Quand les translocations équilibrées engendrent les aneuploidies annexes: Focus sur trois couples marocains

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XXVIe COLLOQUE ACLF
Association des Cytogénéticiens de Langue Française
&
XXXIIe COLLOQUE ATC
Association des Techniciens en Cytogénétique
Du 13 au 15 SEPTEMBRE 2023
Le HAVRE
CARRÉ DES DOCKS

INTRODUCTION

- Les rearrangements chromosomiques structurels équilibrés sont des anomalies frequentes.

- Prevalence de 0,4% en prenatal et 0,2% en Postnatal.

- Production de gamètes déséquilibrés pendant la méiose.

- Problèmes de fertilité, de fausses couches à répétition et descendance présentant des anomalies congénitales et des déficiences cognitives.

Jacobs PA et al. Ann Hum Genet 1974
Van Dyke et al . Am J Hum Genet. 1983

Anomalies chromosomiques observées à la naissance
Incidence p.1000 N Né

Aneuploïdies (y compris mosaïques) :

·	Chromosomes sexuels	2,03 dont :
	sexe masculin	2,53
	sexe féminin	1,50
·	Autosomes	1,45 dont :
	tri 21	1,21
Anomalies de structure		
·	Equilibrées	2,12 dont :
	t.robertsoniennes	0,99
	t.réciproques	0,91
	inversions	0,22
·	Non équilibrées	0,62 dont :
	t.robertsoniennes	0,06
	Total	6,22

1992-2010

GENETIC TESTING AND MOLECULAR BIOMARKERS
Volume 16, Number 6, 2012
© Mary Ann Liebert, Inc.
Pp. 569–573
DOI: 10.1089/gtmb.2011.0265

Cytogenetic Analysis of 5572 Patients Referred for Suspected Chromosomal Abnormalities in Morocco

Nisrine Aboussair,[1,2] Imane Cherkaoui Jaouad,[1] Souad Cherkaoui Dequaqui,[1] Aziza Sbiti,[1] Fatiha Elkerch,[1] Benbouchta Yahya,[1] Abdelhafid Natiq,[1] and Abdelaziz Sefiani[1,3]

Objectives: The aim of this study was (1) to identify the profile of patients being referred for cytogenetic analysis in Morocco, (2) to determine the prevalence and type of chromosomal abnormalities in the different groups, (3) to compare the results with those of similar studies done in other countries. *Material and Methods:* 5572 patients ranging from newborns to 50 years of age were referred to the department of medical genetics, of the Moroccan National Institute of Health between 1993 and 2010, with a variety of clinical disorders such as mental retardation; multiple congenital malformations; clinical features of Down syndrome, Turner's syndrome, and Klinefelter syndrome; ambiguous sex; sterility; amenorrhea; recurrent miscarriage; and chromosome breakage

Déterminer la prévalence et le type des anomalies chromosomiques???

Table 2. Autosomal Chromosome Abnormalities in Patients Referred for Cytogenetic Analysis

Karyotype	*No. of cases*	*%*
I-Numerical aberrations	1096	19.67
Down syndrome (excluded translocations)	1056	18.95
Edwards syndrome	23	0.41
Patau syndrome (excluded translocations)	16	0.28
Partial trisomy 47,XY,+der(15)	1	0.02
II-Structural aberrations	137	2.45
Robertsonian translocation	44	0.78
Reciprocal translocation	25	0.45
Unbalanced derivative chromosome	6	0.1
Deletions (excluded 5p- and 4p-)	12	0.21
Cri du chat syndrome	8	0.14
Wolff Hirschorn syndrome	7	0.12
Microrearrangements	20	0.36
Ring chromosomes	8	0.14
Additions	7	0.12
Marker chromosomes	7	0.12
Inversion	1	0.02
Total	1233	22.13%

Table 4. Comparison of the Frequency of Chromosomal Aberrations of the Moroccan Population of the Current Study with Other Similar Studies Reported by Different Investigators in Other Countries

Other countries	*Total number of patients examined*	*Frequency of chromosomal aberrations found (%)*
Mokhtar (1997)	137	38.7%
Verma and Dosik (1980)	357	27.2%
Singh (1977)	451	28.8%
Duarte *et al.* (2004)	916	29.3%
Navsania (1993)	1000	16.6%
Goud *et al.* (2005)	1800	28.3%
Kim *et al.* (1999)	4117	17.5%
Balkan *et al.* (2010)	4216	32.2%
Current study	5572	27%

interchromosomal effect (ICE)

Review > Pediatrics. 1963 Sep;32:326-37.

AUTOSOMAL DISORDERS

J LEJEUNE

178 TURKISH JOURNAL OF UROLOGY Turk J Urol 2020; 46(3): 178–85 • DOI: 10.5152/tud.2020.19255

ANDROLOGY

Original Article

Investigation of the interchromosomal effects in male carriers with structural chromosomal abnormalities using FISH

Özgür Balasar[1], Hasan Acar[2]

- Quelles conséquences des translocations réciproques et robertsoniennes sur La descendance ????

