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Research Article

Array-Comparative-Genomic-Hybridization (Acgh) Based Preimplantation-Genetic-Diagnosis (PGD) for Balanced Translocation Carriers Improves both Diagnostic and Pregnancy Rates Compared to Fluorescent-In-Situ-Hybridization (FISH) and Polymerase-Chain-Reaction (PCR) Based PGD

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Abstract

Introduction: Preimplantation genetic diagnosis (PGD) of balanced translocations is usually performed using Fluorescence-in-Situ-Hybridization (FISH), and more rarely by Polymerase-Chain-Reaction (PCR). These methods assess only chromosomes involved in the translocation, as opposed to array comparative-genomic-hybridization (aCGH) which screens all chromosomes.

Material and Methods: In this report, we compared the diagnosis and pregnancy rates for balanced translocations using all three techniques in a retrospective study of 75 PGD cycles.

Results: Of 331 embryos analyzed by FISH, 225 (68%) were successfully diagnosed, 34 (15%) were transferable yielding a pregnancy rate of 13% per Ovum-Pick-Up (OPU). With PCR, 80 out of 124 embryos (65%) were diagnosed, 21 (26%) were transferable, and a pregnancy rate of 14.3% per OPU was achieved. Using aCGH, 60 of 71 embryos (85%) were successfully diagnosed, 26 of which (43%) presented with chromosomal aneuploidies not associated with the parental translocation. Nine embryos diagnosed by aCGH were transferable yielding a pregnancy rate of 40% per OPU. The proportion of embryos successfully diagnosed and pregnancy rates per OPU were significantly higher using aCGH compared to FISH or PCR (p= 0.036; p=0.017), respectively.

Conclusion: Altogether, these data indicate that the use of aCGH for chromosomal translocation PGD significantly increases diagnosis and pregnancy rates.

Keywords: Pre-implantation genetic diagnosis; Chromosomal translocations; Single cell fluorescence in situ hybridization; Single cell PCR; Single cell array comparative genomic hybridization

Abbreviations: aCGH-array Comparative Genomic Hybridization; ADO-Allele Drop Out; CMA-Chromosomal Microarray Analysis; CVS-Chorionic Villus Sampling; ESHRE-European Society for Human Reproduction and Embryology; FISH-Fluorescence in Situ Hybridization; ICSI-Intra-Cytoplasmic Sperm Injection; IRB-Institutional Review Board; IUFD-Intra Uterine Fetal Death; IVF-in vitro fertilization; LSI-Locus Specific Identifier; OPU-Ovum Pick Up; PCR-Polymerase Chain Reaction; PGD-Preimplantation Genetic Diagnosis; PGS-Preimplantation Genetic Screening; SD-Standard Deviation; STR-Short Tandem Repeat; WGA - Whole Genome Amplification

Introduction

Chromosomal translocations are a relatively common genetic variation found in ~1 in 380 newborns. They are caused by rearrangement of non-homologous chromosomes and are classified as either reciprocal or Robertsonian. Reciprocal translocations result from an exchange of genetic material between non-homologous chromosomes (~1 in 500-600 newborns) while Robertsonian translocations are caused by breaks at or near the centromeres of two acrocentric chromosomes (~1 in 900 newborns) [1]. By rule, a translocation can be either balanced or unbalanced in terms of chromosomal copy number state. When a translocation is balanced the amount of genetic content is normal and the carrier of the translocation is usually healthy. Balanced translocations are 10 times more common in in vitro fertilization (IVF) patients, particularly those with severe male factor infertility, and are reported in over 3% of people experiencing repeated implantation failure following IVF treatment [2]. The reproductive risks for a translocation carrier can be estimated by studying the translocated chromosomes and their breakpoint locations. In this way, each couple presents with its own distinct risk for reproductive complications that are associated with their particular translocation. These complications include: infertility, increased miscarriage rates, intra uterine fetal deaths (IUFD) and neonatal anomalies [3]. All of these outcomes can be minimized by preimplantation genetic diagnosis (PGD) to eliminate embryos with unbalanced karyotypes [4-8]. PGD is designed to prevent the transmission of genetic disease to offspring and it is an alternative to prenatal diagnosis and pregnancy termination.

