# PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDIES: WHAT TO DO WITH MOSAIC EMBRYOS

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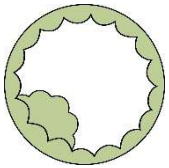
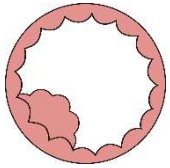
**Barcelona**

# Embryo categories according chromosomal status



euploid

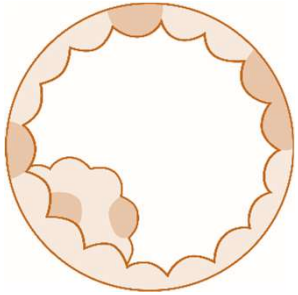


aneuploid

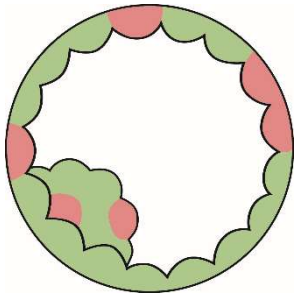
PGT-A 2.0: analysis of multiple cells + high sensitive techniques

mosaic

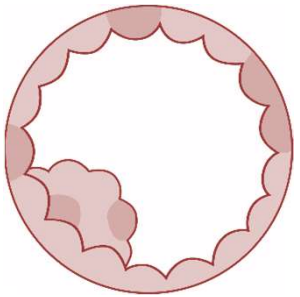
# Mosaicism: definition. Types.



Mosaic embryo: 2 or more distinct cell lines



Aneuploid-euploid mosaic



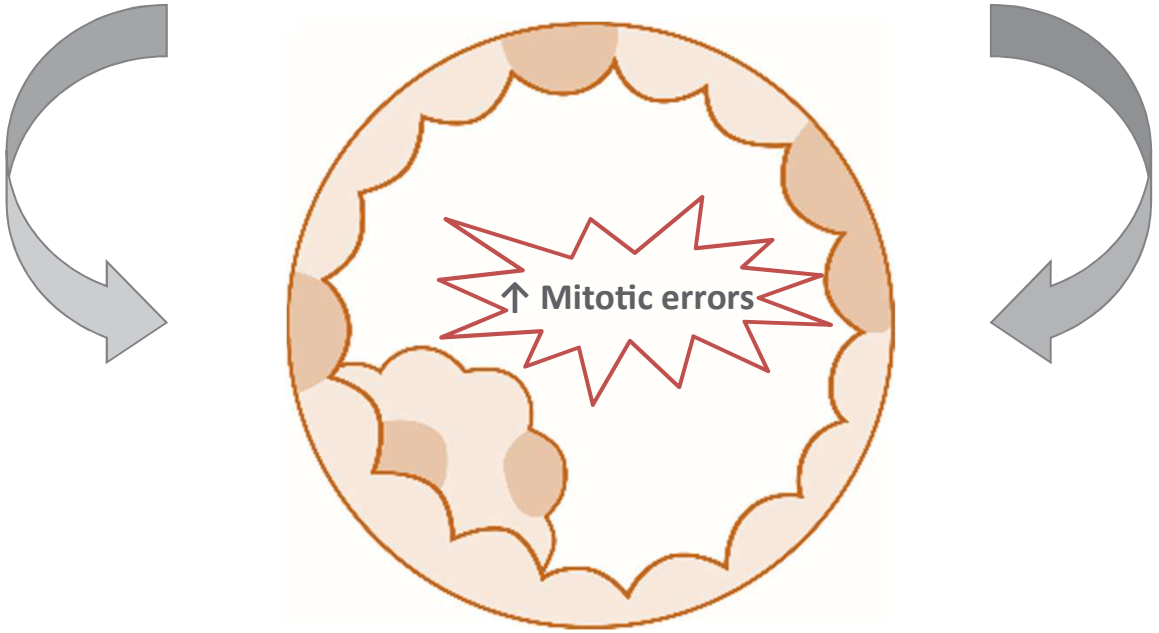
Aneuploid-aneuploid mosaic

# Mosaicism: molecular causes

First mitotic events are fast

Relaxed cell cycle check-points

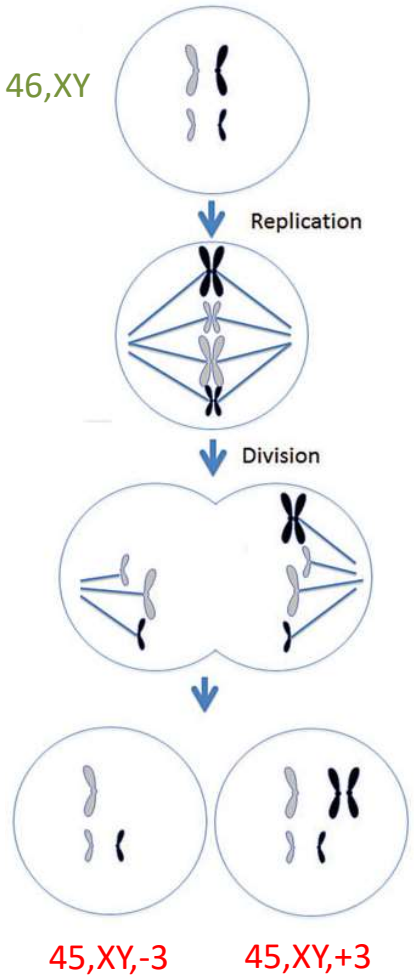
- Centrosome aberrations
- Failed chromatin cohesion
- Cell cycle checkpoints alterations
- …



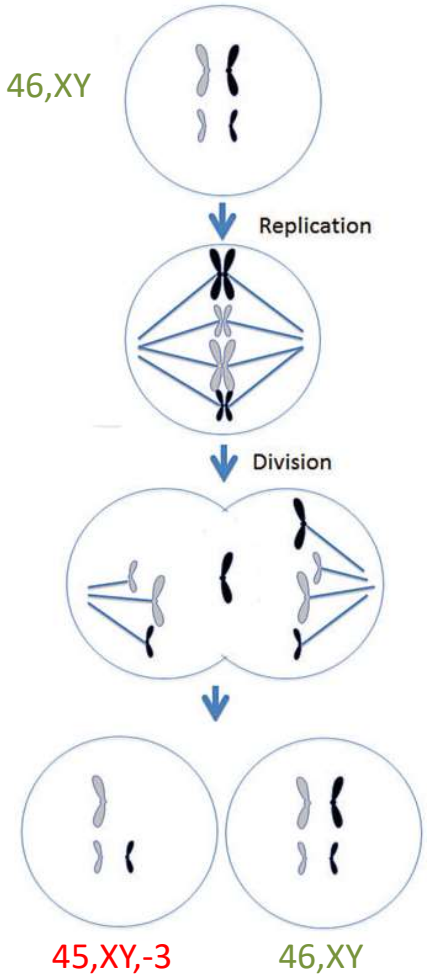
# Mosaicism: origin

(Taylor *et al*., 2014)

