Le PGT-A en 2024: entre Pratique et Contreverse

Pr Abdelhafid Natiq Ph.D

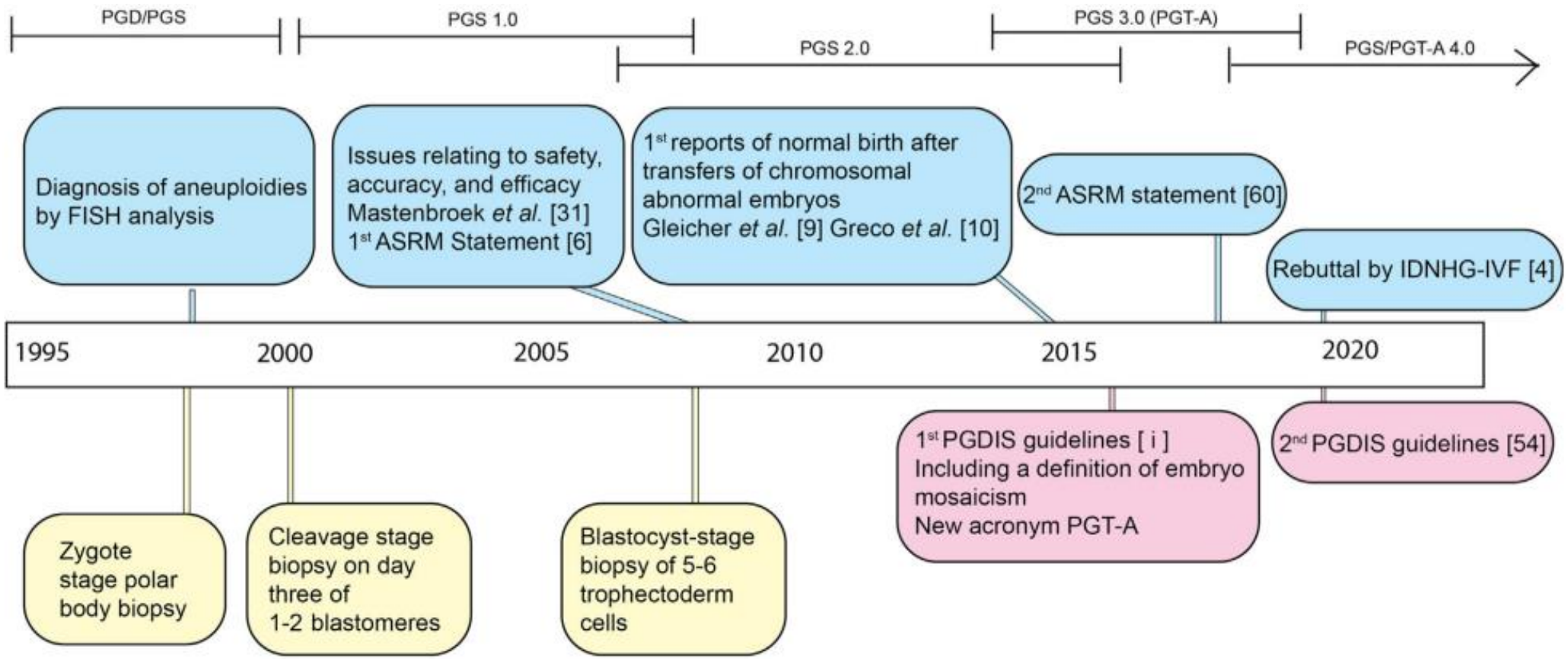
Faculté de médecine et de pharmacie Rabat

Laboratoire Nationale Mohammed VI Fondation Mohammed VI Casablanca

PGT ?

- PGT-A: Preimplantatoire genetic testing des aneuploidies.
- Technique de sélection génétique de l’embryon.
- Consiste à prélever quelques cellules de l'embryon et de déterminer si l'embryon est euploïde et donc transférable.
- Le PGT devrait donc augmenter les chances de mener une grossesse à terme.
- Pratique interdite en France.

Histoire du PGT-A



Norbert Gleicher et al 2021

Article

Preimplantation genetic screening: results of a worldwide web-based survey

Ariel Weissman [a,b,*], Gon Shoham [b], Zeev Shoham [c,d], Simon Fishel [e], Milton Leong [f], Yuval Yaron [a,g]

[a] IVF Unit, Department of Obstetrics and Gynecology, Edith Wolfson Medical Center, 62 Halochamim Street, Holon, 5822012, Israel
[b] Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Tel Aviv, 6997801, Israel
[c] IVF Unit, Kaplan Hospital, Rehovot, 7661041, Israel
[d] Hadassah Medical School, Affiliated to the Hebrew University, Jerusalem, Israel
[e] CARE Fertility Group, John Webster House, 6 Lawrence Drive, Nottingham Business Park, Nottingham, NG14 5GU, UK
[f] The IVF Clinic, 13/F Central Tower, 28 Queens Road Central, Hong Kong, China
[g] Prenatal Genetic Diagnosis Unit, Genetic Institute, Tel Aviv Sourasky Medical Center, 6 Weizmann Street, Tel Aviv, 6423906, Israel

- Etude Prospective
- **386** centres de FIV
- **70** pays
- **342 600** cycles

Contenu de l'enquête

Table 1 – Geographic distribution of IVF units participating in the survey.

Continent	Total				Centers Performing PGS				Centers NOT Performing PGS			
	Annual IVF Cycles	%	Number of units	%	Annual IVF cycles	%	Number of units	%	Annual IVF cycles	%	Number of units	%
USA and Canada	65,800	19.2	97	25.1	63,000	23.9	93	34.3	2800	3.5	4	3.5
South America	18,500	5.4	34	8.8	15,900	6.0	26	9.6	2600	3.3	8	7
Australia and New Zealand	22,300	6.5	21	5.4	20,800	7.9	16	5.9	1500	1.9	5	4.3
Asia	83,900	24.5	78	20.2	62,200	23.6	56	20.7	21,700	27.3	22	19.1
Europe	137,900	40.3	137	35.5	91,600	34.8	70	25.8	46,300	58.2	67	58.3
Africa	14,200	4.1	19	4.9	9600	3.6	10	3.7	4600	5.8	9	7.8
	342,600	100	386	100	263,100	100	271	100	79,500	100	115	100

INDICATIONS

- ✓ Age maternelle avancée (27%)
- ✓ Défaut d'implantation récurrent (32%)
- ✓ Fausses couches à répétition (31%)
- ✓ (10%) offert à toutes les patientes.

› Singapore Med J. 2010 Feb;51(2):133-6.

Cytogenetic and epidemiological profiles of Down syndrome in a Moroccan population: a report of 852 cases

I C Jaouad [1], S Cherkaoui Deqaqi, A Sbiti, A Natiq, F Elkerch, A Sefiani

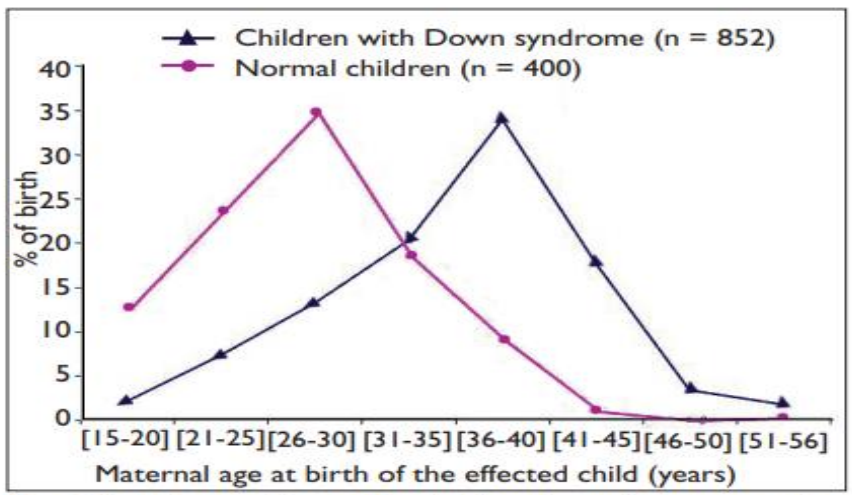


Fig. 3 Prevalence of normal and trisomic newborns according to maternal age at term (current study).

Table II. Frequency of trisomy 21 at delivery according to maternal age.[19]

Maternal age	Risk of trisomy 21
20 years	1/1480
25 years	1/1350
30 years	1/940
35 years	1/353
40 years	1/85
45 years	1/30

Reproductive Sciences (2023) 30:2907–2919
https://doi.org/10.1007/s43032-023-01256-2

REVIEW

The Role of Advanced Parental Age in Reproductive Genetics

Boling Chu[1] · Zhi Liu[2] · Yihong Liu[3] · Hui Jiang[1]

Received: 13 December 2022 / Accepted: 29 April 2023 / Published online: 12 May 2023

ANDROLOGY

REVIEW ARTICLE | Open Access

Impact of paternal age on assisted reproductive technology outcomes and offspring health: a systematic review

Annabelle Gourinat, Charles Mazeaud, Jacques Hubert, Pascal Eschwege, Isabelle Koscinski

First published: 14 January 2023 | https://doi.org/10.1111/andr.13385 | Citations: 3

when comparing fathers aged 25–29 and 45+ years, found that the risk of having a stillborn child increased by 22%. According to research by Astolfi et al., the risk of having a stillborn child increases with paternal age .

genes

MDPI

Review

Impact of Advanced Paternal Age on Fertility and Risks of Genetic Disorders in Offspring

Aris Kaltsas et al , genes 2023

LE PGT-A EST IL EFFICACE EN PMA??