Nevertheless, PGD is challenging for two primary reasons. For one,

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PGD can be performed solely on a miniscule amount of genetic material found in IVF biopsies (which includes single polar body, blastomere, or trophectoderm biopsies). Another issue with PGD is time. Fresh transfer PGD cycles require the diagnosis of IVF biopsies to complete within 24-48 hours so that embryos can be transferred within a proper window for successful implantation. Until recently, PGD for balanced translocations was performed using fluorescence in situ hybridization (FISH). This type of testing is performed with breakpoint spanning probes or centromeric/subtelomeric probe combinations. Although FISH is a relatively direct method of analyzing embryonic cells, it has many well-documented technical constraints [6,9,10] that include: cell loss during the fixation process, signal overlap, signal splitting and variable cell fixation. The latter problem allows residual cytoplasm to interfere with probe attachment thereby complicating signal interpretation. Error rates for translocation FISH protocols, tested on blastomeres from research embryos, have been reported to range from 0% to 10% with an average error rate of 6% [5,9,11,12]. Furthermore, in the event that embryos are not diagnosed due to technical failure of the procedure, transfer is not performed. For these reasons substantial efforts have been made, recently, to devise a more efficient technique for genetic analysis of translocations in IVF biopsies.

One alternative to FISH is a molecular technique involving Polymerase Chain Reaction (PCR) amplification of polymorphic short tandem repeat (STR) markers. PCR has been used in PGD extensively over the last 20 years for the detection of single-gene disorders. Although in theory, PGD for monogenic disorders could be accomplished using mutation analysis alone; this would be accompanied by a high error rate due to allele drop out (ADO) which can reach 10-20%. ADO results from preferential allele-specific amplification and can lead to misinterpretation of the genetic status of the oocyte/embryo. Therefore, PGD protocols need to include several linked informative polymorphic markers (STRs) flanking the disease gene in order to minimize misdiagnosis due to ADO, allowing accuracy rates that approach 100%. In cases of translocations at least two completely informative markers (four different maternal and paternal alleles) on each side of the breakpoint are required. The analysis is performed by counting the number of alleles. To accomplish this, prior to the PGD cycle, informative polymorphic markers need to be detected by analyzing the genomic DNA from the couple. There have been reports on the use of PCR-based translocation PGD [13,14], however, the primary issue with this technique is that ADO resulting from single cell PCR severely complicates allele copy number counting. Moreover, PCR-based translocation PGD (and FISH-PGD) only assesses a limited number of chromosomes. Therefore, these technologies permit the transfer of reproductively incompetent embryos with aneuploidy for chromosomes that were not included in the analysis.

Array comparative genomic hybridization (aCGH) is a universal assay that tests the copy number of all 23 sets of human chromosomes (including the two particular chromosomes involved in the translocation) at once [15-18]. aCGH technology offers higher resolution analysis than FISH and aCGH results are simple to interpret with less inter-observer variability [19-21]. Promising studies have also indicated that array-based PGD for translocation carriers can lead to improved pregnancy rates per transfer [22-27].

The aim of our research was to compare the diagnosis and pregnancy rates for carriers of balanced translocations that performed PGD using the aforementioned three techniques: FISH, PCR, and aCGH.

Materials and Methods

A retrospective study of all PGD cases for balanced translocations performed in the Shaare-Zedek PGD Unit from 01/2010 to 03/2014. Twenty-eight couples carrying 20 reciprocal translocations and 8 Robertsonian translocations.The clinical and demographic patient characteristics are presented in Table 1. aCGH was started gradually in our laboratory in 2013 while still performing both other two techniques. FISH and PCR were performed arbitrary during the previous years.

IVF and embryo biopsy procedure

Cleavage-stage day 3 embryos were obtained using standard IVF procedure. Blastomere biopsy, ICSI, and embryo cultures were performed as previously described [28]. One cell only was removed from each fresh or cryopreserved day 3 embryo, unless the nucleus could not be visualized.

FISH

Three types of probes, including centromere-specific, locus-specific (LSI) and subtelomere-specific were used for FISH-PGD. The designed probe set contained sufficient probes to detect all expected unbalanced forms of the chromosomal rearrangement according to the ESHRE PGD consortium best practice guidelines for FISH-based PGD [29]. The FISH procedure was performed as previously described [30].

