NEWSLETTER

This newsletter centers on reproductive topics with a genetics focus. If there is an organization or upcoming webinar you'd like me to include in a future newsletter, please feel free to reach out at genetics@modernreproduction.org.

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ISSUE 24

NEWSLETTER

The little lit review

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Interpretation of noninvasive prenatal testing results following in vitro fertilization and preimplantation genetic testing for aneuploidy

Amber M. Klimczak MD, Andres Reig MD, Shelby A. Neal MD, Emre Seli MD, Richard T. Scott Jr. MD

A common question that arises from patients during PGT-A consent is, "what's the chance there's a genetic condition in the embryo after normal PGT-A results?" We typically explore the ways PGT-A is limited such as the TE biopsy, accuracy, and kinds of conditions it cannot detect. We explore the testing that's available in pregnancy to address some but not all of the limitations of PGT-A. However, even with normal PGT-A results, prenatal testing, and ultrasounds, there is always a possibility of health conditions in children - uncertainty is the nature of having them.

This article explored the NIPT results of 1139 patients, who transferred euploid embryos. Infrequently, will the NIPT results be discordant to the PGT-A results. From this study and discussion from professionals, it seems that if the two would be discordant, it would be due to sex chromosome differences, particuarly Turner syndrome.

Number of pts	NIPT result	Add't info
1127	Negative	
4	No call	3 underwent diagnostic testing with normal results; all four delivered phenotypically "normal" babies
8	Positive	6 had euploid karyotype after prenatal diagnosis; 1 delivered a "normal" baby, 1 amniocentesis revealed Turner mosaicism (80%)

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The little lit review

Placental, maternal, fetal and technical origins of false-positive cell-free DNA screening results

Yvette Raymond, Shavi Fernando, Melody Menezes, Ben W Mol, Andrew McLennan, Fabricio DA Silva Costa, Tristan Hardy, Daniel L Rolnik

The authors reviewed the literature regarding false positive NIPT results and the explanations of such including confined placental mosaicism, maternal malignancy, maternal aneuploidy, fibroids, vanishing twin, and technical failure.

Confined placental mosaicism is one of the more common causes of false positive results. CPM occurs in 2% of pregnancies, and there are 3 types. The aneuploidy can arise mitotically or meiotically. "Trisomy of chromosomes 2, 3, 7, 8, 10 or 12 tends to arise from mitotic non-disjunction, whilst trisomies of chromosomes 14, 15, 16 or 22 are more likely resultant from meiotic errors".

If meiotically, then trisomy rescue may the underlying mechanism of correction, yet uniparental disomy may result. Within a months time, there were two cases of false positive results in our clinic, both with segmental uniparental disomy as a result. As has been suggested, aneuploid placentas can have adverse outcomes, so once aneuploidy had been ruled out in the baby, the possibility of an aneuploidy placenta and the impact should be considered.

One study estimated vanishing twin as the cause for 15% of FP NIPT results. "A demised twin may release cfDNA for up to 15 weeks post demise, however the likelihood of this cfDNA being detected by NIPT decreases with time, such that co-twin demise is an uncommon cause of false-positive results received after 14 weeks' gestations."

"A 2017 study by Zhou et al. investigating the causes of false-positive screening results for trisomies 21, 18 and 13 revealed that 8.1% were attributable to maternal segmental duplications affecting the flagged chromosome. ***Benign copy number variants exceeding 500 Kb are thought to be present in as many as 10% of the general population*** which could increase false positive NIPT results, although most genome-wide screening panels are only able to detect those exceeding 7 Mb". "One study finding that 8.6% of all high-risk SCA results were due to an abnormal X chromosome karyotype in the mother." Loss of the X chromosome as a woman ages may also be a confounding factor.

The authors urge for more research in this area and to inform patients of the possibility of false positive results

Placental DNA in the pregnant person's bloodstream arises from the cytotrophoblast

Trisomy 16 is almost always meiotic in origin, results in type 3 CPM, and associated with SB, placental insufficiency, and FGR

Maternal blood transfusions or organ donor from XY individual can be a cause of sex discordance of NIPT

RAT and 7q deletions are more likely to be FP due to fibroids than the common trisomies

NEWSLETTER

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Remember, it's just a screening test

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