- Quelle approche diagnostique en Préimplantatoire et Prénatal ????

interchromosomal effect (ICE)

Journal of Assisted Reproduction and Genetics (2019) 36:2547–2555
https://doi.org/10.1007/s10815-019-01593-9

GENETICS

Check for updates

Interchromosomal effect in carriers of translocations and inversions assessed by preimplantation genetic testing for structural rearrangements (PGT-SR)

E. Mateu-Brull[1] · L. Rodrigo[1] · V. Peinado[1] · A. Mercader[2] · I. Campos-Galindo[1] · F. Bronet[3] · S. García-Herrero[1] · M. Florensa[4] · M. Milán[1] · C. Rubio[1]

Results In carriers of translocations, we observed a higher percentage of abnormal embryos from day 3 biopsies compared with day 5/6 biopsies and for reciprocal translocations compared with other rearrangements. We observed a high percentage of embryos with aneuploidies for chromosomes not involved in the rearrangement that could be attributed to total ICE (aneuploid balanced and unbalanced embryos). No significant differences were observed in these percentages between types of rearrangements. Pure ICE (aneuploid balanced embyos) was independent of female age only for Robertsonian translocations, and significantly increased in day 3 biopsies for all types of abnormalities. Furthermore, total ICE for carriers of Robertsonian translocations and biopsy on day 3 was independent of female age too. High ongoing pregnancy rates were observed for all studied groups, with higher pregnancy rate for male carriers.

interchromosomal effect (ICE)

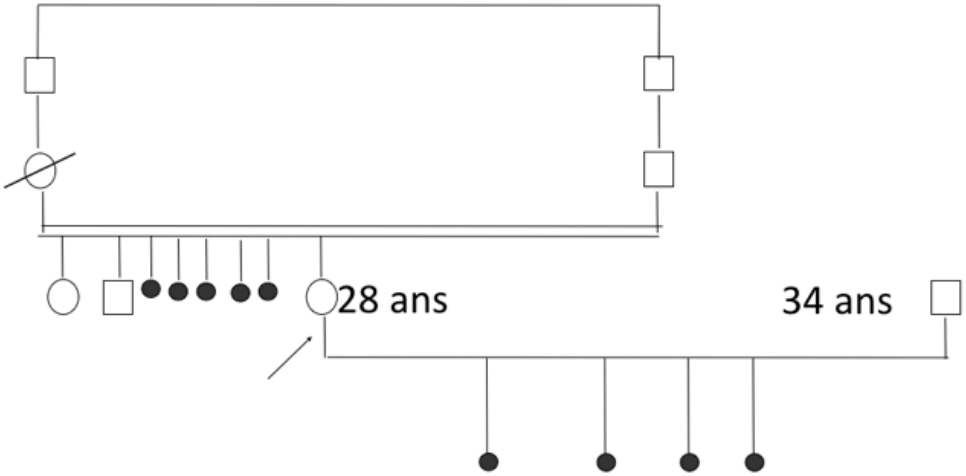
Human Reproduction Vol.20, No.5 pp. 1256–1260, 2005
Advance Access publication February 3, 2005
doi:10.1093/humrep/deh751

Aneuploidy 12 in a Robertsonian (13;14) carrier: Case report

C.Gutiérrez-Mateo[1,4], L.Gadea[2], J.Benet[1], D.Wells[3], S.Munné[2,3] and J.Navarro[1]

