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.

Sign up for the newsletter here

Webinars

ELSI FRIDAY FORUM | THE IMPACT OF DOBBS ON EMERGING REPRODUCTIVE TECHNOLOGIES
3/8 12PM EST

Register

STATE OF PRECISION MEDICINE SUMMIT
3/6 11-3PM EST

Register

PROGENESIS: 'ALABAMA SUPREME COURT RULING: HOW THE LEGAL SYSTEM IS IMPACTING MEDICINE'
3/13 6PM EST

Register

ASRM GC: SINGLE GENE TESTING FOR INFERTILITY
3/13 2PM EST

Register

ISSUE 27

NEWSLETTER

The little lit review

1

Gene selection for genomic newborn screening: moving towards consensus?

Lilian Downie, Sophie E Bouffler, David J Amor, John Christodoulou, Alison Yeung, Ari E Horton, Ivan Macciocca, Alison D Archibald, Meghan Wall, Jade Caruana, Sebastian Lunke, Zornitza Stark

This article highlights the significance of gene selection in genomic newborn screening (gNBS) and endeavors to establish a consensus gene list. A multidisciplinary team curated the list using an open platform, focusing on severe treatable disorders with an onset below 5 years. Among 1,279 genes reviewed, 604 met inclusion criteria, with metabolic conditions (25%), immunodeficiencies (21%), and endocrine disorders (15%) being prevalent. A comparison with five other gNBS projects revealed 55 consensus genes. The study underscores the importance of clear principles in gene inclusion, addressing challenges like treatability definitions and gene-disease association strength. The curated gene list serves as a foundation for international harmonization in gNBS, aiming to navigate complexities such as analytical validity and healthcare system variability.

Question? Do you agree that “the inclusion of non-treatable and/or adult onset conditions would require an extra component of choice and decision-making in the consent process and further consideration regarding the timing of result return”?

Criteria:

1.Age of onset of disease or access to treatment **<5** years
2. Disease causes significant morbidity or mortality
3.Treatment or intervention that significantly alters disease course is available
4. Clinically valid gene-disease association (at least three independent families reported)
5. Common disease-causing variants reliably detected on available genome sequencing platform and bioinformatics pipeline.

Technical difficulties:

1. Mapping: “generally caused by regions of high homology, including pseudogenes, and create regions in which sequencing reads cannot be aligned unambiguously. This reduces accuracy of variant calling and complicates, or can prevent, the analysis of a gene, including some for conditions included in some standard NBS programs (e.g. CYP21A2 and SMN1).”

2. Variant detection issues: “Genes in which common disease variants remain difficult to ascertain by clinically accredited short-read WGS include HBA1/2 and F8, which are frequently disrupted by complex structural variants or recurring inversions, respectively.”

BabyScreen+ gene panel

ISSUE 27

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Common teratogenic medication exposures-a population-based study of pregnancies in the United States

Yanning Wang , Nicole E Smolinski, Thuy Nhu Thai, Amir Sarayani, Celeste Ewig, Sonja A Rasmussen, Almut G Winterstein

This study investigates the prevalence of prenatal exposure to teratogenic medications in the United States from 2011 to 2018. Analyzing data from the MerativeTM MarketScan Commercial Database, the study identifies the 10 most commonly used teratogenic medications, assessing their impact on live and nonlive pregnancies. The findings reveal fluctuations in exposure rates over the study period, with certain medications showing significant increases. Notably, pregnancies with nonlive outcomes exhibit higher exposure rates. Medications like sulfamethoxazole/trimethoprim, fluconazole, and beta-blockers are identified as frequently used with known teratogenic risks. The study emphasizes the need for targeted risk mitigation strategies and highlights evolving trends in prenatal medication exposure, suggesting avenues for clinical and regulatory interventions.

Highest rates of prenatal exposure:

sulfamethoxazole/trimethoprim
high-dose fluconazole
topiramate
lisinopril
warfarin
losartan
carbamazepine
valproate
vedolizumab
valsartan
low-dose fluconazole
metoprolol
atenolol
duloxetine
gabapentin
lidocaine
methimazole
hydralazine
lithium
meloxicam

Of all pregnancies, 2.3% and 4.8% had exposure to at least 1 medication with known or potential teratogenic risk, respectively.

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Community Content:

March of Dimes created resources/website in Spanish

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Modern Reproduction Content:

Substack post number two is up!