Molecular PGD

Couples provided peripheral blood from which DNA was extracted by standard methods. For each translocation, polymorphic markers were detected on relevant chromosomes on each side of the breakpoint. At least four completely informative markers (four different alleles maternal and paternal), two upstream and two downstream of the breakpoints, were included in the genetic analysis. These markers were then used in a single-cell multiplex assay as previously described [31]. Stringent precautions to avoid any source of contamination, as recommended by the European Society for Human Reproduction and Embryology (ESHRE) PGD consortium [32] were used during all the steps. The genetic analysis was performed by counting the number of alleles. For example, the loss of chromosomal material due to an abnormal segregation from the carrier parent results in an allele inherited only from the other parent (a mono-allelic state is present in the embryo). When there is an extra chromosomal segment from the carrier parent, it will be seen as the presence of a tri-allelic state of the marker.

aCGH

Single blastomeres were lysed and genomic DNA amplified using

Variable	FISH	PCR	aCGH
No. of couples*	23	5	10
Reciprocal / Robertsonian (no. of couples)	17/6	2/3	8/2
Female age (mean ± SD)	30.1 ± 5.1	31.2 ± 3.6	30.5 ± 5.5
Male/female carrier ratio	1.1	1.5	1.5
No. of healthy children	0 (0 – 3)	0.5 (0 – 2)	0 (0 – 3)
No. sick/dead children	0 (0 – 2)	0 (0 – 1)	0 (0 – 1)
No. IUFD >20 weeks	0 (0 – 1)	0 (0)	0 (0)
No. spontaneous abortions	2 (0 – 5)	3 (0 – 7)	1 (0 – 5)
No. of TOP d/t unbalanced	0 (0 – 12)	0 (0)	0 (0 – 1)

*Two couples had 1 PCR and 1 FISH cycles; 6 had 1 FISH and 1 aCGH cycle and one couple performed 3 PCR, 1 FISH and 1 aCGH cycle.

TOP-termination of pregnancy; IUFD-intrauterine fetal death; No-number

Values are median (range) unless otherwise indicated

NS (no statistical significance) for all parameters

Table 1: Clinical and demographic patient characteristics.

the SurePlex DNA Amplification System (BlueGnome, Cambridge, UK), according to the manufacturer's instructions. WGA products were processed according to the BlueGnome 24sure+ protocol (available at www.cytochip.com). A laser scanner (Agilent model G2565CA) was used to excite the hybridized fluorophores and read and store the resulting images of the hybridization. Scanned images were then analyzed and quantified by fixed algorithm settings in Blue Fuse Multi Software (BlueGnome, Cambridge, UK). To pass hybridization quality controls, female samples hybridized with a male reference DNA (sex mismatch) had to show a consistent gain on chromosome X and a consistent loss of chromosome Y. The entire procedure from blastomere biopsy until the end of the genetic analysis was completed within 26 h, and the results were obtained in time for an embryo transfer on day 4 or 5, post-oocyte retrieval.

Statistical analysis

Parameters were defined by percentages, means ± SD and medians with interquartile ranges. Comparisons between the study groups included Chi-square test for categorical variables and Kruskal-Wallis test for continuous variables. A two-sided P value of less than 0.05 was considered statistically significant. Analyses were carried out using IBM© SPSS statistics 20.0. Written informed consent was obtained from all couples. Given that PGD is a clinical procedure IRB is not required in our institution.

Results

Seventy five PGD cycles were carried out for the 28 families carrying 20 reciprocal translocations and 8 Robertsonian translocations.Nine couples had genetic analysis carried out with more than one technique during consecutive IVF cycles. Two couples had the analysis performed with PCR in the first cycle and then FISH in the next one; 6 couples performed FISH then aCGH; and one couple performed 5 cycles – the first three were analyzed with PCR, one cycle by FISH and the last one using aCGH.

No significant difference in maternal age or obstetrical history was observed between the three groups. The groups were also similar in the ratio between maternal and paternal translocation carriers. Eighteen of the 28 couples (64%) had already experienced spontaneous abortions before applying for the PGD program (median 2, range 0-7). Four couples (14.2%) went through termination of pregnancy due to an unbalanced embryo; 3 couples (10.7%) had IUFD; and 4 (14.2%) gave birth to a child with congenital anomalies prior to PGD.The IVF cycle parameters are presented in Table 2.

No significant differences in the number of oocytes retrieved, mature oocytes (MII) and number of fertilized oocytes were observed between the three groups. In the aCGH group there were 7 frozen/thawed cycles out of 15 treatment cycles (46.7%), as compared to 6 out of 46 (13%) and 2 out of 14 (14.3%) in the FISH and PCR groups, respectively (p=0.015). The average number of biopsied embryos in the aCGH group was 4.7, which was found to be significantly smaller than in the FISH group (7.2) and PCR group (8.9) (p=0.03).