PGS: RANDOMIZED CLINICAL TRIALS

Selection of single blastocysts for fresh transfer via standard morphology assessment alone and with array CGH for good prognosis IVF patients: results from a randomized pilot study

Zhihong Yang[1], Jiaen Liu[2], Gary S Collins[3], Shala A Salem[1], Xiaohong Liu[2], Sarah S Lyle[1], Alison C Peck[1], E Scott Sills[1*] and Rifaat D Salem[1]

Molec Cytogenet 2012

In vitro fertilization with single euploid blastocyst transfer: a randomized controlled trial

Eric J. Forman, M.D.,[a,b] Kathleen H. Hong, M.D.,[a,b] Kathleen M. Ferry, B.Sc.,[a] Xin Tao, M.Sc.,[a] Deanne Taylor, Ph.D.,[a] Brynn Levy, Ph.D.,[a,c] Nathan R. Treff, Ph.D.,[a,b] and Richard T. Scott Jr., M.D.[a,b]

Fertil Steril 2013

Blastocyst biopsy with comprehensive chromosome screening and fresh embryo transfer significantly increases in vitro fertilization implantation and delivery rates: a randomized controlled trial

Richard T. Scott Jr., M.D.,[a,b] Kathleen M. Upham, B.S.,[a] Eric J. Forman, M.D.,[b] Kathleen H. Hong, M.D.,[b] Katherine L. Scott, M.S.,[a,c] Deanne Taylor, Ph.D.,[a,b] Xin Tao, M.S.,[a] and Nathan R. Treff, Ph.D.[a,b]

Fertil Steril 2013

Le PGT-A augmente les chances des taux d'implantation, de grossesses et de naissance vivantes

Characteristics of included randomized and observational studies.

Study	Design	Indication	Embryo biopsy	Genetic platform	Main outcomes
Randomized studies					
Yang et al., 2012 (24)	Pilot RCT	Good-prognosis patients, 1st IVF cycle	Blastocyst	aCGH	Clinical PR, ongoing PR (>20 wk)
Forman et al. 2013 (22)	Noninferiority trial (RCT)	Normal ovarian reserve, ≤1 previous IVF failure	Blastocyst	qPCR	Ongoing PR (>24 wk), multiple PR
Scott et al., 2013 (75)	RCT	Normal ovarian reserve, ≤1 previous IVF failure	Blastocyst	qPCR	Sustained IR, delivery rate
Observational studies					
Sher et al., 2009 (58)	PCS	AMA + RIF + RPL	Cleavage	mCGH	IR, Live birth rate
Schoolcraft et al., 2010 (55)	PCS	Previous IVF failure	Blastocyst	aCGH	IR
Fishel et al., 2011 (79)	PCS	RIF	Polar Body	aCGH	IR
Forman et al., 2012 (23)	RCS	1st SET cycle	Blastocyst	qPCR	Ongoing PR (>12 wk)
Keltz et al., 2013 (76)	RCC	AMA + RIF + RPL	Cleavage	aCGH	IR
Greco et al., 2014 (43)	PCS	RIF	Blastocyst	aCGH	IR
Lee et al., 2015 (77)	RCS	AMA	Blastocyst	aCGH	IR, Live birth rate
Feichtinger et al., 2015 (78)	RCS	RIF + AMA	Polar Body	aCGH	Live birth rate

Note: aCGH = array comparative genomic hybridization; AMA = advanced maternal age; IR = implantation rate; mCGH = metaphase comparative genomic hybridization; qPCR = quantitative polymerase chain reaction; PCS = prospective cohort study; PR = pregnancy rate; RCC = retrospective case-control; RCS = retrospective cohort study; RCT = randomized controlled trial; RIF = repeated implantation failure; RPL = recurrent pregnancy loss; SET = single-embryo transfer.

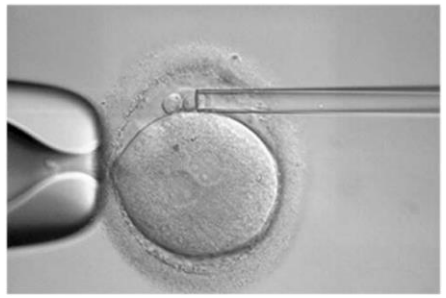
Reserve ovarienne normale → Le PGS augmente les chances du taux d'implantation et de grossesse.

Dahdouh et al., Fertil Steril 2015

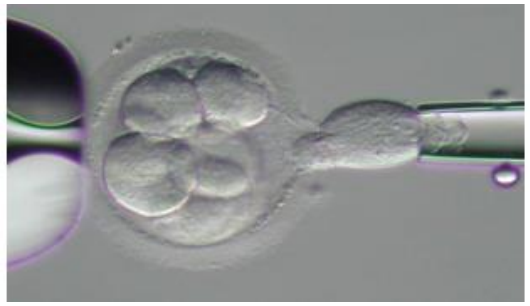
BIOPSIE EMBRYONNAIRE

Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6

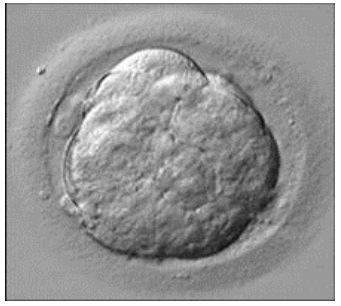
Polar Body Biopsy



Cleavage stage biopsy

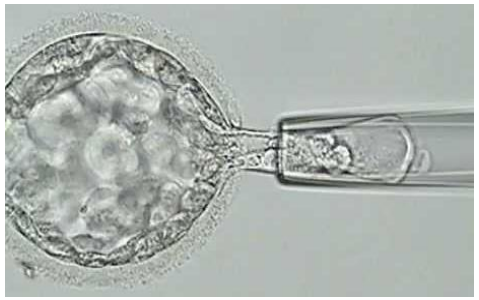


Morula stage biopsy

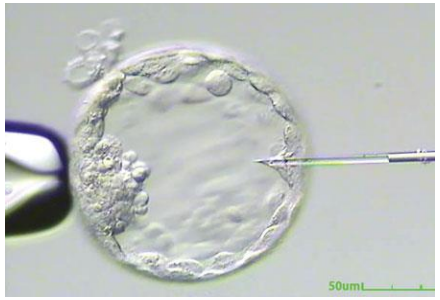


Blastocyst biopsy

Trophectoderm



Blastocoelic fluid



(Dahdouh et al., 2015)

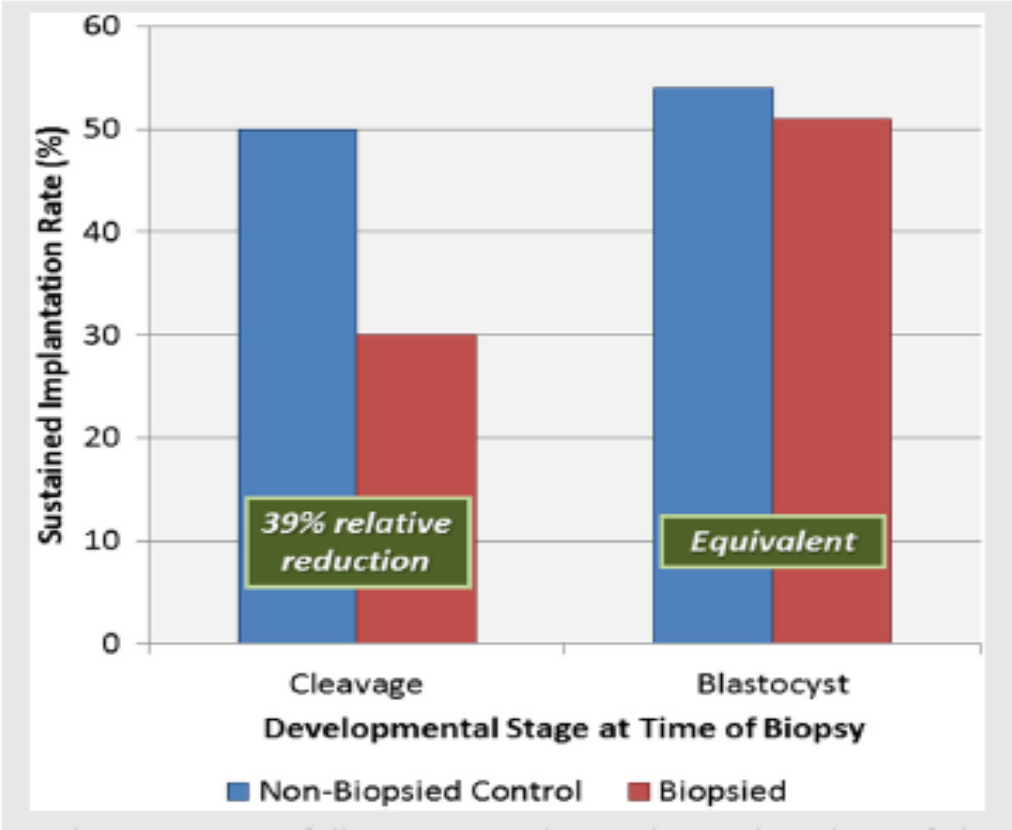
STADE DE BIOPSIE ET IMPACT SUR LE “IR”??

