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Noninvasive preimplantation genetic test for aneuploidy (NIPGT-A) has a lower false positive rate than that of the invasive PGT-A

L.D. Vagnini[2], C.G. Petersen[1,2], A. Renzi[2], J.B.A. Oliveira[1,2], A.H. Oliani[3], R. Nakano[4], C.G. Almodin[5], C. Marcondes[6], A. Ceschin[7], A. Amaral[8], E. Borges Jr[9], A. Castelo Branco[10], J.B. Soares[11], J. Lopes[12], J.G. Franco Jr.[1,2]

[1]Paulista Center for Diagnosis Research and Training, Ribeirao Preto, Brazil.
[2]Centre for Human Reproduction Prof Franco Jr, Ribeirao Preto, Brazil.
[3]Sao Jose do Rio Preto School of Medicine FAMERP, Sao Jose do Rio Preto, Brazil.
[4]Ferticlin Human Fertility Clinic, Sao Paulo, Brazil.
[5]Materbaby, Maringa, Brazil.
[6]Santista Nucleus of Human Reproduction, Santos, Brazil.
[7]Feliccita Fertility Institute, Curitiba, Brazil.
[8]Genesis Human Reproduction Assistance Center, Brasilia, Brazil.
[9]Fertility Medical Group, Research, Sao Paulo, Brazil.
[10]Art Fertil Human Reproduction Clinic, Recife, Brazil.
[11]Alpha Project - Alliance of Assisted Fertilization Laboratories, Sao Paulo, Brazil.
[12]CENAFERT, Salvador, Brazil.

Study question

Does NIPGT-A have lower false positive rates (FPR) than invasive PGT-A?

Methods

This cohort study included a total of 37 blastocysts vitrified on day 5 that were previously biopsied for invasive PGT-A and presented a diagnosis of aneuploidy. The embryos were donated under informed consent by patients following the Human Medical Authority regulations. Blastocysts were thawed and cultured in 15µl drops of culture medium under oil. After their expansion (4-8hours), the blastocysts were transferred to NGS tubes and their corresponding spent media were collected for analysis.

The DNA of all samples (spent culture medium and whole embryo) was amplified by the MALBAC® technology (Yikon Genomics). The samples were subjected to next-generation sequencing (NGS) using Illumina MiSeq® System. The ploidy status results obtained from ChromGo™ software (Yikon Genomics) for culture medium and whole embryo were compared to determine the accuracy of NIPGT-A for screening chromosomal abnormalities in Genomics) for culture medium and whole embryo were compared to determine the accuracy of NIPGT-A for screening chromosomal abnormalities in each embryo.

Table 1. NIPGT-A and Invasive PGT-A results

A) NIPGT-A	Whole Embryo	
	Aneuploidy	Normal
Aneuploidy	29	2
Normal	0	6

PPV: 93.5% FPR: 6.5%

B) Invasive PGT-A	Whole Embryo	
	Aneuploidy	Normal
Aneuploidy	29	8
Normal	----	----

PPV: 78.4% FPR: 21.6%

Results

DNA from all 37 spent media samples and whole embryos were successfully amplified. Comparing the results of NIPGT-A and whole embryos sequencing, the positive predictive value (PPV) was 93.5% and the FPR was 6.5% (Table 1A). On the other hand, comparing the whole embryo and invasive PGT-A results, the PPV was 78.4%, and the FPR was 21.6% (Table 1B). Both NIPGT-A and invasive PGT-A had a negative predictive value (NPV) of 100% and a false negative rate (FNR) of 0%. In the eight cases of disagreement the results are presented in the Table 2.

Conclusion

When DNA sequencing from whole embryo cells was used as the gold-standard, the FPR of NIPGT-A was 3.32-times smaller than that obtained with invasive PGT-A. NIPGT-A has a lower FPR than invasive PGT-A and does not require micromanipulation skills, avoiding trophectoderm biopsies trauma and seems to provide more accurate results corresponding to the ploidy status of the whole embryo. Thereby NIPGT-A should be considered as the test of choice for genetic evaluation of the embryo.

Table 2. Disagreement results of whole embryo, NIPGT-A and invasive PGT-A

Whole embryo	NIPGT-A	Invasive PGT-A
46,XY	46,XY	XY,+1q(x3);+3q(x3)
46,XY	46,XY	XY,-2(x1)
46,XY	XY,-1(x1);-9q(x1)	XY,+9q(x3)
46,XX	46,XX	XX,+9q(x3)
46,XX	46,XX	XX,-4(x1)
46,XY	46,XY	X0, multiple abnormalities
46,XX	46,XX	XX,+13(x3)
46,XY	XY,-1(x1);-9(x1),-19(x1);-21(x1)	XY,-9(x1)