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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Webinars

GENETIC COUNSELING FOR RARE DISEASES: A GLOBAL PERSPECTIVE

12/18/23 10AM EST

Register

EPIGENETICS WEBINAR

12/21/23 6PM EST

Join Zoom

NEWSLETTER

The little lit review

1 Improving the accuracy of noninvasive prenatal testing through size-selection between fetal and maternal cfDNA

Hyuk-Jung Kwon, Seonyoung Yun, Joungsu Joo, Dabin Park, Woo-Jung Do, Sunghoon Lee, Min-Seob Lee

The concept that fetal (placental) DNA fragments are shorter than maternal fragments and can be isolated for improved NIPT detected has been investigated in the last few years (articles A, B, and C). I remember this being introduced with LabCorp's NIPT product a few years ago, though for some reason, I cannot find any information that the lab is still using the approach. Myriad has made it clear they are and had a recent poster presentation at SMFM's annual conference.

High BMI can be a challenge with NIPT as the fetal fraction can lower and cause difficulty in identifying chromosomal abnormalities, possibly resulting in an non reportable result. The authors investigated sizes of fetal and maternal fragments of 60,000 individuals. "By implementing size-selection method, the accuracy of NIPT was improved, resulting in an increase in the overall positive predictive value for all aneuploidies from 89.57% to 97.1%. This was achieved by enriching both fetal and maternal-derived cfDNA, which increased fetal DNA fraction while the number of false positives for all aneuploidies was reduced by more than 70%."

Is this enhancement routine for labs?

When looking for LabCorp's mention of using this approach, I instead came across their fetal mosaicism ratio that is calculated for positive results to help better discern true positives from other biological explanations like cotwin demise or placental mosaicism. I wonder if this will expand to other chromosomes, as it appears to be for the common 5, and how this could be useful for embryos with mosaic PGT-A results.

NEWSLETTER

The little lit review

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Prenatal diagnosis after high chance non-invasive prenatal testing for trisomies 21, 18 and 13, chorionic villus sampling or amniocentesis? Experience at a district general hospital in the United Kingdom

Collins Ejakhianghe Maximilian Okoror and Suruchi Arora

The authors provide a nice review of NIPT's performance against multiple marker screening as well as the endless discussion on whether CVS or amniocentesis should be offered. From this center's experience, they recommend amniocentesis in the setting of positive NIPT and unremarkable ultrasound. If an abnormality is identified on ultrasound, then either CVS or amniocentesis can be considered. The reason for this recommendation is the risk of confined placental mosaicism.

It has been the case there are two clearly different NIPT methodologies: SNP based and massive parallel sequencing. Yet, now, with the above article and mosaicism ratio add-ons, will there need to be more differentiation of the type of NIPT used and the study investigating it? This is the current difficulty with PGT-A testing in that each lab may have slight variation in their methodology, amplification, and thresholds such that outcome studies that do not specify the methodology are difficult to generalize the testing.

P16.08

Non-mosaic Trisomy 21 from CVS and subsequent normal karotype from amniocentesis: a rare case of fetoplacental discordance

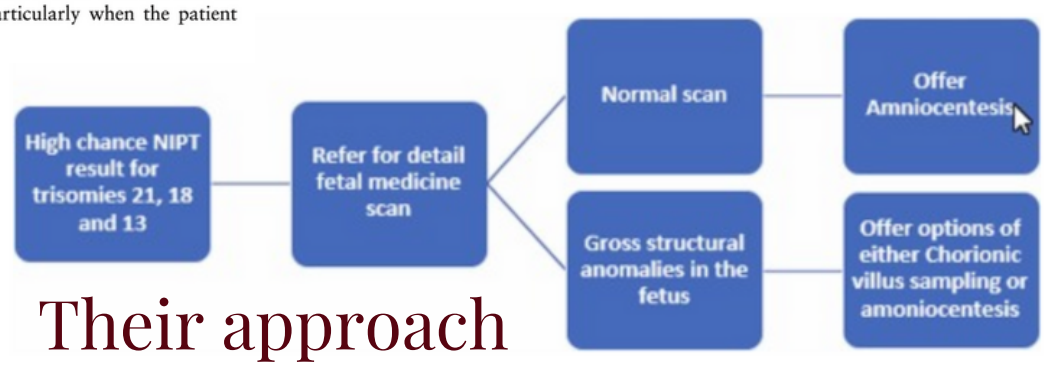
E. Thia[1], C. Choi[1], J. Zheng[1], M. Lin[1], M. Yong[2], H. Law[2], C. Tee[2], S. Yeo[1]

[1]Maternal Fetal Medicine, KK Women's and Children's Hospital, Singapore; [2]KK Women's and Children's Hospital, Singapore

Chorionic villus sampling (CVS) and amniocentesis are well established procedures for prenatal diagnosis. When CVS shows a non-mosaic Trisomy 21, the accepted clinical practice is to disclose the diagnosis as Trisomy 21 at prenatal counselling and facilitate the patient's choice, be it termination of pregnancy. However, cytogenetic diagnosis through CVS may not always reflect the true chromosomal constitution of the fetus. Confined placental mosaicism (CPM) is well known to occur and can cause conflicting results with cytogenetic report.