Fertil Steril. 2013 Sep;100(3):624-30. doi: 10.1016/j.fertnstert.2013.04.039. Epub 2013 Jun 15.

Cleavage-stage biopsy significantly impairs human embryonic implantation potential while blastocyst biopsy does not: a randomized and paired clinical trial.

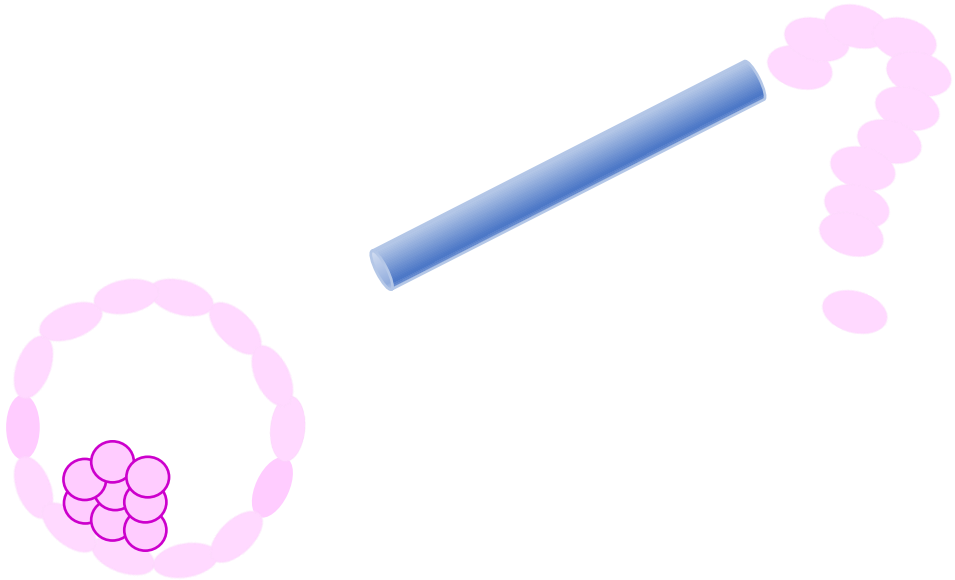
Scott RT Jr[1], Upham KM, Forman EJ, Zhao T, Treff NR.

- La Biopsie au stade j3: réduit de façon remarquable le taux d’implantation embryonnaire.
- Au stade J5: aucun impact sur le taux d’implantation.



Scott et al., 2013

Biopsie de Trophoectoderme



Nombre de cellules à biopsier?

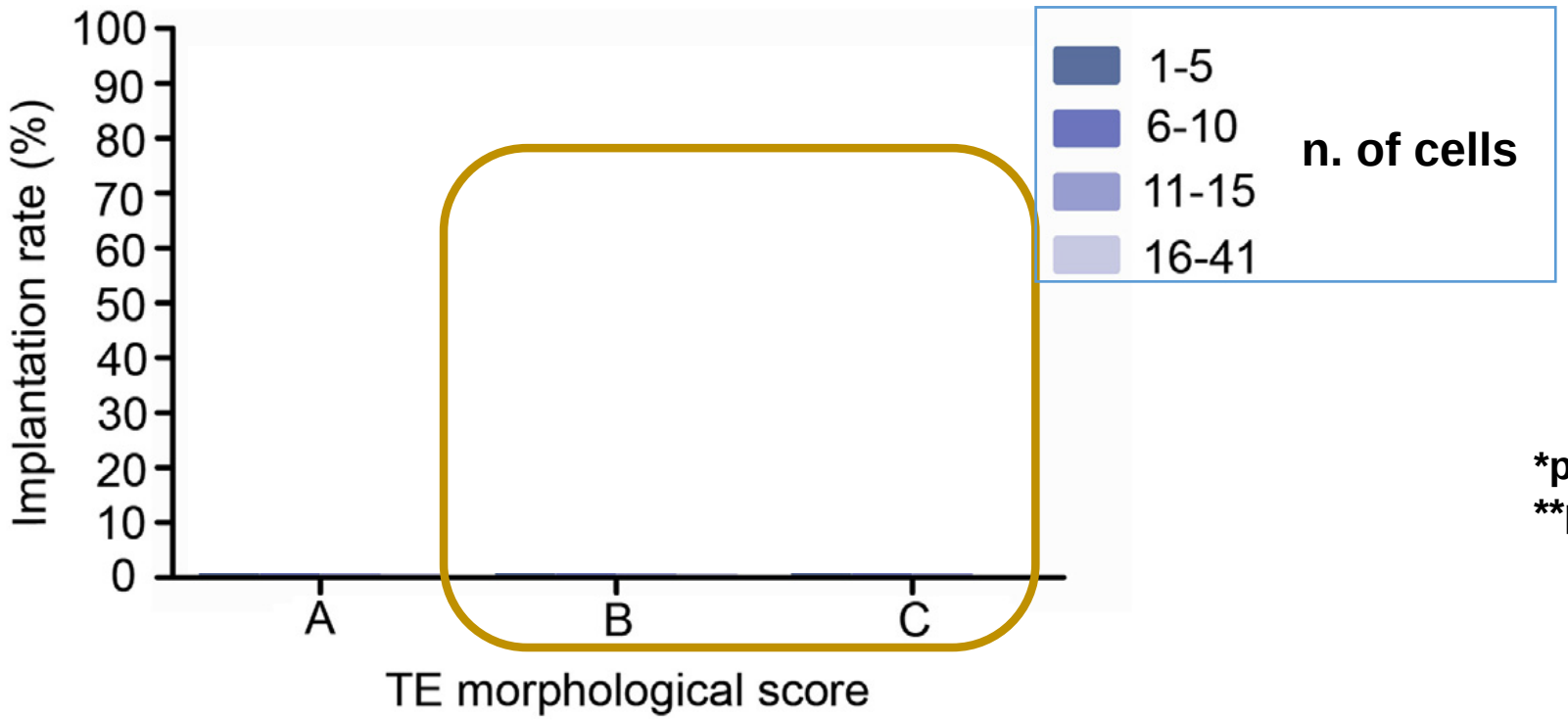
CrossMark

Number of biopsied trophectoderm cells is likely to affect the implantation potential of blastocysts with poor trophectoderm quality

Shuoping Zhang, M.Sc.,[a,b] Keli Luo, M.D., Ph.D.,[a,b,c] Dehua Cheng, M.Sc.,[a,b] Yueqiu Tan, Ph.D.,[a,b,c] Changfu Lu, Ph.D.,[a,b,c] Hui He, M.Sc.,[a,c] Yifan Gu, Ph.D.,[a,b,c] Guangxiu Lu, M.D.,[a,b,c,d] Fei Gong, M.D., Ph.D.,[a,b,c] and Ge Lin, M.D., Ph.D.[a,b,c,d]

[a] Institute of Reproduction and Stem Cell Engineering, Central South University, [b] Reproductive and Genetic Hospital of Citic-Xiangya, [c] Key Laboratory of Stem Cells and Reproductive Engineering, Ministry of Health, and [d] National Engineering and Research Center of Human Stem Cell, Changsha, People's Republic of China

TROPHECTODERM BIOPSY



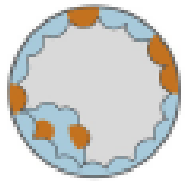
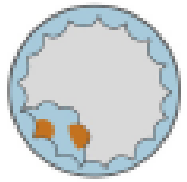
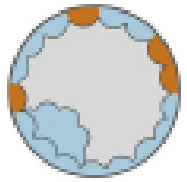
*p<0.05
**p<0.01

Dans les embryons à faible score, le nombre de cellules biopsiés impact negativement les taux d'implantation.

Zhang et al., Fertil Steril 2016

LE STATUT CHROMOSOMIQUE DE L'EMBRYON??

LE PGS ET MOSAICISME

Mosaicism type	Possible TE biopsy	Diagnoses accuracy
Total Mosaic 	Euploid	Misdiagnosis
	Mosaic	Accurate
	Aneuploid	Misdiagnosis
ICM Mosaic 	Euploid	Misdiagnosis (Mosaicism never detectable)
TE Mosaic 	Euploid	Misdiagnosis
	Mosaic	Accurate
	Aneuploid	Misdiagnosis
ICM/TE Mosaic Type I 	Euploid	Misdiagnosis (Mosaicism never detectable)
ICM/TE Mosaic Type II 	Aneuploid	Misdiagnosis (Mosaicism never detectable)

Assessing the true incidence of mosaicism in preimplantation embryos

Maria Vera-Rodriguez, Ph.D. and Carmen Rubio, Ph.D.
Igenomix and Igenomix Foundation, Valencia, Spain

(Fertil Steril 2017;107: 1107–12. 2017 by American Society for Reproductive Medicine.)

