# 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

### COGEN -IVF WORLDWIDE ONLINE CONGRESS

November 3rd, 2023 @ **5:30 am** ET

Register

### FDA PUBLIC HEARING FOR GENE THERAPY

October 31, 2023 @ 12:30 pm ET

Register

ISSUE 17

# NEWSLETTER

## *The little lit review*

### 1 The potential impact of implementation of expanded carrier screening on pediatric patient diagnoses: A retrospective chart review of patients who receive care in an outpatient genetics clinic in the northeast

Kelly Roche | Shama P. Khan | Christina Botti | Philip Giampietro | Sharon Anderson | Elena Ashkinadze

| Diagnosis |
|---|
| ABCA12-related congenital ichthyosis |
| Alport syndrome |
| AR primary microcephaly |
| Arginase deficiency |
| Aromatic L-amino acid decarboxylase deficiency |
| ARX-related disorder |
| Bardet-Biedl syndrome |
| Carnitine palmitoyltransferase II (CPT II) deficiency |
| Carnitine uptake deficiency |
| Charcot Marie Tooth Type 4C |
| Cobalamin C deficiency |
| Congenital adrenal hyperplasia |
| Dents disease, XL |
| DFNB4/Pendred syndrome |
| Duarte variant galactosemia (D2) homozygosity |
| Duchenne/Becker muscular dystrophy |
| Fabry disease |
| Familial Mediterranean Fever |
| Fanconi anemia type L |
| Fragile X |
| Friedreich's ataxia |
| Fructose 1,6 biphosphatase deficiency |
| Gilbert syndrome |
| Glucose-6-phosphate-dehydrogenase (G6PD) deficiency |
| Gaucher disease |
| GJB2 and GJB6-related hearing loss, digenic |
| GJB2-related hearing loss |
| GLDC-related disorder |
| Glycogen storage disease type IXa |
| GM1 gangliosidosis |
| HSD10-related disorder |
| Hunter syndrome |
| HUWE1-related intellectual disability syndrome |
| Hyperphenylalanemia |
| Hypohydrotic ectodermal dysplasia |
| Isovaleric acidemia |
| Mainzer-Saldino syndrome |
| Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency |
| Methylmalonic acidemia (cobalamin B deficiency) |
| MICRO syndrome |
| MSTO1-related disorder |
| Mucolipidosis type III gamma |
| Mucopolysaccharidosis type IIIB, Sanfillippo type B |
| MYO15A-related hearing loss |
| NSUN2-related disorder |
| Osteogenesis imperfecta |
| Partial biotinidase deficiency |
| PCDH15-related hearing loss |
| PIGN-related disorder |
| Polycystic kidney disease, AR |
| POU3F4-related hearing loss |
| PGAP1-related disorder |
| Primary ciliary dyskinesia |
| Progressive pseudorheumatoid arthropathy of childhood |
| Pycnodysostosis |
| Ribose-5-phosphate deficiency |
| Senior Loken syndrome |
| Spinal muscular atrophy Type 3 |
| Usher syndrome |
| Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency |
| Wilson syndrome |
| Xeroderma pigmentosum |

The authors performed a retrospective analysis from June 2017-2020 of one institute to identify if patients diagnosed with an autosomal recessive, x-linked recessive, or Fragile X would have otherwise been identified via expanded carrier screening.

There were 1189 families identified excluding those diagnosed with CF, SMA, hemoglobinopathies, thalassemia, endocrine disorders, PCDH19-related epilepsy, autosomal dominant, and x-linked dominant conditions. Of these families, 8% or 99 were included in the analysis.

60/99 cases would have been expected to be detected via a 526 gene panel.

For the 39/99, the reasons the diagnosis would not have been made with the 526 gene panel include:

1. 26/39 cases, the gene was not on the panel
2. 11/39 cases, the gene was on the panel but the individual had at least one VUS which would not have been expected to be reported out given carrier screening typically only reports out pathogenic and likely pathogenic variants
3. 2/39 were de novo variants

Importantly, one of the limitations of the analysis is that parents were not tetsed with the 526 panel, so carrier status was not confirmed. Additional cases may have been de novo or it is possible that even with screening, the parental variants may have been a false negative and still missed.

The authors pose that carrier screening is not only helpful for preimplantation genetic testing and prenatal diagnosis options but also for a reduction in the diagnostic odyssey, possible decrease cost in overall testing, targeted and earlier treatment, and reduction of potential irreversible harm for some conditions.

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## *The little lit review*

### Genetic causes of sporadic and recurrent miscarriage

Pedro Melo, Ph.D., Rima Dhillon-Smith, Ph.D., Md Asiful Islam, Ph.D., Adam Devall, Ph.D., and Arri Coomarasamy, M.D

The authors explored the genetic causes of both sporadic and recurrent miscarriage. Data is emerging but also not robust enough to determine genetic causes other than chromosomal abnormalities. Studies indicate genes involved in the immune response, coagulation, metabolism, and angiogenesis may underlie miscarriages.

Prevalence of chromosome abnormalities is similar for sporadic and recurrent miscarriage, indicating other factors as a cause for recurrent miscarriage such as uterine malformations, endocrine disorders, heightened immunity due to inflammation or infection, and 2-5% of cases secondary to parental translocation.

Male and female age are considered risk factors for miscarriage, particularly female age <20 and >40. Disorders associated to miscarriage include: inherited and acquire thrombophilia, subclinical hypothyroidism, thyroid autoimmunity, PCOS, and prolactin disorder.

>50% of first trimester miscarriages are due to genetic defects

30-60% = trisomies
11-13% = triploidy
10-15% = Monosomy X
9% = tetraploidy
2-6% = structural chromosome rearrangement
8% = mosaicism

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## Community Content:


BORN Ontario has done a great job at provider guides for what genetic tests to offer to patients. Of course, there may be differences from country to country pertaining to access and coverage.

## Modern Reproduction Content:

Just like the weekly newsletter, we have a weekly blog post. Typically, the general population is the intended audience, but I know I like to take a peek at what general content is out there.