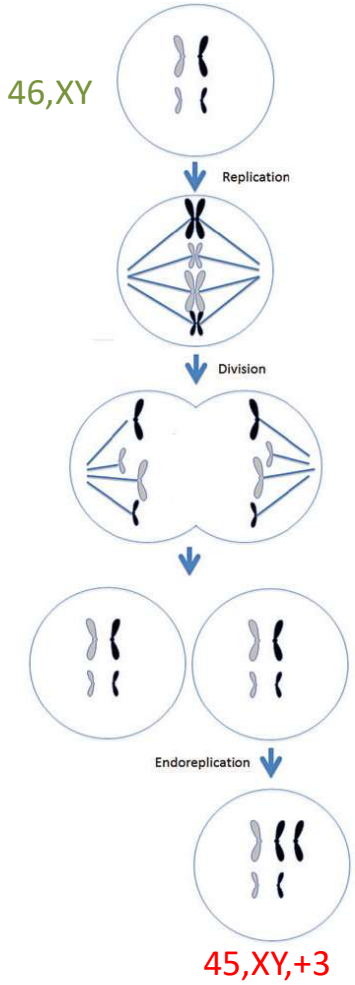
## Mitotic non-disjunction



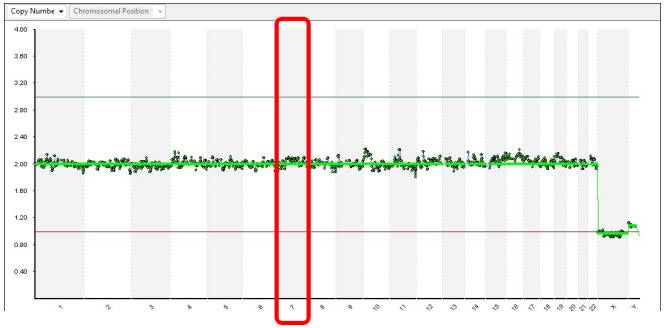

## Anaphase lag

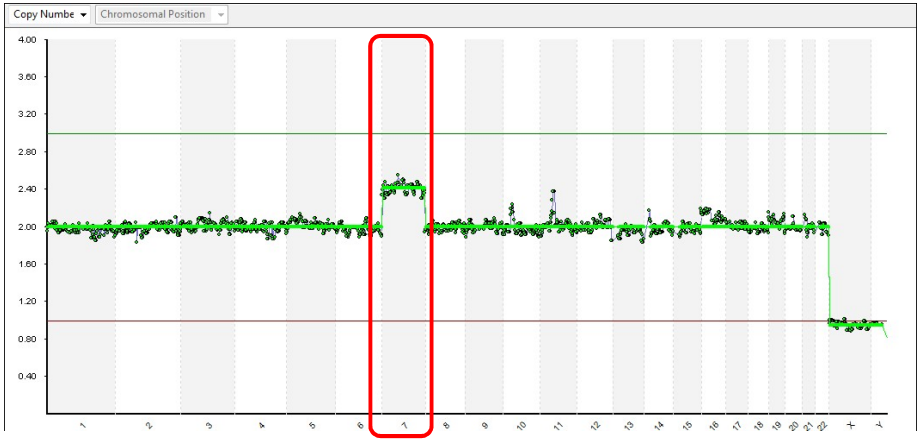


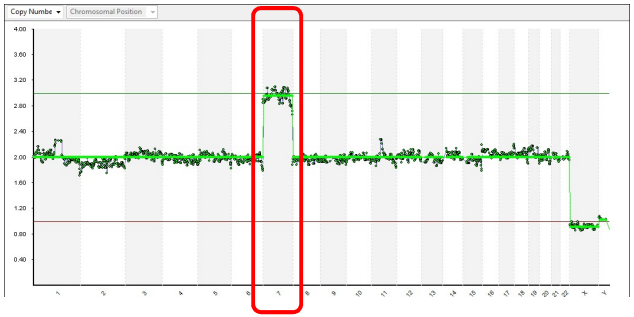

## Endoreduplication



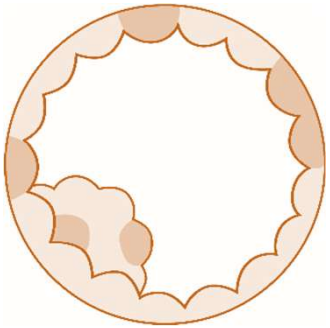
# Mosaicism: how is it detected?



# Mosaicism: incidence



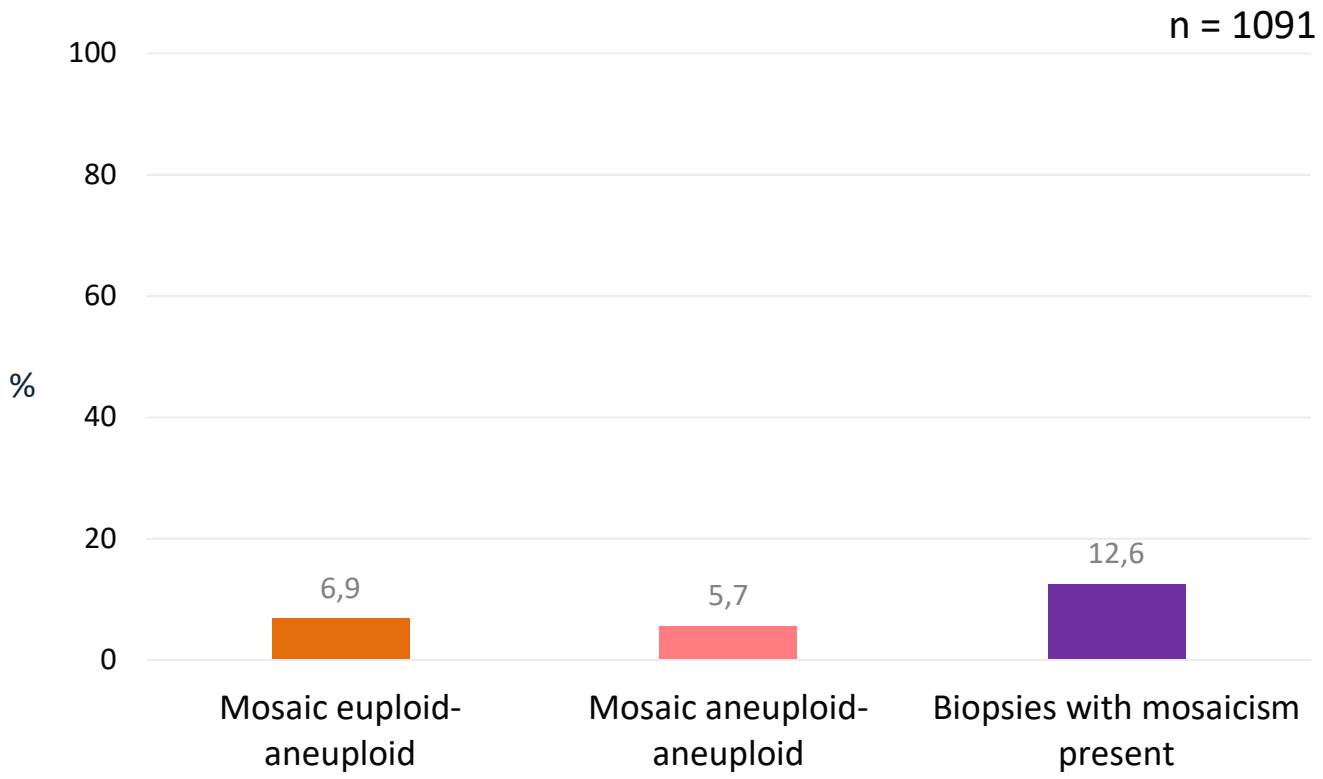
What is the incidence of embryonic mosaicism?