MOSAICISME - ANEUPLOIDIE RESCUE

Incidence du mosaicisme

de 15 to 90% au stade clivage

de 15 to 30% au stade blastocyste

de 1 to 2% en DPN

Un mécanisme de sélection contre le mosaïcisme / la correction de l'aneuploïdie aux stades ultérieurs du développement embryonnaire

Hum Reprod Update. 2014 Jul-Aug;20(4):571-81. doi: 10.1093/humupd/dmu016. Epub 2014 Mar 25.

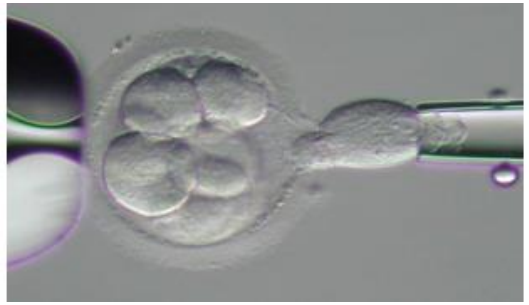
The origin, mechanisms, incidence and clinical consequences of chromosomal mosaicism in humans.

Taylor TH[1], Gitlin SA[2], Patrick JL[3], Crain JL[3], Wilson JM[3], Griffin DK[4].

Fertil Steril. 2009 Sep;92(3):890-6. doi: 10.1016/j.fertnstert.2008.07.1761. Epub 2008 Sep 30.

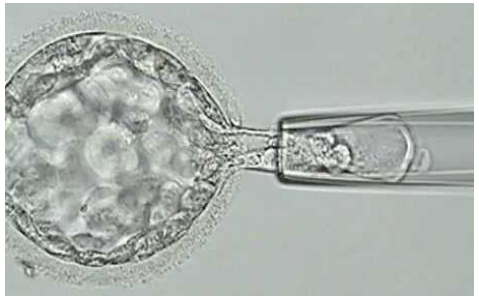
Preimplantation aneuploid embryos undergo self-correction in correlation with their developmental potential.

Barbash-Hazan S[1], Frumkin T, Malcov M, Yaron Y, Cohen T, Azem F, Amit A, Ben-Yosef D.



83 embryons aneuploïdes à J3

Ré analyser à j5



27 embryons euploïdes à j5

Au stade blastocyste 32,6% de self correction

ANEUPLOIDIE RESCUE

Healthy Babies after Intrauterine Transfer of Mosaic Aneuploid Blastocysts

N Engl J Med 2015; 373:2089-2090 | November 19, 2015 | DOI: 10.1056/NEJMc1500421

Greco E, et al.

Table 1. Clinical Outcomes of Single Mosaic Blastocysts Transferred.*

Patient No.	Chromosomal Constitution	Mosaicism†	Karyotype‡	Clinical Outcome
		percent		
1	arr(4)x1,(10)x1	40	46,XX	Baby healthy at birth
2	arr(6)x1,(15)x1	50	46,XX	Baby healthy at birth
3	arr(2)x1	40	46,XX	Baby healthy at birth
4	arr(2)x1	35	46,XY	Baby healthy at birth
5	arr(5)x1	50	46,XX	Baby healthy at birth
6	arr(5)x1,(7)x1	40	46,XX	Baby healthy at birth
7	arr(11)x1,(20)x3,(21)x3	30	NA	No pregnancy
8	arr(1)x1,(6)x3,(10)x3,(12)x3,(13)x3,(14)x3,(21)x3	50	NA	No pregnancy
9	arr(3)x1,(10)x3,(21)x3	35	NA	No pregnancy
10	arr(1)x3	50	NA	Biochemical pregnancy§
11	arr 9p21.2q34.3(26,609,645-140,499,771)x3	45	NA	Biochemical pregnancy§
12	arr(15)x3	30	NA	No pregnancy
13	arr(18)x1	50	NA	No pregnancy
14	arr(18)x1	50	NA	No pregnancy
15	arr(18)x1	40	NA	No pregnancy
16	arr(4)x1	50	NA	No pregnancy
17	arr(5)x3	40	NA	No pregnancy
18	arr 10q21.3q26.3(67,216,644-134,326,648)x3	50	NA	No pregnancy

* NA denotes not available.
† The approximate percentage of aneuploid cells in the transferred blastocyst is listed (see the Supplementary Appendix).
‡ The karyotype was determined by means of chorionic-villus sampling.
§ Biochemical pregnancy was defined by the presence of a low peak in levels of the beta subunit of human chorionic gonadotropin (β-hCG) (<100 mIU per milliliter), a rapid decrease in the urinary or serum β-hCG concentration, and no substantial delay in the onset of the next menstrual period, but with no detection of an identifiable pregnancy by means of ultrasonographic examination.

The NEW ENGLAND JOURNAL of MEDICINE

ANEUPLOIDY RESCUE

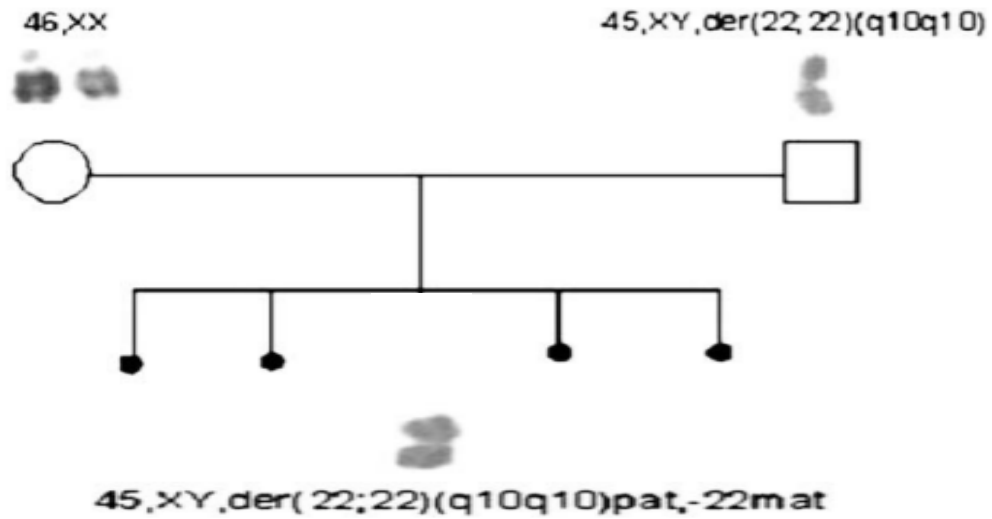
Case Reports > Fertil Steril. 2008 Nov;90(5):2013.e13-5. doi: 10.1016/j.fertnstert.2008.03.067. Epub 2008 Jun 20.

Unexpected fertility and paternal UPD 22

Karim Ouldim [1], Aziza Sbiti, Abdelbafid Natiq, Fatiha El-Kerch, Souad Cherkaoui, Abdelaziz Sefiani

FIGURE 1

Family pedigree and partial karyotype.



99,999 %

- Possibilité d'une paternité par **trisomy rescue.**
- Pas de gène à empreinte paternelle avec des effets symptomatologiques sur le 22.

Reprod Biol Endocrinol. 2017; 15: 6.
Published online 2017 Jan 10. doi: 10.1186/s12958-016-0225-2

PMCID: PMC5223447
PMID: 28069012

Systematic review of worldwide trends in assisted reproductive technology 2004–2013

Vitaly A. Kushnir,[1,2] David H. Barad,[1,3] David F. Albertini,[1,4,6] Sarah K. Darmon,[1] and Norbert Gleicher[1,3,5,6]

© Can Stock Photo - csp28806982

Reprod Biomed Online. 2018 Mar;36(3):288-289. doi: 10.1016/j.rbmo.2017.12.012. Epub 2017 Dec 29.

Time-lapse systems for ART.

Armstrong S[1], Bhide P[2], Jordan V[2], Pacey A[2], Farquhar C[2].

RBM ONLINE

ELSEVIER

Letter

How PGS/PGT-A laboratories succeeded in losing all credibility

Norbert Gleicher MD et all (2018)

REPRODUCTIVEBIOMEDICINEONLINE37(2018)242–245

« (…)resulted in couples paying more money for a less effective treatment."

