P745

Early Laboratory Experience with a Prenatal Screening Assay for Simultaneous Prenatal Aneuploidy, Recessive Disease and Serology Compatibility Screening

Summer Pierson[1], Ariel Gershman[1], Heather LaBreche[1], Harshal Tandel[1], Helen Wan[1], Katie Johansen Taber[1], Dale Muzzey[1]

1 Myriad Genetics, Inc., Salt Lake City, UT

Background

- Genetic risk assessment in pregnancy includes fetal risk assessment for both aneuploidies and recessive disease, traditionally achieved via carrier screening for each reproductive partner along with a separate prenatal cell-free DNA (pcfDNA) screen for aneuploidies
- Carrier screening is often incomplete because only one reproductive partner is screened, limiting the ability to identify fetuses at risk
- We present initial performance data for a scalable assay that simultaneously assesses fetal aneuploidy, fetal and maternal recessive disease carrier status, and fetal serological compatibility using pcfDNA in maternal blood

Methods

- Data from samples run on a multiple pcfDNA screen (FirstGene; Myriad Genetics, Inc.) as part of the prospective, IRB-approved CONNECTOR study were analyzed

The pcfDNA assay includes:

- Carrier screening and fetal risk assessment for 10 (ACMG Tier 2+) severe and profound recessive conditions common in a US pan-ethnic population
- Common aneuploidies
- Sex chromosome abnormalities (SCAs)
- 22q11.2 microdeletion
- Maternofetal RhD incompatibility

Metrics analyzed:

- Turnaround time (TAT)
- Fetal fraction (FF)
- Sample failure rate
- Result type

Table 1. Recessive Conditions Assessed

Gene/Recessive Condition	Carrier Screen	Fetal Risk Assessment
CFTR / cystic fibrosis	✕	✕
SMN1 / spinal muscular atrophy	✕	✕
HBA 1&2 / hemoglobin Barts	✕	✕
HEXA / Tay-Sachs disease	✕	✕
PMM2 / congenital disorder of glycosylation type 1A	✕	✕
ACADM / medium chain acyl-CoA dehydrogenase deficiency	✕	✕
ASPA / Canavan disease	✕	✕
DHCR7 / Smith Lemli Optiz syndrome	✕	✕
PAH / phenylalanine hydroxylase deficiency	✕	✕
FMR1 / fragile X syndrome	✕	

Results

- 406 patients with complete assay results
- Median TAT: 10 days (**Figure 1**)
- Median FF: 10.1% (range 3.0%-40.6%) (**Figure 2**)
- Assay failure rate due to low FF: 1.2%
- Screen-negative for aneuploidies and recessive conditions: 84.7% (n=344)
- Fetuses identified as carriers of recessive conditions: 6.6% (n=27)
  - 37% (n=10): cases in which the pregnant patient was a carrier of the same variant identified in the fetus
  - 63% (n=17): cases in which the variant detected in the fetus was NOT present in the pregnant person