# Mosaicism: incidence

| PUBLICATION | N | METHODOLOGY | CUT-OFF | MOSAICISM INCIDENCE (%) |
|---|---|---|---|---|
| Fragouli *et al.*, 2011 | 52 | FISH/CGH/aCGH | NA | 32,4 |
| Capalbo *et al.*, 2013 | 70 | FISH/aCGH | NA | 18,6 |
| Novik *et al* ., 2014 | 551 | FISH/aCGH | Log ratios | 28,3 |
| Greco *et al.*, 2015 | 3802 | aCGH | 35-50% | 4,8 |
| Ruttanajit *et al.*, 2016 | 399 | NGS | 10-90% | 13,0 |
| Munné *et al.*, 2017 | 29195 | NGS | 20-80% | 21,81 |
| Fragouli *et al.*, 2017 | 150 | NGS | >0 - <100% | 29,3 |
| Sachdev *et al.*, 2017 | 1492 | NGS | 20-80 % | 17-47 |
| Nakhuda *et al.*, 2018 | 1547 | NGS | 20-80% | 30,1 |
| Lorenzi *et al.*, 2018 | 655 | NGS | 20-80% | 26 |
| Xu *et al.*, 2018 | 4423 | NGS | 25-80% | 6,6 |
| Morin *et al.*, 2018 | 13465 | NGS | NA | 3,6 |
| Lin *et al.*, 2018 | 1872 | NGS | NA | 20 |
| McReynolds *et al.*, 2018 | 27755 | NGS | NA | 2,3 |
| Brezina *et al.*, 2018 | 21212 | NGS | NA | 3,6 |

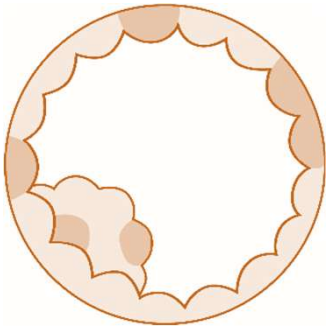
# Mosaicism: incidence

- Sigle-step media + Time-lapse culture (low $O_2$ concentration)
- hr-NGS (VeriSeq® Illumina®)
- Dexeus' mosaicism threshold: 30-70%




(Dexeus, unpublished data)

# Mosaicism: incidence



Mosaicism = Intrinsic ?

# Intrinsic factors and mosaicism incidence

First cleavages guided by maternal products

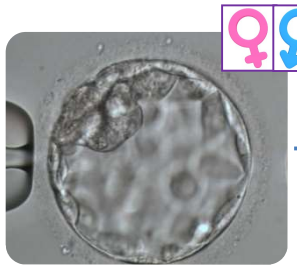
- Female age
- Ovarian reserve
- BMI
- Infertility reason

Centrosome provided by sperm

- Seminal parameters
- Male age
- Infertility reason

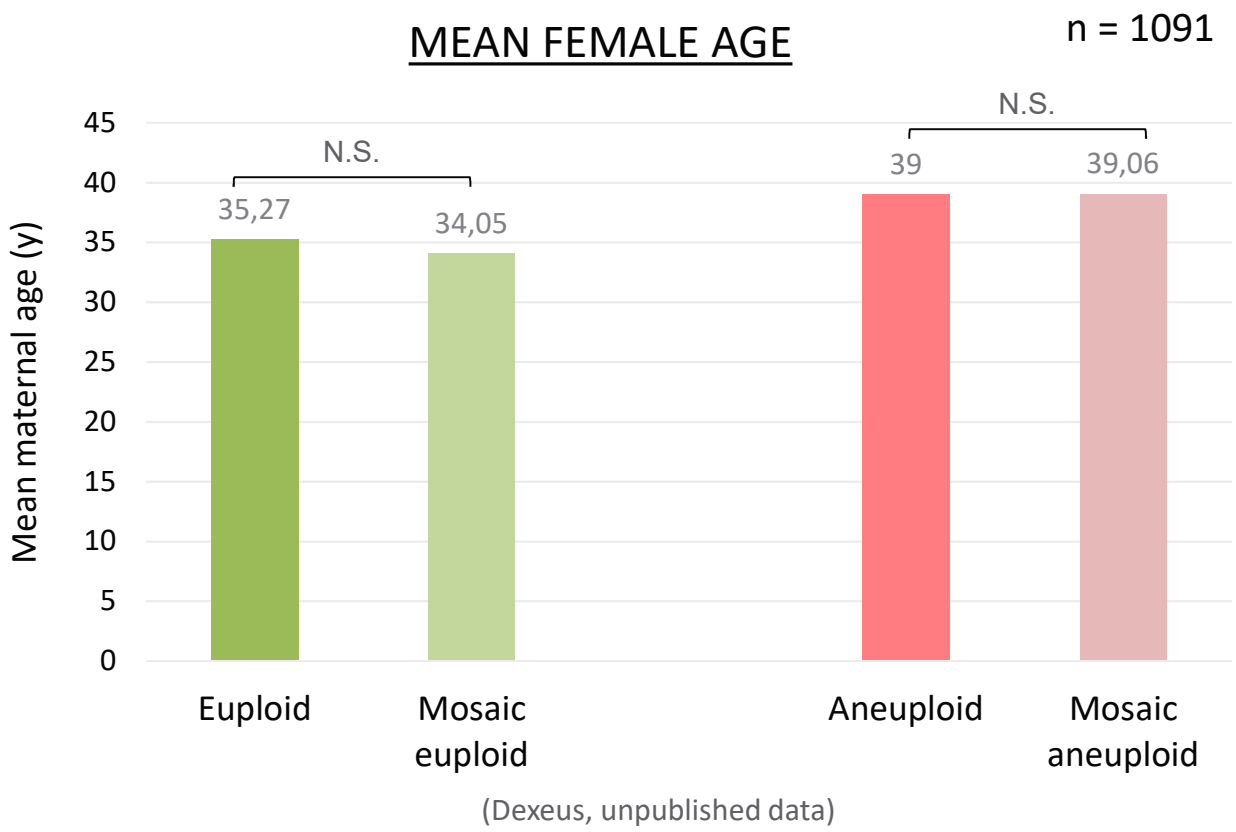
DNA damage

- Altered DNA fragmentation



# Intrinsic factors and mosaicism incidence

Patient factor ♀



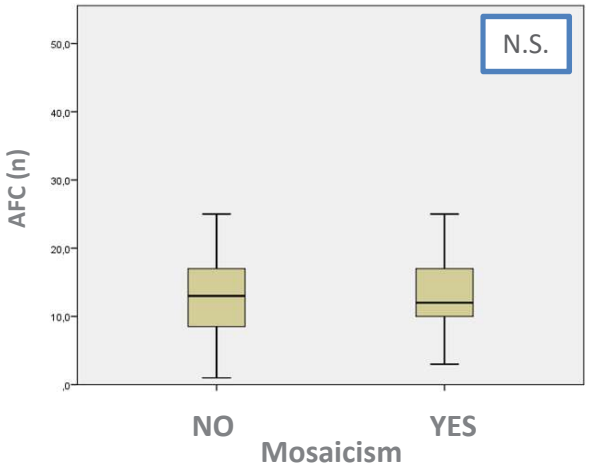

(Dexeus, unpublished data)

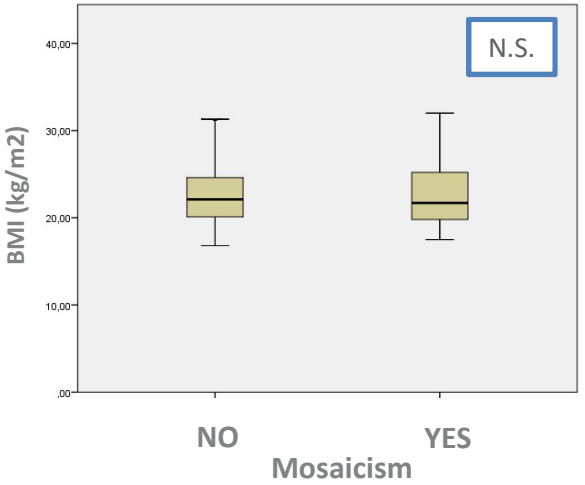
- There is no correlation between female age and level of mosaicism (Minasi *et al*, ESHRE 2018).