Trends in
Molecular Medicine

Special Issue: Reproductive and Sexual Health

Opinion

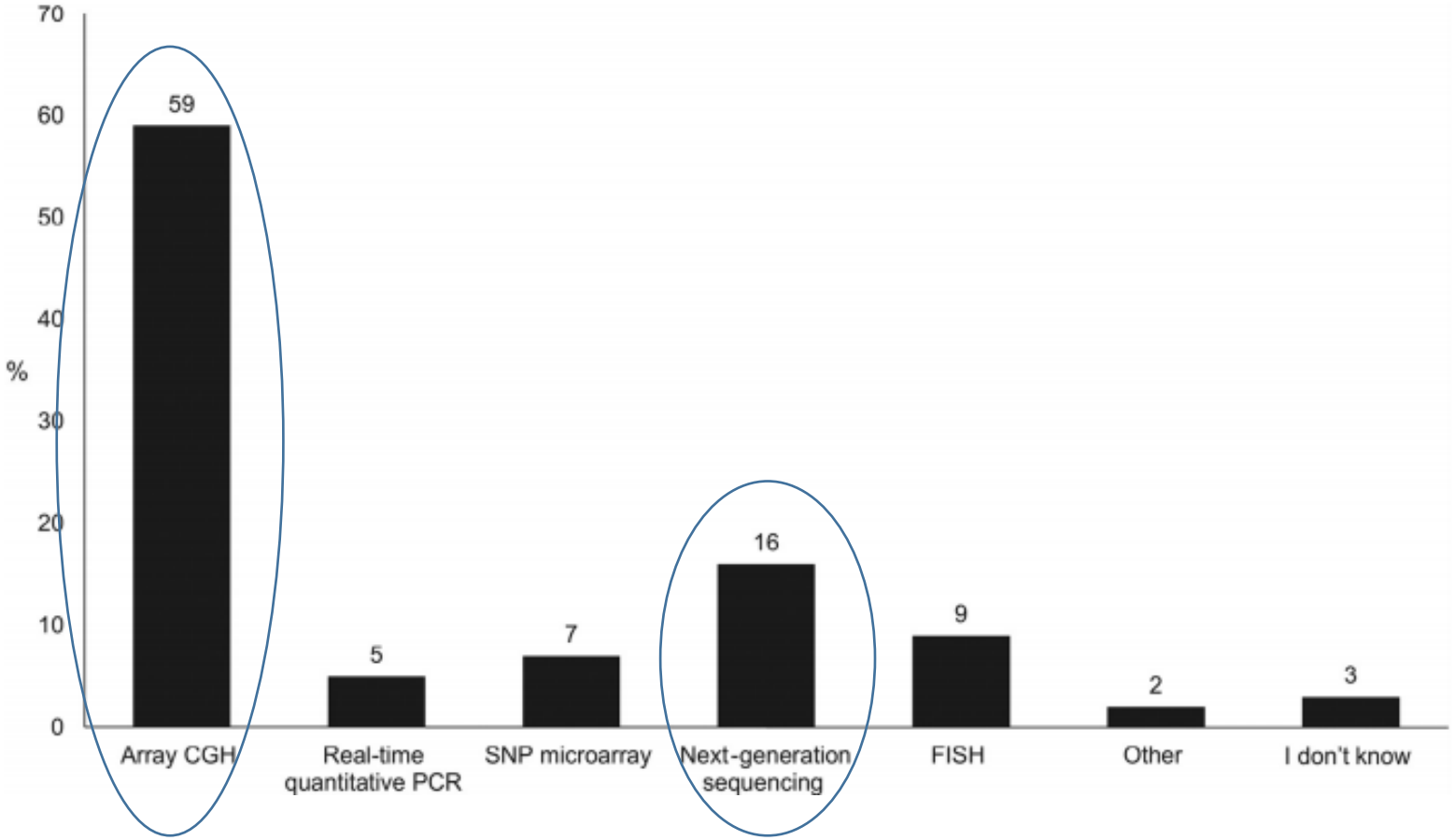
Preimplantation Genetic Testing for Aneuploidy – a Castle Built on Sand

Norbert Gleicher,[1,2,3,4,*] Pasquale Patrizio,[1,5] and Ali Brivanlou[3]

We here demonstrate that **both assumptions are false**, PGT-A, therefore, does neither improve IVF outcomes nor, likely, significantly reduces **miscarriages** and, in women with small embryo numbers, actually reduces **pregnancy and live birth chances**.

Trends in Molecular Medicine, August 2021, Vol. 27, No. 8

TECHNIQUES DE GENETIQUE ET PGT-A



PGS 2.0

Figure 3 – Which method of genetic testing is predominantly used in your clinic for determination of embryo ploidy status? Results are expressed in percentage, which represents the proportion of replies from the clinics relative to the number of cycles performed in each clinic. CGH, comparative genomic hybridization; FISH, fluorescence in-situ hybridization; PCR, polymerase chain reaction; SNP, single nucleotide polymorphism. Figure adapted the IVF-Worldwide (2017).


ACPA
NGS
???

J Assist Reprod Genet
DOI 10.1007/s10815-017-0954-y

GENETICS

Complex chromosomal rearrangement—a lesson learned from PGS

Tsvia Frumkin[1] · Sagit Peleg[1] · Veronica Gold[1] · Adi Reches[1,2] · Shiri Asaf[1] · Foad Azem[1] · Dalit Ben-Yosef[1,3,4] · Mira Malcov[1]

J Assist Reprod Genet. 2017 Aug; 34(8): 1095–1100

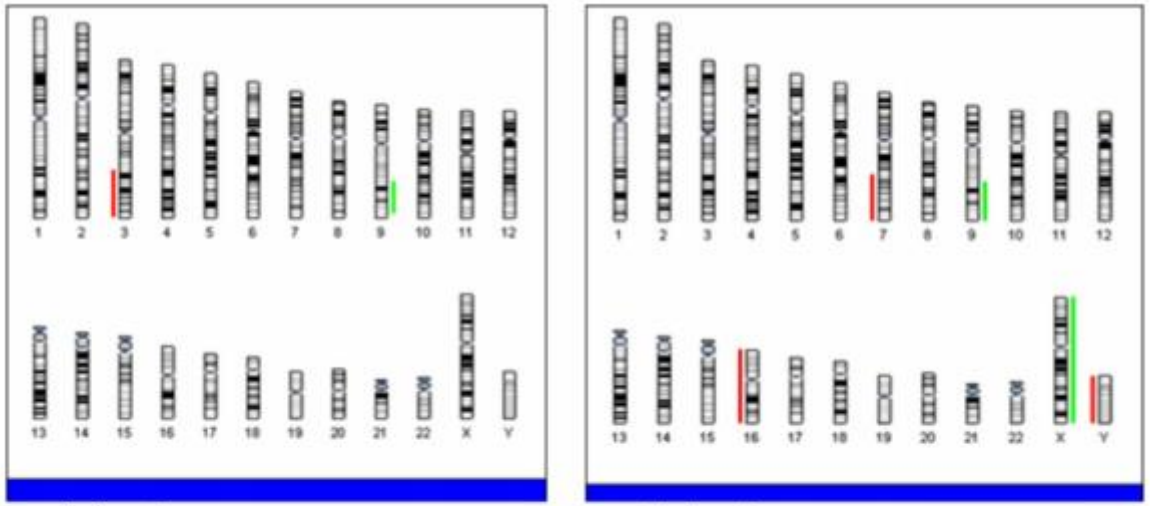


Fig. 1 Representative figure of CMA results of abnormal embryos that were diagnosed by PGS. The *green lines* demonstrate a gain of chromosomal regions and *red lines* demonstrate a loss of chromosomal regions

Table 1 Results of all embryos analyzed in the first CMA cycle

Embryo ID	Result
1	Unbalanced (−3s, +9s)
2	Unbalanced (−7s, −16, +9s)
3	Unbalanced (−9s, +7s, +22)
8	Abnormal (−8)
12	Unbalanced (−9s, +3s)
14	Unbalanced (−7s, +3s, +22)
16	Unbalanced (−3 s, +7s)

s structural aberration

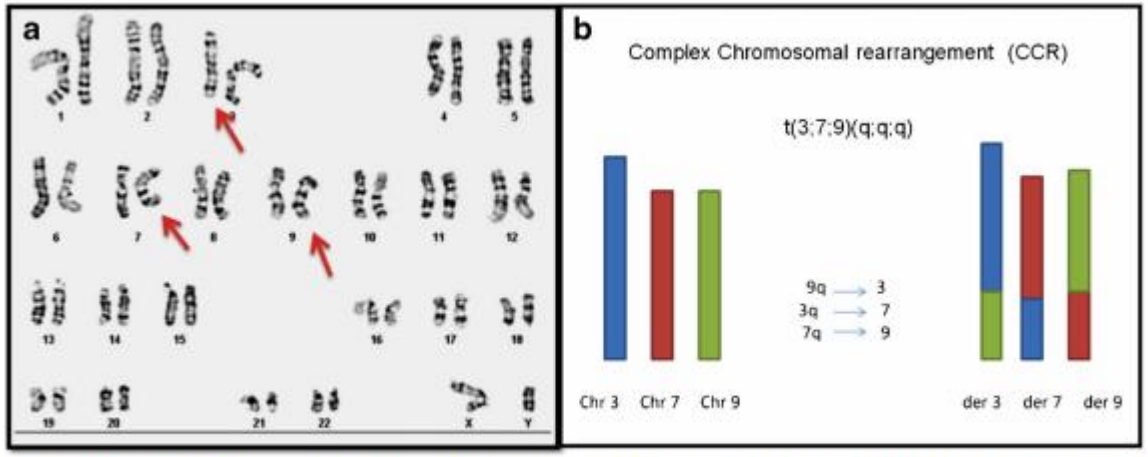
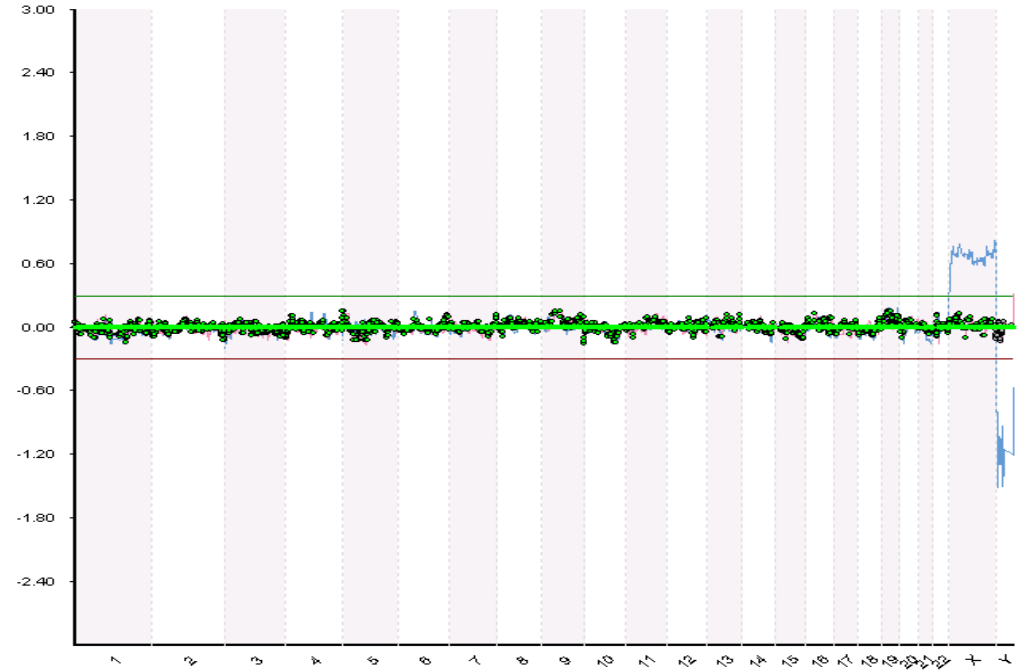