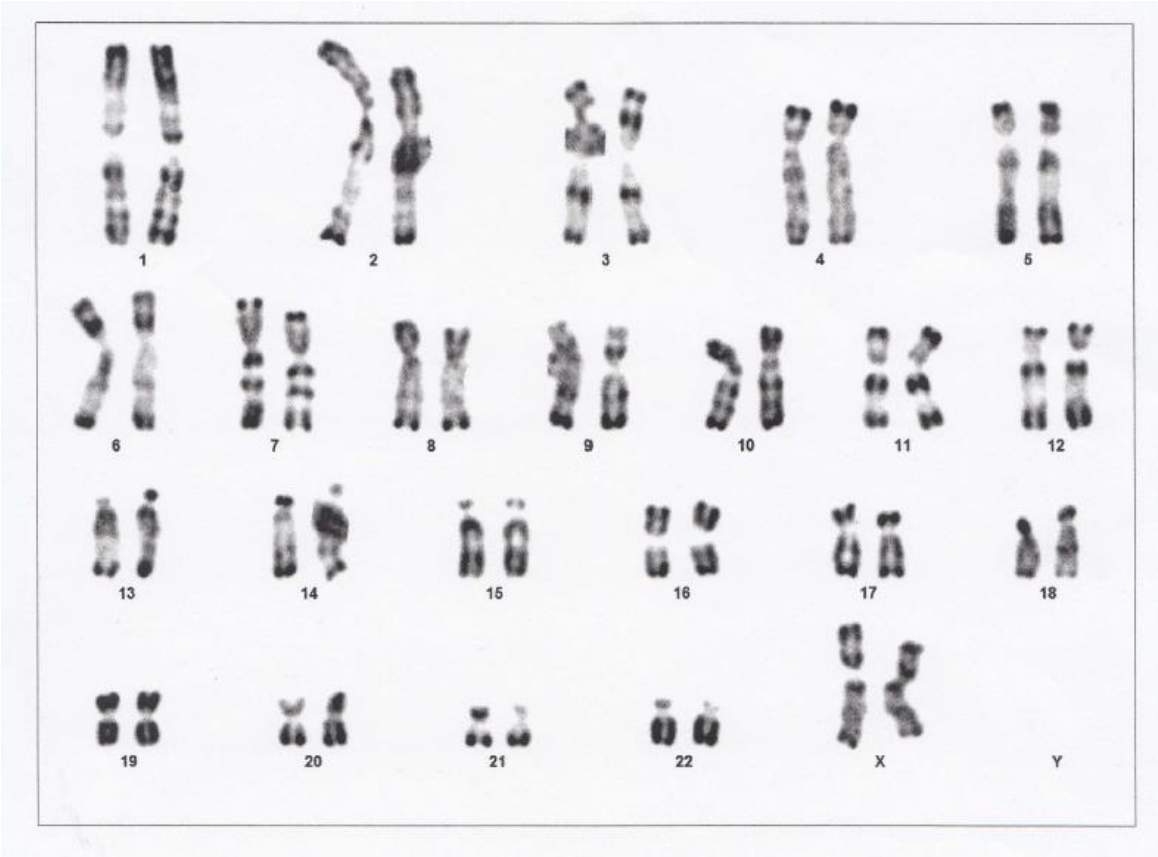
In translocation carriers, the presence of aneuploidy for the chromosomes unrelated to the rearrangement may lead to an additional risk of abnormal pregnancy or implantation failure. Consequently, it may be important to analyse not only the chromosomes involved in the rearrangement but also the rest of chromosomes. We combined spectral karyotyping (SKY) and comparative genomic hybridization (CGH) to karyotype one unfertilized oocyte and its first polar body (1PB) from a Robertsonian translocation carrier t(13;14) aged 29 years who was undergoing IVF and preimplantation genetic diagnosis (PGD) for translocations and aneuploidy screening. Two out of four embryos were aneuploid, as a result of an adjacent segregation. The unfertilized oocyte had a normal/balanced constitution of the chromosomes involved in the reorganization. However, this 1PB–metaphase II doublet was aneuploid for chromosome 12, the oocyte being hyperhaploid (24, X, +12) and its 1PB hypohaploid (22, X, −12). The application of CGH for the study of Robertsonian translocations of maternal origin will be useful to study imbalances of the chromosomes involved in the rearrangement, as well as alterations in the copy number of any other chromosome. The combination of PGD for translocations with aneuploidy screening could help to reduce the replacement of chromosomally abnormal embryos.

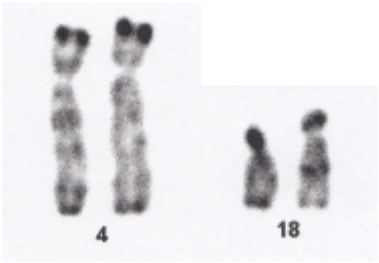
- Jeune couple
- 4 FCS entre 5 et 8 SA
- Caryotype du couple:

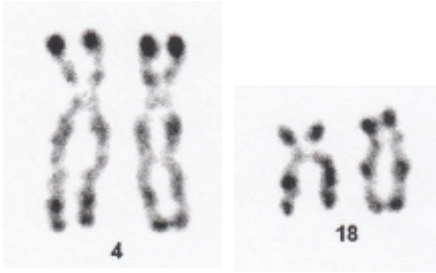


  - ✓ Homme: 46,XY
  - ✓ Femme: 46,XX,der(18)t(18;?)(q22,?)