Variable	FISH	PCR	aCGH
No. of cycles	46	14	15
Frozen cycles	6 (13%)	2 (14.3%)	7 (46.7%)*
No. of oocytes retrieved	19 ± 10.1	20 ± 7.4	16.4 ± 6.4
No. of MII oocytes	15.3 ± 8.4	16 ± 5.1	14.4 ± 6.7
No. of oocytes fertilized	10.6 ± 6.2	11.7 ± 6.3	11.8 ± 5.7
No. of embryos biopsied	7.2 ± 3.9	8.9 ± 4.8	4.7 ± 1.8**

No.=number; *p = 0.015 ; **p = 0.03

Table 2: IVF cycle parameters.

Patients with Robertsonian translocations produced a larger number of normal/balanced embryos than those with reciprocal translocations, 30 of 83 diagnosed embryos (36%) versus 34 of 282 diagnosed embryos (12%) (p<0.001). The PGD Cycle outcome by type of translocation is presented in Table 3.

Five couples (14 cycles) performed PGD with the PCR-based method. A total of 239 different STR markers with an average of 47.8 STR's per couple were tested. An average of only 7.8 STR's per couple were found to be completely informative and used for analysis. The average ADO per cycle was 20%, as well as the ADO per STR ratio.The IVF-PGD overall cycle outcome is presented in Table 4.

The diagnosis rate with aCGH was 60 out of 71 (85%) which was significantly higher than that of FISH (225 out of 331 embryos; 68%) and PCR (80 out of 124 embryos; 65%) (p= 0.036).The pregnancy rate per embryo transfer as well as pregnancy rate per OPU were significantly higher when using aCGH: Pregnancy rate per embryo transfer was 75% for aCGH as compared to 27.3% and 18.2% for FISH and PCR, respectively (P=0.022). Pregnancy rate per OPU was 40% for aCGH as compared to 13% and 14.3% for FISH and PCR, respectively (P=0.017).

When aCGH was used for analysis, twenty six embryos (43%) showed aneuploidies unrelated to the familial translocation, and therefore were not transferred. These aneuploidies would not have been diagnosed by the other two methods.The aneuploidies resulted from the specific translocations are presented in Table 5.

Of the 14 clinical pregnancies achieved, 4 were as a result of a frozen cycle (29%). Of them, one was in the PCR group, and 3 in the aCGH. In the aCGH group, clinical pregnancy and term delivery of a healthy child was achieved in 3 out of 8 fresh cycles (38%), and in 3 out of 7 frozen cycles (43) (p=NS).

Discussion

Balanced translocation carriers generally choose to perform PGD in order to increase the chance of conceiving and giving birth to a normal healthy child [4-8]. As shown in our study, most of the carrier couples admitted to our IVF-PGD unit already endured at least one obstetrical mishap including the birth of a newborn with unbalanced karyotype; recurrent miscarriage; or pregnancy termination due to malformations or prenatal diagnosis of an unbalanced karyotype. The objective of this study was to find the most efficient of the three known techniques: FISH, PCR, and aCGH, for diagnosis of their embryos. We found that aCGH enhanced our ability to diagnose as many biopsied embryos as possible. This technique also gave the highest pregnancy rate per transfer and per OPU.

In our hands, FISH-PGD was hindered by typical technical constraints as described in the Introduction. Accordingly, our ability to accurately diagnose embryos with FISH was low and consequently the low transfer rate was reflected in low pregnancy rates per OPU. Still, our FISH diagnosis rate (68%) was somewhat lower than previously published [33]. This may be due to the fact that we biopsied only one cell per embryo unlike others who routinely extract two cells for simultaneous FISH analysis. Another contributor to the relatively low diagnostic rate is the fact that many of our patients are strict religious and would not accept prenatal diagnosis. Thus we did not transfer embryos with even the slightest doubt regarding the diagnosis.

