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

INCIDENTAL FINDINGS ON CARRIER SCREENING

Kristen Miller, MGC CGC
Johns Hopkins Prenatal Diagnosis & Treatment Center
Aug 28, 2023 | 1 - 2 pm ET / 10 - 11 am PT

Register

INNOVATIONS IN VARIANT INTERPRETATION: NAVIGATING THE VUS LANDSCAPE

Britt Johnson, PhD, FACMG, Senior Medical Affairs Director, Invitae | Moderator: Flavia M. Facio, MS, CGC, Invitae
Aug 30, 2023 | 12 - 1 pm ET / 9 - 10 am PT

Register

ISSUE 10

NEWSLETTER

The little lit review

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Reproductive Carrier Screening Results With Maternal Health Implications During Pregnancy

Souter, Vivienne MD; Prigmore, Brittany MS; Becraft, Emily MS, CGC; Repass, Elizabeth MS, CGC; Smart, Trevor MS; Sanapareddy, Nina PhD; Schweitzer, Melissa MS, CGC; Ortiz, J. Bryce PhD; Wang, Yang PhD; Benn, Peter DSc

WHEN/WHO: 2020-2022, women between 18-55 years of age

WHAT: test results for pathogenic or likely pathogenic variants from Natera's 274 gene panel which encompassed 76 of ACMG's 113 recommended genes.

WHY: identify variants that had maternal health implications during pregnancy. Excluded any late disease onset as well as carriers of alpha thalassemia trait and other mild hemoglobinopathy variants.

RESULTS: 2.3% (2139/91637) were a carrier for one of the 12 genes identified to have maternal implications; 2.0% (1826/91637) identified as carriers for the 9 genes that have implications regardless of the fetal status.

Maternal health implication
irrespective of fetal status

Gene	Health concern
ABCB11	intrahepatic cholestasis of pregnancy
COL4A3/ COL4A4/ COL4A5	HTN, renal disease, nephrotic syndrome
DMD	Cardiomyopathy
F9/F11	Hemorrhage
GLA	Proteinuria, HTN, preeclampsia
OTC	Hyperammonemic crisis

Maternal health implication
dependent on fetal status

Gene	Health concern
CPT1A	Acute fatty liver of pregnancy
CYP19A1	maternal virilization
HADHA	acute fatty liver of pregnancy or HELLP syndrome - fetal complications of FGR, preterm birth poss

*above is a snippet of information - refer to article for more detail of recommendations for each gene

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The little lit review

Prenatal Diagnosis of Chromosomal Mosaicism in Over 18,000 Pregnancies: A Five-Year Single-Tertiary-Center Retrospective Analysis

Shuyuan Li , Yiru Shi , Xu Han, Yiyao Chen, Yinghua Shen, Wenjing Hu, Xinrong Zhao and Yanlin Wang

A concerning case came up by a colleague in which the patient had a positive cfDNA screen for T21 and an unremarkable ultrasound. Amniocentesis karyotype was normal. Microarray, however, identified mosaicism of Trisomy 21 and a revised karyotype followed confirming the microarray results.

Why is this concerning? Well had this been a FISH negative result, then the positive array would not be such a dramatic surprise. FISH has its limitations, so it is recommended to confirm with additional testing. However, the karyotype is believed to be more diagnostic. This case, however, highlights even the karyotype's limitations. Karyotyping is performed on the available and select number of cells. It could miss a cell population's genotype whereas microarray is the combination of cells' DNA. Array may be more sensitive to mosaicism in some cases, but it's important to verify with the performing lab their array's sensitivity compared to karyotype.

This article reviews 23 cases of discordance. 16 cases were discordant amniocentesis results of karyotype and either array or FISH. 5 cases were normal karyotypes with mosaic microarray results involving chromosomes X, 14, 15, 16, and 7. The other cases were of abnormal mosaic karyotypes and normal arrays. Explanations for the latter cases were the lower mosaicism thresholds being missed by the array and the marker chromosome being of heterochromatin origin. Given there are both instances of normal/abnormal karyotype/array, it can be worthwhile to order both assessments for patients. This approach can add cost and time as well as increase the possibility of uncertainty. I'd love to hear about others' approaches to diagnostic testing given these case examples. I've utilized the FISH reflex approach (if FISH is abnormal, reflex to karyotype; if normal, reflex to microarray).

The article has a wealth of information, and I only focused on one aspect of what this review contributes. Check out the full article !

# **of cases**	**karyotype**	**microarray**
5	normal	abnormal (involving chr X, 14, 15, 16, 7)
11	abnormal	normal

NEWSLETTER

Community Content:

Great content on anything related to treatment and therapies for conditions such as sickle cell disease and leukemia. These organizations were mentioned in the recent webinar from Expecting Health.

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Fertility Preservation Grants

Modern Reproduction Content:

Every week, a blog entry is posted directed to the general population on Modern Reproduction's website. A recent post was on why PGT-M is not like other genetic tests. It requires a specialized test design period given the linkage analysis methodology utilized whereas other genetic tests use other methods that are not specific to the family's DNA. It can be described as a curated test as opposed to an off the shelf test.

8/16/23

Why is PGT-M different from other genetic tests?

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