into prenatal care since it became clinically available in 2011.

The sensitivity and specificity of NIPS is highly dependent on the percentage of the maternal cfDNA sample that is fetal-derived (the fetal fraction; FF). Certain NIPS platforms will not deliver a result for >20% of women with high body-mass index (and >5% overall) due to low FF (<4%).[1]

The Myriad Prequel™ Prenatal Screen utilizes a customized, proprietary whole genome sequencing (WGS) approach to NIPS. Prequel has always delivered results with high quality, specificity, and sensitivity at all fetal fractions without a fetal fraction cutoff. Now, Prequel with Amplify technology further enhances these results by enriching fetal fraction for all patients including those with high body-mass index. This new technology opens the door to future enhancements that deliver the information individuals need to plan their family.

Prequel with Amplify™ Technology

In 2020, Myriad Genetics announced the launch of Prequel with Amplify technology, a revolutionary advancement in NIPS that is better able to detect fetal DNA by enriching fetal fractions for ALL patients.

The Amplify technology benefits those who need it most, like patients with high BMI, which make up approximately 50% of pregnancies in the United States.[2] Amplify uses a scalable fetal fraction amplification (FFA) technology that increases FFA by a 3.9-fold on average for samples with low FF (2.3-fold overall). The technology was analytically validated on 1,264 samples tested in Myriad Genetics' laboratories yielding zero samples that had FF<4% whereas 1 in 25 of these same patients had FF<4% without FFA.[1]

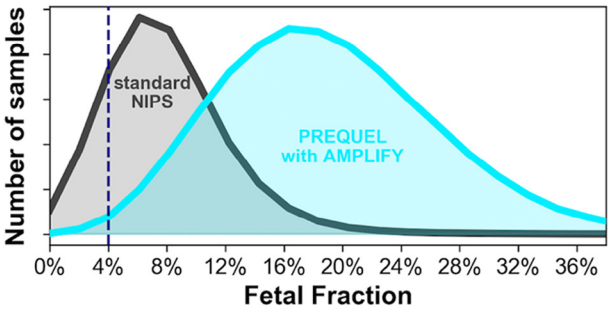
Amplify essentially eliminates the issue of low fetal fraction while maintaining an industry-leading test failure rate of 0.1%. This provides equity in care for all patient types, regardless of BMI, ethnicity, or race.

Myriad Genetics clinical experience

In the poster presentation Avoiding Unnecessary Trade-offs: Clinical Experience for a Noninvasive Prenatal Screen with Both Low-Test Failure Rate and High Accuracy[3], Myriad Genetics described clinical experience from its laboratory.

Myriad's experience demonstrates that Prequel achieves high accuracy while maintaining a low test-failure rate of 0.1% in a general obstetric population. Use of a fetal fraction threshold to determine test failure would have impacted thousands of patients, unnecessarily delaying the identification of a number of affected pregnancies. Failing samples based solely on fetal fraction is not necessary with Myriad's WGS approach to NIPS.

A deeper look at the first 100K samples: >99% of samples had a fetal fraction of >4%



Average FF without AMPLIFY **8.3%**

Average FF with AMPLIFY **20.2%**

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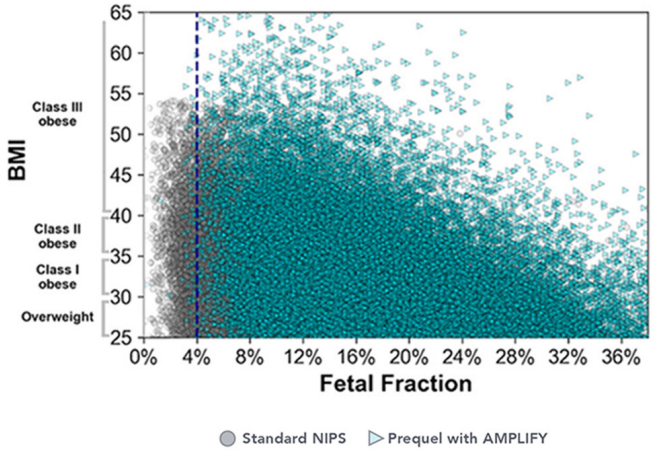
The effect of Amplify in the most difficult-to-call (high BMI) samples



Key takeaways

- Average fetal fraction (FF) of the high BMI samples was 18.4%
- Of patients with BMI >40 drawn as early as 10 weeks, the lowest FF sample was 3%
  - >99% of patients had a fetal fraction >4%

Patient	Gestational age (weeks)	BMI	Other lab result (FF)	Prequel with Amplify result	Amplified FF
A	10	25	FAILED (2%)	NEGATIVE	Received a confident result with 20% FF
B	10	39	FAILED (3%)	NEGATIVE	Received a confident result with 9% FF
C	11	>40	FAILED (3%)	NEGATIVE	Received a confident result with 12% FF
D	12	45	FAILED (2%)	NEGATIVE	Received a confident result with 9% FF
E	13	25	FAILED due to “Low FF”	POSITIVE T21 & later confirmed with amnio	Received a confident result with a 6% FF . . . and was able to better prepare for having a baby with Down syndrome

Actual patient cases

Myriad is focused on providing equity of care for all patients. In looking at actual patient cases, these patients received a failed result due to low fetal fraction with another lab. Myriad was subsequently able to give these patients the results they needed.

Bottom line

Fetal fraction with amplification helps provide more equitable care, by reducing the number of patients entering the complex workflows associated with no-calls. As guidelines recommend that patients with a failed result (no-call) be offered an invasive diagnostic procedure, these patients may be exposed to unnecessary risk in a healthy pregnancy. Offering all patients Prequel with Amplify helps solve this.

REFERENCES: 1. Welker, N.C., Lee, A.K., Kjolby, R.A.S. et al. High-throughput fetal fraction amplification increases analytical performance of noninvasive prenatal screening. Genet Med (2020). https://doi.org/10.1038/s41436-020-01009-5.2. 2. Deputy, N. P., Dub, B. & Sharma, A. J. Prevalence and Trends in Pre-pregnancy Normal Weight - 48 States, New York City, and District of Columbia, 2011-2015. MMWR Morb. Mortal. Wkly. Rep. 66, 1402–1407 (2018). 3. Hancock, S., Ben-Shachar, R., Adusei, C., Haverty, C., Muzzey, D. Avoiding Unnecessary Trade-offs: Clinical Experience for a Noninvasive Prenatal Screen With Both Low Test Failure Rate and High Accuracy. ISPD 2019. Myriad Womans Health.

About Myriad Genetics

Myriad Genetics is a leading genetic testing and precision medicine company dedicated to advancing health and wellbeing for all, empowering individuals with vital genetic insights and enabling healthcare providers to better detect, treat and prevent disease. Myriad discovers and commercializes genetic tests that determine the risk of developing disease, accurately diagnose disease, assess the risk of disease progression, and guide treatment decisions across medical specialties where critical genetic insights can significantly improve patient care and lower healthcare costs.

For more information, visit the Company’s website: www.myriad.com.

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