Regarding PCR-based translocation PGD, we noted not only a modest diagnosis rate (68%) but also a massive pre-case laboratory

Case no.	Karyotype	Type of analysis	No. cycles performed	Clinical pregnancy	Pregnancy outcome	Diagnosis confirmed
	Reciprocal					
1	t(8;10)(p21.1;q21.2)	FISH	1	no		
		PCR	3	no		
		CGH	1	no		
2	t(8:10)(q22.3;q21.2)	FISH	3	no		
3	46,XY,t (16;19)(p12;q13)	FISH	2	no		
4	46,XY,t(13;18)(q34;q12)	FISH	2	no		
5	t(11;14)(q23;q32)	FISH	1	yes	Term delivery	yes
		CGH*	3	no		
6	t(6;12)(q22.2;q22)	FISH	1	no		
7	t(11;13)(q23;q12.3)	FISH	5	no		
8	t(9;11)(p21.2;q21)	FISH	3	no		
9	46,XX,t(9;11)(p21.2;q21)	FISH	2	no		
		CGH	1	yes	Term delivery	yes
10	46,XX,t(4;10)(q31.3;q11.2)	FISH	2	no		
11	46,XY,t(13;15)(q14;q22)	FISH	2	no		
		CGH	1	yes	Term delivery	yes
12	t(10;16)(p11.2;q24)	FISH	2	no		
13	t(2;7)(q23;q31)	FISH	4	yes	Term delivery	yes
14	t(11;22)(q23;q11.2)	FISH	4	yes	Term delivery	yes
15	46,XX,t(1;14)(p13.3;q11.2)	FISH	1	no		
		CGH	2	yes	Term delivery	yes
16	t(9:16)(p24;q22)	FISH	1	no		
		CGH	3	yes	Term delivery	yes
17	46,XX,t(11;22)(q23;q11.2)	FISH	2	yes	missed abortion	no
		FISH		yes	Term delivery	yes
18	t(8;10)(p21.1;q21.2)	PCR	3	no		
19	46, XY, t (2,7)(p16;p22)	CGH	1	yes	Term delivery	yes
20	46XX t(5;13)(p12;q14.3)	CGH	1	yes	Term delivery	yes
	Roberstosnian					
21	45,XY,der(14;21)(q10;q10)	FISH	2	no		
		CGH	1	no		
22	45,XY,der(14;21)(q10;q10)	FISH	1	no		
23	45,XX,der(14;21)(q10;q10)	FISH	2	no		
24	45,XX,der(13;14)(q10;q10)	FISH	1	yes	Term delivery	yes
		PCR	4	yes	EUP	no
25	45,XX,der(15;21)(q10;q10)	FISH	1	no		
26	45,XX,der(13;14)(q10;q10)	FISH	1	no		
		PCR	1	no		
27	45XY t(13;14)	PCR	3	yes	Term delivery	yes
28	45,XY,der(14;21)(q10;q10)	CGH	1	no		

*Returned after delivery for a second child

Table 3: Cycle outcome by type of translocation.

Variable	FISH	PCR	aCGH
No. of embryos biopsied	331	124	71
No. of embryos successfully diagnosed	225 (68%)	80 (65%)	60 (85%)*
No. embryos transferable	34	21	9
No. cycles with transfer	22	11	8
Clinical pregnancy	6	2	6
Pregnancy rate/ET	27.3%	18.2%	75% **
Pregnancy rate/OPU	13%	14.3%	40%***

No-number; OPU (oocyte pickup); ET=embryo transfer; *p= 0.036; **p= 0.022; ***P = 0.017

Table 4: IVF-PGD overall cycle outcome.

Case no.	Translocation	No. embryos :					Additional aneuploidies
		Biopsied	Diagnosed	Normal/ balanced	Unbalanced	Aneuploid	
	Reciprocal						
1	t(8;10)(p21.1;q21.2)	3	3	0	1	2	(-14; -18), (+19)
2	46,XX,t(9;11)(p21.2;q21)	2	2	2	0	0	
3	t(11;14)(q23;q32)	14	11	1	6	4	(+20; +16), (+13s), (-2; -10s), (-X)
4	46,XX,t(1;14)(p13.3;q11.2)	9	8	1	3	4	(chaotic*1), (-22), (-21s), (-9s)
5	t(9:16)(p24;q22)	16	12	2	3	7	(chaotic*4), (+22), (-14), (-18s)
6	46, XY, t (2,7)(p16;p22)	6	6	1	2	3	(chaotic*3)
7	46,XY,t(13;15)(q14;q22)	7	7	1	1	5	(chaotic*2), (-5; -Y), (-Y), (-6s)
8	46XX t(5;13)(p12;q14.3)	4	4	1	3	0	
	Roberstosnian						
9	45,XY,der(14;21)(q10;q10)	6	3	0	0	3	(chaotic*1), (-10; -7s), (-5s; -11)
10	45,XY,der(14;21)(q10;q10)	4	4	0	0	4	(chaotic*2), (+20; +X), (+7; +12; +19)