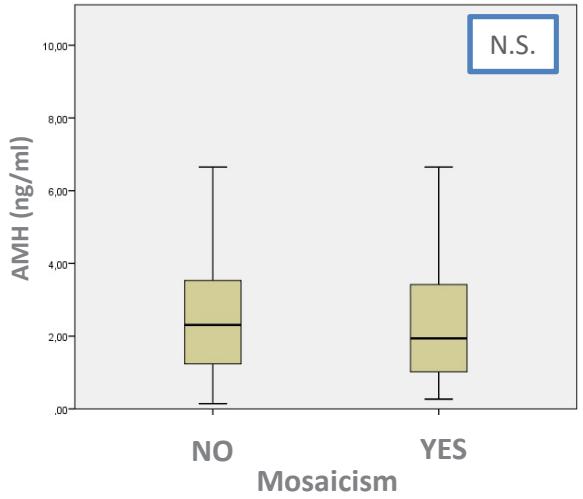
# Intrinsic factors and mosaicism incidence

Patient factor ♀

n = 1091



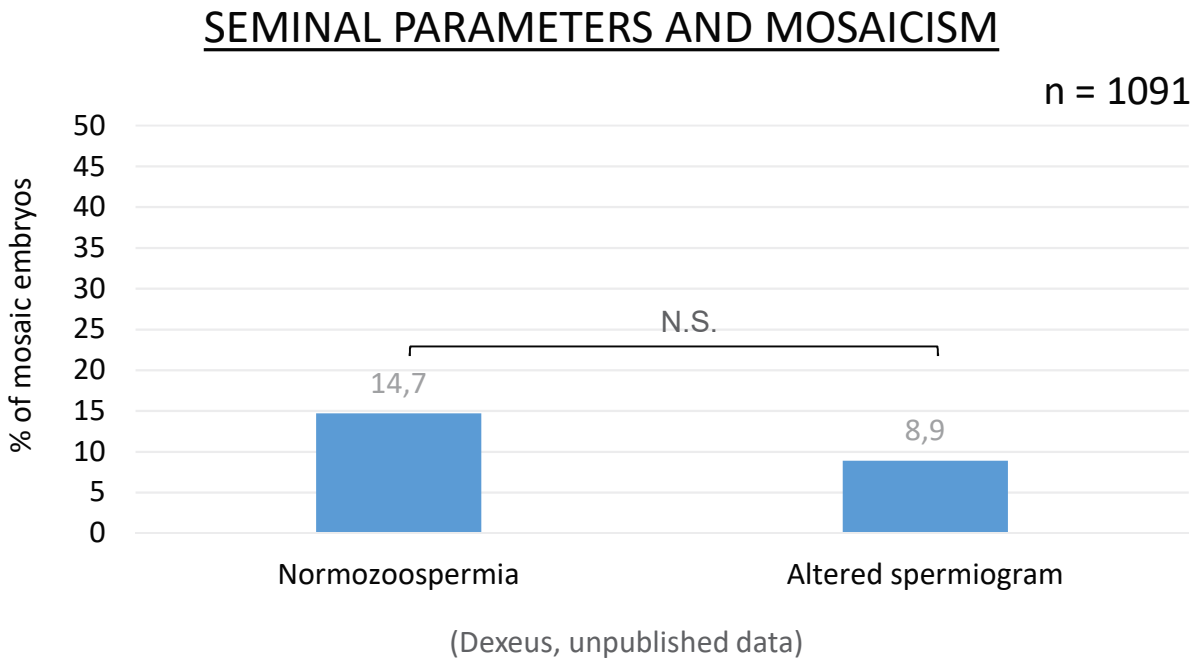




(Dexeus, unpublished data)

- There is no correlation between female characteristics and level of mosaicism (Minasi *et al*, 2018).

# Intrinsic factors and mosaicism incidence

Patient factor ♀




(Dexeus, unpublished data)

- There is no correlation between seminal parameters and level of mosaicism (Minasi *et al*, 2018).

# Intrinsic factors and mosaicism incidence

Patient factor ♀

## ALTERED DNA FRAGMENTATION

Int J Radiat Biol. 2011 Mar;87(3):320-9. doi: 10.3109/09553002.2011.530334. Epub 2010 Nov 19.

**Structural chromosomal aberrations, aneuploidy, and mosaicism in early cleavage mouse embryos derived from spermatozoa exposed to γ-rays.**

Tateno H[1], Kusakabe H, Kamiguchi Y.

**CONCLUSIONS:**

Mouse sperm DNA is highly vulnerable to γ-rays. The structural chromosomal aberrations of sperm origin are unstable in their behaviour and structure during cleavage, and therefore cause secondary aneuploidy and mosaicism in the early cleavage embryos.

# Intrinsic factors and mosaicism incidence

## Reason for infertility

- 200 cycles from the same IVF laboratory.
- 655 blastocysts biopsied by the same embryologist and analyzed by NGS.
- Mosaicism threshold: 20-80%

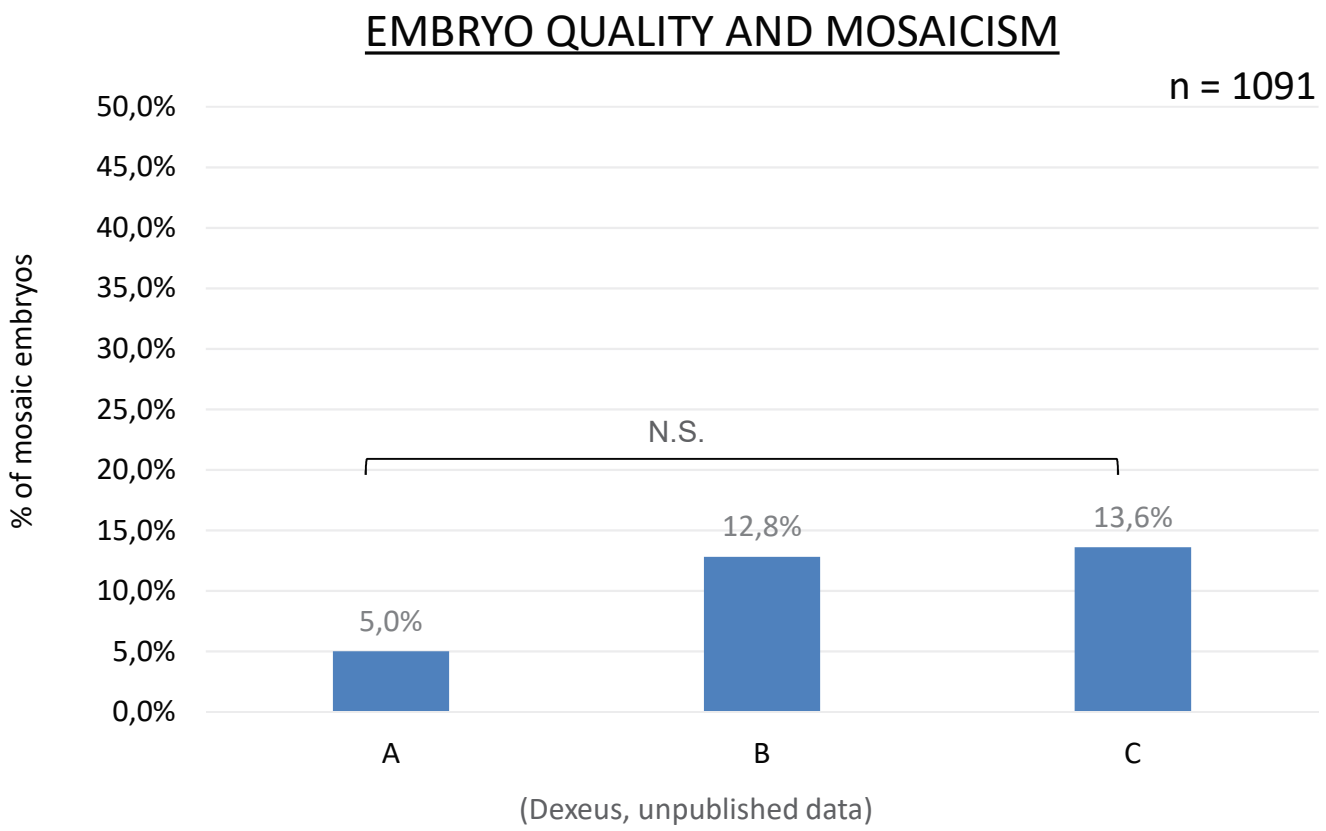
| ANALYZED FACTOR | | EUPLOID | ANEUPLOID | MOSAICISM | P-VALUE |
|---|---|---|---|---|---|
| Maternal age | Maternal age <30 | 108 (57.8%) | 26 (13.9%) | 53 (28.3%) | NS (0.124) |
| | Maternal age 30-34 | 47 (55.3%) | 18 (21.2%) | 20 (23.5%) | |
| | Maternal age 35-39 | 71 (32.3%) | 82 (37.3%) | 67 (30.4%) | |
| | Maternal age >40 | 23 (14.1%) | 107 (65.6%) | 33 (20.3%) | |
| PGT-A indication | Advanced maternal age (≥ 38 y/o) | 42 (19.2%) | 129 (58.9%) | 48 (21.9%) | NS (0.325) |
| | Recurrent pregnancy loss (≥ 2 miscarriages) | 16 (36.4%) | 16 (36.3%) | 12 (27.3%) | |
| | Repeated implantation failure | 27 (39.1%) | 21 (30.5%) | 21 (30.4%) | |
| | Time to pregnancy | 155 (54.4%) | 49 (17.2%) | 81 (28.4%) | |
| Presence of male factor | Male factor | 63 (34.3%) | 72 (39.1%) | 49 (26.6%) | NS (0.799) |
| | No male factor | 163 (41.4%) | 130 (33.0%) | 101 (25.6%) | |
| day of biopsy | Day 5 biopsy | 47 (44.7%) | 28 (26.7%) | 30 (28.6%) | NS (0.939) |
| | Day 6 biopsy | 130 (38.6%) | 112 (33.2%) | 95 (28.2%) | |
| Type of OS | Low-dose of gonadotropins | 149 (45.7%) | 84 (25.8%) | 93(28.5%) | NS (0.246) |
| | High-dose of gonadotropins | 96 (32.5%) | 127 (41.3%) | 72 (24.4%) | |
| OS legth | ≤ 10 days of OS | 179 (42.2%) | 131 (30.9%) | 114 (26.9%) | NS (0.793) |
| | > 10 days of OS | 66 (33.5%) | 80 (40.6%) | 51 (25.9%) | |

