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:

PATH TO PRECISION HEALTH BY SARAH LAWERENCE'S GENOMIC INSTITUTE
4/16 @ 2PM EST

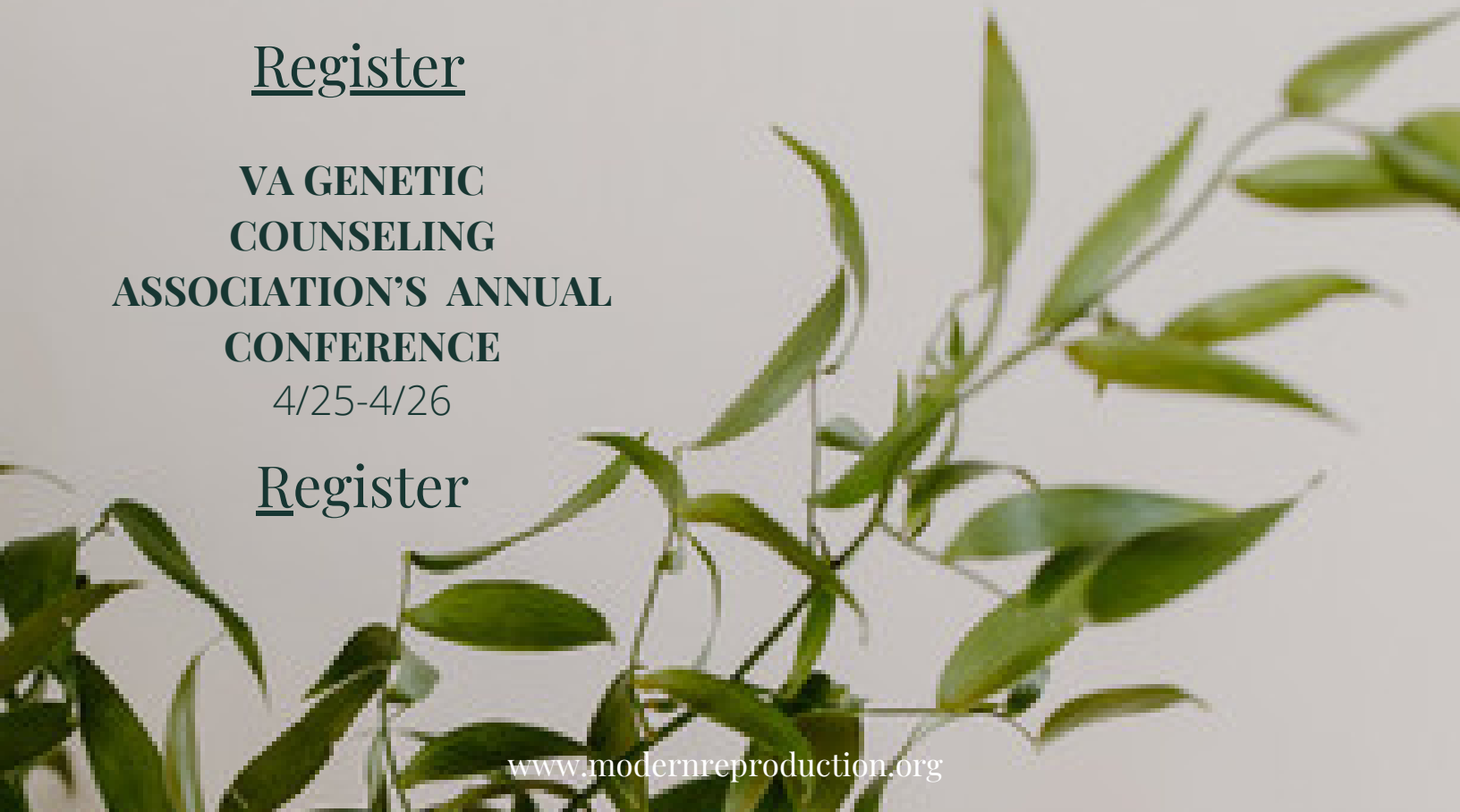
Register

ETHICAL SCRUTINY OF GAMETE DONATION GUIDELINES & PRACTICES
4/24/24 @ 1PM EST

Register

VA GENETIC COUNSELING ASSOCIATION'S ANNUAL CONFERENCE
4/25-4/26

Register



ISSUE 30

NEWSLETTER

The little lit review

1

Epigenetics of pregnancy: looking beyond the DNA code

Daniela Zuccarello, Ugo Sorrentino, Valeria Brasson, Loris Marin, Chiara Piccolo, Antonio Capalbo, Alessandra Andrisani & Matteo Cassina

The article dove into the main epigenetic mechanisms such as DNA methylation, histone post translational modifications, non-coding RNAs, and imprinting. There was particular focus on these epigenetic actors in gametes, embryo stages, and fertilization including mention on pre-receptive and receptive endometrium, decidualization, and endometrial fluid. The placenta and brain development were also discussed as well as impacts from maternal nutrition, teratogenic exposures, and stress hormones. Attention to this area can expose additional research areas particularly to explore other causes of infertility. At this time, about 50% of infertility patients are left without an explanation. Epigenetic factors may reduce the number of unexplained infertility diagnoses.

"There is an association between assisted reproductive treatment (ART) procedures and slightly higher frequencies of imprinting syndromes may be due to ART causing an abnormal epigenome in the offspring."