Case report



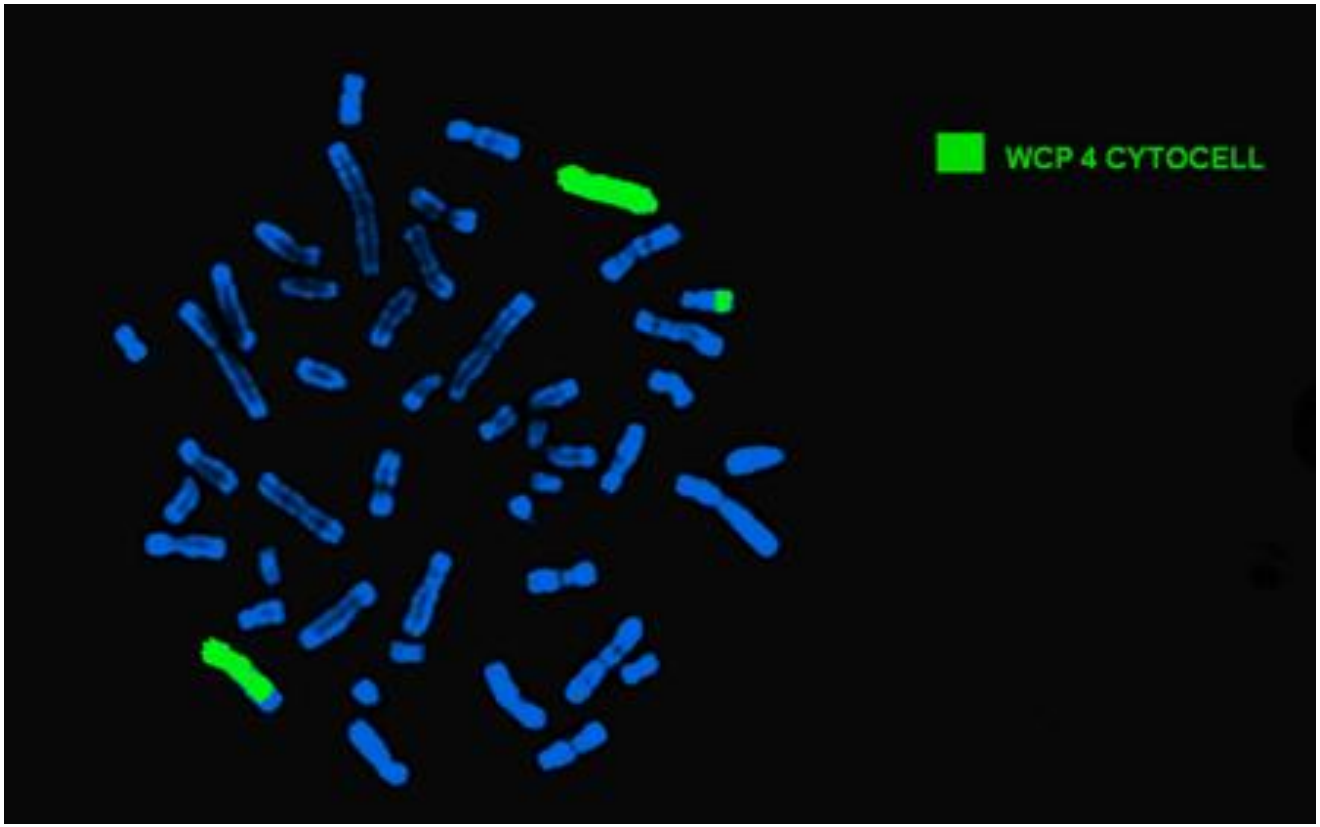




Caryotype de la proposante

Case report

FISH avec WCP 4



46,XX,der(18)t(18;?)(q22,?) → 46,XX,t(4;18)(q34;q21)

Diagnostic préimplantatoire (DPI)

[redacted]

Identification:	**31002**	**Patients:**	[redacted]
Analyse:	PGT-SR (NGS)	**Date de naissance**	
Cycle d'identification:	-	**Identifiant:**	
Type d'échantillon:	Trofoectoderme	**Sexe:**	
Date de réception:	21/04/2021	**Date du rapport:**	
Personne à contacter:	[redacted]	**Clinique de fertilité:**	

PGT-STRUCTURAL (PGT-SR)

Indication

Etude du PGT-SR (Test Génétique Préimplantatoire pour la détection des altérations structurelles) sur la biopsie d'embryons du cycle de reproduction assistée. Le patient présente le caryotype altéré 46,XX,t(4;18)(q31;q21).

Résultats

ID Embryon	Altérations détectées	Chr. Sexuels	Interprétation clinique	Transférable (*)
#Embryon	dup11p,del11q	Normal	Anormal	Non

(*) La colonne "Transférable" n'est qu'une suggestion, elle n'a pas de valeur diagnostique. Il a été généré à partir du résultat obtenu.