Figure 1. pcfDNA Assay TAT Metrics

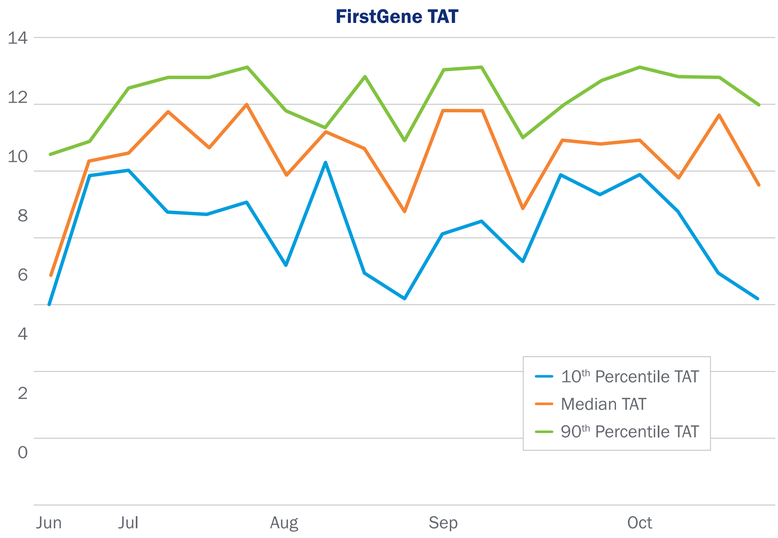
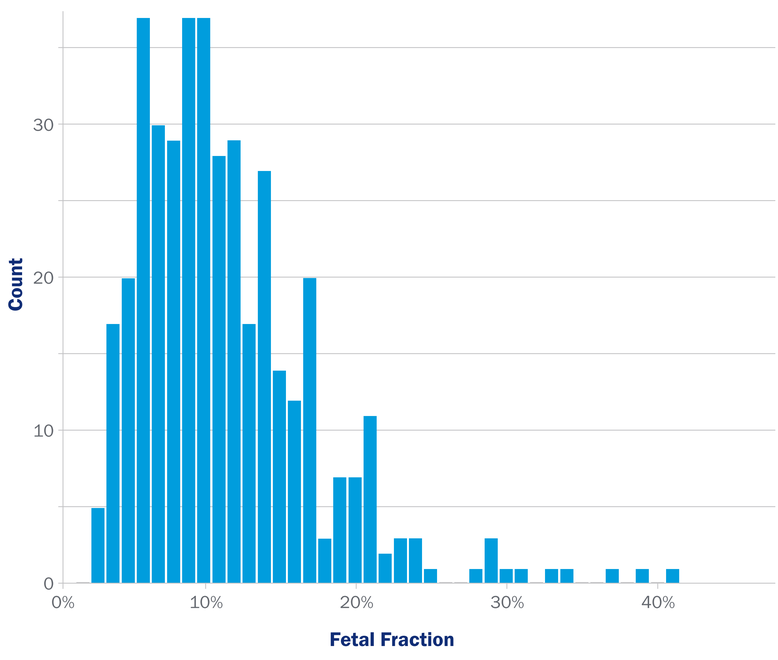
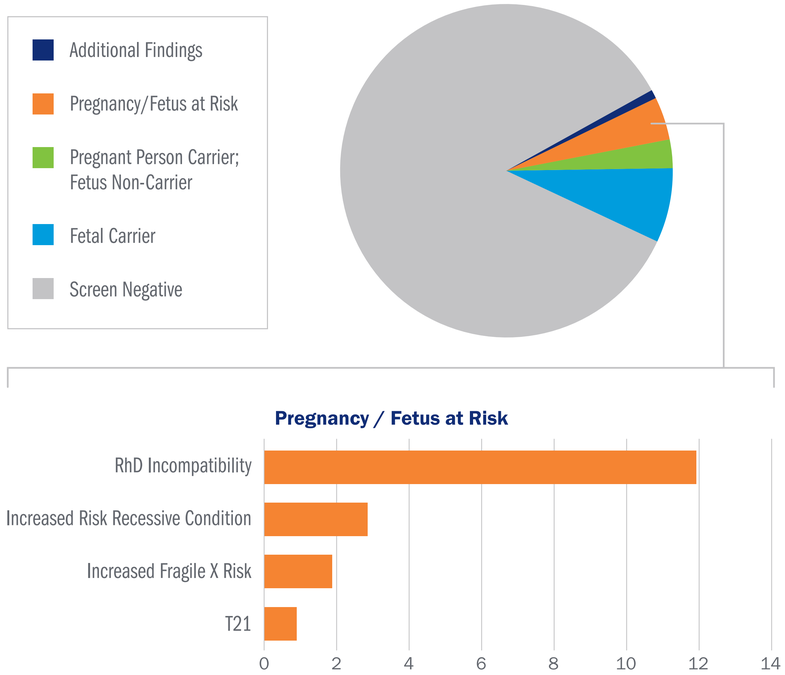


Figure 2. Fetal Fraction Distributions



- 3.2% (n=13) identified the pregnant person as a carrier while the fetus was found to not be a carrier for the condition
- 4.4% (n=18) of pregnancies/fetuses categorized as high risk for one of the tested conditions:
  - 66.7% (n=12) of pregnancies at risk for maternofetal RhD incompatibility
  - 16.6% (n=3) of fetuses at increased risk for recessive disease
  - 11.1% (n=2) of fetuses at risk for Fragile X (based on a premutation detected in the pregnant person)
  - 5.6% (n=1) of fetuses predicted to have a chromosomal aneuploidy
- Remaining reports (0.99%; n=4) included additional findings (**Figure 3**)

Figure 3. Report Types



Conclusions

- Early performance of this pcfDNA assay demonstrates that relevant genetic risk information (fetal aneuploidy, fetal recessive disease risk and RhD compatibility) can be reliably delivered within a timeframe that allows for prompt pregnancy management
- The assay can assess fetal risk when the pregnant person is identified as a carrier, as well as detect fetal variants regardless of inheritance
- The assay maintains a low failure rate

Disclosures: All authors were employees of Myriad Genetics, Inc. at the time of this study and received salary and stock as compensation.

Email for questions:
summer.pierson@myriad.com