(Lorenzi *et al.,* ASRM poster 2018)

*All analyzed factors have no significant impact on the results of mosaic embryos formation.*

# Mosaicism: incidence

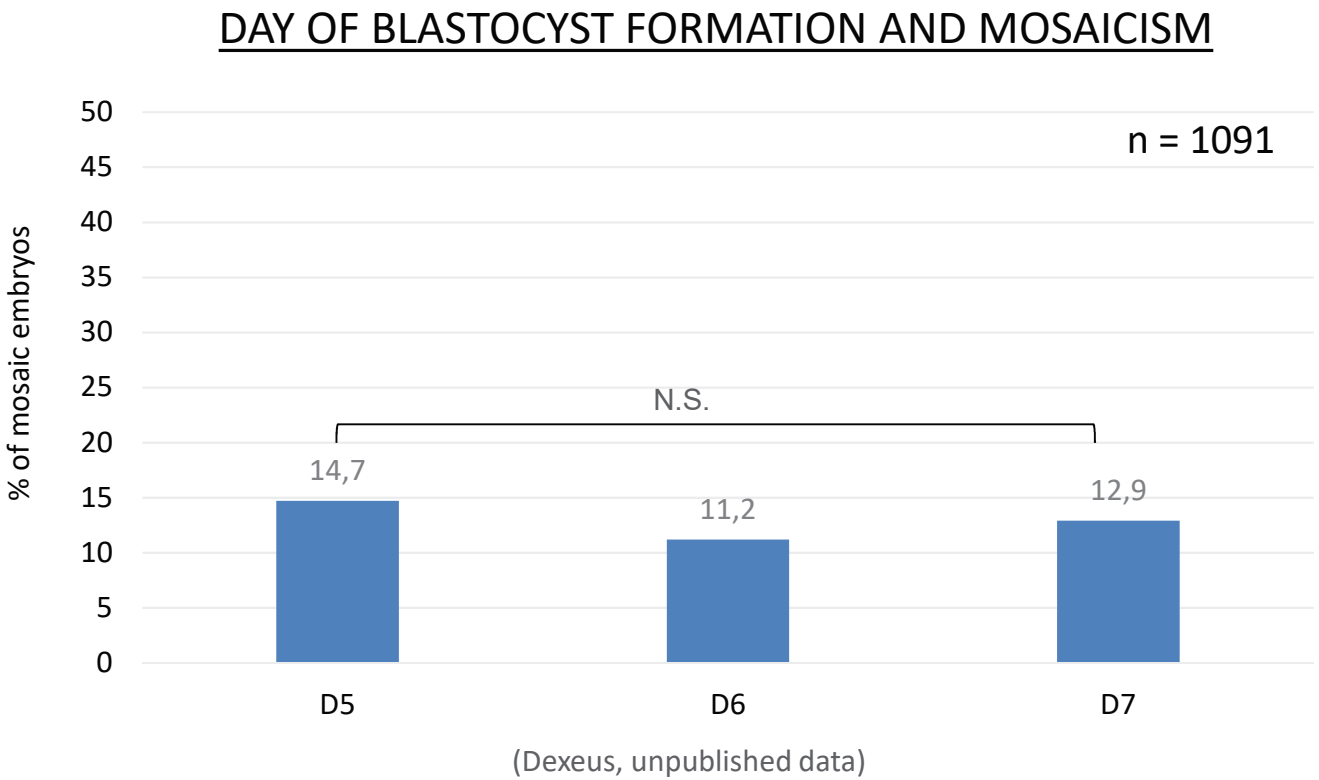
Embryo factor




(Dexeus, unpublished data)

# Mosaicism: incidence

Embryo factor



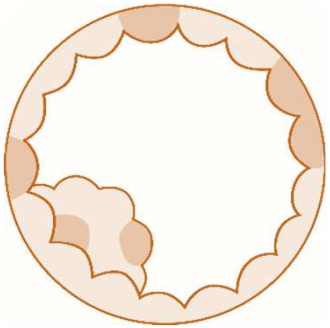

- There is no correlation between embryo quality and level of mosaicism (Minasi et al, ESHRE 2018).

# Mosaicism: incidence

Intrinsic factors and mosaicism:

- Maternal age: ✗
- Female characteristics (AMH, AFC, BMI): ✗
- Paternal age: ✗
- Sperm quality: ✗
- Reason for PGT-A: ✗
- Blastocyst morphology: ✗
- Day of blastocyst formation: ✗

# Mosaicism: incidence



Mosaicism = Intrinsic + ?

# Mosaicism: incidence

- 1492 blastocysts, 192 cycles from 9 different IVF clinics.
- Embryos derived from oocyte donors.
- Analyzed by NGS at a single reference genetic laboratory.
- Significant differences in mosaicism and aneuploidy rates between centers.
- Proportion of embryos with mosaicism: 17-47% depending on the clinic.

| No. Cycles per Center (a-i) | Avg Donor Age | Avg No. Biopsy per Patient | Euploid (%)[b] | Aneuploid(%)[b] | Mosaic (%)[b] |
|---|---|---|---|---|---|
| a-16 | 24.00±2.31 | 7.06±2.86 | 44.95±28.11 | 32.11±26.90 | 22.94±13.58 |
| b-23 | 25.27±2.35 | 6.55±3.53 | 52.08±27.70 | 18.06±18.98 | 29.86±26.63 |
| c-12 | 22.92±1.44 | 7.75±3.14 | 43.68±20.17 | 39.08±19.18 | 17.24±12.20 |
| d-41 | 25.50±2.44 | 7.30±3.83 | 56.29±25.07 | 26.22±22.86 | 17.48±18.73 |
| e-14 | 24.00±2.04 | 10.43±4.11 | 50.35±21.62 | 17.48±10.69 | 32.17±19.79 |
| f-19 | 25.42±3.02 | 9.21±5.48 | 38.82±20.88 | 27.65±19.82 | 33.53±15.07 |
| g-18 | 25.41±3.10 | 8.53±4.52 | 47.92±24.64 | 18.06±21.02 | 34.03±21.67 |
| h-36 | 26.14±2.58 | 8.03±4.74 | 45.49±23.29 | 26.74±17.13 | 27.78±26.31 |
| i-13 | 25.31±2.36 | 5.31±2.56 | 37.31±22.20 | 14.93±12.18 | 47.76±21.26 |
| p | **0.005** | 0.055 | 0.169 | **0.018** | **<0.001** |