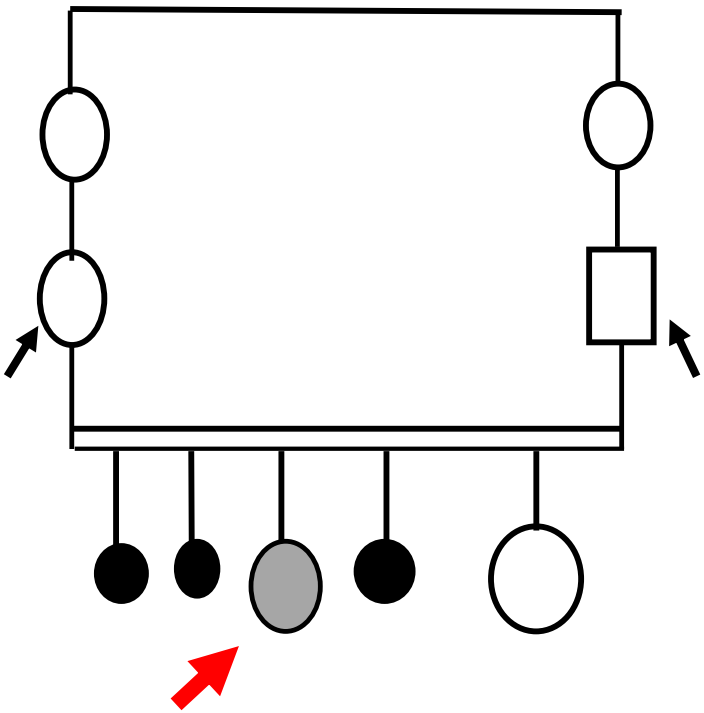
Résultat du PGT-SR

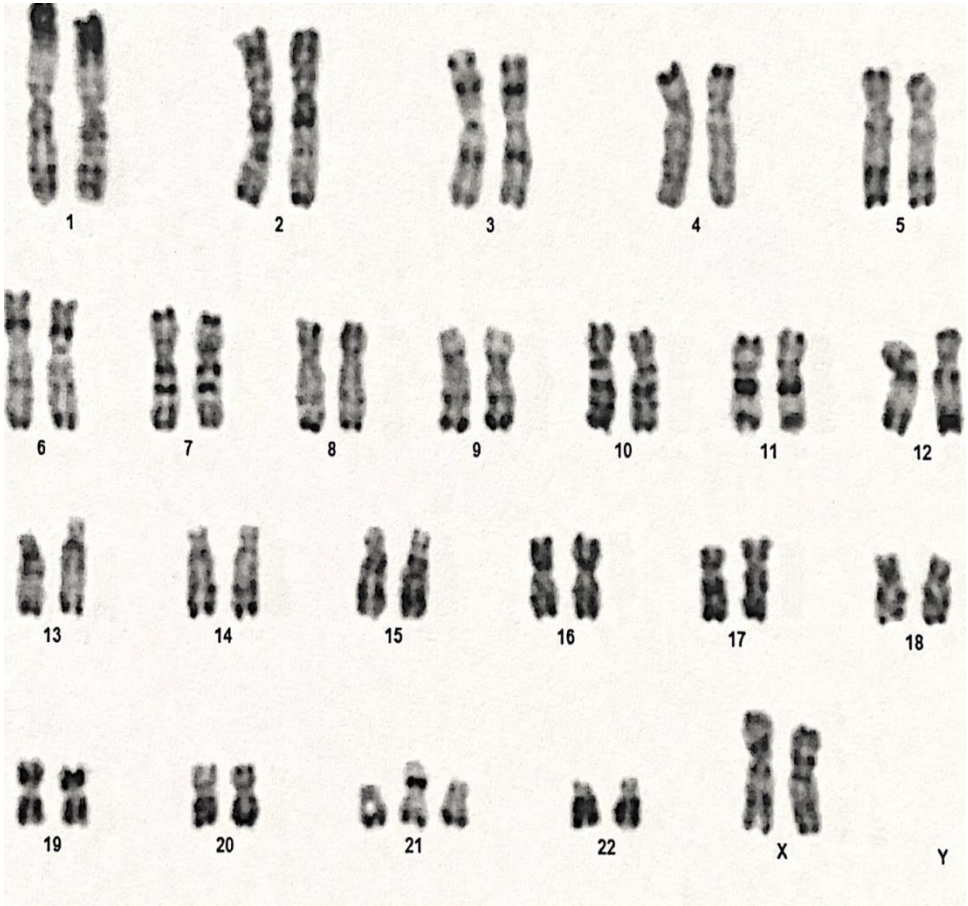
Résultats

ID Embryon	Altérations détectées	Chr. Sexuels	Interprétation clinique	Transférable (*)
#Embryon	dup11p,del11q	Normal	Anormal	Non

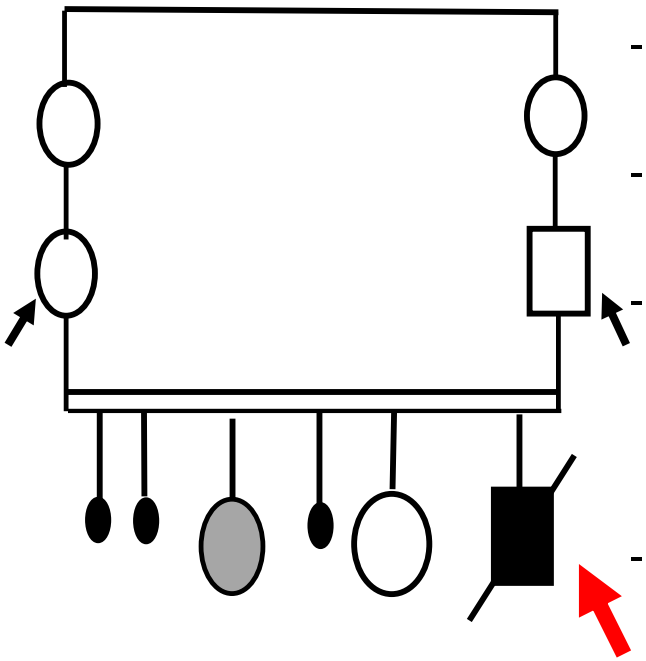
(*) La colonne "Transférable" n'est qu'une suggestion, elle n'a pas de valeur diagnostique. Il a été généré à partir du résultat obtenu.

- Caryotype de la femme: 46,XX,t(4;18)(q34;q21)



