Whose Y is it anyway? Transplantation as a biological cause of noninvasive prenatal testing (NIPT) gender discrepancies

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INTRODUCTION

Since the introduction of noninvasive prenatal testing (NIPT) in 2011, more than 400,000 clinical samples have been run in Sequenom Laboratories. Discrepant results often have biological explanations, including confined placental mosaicism, maternal mosaicism, co-twin demise, and maternal neoplasm. As cell-free DNA is comprised of maternal and trophoblast placental DNA, tissue from foreign organs can contribute its DNA to the pool.

Here we describe three cases of NIPT fetal sex discrepancies in patients who had undergone bone marrow and liver transplants.

METHODS

Maternal blood samples submitted to Sequenom Laboratories for MaterniT21® PLUS testing 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 select microdeletions.[2]

CASES

CASE #1, NIPT result:

Male, negative for aneuploidies. Provider informed us that ultrasound was consistent with a female fetus. 2nd aliquot of sample was run. Both samples showed a strong Y signal. Provider later informed the lab that the patient had a liver transplant due to Wilson's disease 16 years prior, from a male donor.

CASE#2, NIPT result:

Male, negative for aneuploidies. Provider informed us that ultrasound was consistent with a female fetus. Provider later informed the lab that the patient had a bone marrow transplant from her brother in '85. Normal female anatomy at birth.

CASE #3, NIPT result:

Male, negative for aneuploidies. Provider informed us that ultrasound was consistent with a female fetus and that the patient had a bone marrow transplant from her brother in '02 due to aplastic anemia. In reviewing the data, the sample showed a strong Y signal.

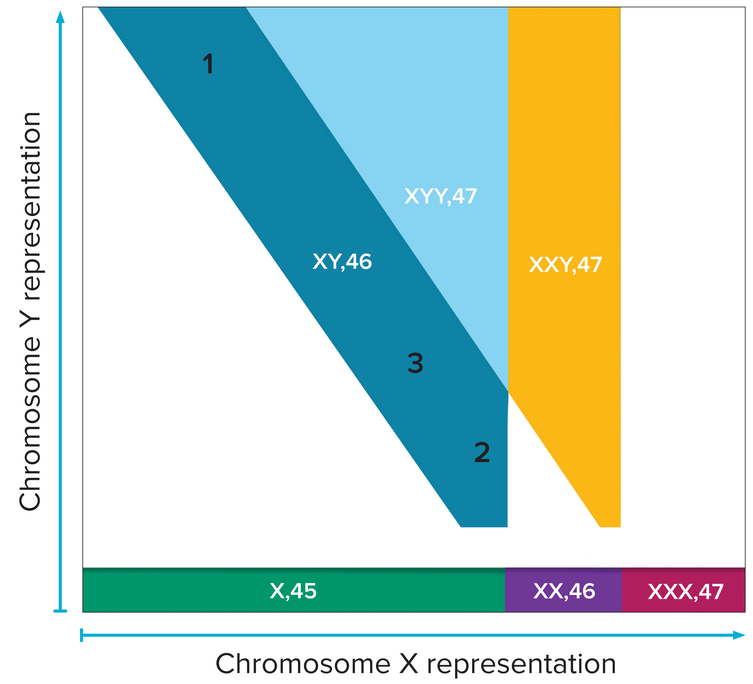

Figure 1. Sex Chromosome Plot

CONCLUSIONS

Obtaining a detailed clinical history in cases of NIPT discrepancy can provide unexpected and valuable clues toward resolution and understanding. As NIPT becomes increasingly available to all populations, pre-test counseling about maternal conditions is essential.

REFERENCES

1. Jensen TJ[1], Zwiefelhofer T, Tim RC, et al. High-throughput massively parallel sequencing for fetal aneuploidy detection from maternal plasma. *PLoS One*. 2013;8(3):e57381. doi: 10.1371/journal.pone.0057381. Epub 2013 Mar 6.
2. Zhao C, Deciu C, Ehrich M, et al. Detection of fetal subchromosomal abnormalities by sequencing circulating cell-free DNA from maternal plasma. PLoSone. In press.

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