(Sachdev *et al.*, ASRM 2016)

# Mosaicism: incidence

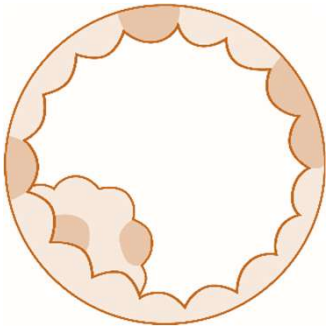
**O-058 Evidence that differences between embryology laboratories can influence the rate of mitotic errors, leading to increased chromosomal mosaicism, with significant implications for IVF success rates**

D. Wells[1], S. Alfarawati[2], S. Taylor[2], N. Kubikova[2], K. Spath[2], K. Turner[3], C. Hickman[4], E. Fragouli[2]

- 623 blastocysts derived from 7 different IVF clinics.
- Analyzed by NGS at a single reference genetic laboratory.
- Similar aneuploidy rates between clinics (meiotic error unaffected).
- Proportion of embryos with mosaicism: 32-60% depending on the clinic.

*Variation in laboratory procedures could be responsible for the observed differences between centers.*

# Mosaicism: incidence



Mosaicism = Intrinsic + (Iatrogenic + Artifactual)

# Mosaicism: incidence

Mosaicism = Intrinsic + (Iatrogenic + Artifactual)

Highly variable in different IVF settings.
Diagnostic platform.
Diagnostic criteria.

Almost impossible to determine
***"the real incidence of mosaicism"*** in the human blastocyst

# Iatrogenic mosaicism: incidence

Iatrogenic: Mosaicism induced by the performance of an IVF cycle.

- Altered gamete maturation
  - Ovarian stimulation.

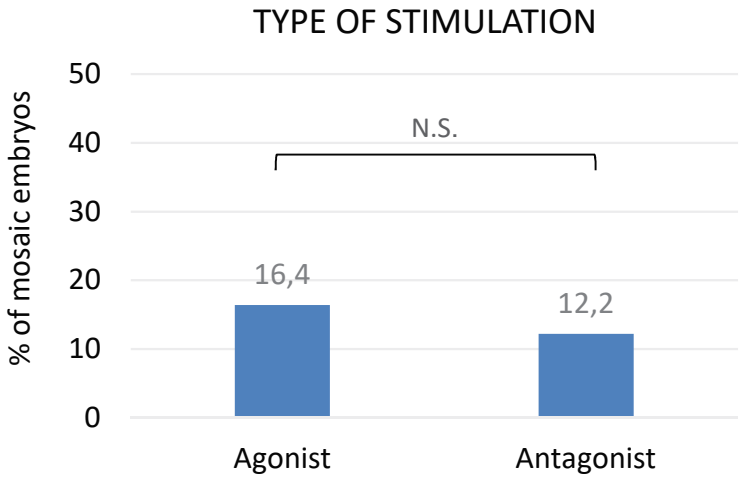
- Culture conditions:
  - Culture type: sequential culture vs single-step media & uninterrupted vs standard culture.
  - Composition of the comercial media.
  - Oxygen concentration: Low vs standard.

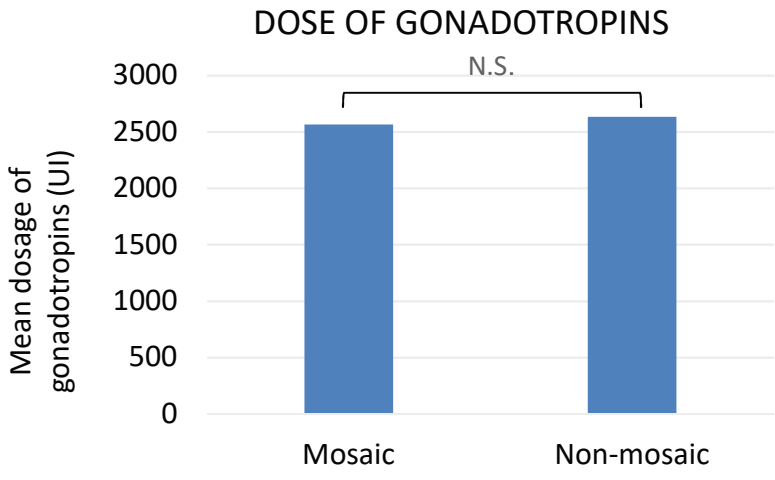
- IVF laboratory quality standards.

# Iatrogenic mosaicism: incidence

## OVARIAN STIMULATION

n = 1091



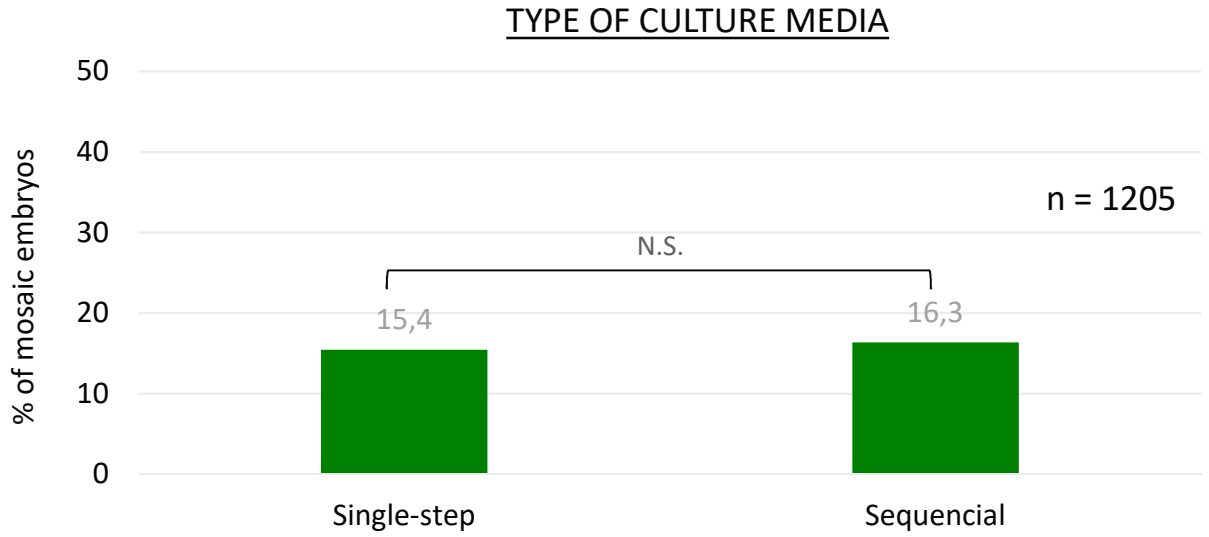

(Dexeus, unpublished data)