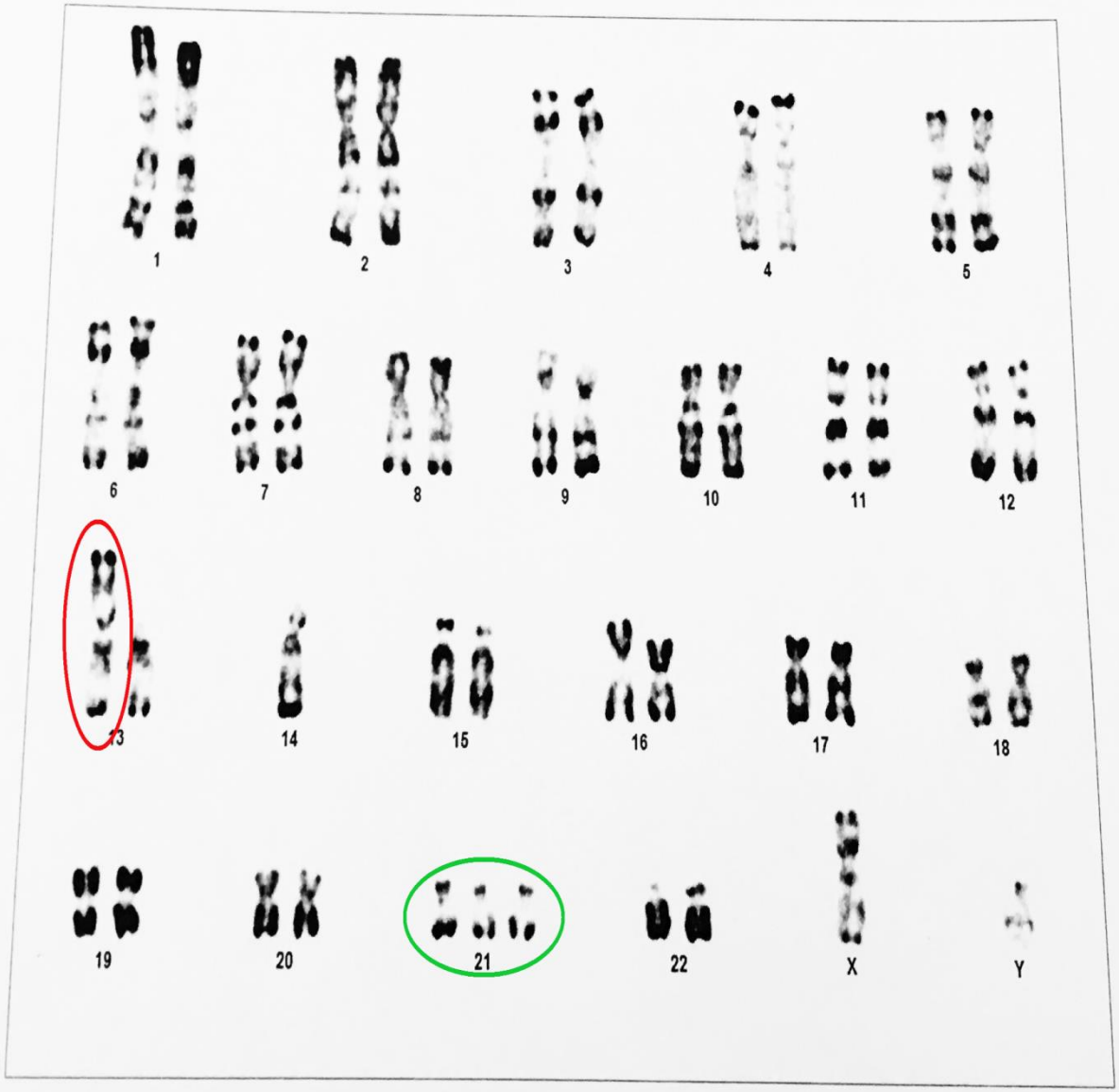


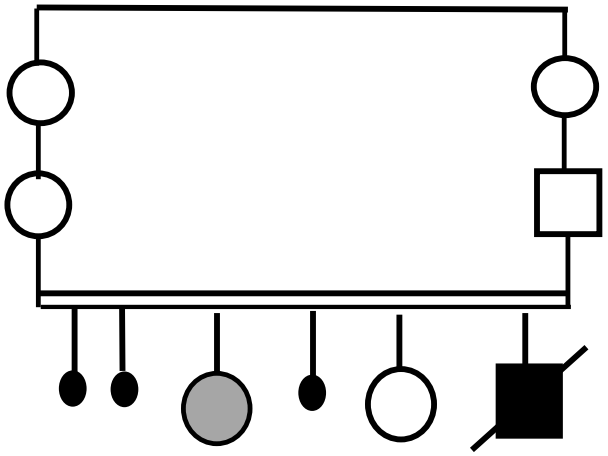
47,XX,+21

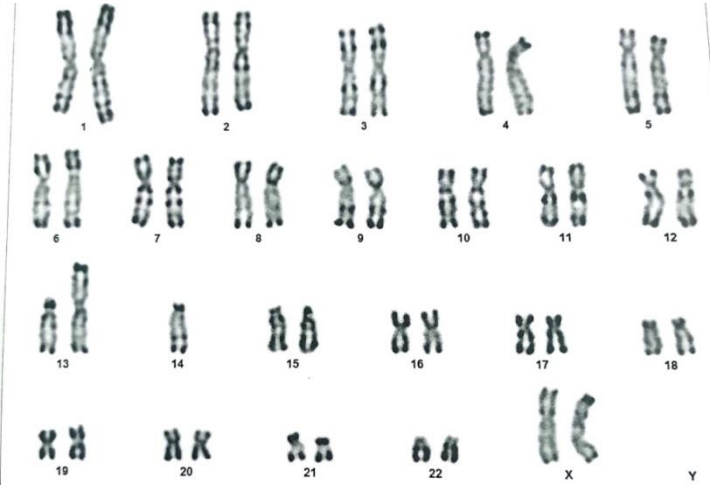


46,XY,der(13;14)(q10;q10),+21

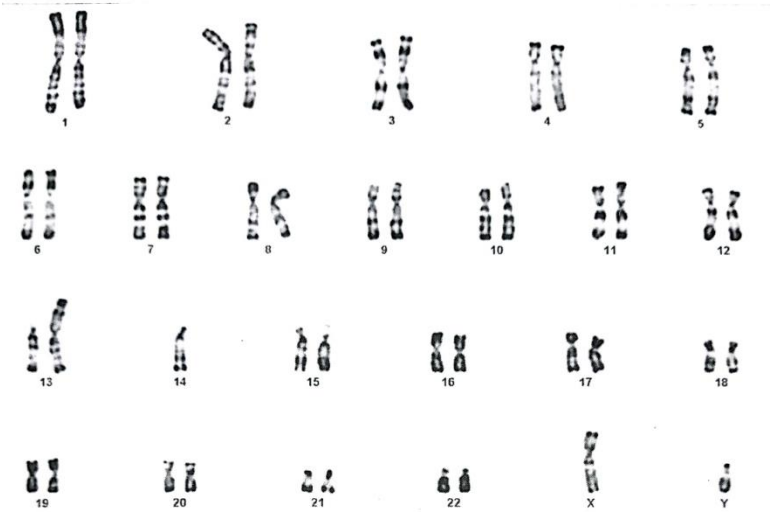
Dossier: 17CG20



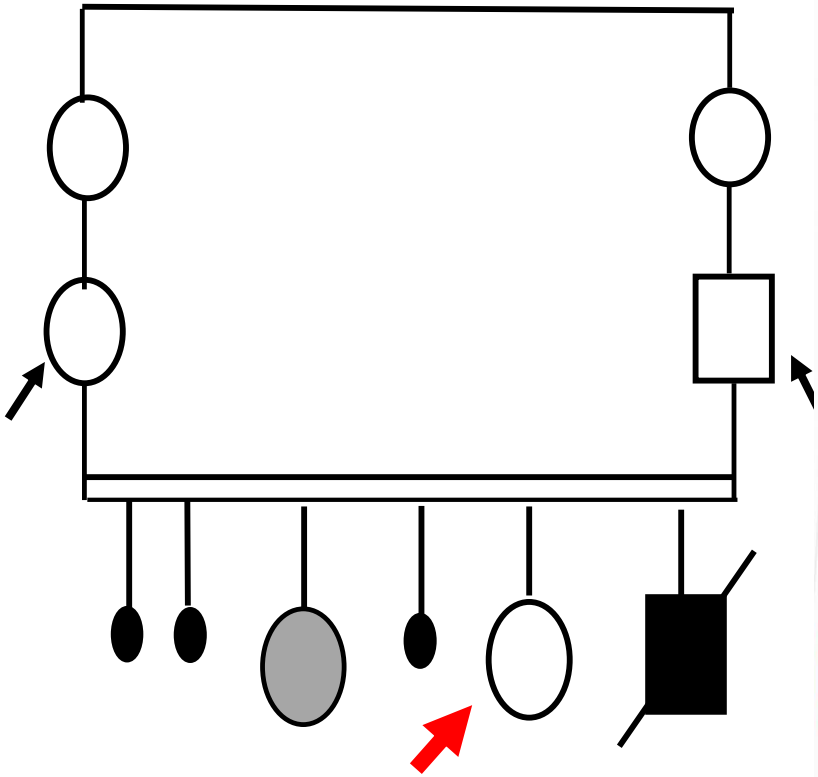