*chaotic ≥ 5 chromosomes with either monosomy or trisomy

Table 5: The aneuploidies resulted from the specific translocations.

expense. For each translocation couple we needed to test a very large number of STRs in order to identify enough informative markers for PGD. On average, we tested translocation couples with the same amount of STRs as we would normally test for 3 to 4 different monogenic disorders. This pre-case burden is quite expensive, laborious, and time consuming. The relatively low diagnostic rate was also not related to the single cell multiplex PCR technique since in cases of PCR for monogenic diseases, we achieve a diagnostic rate of 92% in average, and diagnostic accuracy of 99.5%, consistent with ESHRE PGD consortium best practice guidelines for amplification-based PGD [34].

Traditionally, investigation into the genetic cause of children with mental retardation or anatomic malformations began with karyotype testing. Today, chromosomal microarray analysis (CMA) for postnatal diagnosis has replaced the classical karyotype in most cases and is the standard of care. It is also widely used in prenatal testing – gradually replacing karyotype testing during amniocentesis and chorionic villus sampling (CVS). Its use in PGD is also gaining more and more volume – for diagnosing chromosomal aberrations, preimplantation genetic screening (PGS) and even for single-gene disorders [35,36]. The most widely used platform for PGD is the Bluegnome platform and this platform applies a variation of CMA called aCGH. One of the major advantages of the aCGH method is enhanced diagnostic confidence. This advantage arises from the ability of aCGH to provide a large sampling of informative genetic markers per embryo in high throughput. Thus, there is no need for pre-case family workup as opposed to the lengthy procedure prior to using PCR. In addition, unlike for FISH, data analysis is fully automated to prevent subjective signal scoring. This facilitates easier and more reliable data interpretation.

Due to the high cost per embryo for the aCGH technique, some couples requested analysis of a limited number of embryos, while the surplus good quality embryos were cryopreserved for further testing. Despite the lower number of embryos analyzed in each cycle the pregnancy rate per OPU and ET was significantly higher compared to the other two methods. There was a tendency towards higher pregnancy rates in the cryopreserved aCGH compared to the fresh embryo transfer (43% vs 38%, p=NS), in accordance with recent published studies showing advantages for frozen embryo transfer [37,38].

There is no doubt that one of the greatest advantages, that probably has a crucial part in the improved pregnancy rate outcome in aCGH PGD, is the fact that aCGH simultaneously screens embryos for the unbalanced derivatives associated with the specific translocation, as well as for aneuploidy of all 23 sets of chromosomes. PGD of chromosomal translocations can be combined with aneuploidy screening using both FISH and PCR, but these methods can only identify aneuploidies for a limited number of chromosomes which can lead to the transfer of reproductively incompetent embryos with aneuploidy for chromosomes not analyzed. In general, screening the entire set of human chromosomes and not only a few chromosomes is probably even more important when analyzing embryos of translocation carriers, than with routine PGS. It has been postulated that due to inter-chromosomal effects, carriers of chromosomal translocation are prone to increased meiotic nondisjunction leading to aneuploidies affecting chromosomes not implicated in the translocation. Indeed, previous studies have identified higher aneuploidy rates in embryos from translocation carriers [39-43] and this has led to the recommendation for addition of comprehensive aneuploidy screening to translocation analysis during PGD. In our study, 43% of the embryos diagnosed by aCGH were found to carry aneuploidies unrelated to the two chromosomes involved in the translocation, and therefore were not transferred.

The main limitation of aCGH at the present time is still the monetary cost of this method, per embryo, which is relatively high due to marked up microarray prices. However, we do anticipate that the cost, per array, will decrease in the future.

In conclusion, our preliminary data demonstrates that PGD using aCGH for translocations carriers increases the efficiency of successful genetic analysis. In addition, the aCGH platform, which screens all chromosomes, significantly improves pregnancy rates. We also show that aCGH detects a significant number of embryos carrying aneuploidies unrelated to the familial translocation. In light of these findings, single cell aCGH for chromosomal translocations analysis appears to be an attractive method in PGD.

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