# Iatrogenic mosaicism: culture media

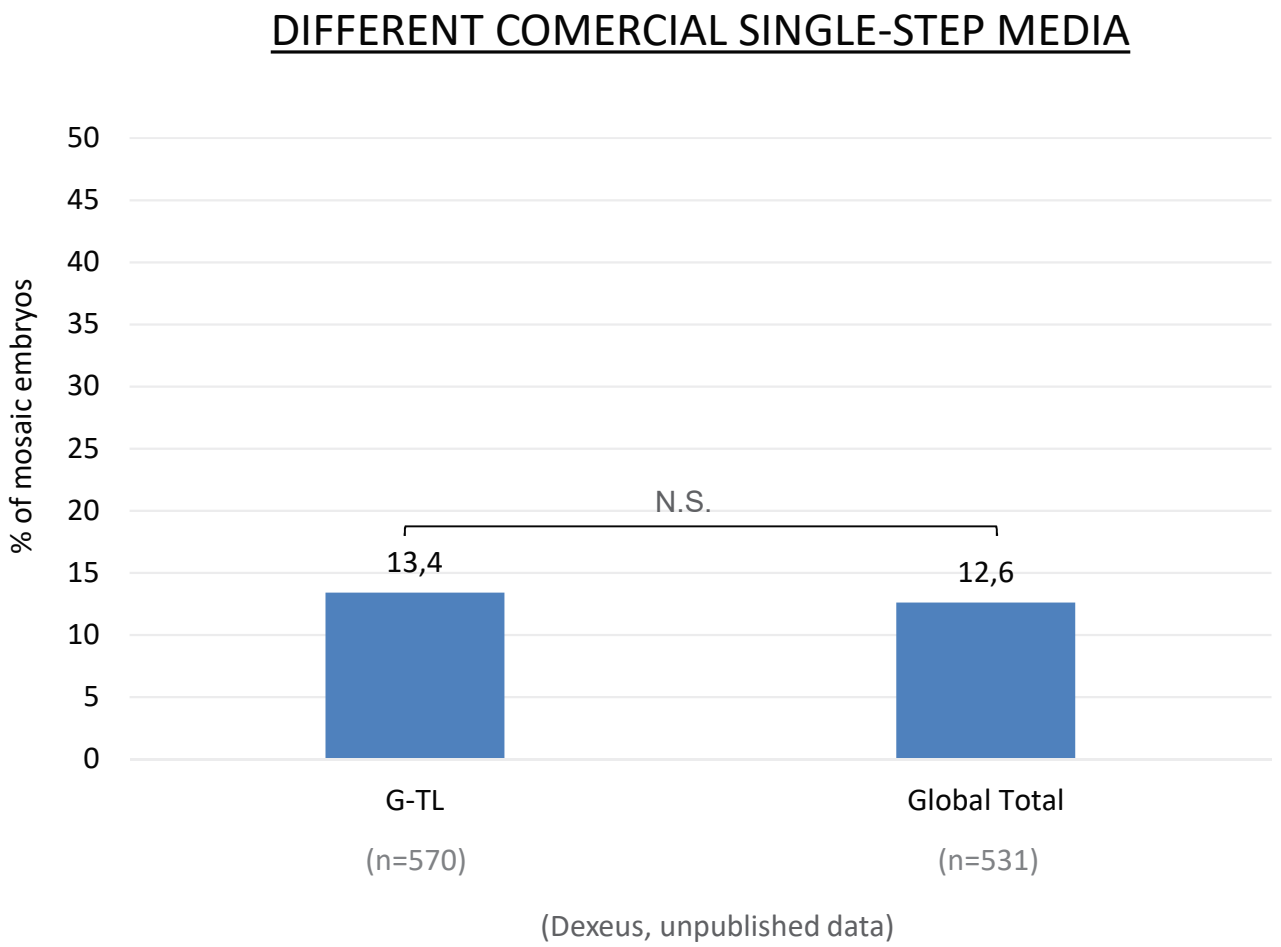
**O-117 Time-lapse and NGS evaluation of human embryos cultured in single medium versus sequential media: a prospective randomized pilot study**

**Z. Yang[1], Y. Kuang[2], X. Zhang[3], Y. Meng[3], L. Tang[4], Q. Lyu[2], L. Su[5], S. Zhang[6], J. Lin[1]**

- Low $O_2$ concentration culture.
- Prospective randomized study. Sibling MII oocytes distributed in single or sequential medium.



# Iatrogenic mosaicism: culture media



# Iatrogenic mosaicism: oxygen concentration/quality standards

**O-268** Wednesday, October 10, 2018 11:30 AM

**CHROMOSOMAL MOSAICISM IS IMPACTED BY COMPROMISED EMBRYO CULTURE CONDITIONS.**

M. Katz-Jaffe,[a] J. Parks,[a] S. McReynolds,[b] L. Henry,[c] W. B. Schoolcraft.[a] [a]Colorado Center for Reproductive Medicine, Lone Tree, CO; [b]Fertility Genetics, Colorado Center for Reproductive Medicine, Lone tree, CO; [c]Fertility Genetics, Colorado Center For Reproductive Medicine, Lone Tree, CO.

- Warmed vitrified zygotes were cultured to the blastocyst stage utilizing 5 % $O_2$ and appropriate $CO_2$ or 20 % $O_2$ and reduced $CO_2$.
- Significant increase in the incidence of mosaicism for embryos cultured under compromised conditions.
- The majority of mitotic errors observed were anaphase lag.

*There is an impact of compromised culture conditions on mitotic cell division and chromosome segregation.*

# Mosaicism: incidence

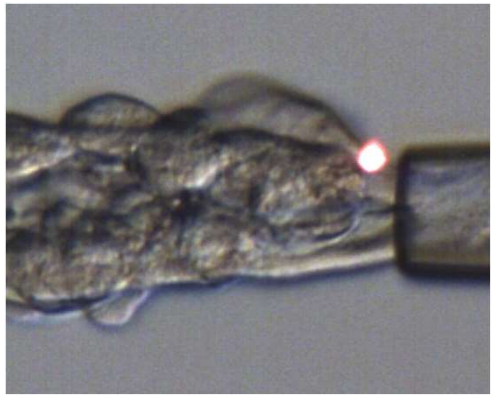
- Artifactual or false mosaicism
  - Biopsy procedure
  - DNA contamination
  - Whole-genome amplification
  - Bioinformatics

- Diagnostic platform/ Diagnostic criteria/ Diagnostic experience

# Mosaicism: incidence

- Artifactual or false mosaicism

  - Biopsy procedure



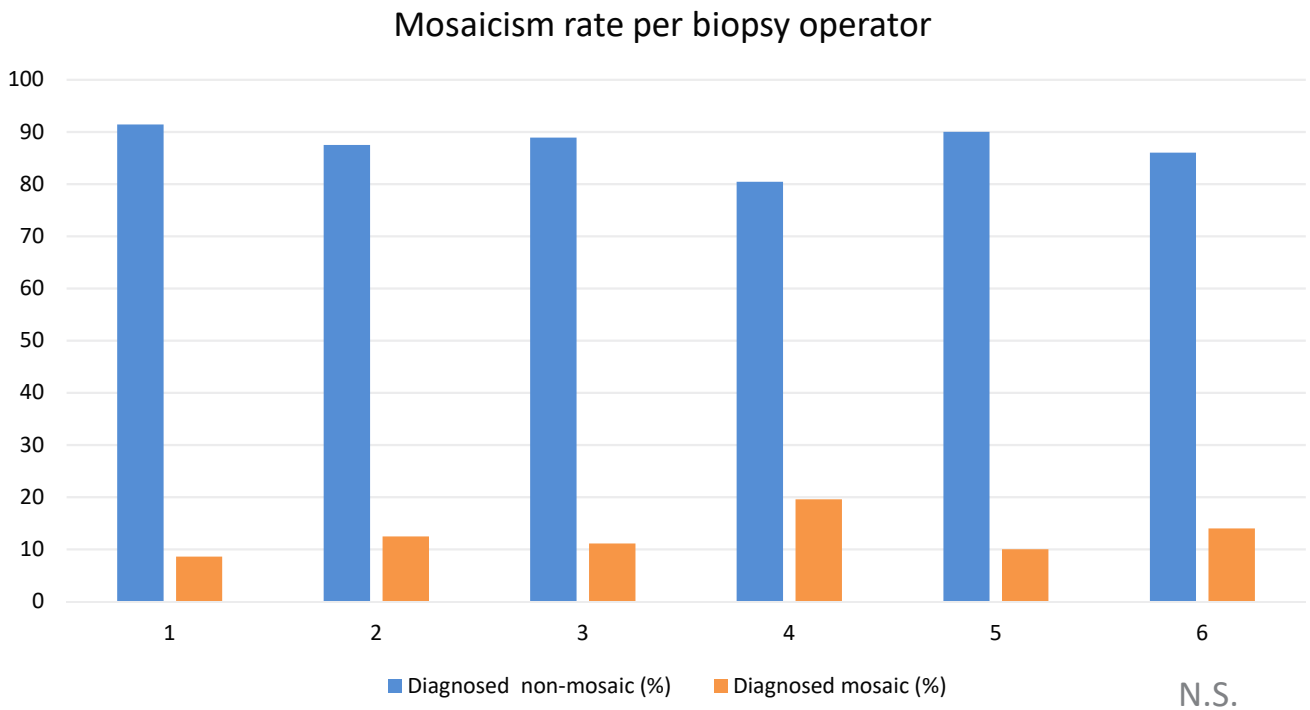
Induced cellular lysis and increased laser exposure during trophectoderm biopsies can generate low-level mosaic profiles: A prospective study.

