FINAL RESULTS OF A MULTICENTER STUDY COMPARING CELL-FREE DNA AND TROPHECTODERM BIOPSIES IN 2,539 HUMAN BLASTOCYSTS

L. NAVARRO-SÁNCHEZ[1], D. SAKKAS[2], N. FRANTZ[3], D. M. SOSCIA[4], W. VENIER[5], E. DE LA FUENTE[1], C. BISIOLI[6], B. TEKE[7], G. BARROSO[8], D. VALBUENA[1], C. SIMON[9], AND C. RUBIO[1]

[1]Igenomix, part of Vitrolife group, Paterna, Valencia, Spain; [2]Boston IVF, Waltham, MA, USA; [3]Nilo Frantz Reproductive Medicine, Porto Alegre, Brazil; [4]Ivirma Global Research Alliance, Genera, Roma, Italy; [5]World Embryology Skills & Training (WEST), Carlsbad, CA, USA; [6]Pregna Medicina Reproductiva, Buenos Aires, Argentina; [7]Bahçeci Health Group, Istanbul, Turkey; [8]Nascere, Mexico City, DF, Mexico; [9]University of Valencia; BIDMC Harvard University; Carlos Simon Foundation, Valencia, Spain

ASRM 2024
Equity, Access, and Innovation
Denver, Colorado
October 19-23, 2024

PURPOSE & OBJECTIVES

This study aimed to evaluate the intrinsic and extrinsic factors that can have an impact in the concordance rate, when testing for chromosomal abnormalities in cell-free DNA (cfDNA) and trophectoderm (TE) biopsies obtained from the same blastocysts.

MATERIAL & METHODS

We carried out a prospective study to investigate the concordance of cfDNA present in spent blastocyst medium with the corresponding TE biopsy in 10 IVF clinics. A total of 2,539 day-6/7 human blastocysts from 716 patients underwent media collection and TE biopsy from April 2018 to December 2022 (Figure 1).
Embryos were cultured in routine conditions up to day 4, when embryos were washed, transferred to a new 10µl medium droplet, and cultured for at least a further 48 hours. Then, on day 6, culture media were collected and frozen at -20ºC. Assisted hatching, TE biopsy and vitrification were performed after media collection. All samples were analyzed by next generation sequencing (NGS) using the Ion ReproSeq PGS Kit (ThermoFisher Scientific), the Ion Chef plus and the Ion S5 XL Sequencer.
R (version 4.2.1) was used for the statistical analysis. A multivariate logistic regression analysis was performed to identify the variables affecting the concordance rate, their adjusted odds ratio (aOR) and confidence interval (CI).

RESULTS

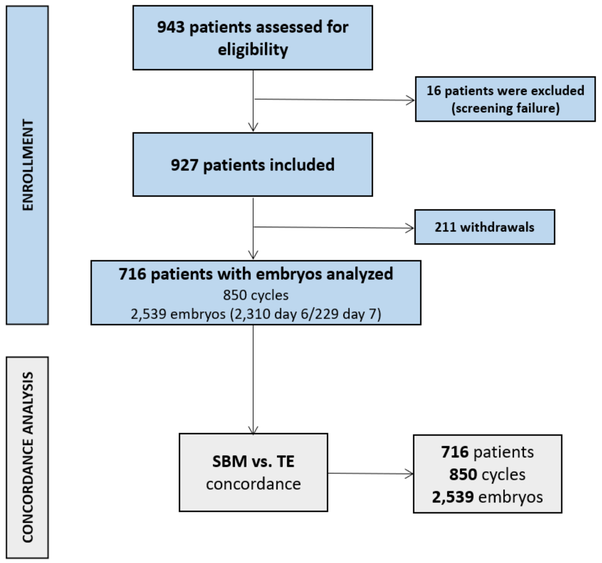
From the 2,539 embryos analyzed, we obtained a result in 2,208 cfDNA-TE pairs. In 1,726 of them, both cfDNA/TE were euploid or aneuploid, corresponding to a ploidy concordance rate of 78.2%. It was not statistically different between the 10 participating centres (73.8 - 83.1%, p=0.12) but it showed a statistically significant increase directly related to female age (p<0.0001) (Figures 2 and 3). The multivariant analysis showed that only the number of NGS reads in the media was significantly related to the concordance rate. See Table 1.