45, XX, der (13; 14)(q10;q10)



45, XY, der (13; 14)(q10;q10)



44, XX, der (13; 14) (q10 ; q10) x 2

Phénotypiquement Normale

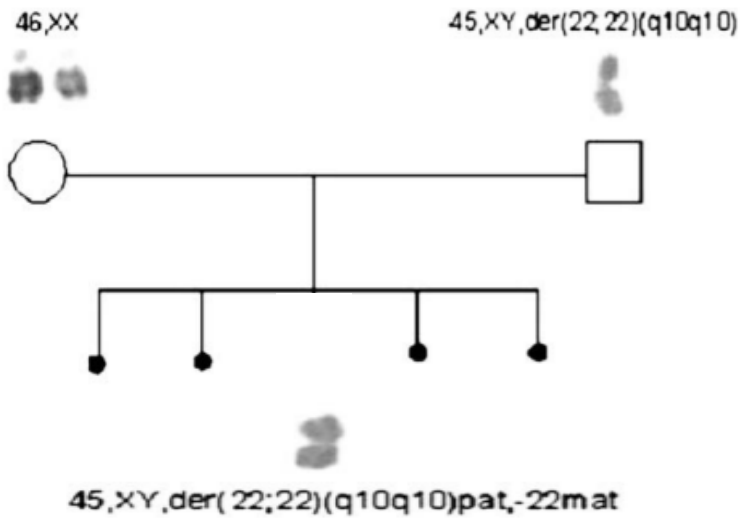
Case Reports > Fertil Steril. 2008 Nov;90(5):2013.e13-5. doi: 10.1016/j.fertnstert.2008.03.067. Epub 2008 Jun 20.