We report a case in which the CVS showed non-mosaic Trisomy 21 whilst the amniocentesis showed a normal karyotype. A healthy baby was delivered. CPM does occur despite CVS showing non-mosaic Trisomy 21. The question of whether amniocentesis should be performed for all cases where CVS showed mosaic Trisomy 21 remains to be debated, particularly when the patient opts for termination of pregnancy.

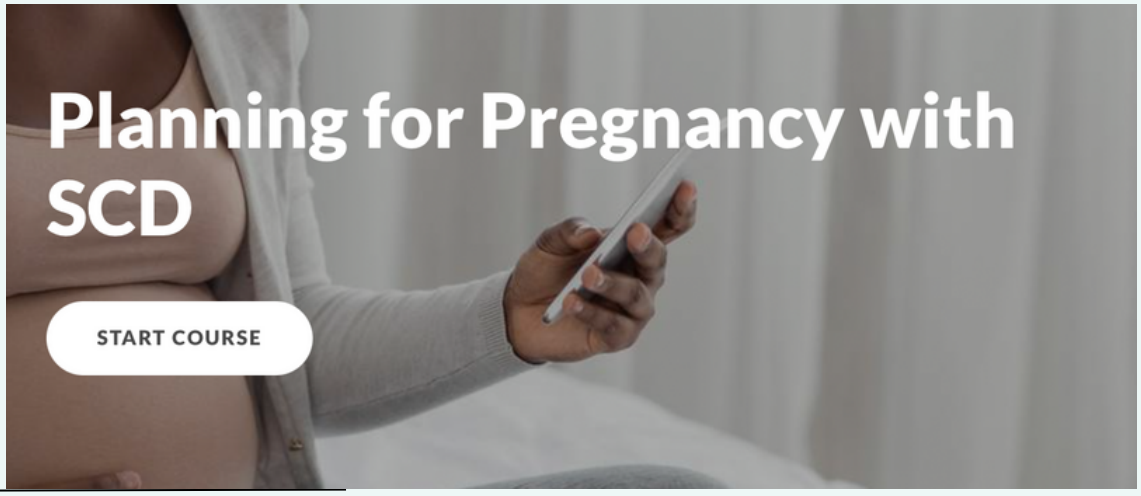
Food for thought



Their approach

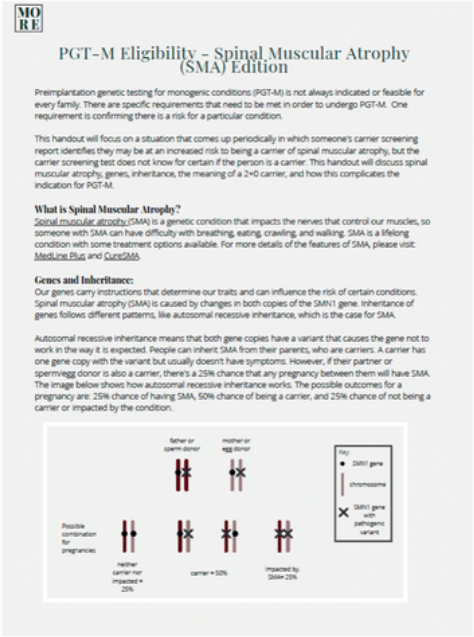
NEWSLETTER

Community Content:



Modern Reproduction Content:

One test result that just continuous complicates things is the increased risk for 2+0 carrier status for SMA. The handout discusses the result itself but also the importance of resolution for PGT-M.


MO RE

PGT-M Eligibility - Spinal Muscular Atrophy (SMA) Edition

Preimplantation genetic testing for monogenic conditions (PGT-M) is not always indicated or feasible for every family. There are specific requirements that need to be met in order to undergo PGT-M. One requirement is confirming there is a risk for a particular condition.

This handout will focus on a situation that comes up periodically in which someone's carrier screening report identifies they may be at an increased risk to being a carrier of spinal muscular atrophy, but the carrier screening test does not know for certain if the person is a carrier. This handout will discuss spinal muscular atrophy, genes, inheritance, the meaning of a 2+0 carrier, and how this complicates the indication for PGT-M.

What is Spinal Muscular Atrophy?

Spinal muscular atrophy (SMA) is a genetic condition that impacts the nerves that control our muscles, so someone with SMA can have difficulty with breathing, eating, crawling, and walking. SMA is a lifelong condition with some treatment options available. For more details of the features of SMA, please visit: MedLine Plus and CureSMA

Genes and Inheritance:

Our genes carry instructions that determine our traits and can influence the risk of certain conditions. Spinal muscular atrophy (SMA) is caused by changes in both copies of the SMN1 gene. Inheritance of genes follows different patterns, like autosomal recessive inheritance, which is the case for SMA.

Autosomal recessive inheritance means that both gene copies have a variant that causes the gene not to work in the way it is expected. People can inherit SMA from their parents, who are carriers. A carrier has one gene copy with the variant but usually doesn't have symptoms. However, if their partner or sperm/egg donor is also a carrier, there's a 25% chance that any pregnancy between them will have SMA. The image below shows how autosomal recessive inheritance works. The possible outcomes for a pregnancy are: 25% chance of having SMA, 50% chance of being a carrier, and 25% chance of not being a carrier or impacted by the condition.

Handout: PGT-M Eligibility- SMA Edition