Fig. 3 **a** Re-karyotyping for the male partner demonstrates CCR 46,XY,t (3;7;9)(q23;q22;q22). The *red arrows* point at derivatives 3, 7, and 9. **b** A schematic presentation of the balanced CCR of the male partner. *Chr* chromosome, *der* derivative

Table 2 Results of all embryos analyzed in the second CMA cycle

Embryo ID	Result
1	Unbalanced (−9s, +7s)
3	Unbalanced (+3s, +7s)
4	Unbalanced (−7s, +3s)
6	Unbalanced (+3s, +7s)
9	Balanced
16	Unbalanced (−3s, +7s)
17	Balanced

s structural aberration



***PGT* + *ACPA* = *méthode de choix pour la détection de RCC*.**

Fertil Steril. 2016 Nov;106(6):1414-1419.e5. doi: 10.1016/j.fertnstert.2016.08.017. Epub 2016 Sep 28.

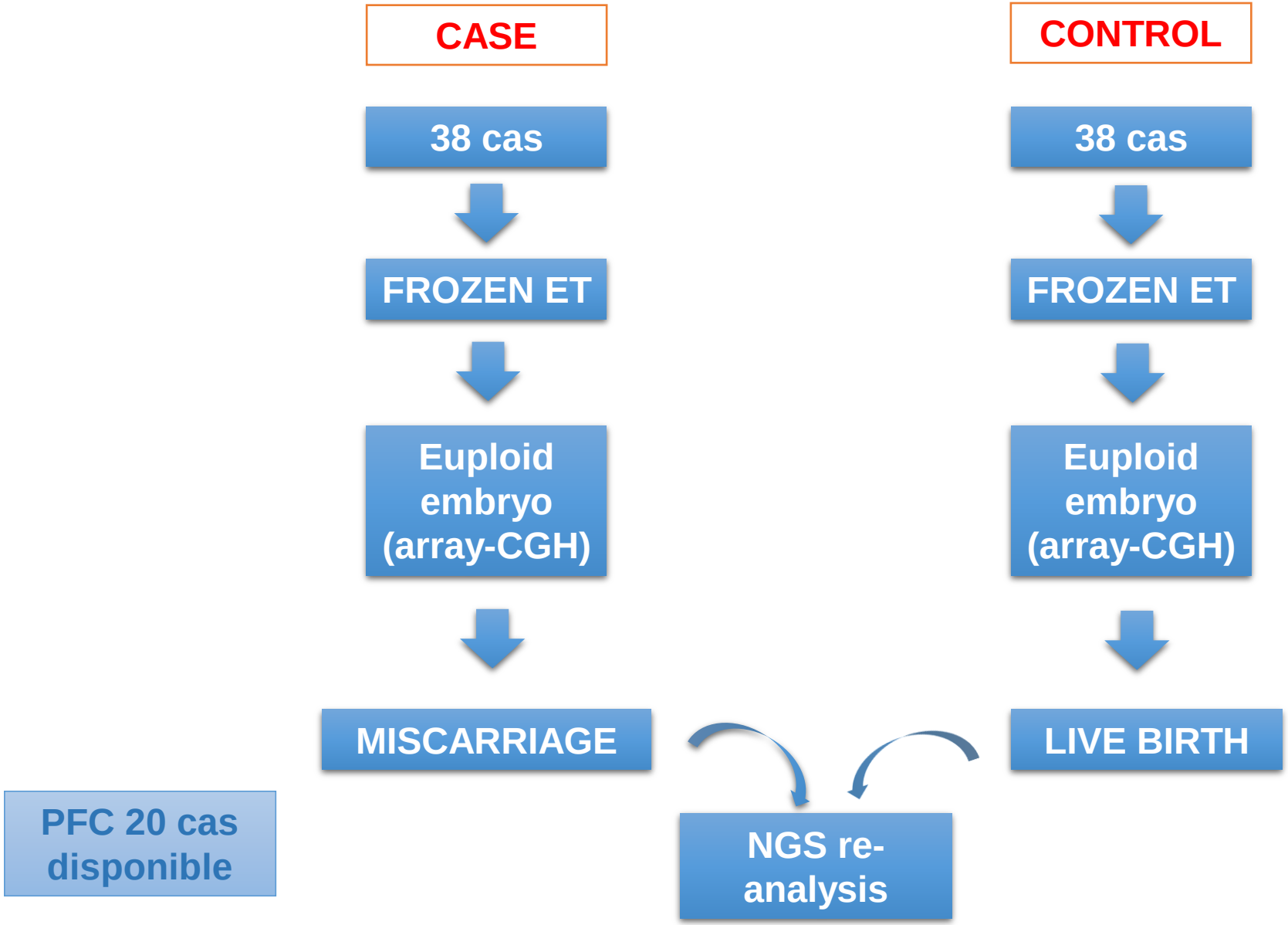
Why do euploid embryos miscarry? A case-control study comparing the rate of aneuploidy within presumed euploid embryos that resulted in miscarriage or live birth using next-generation sequencing.

Maxwell SM[1], Colls P[2], Hodes-Wertz B[3], McCulloh DH[3], McCaffrey C[3], Wells D[4], Munné S[2], Grifo JA[3].

⊕ Author information

Abstract

OBJECTIVE: To determine whether undetected aneuploidy contributes to pregnancy loss after transfer of euploid embryos that have undergone array comparative genomic hybridization (aCGH).



Maxwell et al., 2016

RESULTATS

TABLE 3

Euploid embryos by aCGH resulting in spontaneous abortion with results of POC and reanalysis with NGS.

Euploid embryo no.	Cytogenetic method	Cytogenetic result	NGS result
1	SNP	46 XY	46 XY
2	SNP	47 XX+7	46 XX
3	SNP	46 XX	46 XX
4	Cell culture, G-banding	46 XX	46 XX
5	SNP	46 XX	46 XX
6	Cell culture, G-banding	46 XY →	Mosaic partial trisomy 11pter-p15.1
7	Cell culture, G-banding	46 XX →	Mosaic monosomy 1, mosaic monosomy 17
8	Cell culture, G-banding plus FISH	Mosaic trisomy 21	Mosaic trisomy 21
9	SNP	46 XY	46 XY
10	Cell culture, G-banding	46 XY	46 XY
11	Cell culture, G-banding	46 XX	46 XX
12	SNP	Mosaic trisomy 13	46 XX
13	SNP	46 XX	46 XX
14	Cell culture, G-banding	46 XY	46 XY
15	Cell culture, G-banding	46 XY →	Mosaic partial monosomy 11pter-p11.12, Mosaic partial monosomy 22q12.1qter
16	SNP	46 XX	46 XX
17	Cell culture, G-banding	46 XY	46 XY
18	SNP	Mosaic trisomy 11	Mosaic trisomy 11
19	SNP	46 XY	46 XY
20	Cell culture, G-banding	46 XY →	Mosaic partial monosomy 1, Mosaic monosomy 8

Note: aCGH = array comparative genomic hybridization; FISH = fluorescent in situ hybridization; NGS = next-generation sequencing; POC = products of conception; SNP = single nucleotide polymorphism.

Maxwell. NGS reanalysis of aCGH euploid embryos. Fertil Steril 2016.