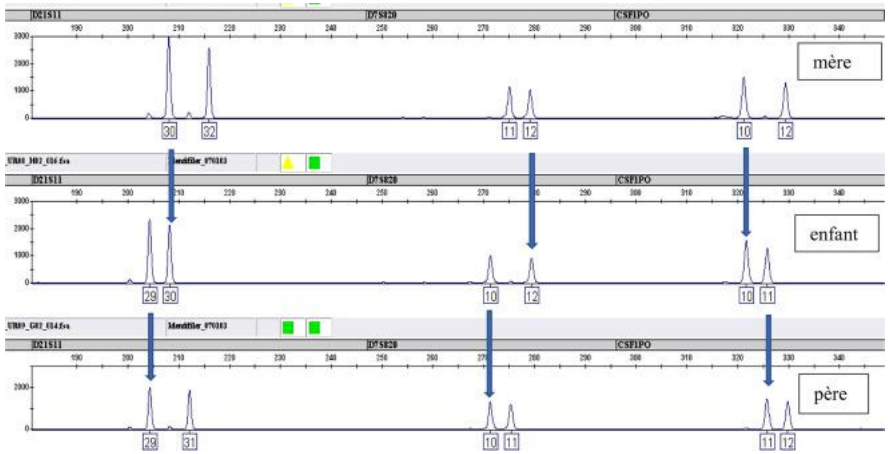
Unexpected fertility and paternal UPD 22

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

FIGURE 1

Family pedigree and partial karyotype.





99,999 %

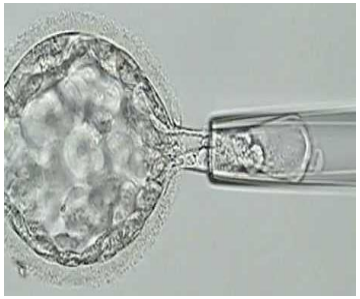
- Possibilité d'une paternité par **trisomy rescue.**
- Pas de gène à empreinte paternelle avec des effets symptomatologiques sur le 22.

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.

Ré analyser à j5



83 embryons aneuploïdes à J3

27 embryons euploïdes à j5

Au stade blastocyste 33% 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.

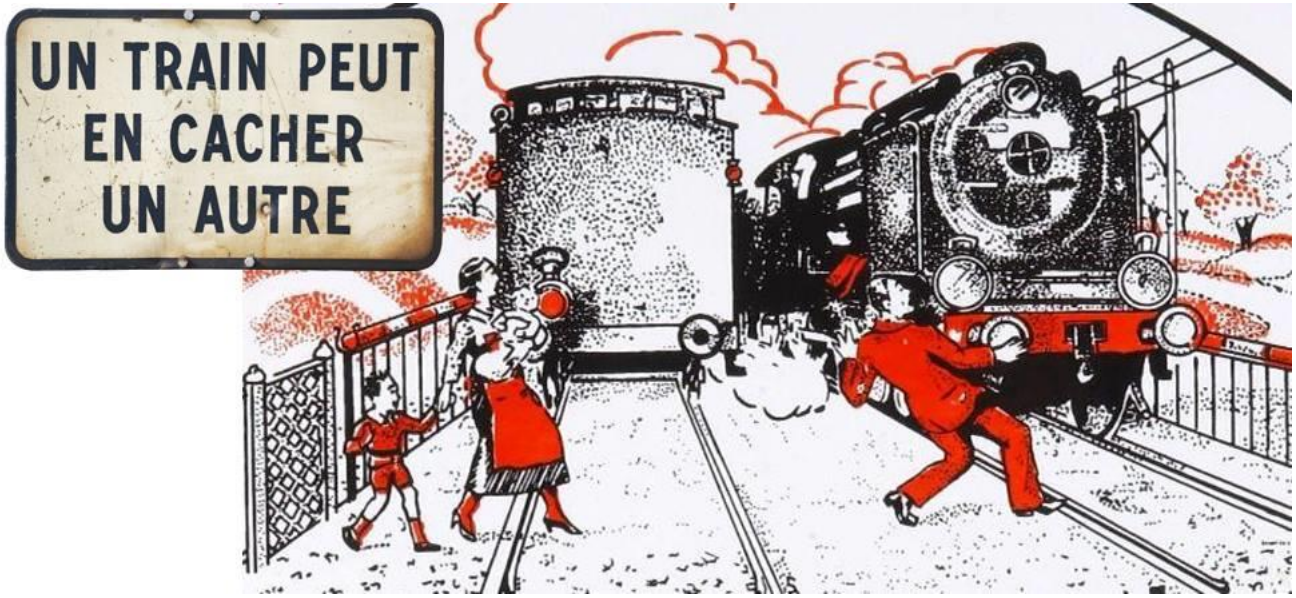
Table 1. Clinical Outcomes of Single Mosaic Blastocysts Transferred.*

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

Conseil Génétique +++



Choix du type de PGT: PGT-SR +++

RCP ET ROB: Evaluation du risque de transmission

Je tiens à remercier L'ATC et tous ces membres pour leurs collaboration précieuse durant ces 30 années.

La fraternité n'est qu'une idée humaine, la solidarité est une idée universelle. Victor Hugo