Background

- 22q11.2 deletion syndrome occurs in approximately 1 in 2,000 to 1 in 6,000 births.1,2
- Prenatal cell-free DNA screening (pCDNA) can detect fetuses affected by deletions as small as 2.5 Mb.3
- Fetal fraction amplification (FFA), which has been shown to increase fetal fraction (FF) by 2.3x, may further enhance pCDNA detection of these deletions.4
- Positive predictive values (PPV) of pCDNA screening for 22q11.2 microdeletion have been reported between approximately 20%-98%.5-10

Here, we sought to describe the impact of FFA on the PPV of 22q11.2 microdeletion screening using a whole-genome sequencing (WGS)-based pCDNA platform.

Study Design and Methods

- We retrospectively analyzed data from patients who underwent WGS-based pCDNA screening with FPA (Prequel™, Myriad Genetics, Inc.) between 8/20-10/22.
- For screen-positive patients, pregnancy outcome data were requested via a routine HIPAA-compliant process.
- All samples with diagnostic confirmation were used to calculate PPV, defined as: true positives/true positives + false positives.
- Confidence interval (CI) was estimated using the two-sided Exact Binomial Test.

Figure 1 shows processed WGS data for two samples called positive for 22q11.2 microdeletion: A: A-D deletion; B: A-B deletion.

Results

- 76 patients screened positive for 22q11.2 microdeletion, comprised of 69 (90.8%) A-D, 5 (6.6%) A-B, and 2 (2.6%) A-C deletions.
- 22 screen-positive patients underwent molecular diagnostic testing; all 22 were confirmed as true positives (PPV=100%; 95% CI 84.6%-100%).
- 20/22 had ultrasonic findings strongly or moderately associated with 22q11.2 microdeletion (Figure 2).
- 52 patients had no diagnostic testing; 33 had ultrasound information. Of those 33, 18 were strongly or moderately associated with 22q11.2 deletion syndrome (e.g., cardiac defects, polyhydramnios, skeletal defects, intrauterine growth restriction) (Figure 2).

Conclusion

- A pCDNA screen that incorporates FFA amplification has a 22q11.2 microdeletion PPV that is among the highest reported and comparable to that of the common trisomies.