Mosaicisme détecté par NGS non présent dans le PFC

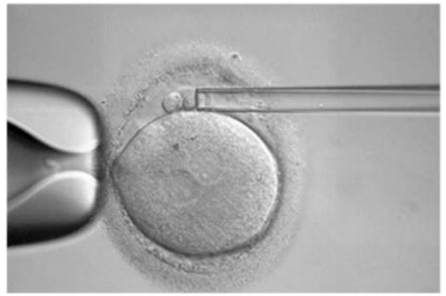
Maxwell et al., 2016

L'ACPA est incapable de détecter certain cas de mosaicisme

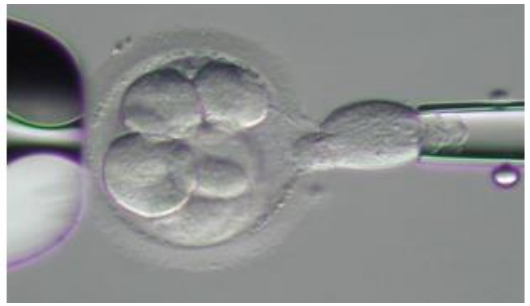
BIOPSIE EMBRYONNAIRE

Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6

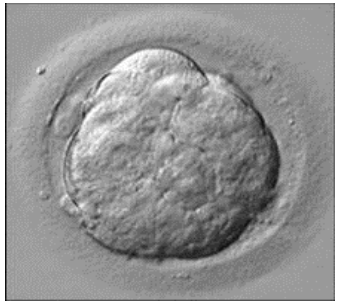
Polar Body Biopsy



Cleavage stage biopsy

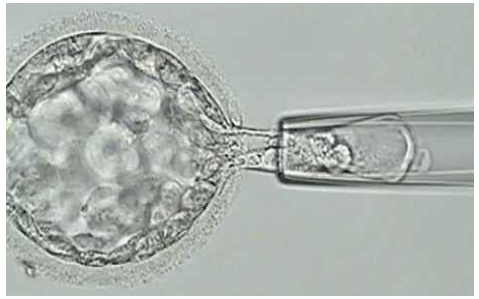


Morula stage biopsy

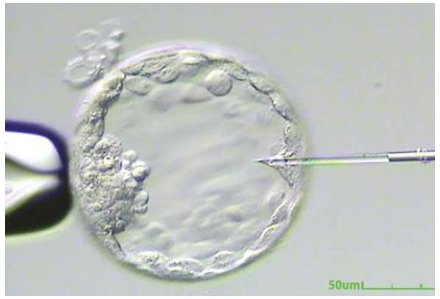


Blastocyst biopsy

Trophectoderm

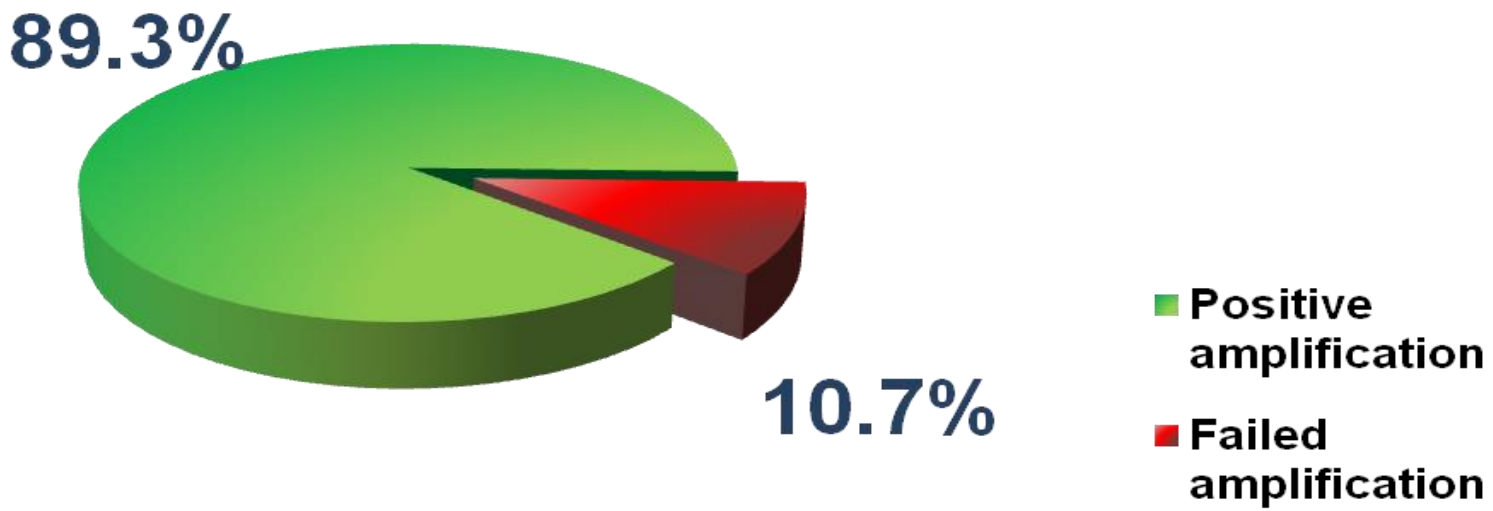


Blastocoelic fluid



DETECTION de L'ADN DANS LE LIQUIDE BLASTOCOELIQUE

SAMPLES: 206



S.I.S.Me.R. Data Reproductive Medecine Unit, Bologne Italy

Medical Hypotheses 83 (2014) 506–508

Contents lists available at ScienceDirect

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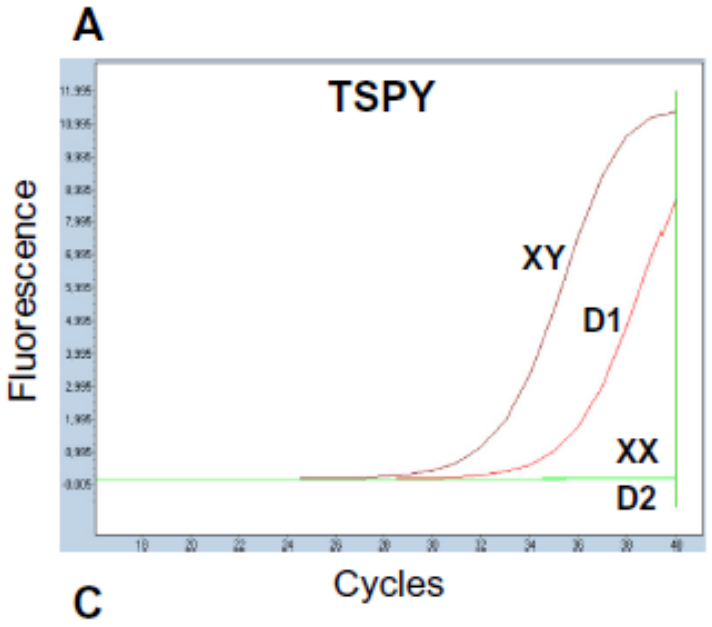
journal homepage: www.elsevier.com/locate/mehy

Non-invasive pre-implantation genetic diagnosis of X-linked disorders

Said Assou [a,b], Ounissa Aït-Ahmed [a,b], Safia El Messaoudi [c], Alain R. Thierry [c], Samir Hamamah [a,b,d,*]

[a] Université Montpellier 1, UFR de Médecine, Montpellier, France
[b] CHU Montpellier, Institute for Regenerative Medicine and Biotherapy, Hôpital Saint-Eloi, INSERM U1040, Montpellier, France
[c] Institut de Recherche en Cancérologie de Montpellier, INSERM U896, Montpellier, France
[d] ART-PGD Department, CHU Montpellier, Hôpital Arnaud de Villeneuve, Montpellier, France



Pushing the limits of detection: investigation of cell-free DNA for aneuploidy screening in embryos

Jacqueline R. Ho, M.D.,[a] Nabil Arrach, Ph.D.,[b,c] Katherine Rhodes-Long, M.S.,[a] Ali Ahmady, Ph.D.,[a] Sue Ingles, Ph.D.,[d] Karine Chung, M.D., M.S.C.E.,[a] Kristin A. Bendikson, M.D.,[a] Richard J. Paulson, M.D., M.S.,[a] and Lynda K. McGinnis, Ph.D.[a]

[a] Department of Obstetrics and Gynecology, University of Southern California, Los Angeles; [b] Department of Microbiology and Molecular Genetics, University of California, Irvine; [c] Progenesis, La Jolla; and [d] Department of Preventative Medicine, University of Southern California, Los Angeles, California

Concordance rates between cell-free DNA (cfDNA), trophectoderm biopsy, and whole embryos, n (%).

	Concordance for ploidy				Concordance for sex			
Pair	**Total**	**AH**	**No AH**	***P* value[c]**	**Total**	**AH**	**No AH**	***P* value[c]**
Day 3 cfDNA vs. whole embryo[a] (n = 16)	9/16 (56.3%)	4/8 (50.0%)	5/8 (62.5%)	.61	13/16 (81.3%)	5/8 (62.5%)	8/8 (100%)	.06
Day 5 cfDNA vs. whole embryo[a] (n = 33)	15/33 (45.5%)	5/16 (31.3%)	10/17 (58.8%)	.11	26/33 (78.7%)	12/16 (75.0%)	14/17 (82.4%)	.61
Day 5 cfDNA vs. trophectoderm biopsy[b] (n = 40)	26/40 (65.0%)	16/28 (57.1%)	10/12 (83.3%)	.16	28/40 (70.0%)	17/28 (60.7%)	11/12 (91.7%)	.07
Day 5 trophectoderm biopsy vs. whole embryo[a] (n = 27)	25/27 (92.6%)	12/14 (85.7%)	13/13 (100%)	.22	26/27 (96.3%)	14/14 (100%)	12/13 (92.3%)	.48

Note: AH = assisted hatching.
[a] Includes research embryos only.
[b] Includes both research embryos and clinical samples.
[c] Chi-square analysis or Fisher exact test used to compare AH vs. no AH groups; $P<.05$ was considered to be significant.