CONCLUSIONS

Only the number of NGS reads in the media was significantly related to the concordance rate, showing that sample quality (cfDNA concentration in the culture media) deeply impacts in the results.

Embryo cfDNA analysis shows very robust results independently of the patient infertility background, stimulation response, culture conditions and blastocyst quality. Therefore, it can be widely applied as a non-invasive approach.

Figure 1. Study workflow.



ACKNOWLEDGEMENTS

We thank all the patients who kindly agreed to participate in this study and the embryology teams and the medical staff at all participating centres for their ongoing assistance with patient recruitment, embryo culture, sample and data collection.

RESULTS

Figure 2. cfDNA-TE concordance rate per centre.

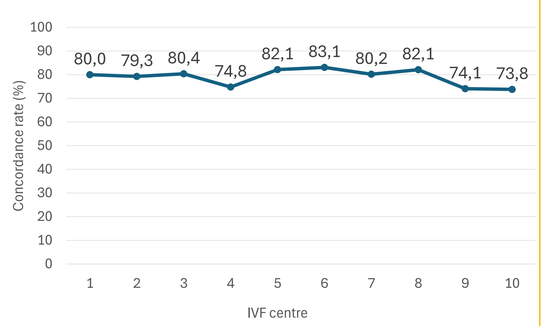


Figure 3. cfDNA-TE concordance rate depending on female age.

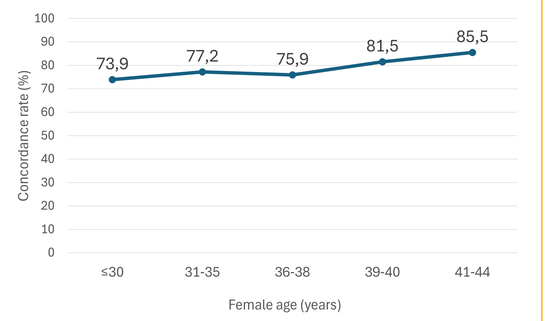


Table 1. Multivariate logistic regression analysis.

Variable	aOR	95% CI	p-value
Female age	1.03	0.98 - 1.08	0.27
Body mass index	1.00	0.97 - 1.04	0.85
No. previous implantation failure	1.02	0.90 - 1.18	0.73
No. previous miscarriages	1.10	0.93 - 1.31	0.29
No. previous live birth	1.08	0.88 - 1.34	0.49
Oocyte origin (own/donated)	0.73	0.19 - 2.27	0.61
No. MII oocytes	0.96	0.91 - 1.02	0.19
Type of fertilization (ICSI/IVF)	-	-	0.53
No. 2PN	1.04	0.97 - 1.12	0.26
Culture conditions (media and incubator used)	-	-	0.67
No. blastocysts analyzed	1.05	0.99 - 1.11	0.14
Embryo quality	0.79	0.52 - 1.19	0.26
Expansion degree	-	-	0.68
Day of media collection	1.33	0.34 - 5.34	0.68
No. NGS media reads	1.19	1.01 - 1.40	**0.04**
Media result (euploid/aneuploid)	1.09	0.79 - 1.49	0.61

REFERENCES

1. Rubio C, Navarro-Sánchez L et al. “Multicenter prospective study of concordance between embryo cell-free DNA and trophectoderm biopsies from 1,301 human blastocysts”. *Am J Obstet Gynecol*. 2020; **223**(5):751.e1-13.
2. Navarro-Sánchez L, García-Pascual C et al. “Non-invasive preimplantation genetic testing for aneuploidies: an update.” *Reprod Biomed Online*. 2022; **44**(5):817-828.
3. Sakkas D, Navarro-Sánchez L et al. “The impact of implementing a non-invasive preimplantation genetic testing for aneuploidies (niPGT-A) embryo culture protocol on embryo viability and clinical outcomes”. *Human Reprod*. 2024; **39**(9): 1952–1959.

CONTACT INFORMATION