I. Background

Recent adoption of genome-wide cell-free DNA (cfDNA) prenatal screening provides unique insight into placental findings not previously recognized. Here we present data from our first 28,760 clinical samples for expanded cfDNA screening, including genome-wide identification of aneuploidy and subchromosomal copy number variants (CNVs) ≥7 Mb, with specific attention to complex chromosomal rearrangements.

II. Methods

Maternal blood samples submitted to Sequenom Laboratories® for MaterniT® GENOME screening were subjected to DNA extraction, library preparation, and whole-genome massively parallel sequencing as described by Jensen et al.1 Sequence data were analyzed using a novel algorithm as described by Lefkowitz et al.2

IV. Conclusions

Identification of complex chromosomal rearrangements via cfDNA prenatal screening marks a new era in prenatal testing. These findings tend to segregate with significant high risk prenatal indications, however it should be noted that 22% of these pregnancies had no known family history or overt ultrasound findings at the time of screening.

Many known familial rearrangements not previously amenable to cfDNA screening may now benefit from early identification or added reassurance. Providers have relayed that these high risk patients often use such information for diagnostic testing plans, deciding to wait for an amniocentesis if normal vs. chorionic villus sampling if abnormal. When diagnostic testing is declined or otherwise not an option, results can help mentally prepare patients and providers alike for the likely outcome, and if need be, assist with planning medical intervention at birth in the event of abnormal screening results.

In addition, new discovery of families at risk of carrying a recombinant event often helps to explain past pregnancy complications, as well as clarify future reproductive risks. Identification of both balanced translocation and inversion carriers earlier in their reproductive lives can assist with improved pregnancy surveillance, maximizing patient options and overall medical management.

V. References