Ho. Cell-free DNA for aneuploidy screening.. Fertil Steril 2018.

CfDNA du milieu de culture embryonnaire n'est pas actuellement optimisé pour dépistage des aneuploïdies , mais il reste un outil

Human Reproduction, Vol.33, No.12 pp. 2162–2167, 2018
Advanced Access publication on October 24, 2018 doi:10.1093/humrep/dey314

human reproduction

MINI-REVIEW *Developments in Reproductive Biology and Medicine*

Non-invasive pre-implantation genetic testing of human embryos: an emerging concept

C. Farra[1], F. Choucair[2], and J. Awwad[2,*]

[1]Department of Pathology and Laboratory Medicine, Medical Genetics Unit, American University of Beirut Medical Center, PO Box 11-236, Riad El-Solh, Beirut 1107 2020, Lebanon [2]Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, American University of Beirut Medical Center, PO Box 11-236, Riad El-Solh, Beirut 1107 2020, Lebanon

*Correspondence address. AUBMC Fertility Center, American University of Beirut Medical Center, PO Box 11-236. Riad El-Solh, Beirut 1107 2020, Lebanon, Tel: +961-1350000 ext. 5606; Fax: +961-1370829; E-mail: jawwad@aub.edu.lb

Submitted on June 3, 2018; resubmitted on September 20, 2018; accepted on October 12, 2018

genetic information. The genetic analysis of cell-free embryonic DNA has been reported, to be useful in evaluating the genetic constitution of embryos; thus, providing a potential alternative to conventional biopsy-derived pre-implantation genetic testing (PGT). In this review, we have summarized these

	Amplification method	Amplification failure	Sample volume (µl)	Collection day	Media change	DNA analysis	Ploidy concordance
Blastocoel fluid							
Palini et al. (2013)	RepliG WGA	43.75% (7/16)	4	Day 5	NA	aCGH	—
Gianaroli et al. (2014)	SurePLEX WGA	23.5% (12/51)	1	Day 5	NA	aCGH	70.0% vs PB 88.9% vs EB 82.0% vs TE
Tobler et al. (2015)	SurePLEX WGA	37.5% (36/96)	1	Day 5	NA	aCGH	62.0% vs TE
Gallusti et al. (2015)	PicoPLEX WGA	55.6% (5/9)	4	Day 5/6	NA	qPCR	—
Magli et al. (2016)	SurePLEX WGA	18.1% (21/116)	0.01	Day 5	NA	aCGH	95.0% vs PB 94.0% vs EB 97.1% vs TE
Embryo-spent culture medium							
Gallusti et al. (2015)	PicoPLEX WGA	6.25% (2/32)	10	Day 3	NA	qPCR	—
		5.55% (3/54)	10	Day 5/6	Yes	qPCR	—
Shamonki et al. (2016)	Repli-G WGA	3.5% (2/57)	15	Day 5/6	Yes	aCGH	—
Xu et al. (2016)	MALBAC WGA	0% (0/42)	5–20	Day 5	Yes	HiSeq NGS	87.7% vs WB
Liu et al. (2017)	MALBAC WGA	9.1% (8/88)	30	Day 5	No	HiSeq NGS	64.5% vs EB
Hammond et al. (2017)	TaqMan PreAmp system	0% (0/51)	20	Day 3	NA	qPCR	—
		0% (0/51)		Day 5	Yes		—
		0% (0/52)		Day 6	No		—
Feichtinger et al. (2017)	SurePLEX WGA	18.2% (4/22)	5	Day 5	No	aCGH	72.2% vs PB
Vera-Rodriguez et al. (2018)	SurePLEX WGA	8.9% (5/56)	20	Day 5	Yes	ReproSeq	33.0% vs TE
Combined embryo-spent culture medium and blastocoel fluid							
Kuznyetsov et al. (2018)	SurePLEX WGA	0% (0/28 frozen)	—	Day 5/6	NA	MiSeq NGS	87.5% vs TE 96.4% vs WB
		0% (0/19 fresh)	—	Day 5/6	Yes	MiSeq NGS	100% vs TE 99.7% vs WB
Li et al. (2018)	MALBAC WGA	2.5% (1/40)	25	Day 5	Yes	HiSeq NGS	45.0% vs TE 50.0% vs WB

- ❑ mean DNA concentration 26,16 ng/µl

- ❑ pooled culture medium/BF samples were associated with 97.5 and 100% DNA amplification rates, After WGA.

Concept Prometteur

PGDIS POSITION STATEMENT ON CHROMOSOME MOSAICISM AND PREIMPLANTATION ANEUPLOIDY TESTING AT THE BLASTOCYST STAGE

- ***Pour déclarer un mosaicism embryonnaire, le seuil suggéré doit être > 20%, donc les niveaux inférieurs doivent être traités comme normaux (euploïdes), > 80% anormaux (aneuploïdes) et les autres entre 20-80% mosaïque (mosaïques euploïdes-aneuploïdes).***

July 2019

Les guidelines suggérées pour prioriser les embryons mosaïques à transférer

Les embryons présentant une mosaïque euploïdie / monosomie sont préférables à l'euploïdie / trisomie, étant donné que les embryons monosomiques (sauf 45, X) ne sont pas viables.

Si une décision est prise de transférer des embryons trisomiques mosaïque pour un seul chromosome, on peut prioriser la sélection en fonction du chromosome impliqué:

- ***Transfert préférable** pour des embryons trisomiques en mosaïque concernant **les chromosomes 1, 3, 4, 5, 6, 8, 9, 10, 11, 12, 17, 19, 20, 22, X, Y.***

- ***Transfert moins prioritaire**:*

  - *embryons mosaïques pour les trisomies associées à un retard de croissance intra-utérin (**chromosomes 2, 7, 16) .***

  - *embryons pour les trisomies capables de donner des naissances viables !!!!!! **(chromosomes 13, 18, 21)** .*

Lancet Digit Health. 2023 Jan;5(1):e28-e40. doi: 10.1016/S2589-7500(22)00213-8.

A non-invasive artificial intelligence approach for the prediction of human blastocyst ploidy: a retrospective model development and validation study

Josue Barnes [1], Matthew Brendel [1], Vianne R Gao [2], Suraj Rajendran [3], Junbum Kim [1], Qianzi Li [2], Jonas E Malmsten [4], Jose T Sierra [5], Pantelis Zisimopoulos [6], Alexandros Sigaras [6], Pegah Khosravi [7], Marcos Meseguer [8], Qiansheng Zhan [4], Zev Rosenwaks [4], Olivier Elemento [9], Nikica Zaninovic [4], Iman Hajirasouliha [10]

Background: One challenge in the field of in-vitro fertilisation is the selection of the most viable embryos for transfer**. Morphological quality assessment** and **morphokinetic analysis** both have the disadvantage of intra-observer and inter-observer variability. A third method, preimplantation genetic testing for aneuploidy (PGT-A), has limitations too, including its invasiveness and cost. We hypothesised that differences in aneuploid and euploid embryos that allow **for model-based classification are reflected in morphology, morphokinetics, and associated clinical information.**

Review > Reprod Sci. 2023 Jul 29. doi: 10.1007/s43032-023-01301-0. Online ahead of print.

Current Applications and Controversies in Preimplantation Genetic Testing for Aneuploidies (PGT–A) in In Vitro Fertilization

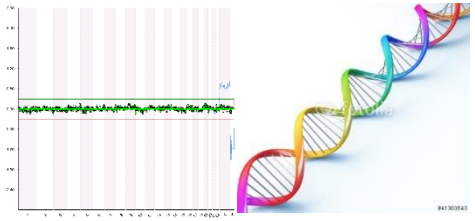
Carmen Morales [1]

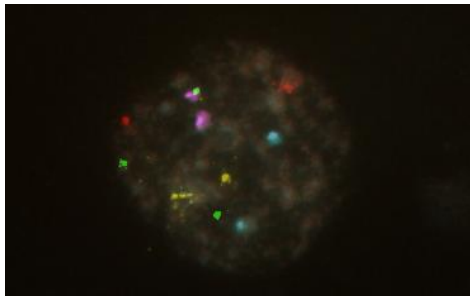
It has to be considered that PGT-A may not be a **universal test** to improve the reproductive potential in IVF patients, rather each clinic should **evaluate the efficacy** of PGT-A in their IVF program based on **their population, skills, and limitations**.

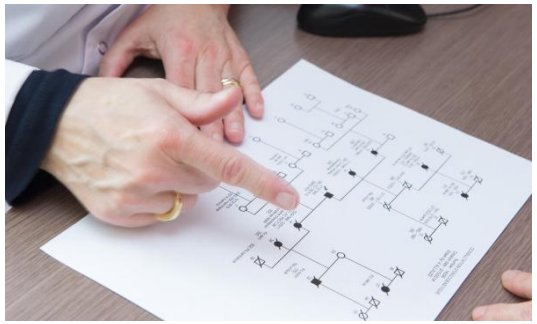
« L'important n'est pas de convaincre, mais de donner à réfléchir. »

Bernard Werber

THE TAKE-HOME MESSAGE





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2024


Obrigado
감사합니다
Gracias
Merci
شكرا لك
Thank you
Danke
謝謝
Ευχαρισ