I. Introduction

Traditional noninvasive prenatal testing (NIPT) is a valuable screening tool for common aneuploidies. With MaterniT® GENOME, noninvasive detection of additional cytogenetic abnormalities is possible. Pallister-Killian mosaic syndrome is uniquely characterized by the presence of supernumerary isochromosome 12p, i(12p). The tissue specificity and clinical variability of Pallister-Killian mosaic syndrome can make diagnosis challenging. Herein we describe three cases of i(12p) and their NIPT results.

II. Methods

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

III. Cases

Case 1:
Indication: congenital diaphragmatic hernia. MaterniT® GENOME result: 34.3Mb gain 12p(11.1-p13.33), as displayed in the ideogram below. Suggestive of 40% mosaicism for 12p (20% i(12p)), established by comparing fetal fraction to the fraction of the observed event. Amniocentesis karyotype confirmed 80% mosaic i(12p) consistent with Pallister-Killian mosaic syndrome.

Case 2:
Indication: congenital diaphragmatic hernia. MaterniT® GENOME result: 34.3Mb gain 12p(11.1-p13.33), as displayed in the ideogram below. Suggestive of 40% mosaicism for 12p (20% i(12p)), established by comparing fetal fraction to the fraction of the observed event. Amniocentesis karyotype confirmed 80% mosaic i(12p) consistent with Pallister-Killian mosaic syndrome.

Case 3:
Indication: congenital diaphragmatic hernia, club foot, increased nuchal fold. MaterniT® GENOME result: 34.3Mb gain 12p(11.1-p13.33), as displayed in the ideograms below. Suggestive of 64% mosaicism for 12p (32% i(12p)), established by comparing fetal fraction to the fraction of the observed event. Amniocentesis karyotype and microarray confirmed 80% mosaic i(12p) consistent with Pallister-Killian mosaic syndrome.

IV. Conclusion

MaterniT® GENOME is uniquely positioned to report esoteric abnormalities ≥7Mb, including gains of 12p, which may suggest i(12p). This de novo isochromosome is more commonly observed in advanced maternal age pregnancies, resulting from maternal meiotic errors with subsequent i(12p) retention or loss. The mosaic nature of the syndrome poses a challenge for both screening and diagnostic testing, as the mosaicism can be highly variable and tissue dependent. The ability of NIPT to view the placental (trophoblast) genome may capture the early formation of a de novo i(12p) abnormality.

V. References