RNA is not just involved in encoding for proteins. Non-coding RNAs (ncRNAs) have been identified to be involved with regulation and gene silencing such as during decidualization

NEWSLETTER

The little lit review

Adverse pregnancy outcome in fetuses with early increased nuchal translucency: prospective cohort study

B. B. Bet, M. A. Lugthart, I. H. Linskens, M. C. van Maarle, E. van Leeuwen, E. Pajkrt

The article explores the potential for adverse outcomes when pregnancies are identified to have increased nuchal translucency earlier in pregnancy. This prospective study recruited women, whose pregnancies were identified to have NTs >2.5mm (99th%tile) at <45mm, incidentally discovered at a dating scan. A second ultrasound was conducted once the pregnancies were >45mm and monitored until 4 weeks after delivery or after TOP. After the second scan, two groups emerged: those that normalized and were <3.5mm and those that persistent at >3.5mm. Additionally, the authors considered the NT size and correlation to adverse outcomes: 2.5-3.4mm, 3.5-4.4mm, and >4.5mm.

Ultimately, the authors found that 1. an early increased NT is associated with adverse outcomes such as chromosomal conditions, miscarriage, or birth defects and 2. even with early resolution, there remains an increased risk compared to the general population

Table 2. **Degree of early NT enlargement and relationship with adverse pregnancy outcome, N (%)**

		Adverse pregnancy outcome					
		Congenital anomalies					
NT at inclusion (mm)	Total cases	Aneuploidies	Other genetic disorders	Structural anomalies *	Pregnancy loss †	Total	Live birth, no defects
2.5 – 3.4	41	6 (14.6)	1 (2.4)	2 (4.9)	-	9 (22.0)	32 (78.0)
3.5 – 4.4	45	13 (28.9)	4 (8.9)	-	1 (2.2)	18 (40.0)	27 (60.0)
≥ 4.5	23	6 (26.1)	2 (8.7)	2 (8.7)	2 (8.7)	12 (52.2)	11 (47.8)
Total	109	25 (22.9)	7 (6.4)	4 (3.7)	3 (4.6)	39 (35.8)	70 (64.2)

** Structural anomaly without the diagnosis of a chromosomal or genetic disorder.*

† Pregnancy loss (miscarriage or fetal death) without another diagnosis, thus no aneuploidy, no other genetic or structural anomalies.

Table 3. **Overview of abnormal findings grouped by type of test. Subdivided for normalized and persistently increased NT groups, N (%)**

	Total (n=109)	Normalized NT (n=63)	Pers. increased NT (n=46)
Abnormal NIPT	*5 (4.6)*		
Trisomy 21	2 (1.8)	1 (1.6)	1 (2.2)
Trisomy 18	1 (0.9)	-	1 (2.2)
Trisomy 13	2 (1.8)	1 (1.6)	1 (2.2)
Abnormal QF-PCR	*20 (18.3)*		
Trisomy 21 *(in total, n=7, 6.4%)*	5 (4.6)	1 (1.6)	4 (8.7)
Trisomy 18 *(in total, n=11, 10.1%)*	10 (9.2)	-	10 (21.7)
Trisomy 13 *(in total, n=4, 3.7%)*	2 (1.8)	1 (1.6)	1 (2.2)
Klinefelter syndrome (XXY) *	1 (0.9)	1 (1.6)	-
Monosomy X	2 (1.8)	-	2 (4.3)
Abnormal Microarray	*3 (2.8)*		
22q11 deletion syndrome	1 (0.9)	-	1 (2.2)
13q31.1q34 microdeletion	1 (0.9)	1 (1.6)	-
15q11.2 microdeletion ‡	1 (0.9)	-	1 (2.2)
Abnormal WES	*4 (3.7)*		
MYRF gene mutation	1 (0.9)	-	1 (2.2)
MED13L gene mutation	1 (0.9)	-	1 (2.2)
MED12L gene mutation	1 (0.9)	1 (1.6)	-
CBL-gene mutation ‡	1 (0.9)	-	1 (2.2)
Abnormal FTAS	*3 (2.8)*		
Fetal hydrops	2 (1.8)	-	2 (4.3)
Bilateral radial aplasia §	1 (0.9)	1 (1.6)	-
Abnormal STAS	*1 (0.9)*		
Sacrococcygeal teratoma *	1 (0.9)	1 (1.6)	-
Total	36 (33.0)	9 (14.3)	27 (58.7)

** Potentially missed by routine first-trimester screening consisting of NIPT and FTAS, as the Dutch NIPT does not include sex chromosomes and no ultrasound abnormalities were seen in the first trimester.*

† Additional finding, definite relation with increased NT could not be made.

‡ Noonan-like syndrome

§ No underlying genetic cause was found with QF-PCR, microarray or WES.

Abbreviations: FTAS; first-trimester anomaly scan, NIPT; non-invasive prenatal test, NT; nuchal translucency, QF-PCR; Quantitative Fluorescence-Polymerase Chain Reaction, STAS; second-trimester anomaly scan, WES; whole exome sequencing.

ISSUE 30

NEWSLETTER

Community Content:

Flo pregnancy app/website is one of many groups coming together to assist people with tracking their cycles and subsequent pregnancies. There are tons of articles on these sites for patients to navigate both of these life events.

Modern Reproduction Content:

Blog posts are available on the site, suited for patients, on a variety of topics.