Whitney John B.

# Mosaicism: incidence

- Artifactual or false mosaicism

  - Biopsy procedure




N.S.
(Dexeus, unpublished data)

Same set-up
Same training
→ Same % of mosaicism

# Mosaicism: Incidence

- Diagnostic experience

Figure 9 Artifact Showing Alternating Steps for Chromosomes 1–10

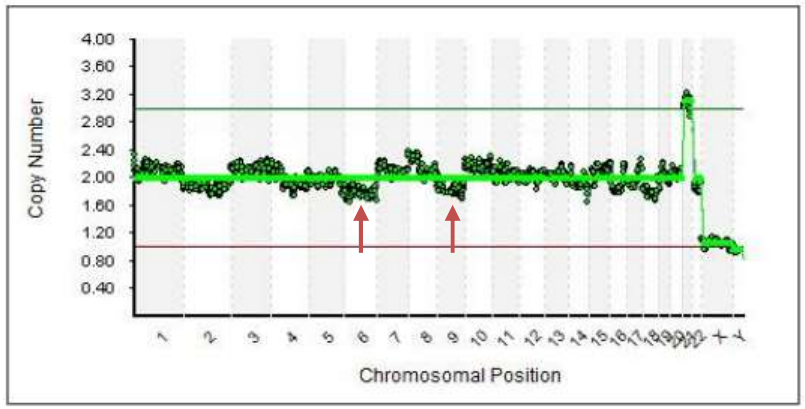
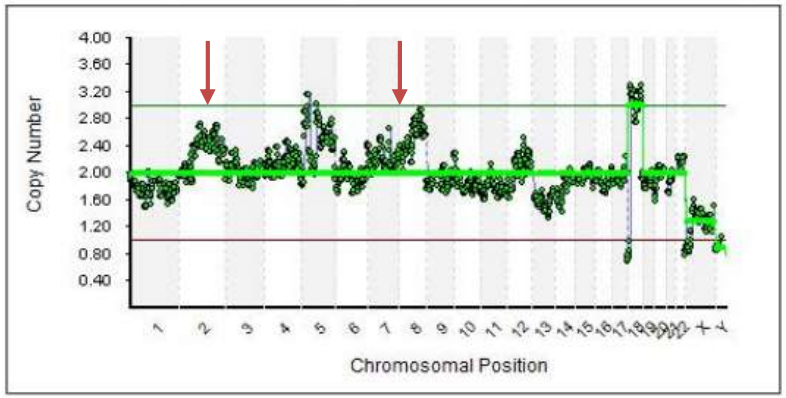



Figure 10 Sample with Increasing Chromosome "Ramp" from Chromosomes 6–8 from a Cell Line Sample with the Expected Karyotype of 46, XY, i(18)(q11.1), i(18)(q11.1)



# Mosaicism: Incidence

Iatrogenic and artifactual factors and mosaicism:

- Mosaicism can be affected by IVF setting.
- Concrete parameters in terms of culture conditions have not been yet identified.
- Exception: Substandard culture and operating protocols.

# Mosaicism: to transfer or not to transfer?

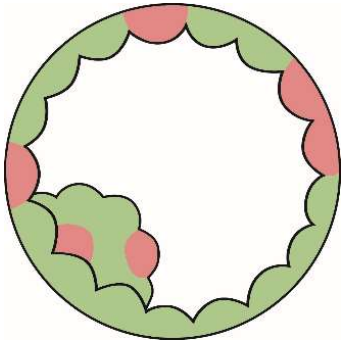
… embryonic mosaicism is a reality

…mosaic embryos can give rise to healthy childs


**Healthy Babies after Intrauterine Transfer of Mosaic Aneuploid Blastocysts**

Ermanno Greco, M.D.
Maria Giulia Minasi, M.Sc.
Francesco Fiorentino, Ph.D.

# Mosaicism: to transfer or not to transfer?



What to do with mosaic embryos?

1. Prioritise euploid embryos.

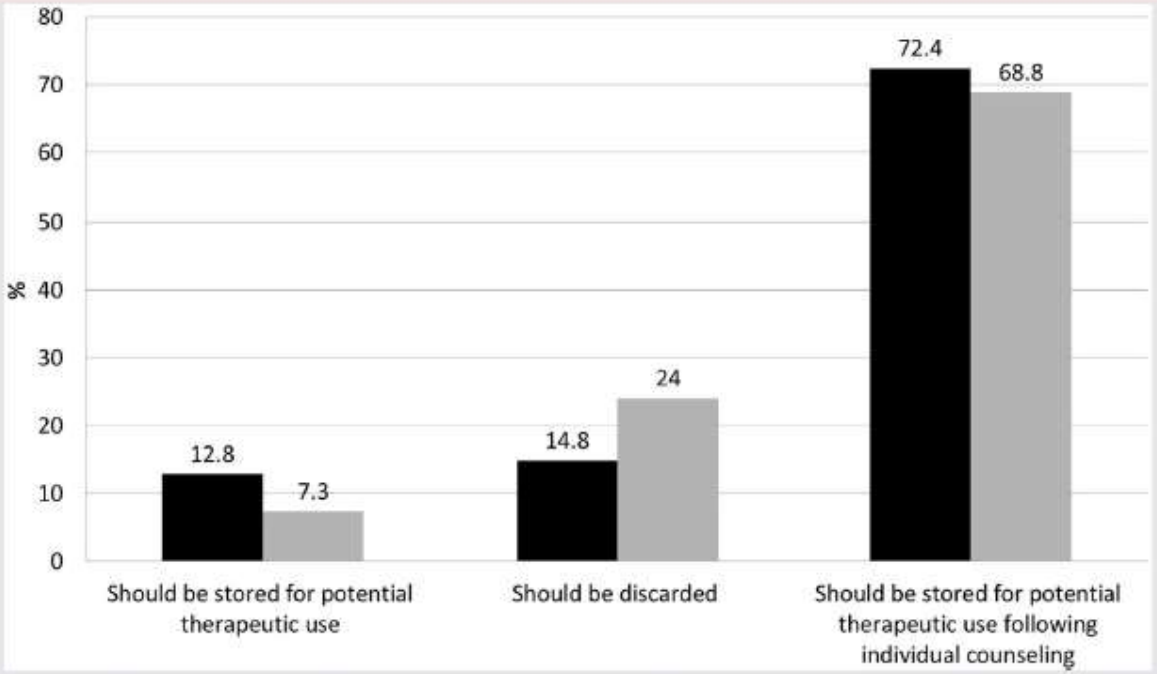
2. Transfer of mosaic embryos?

# Mosaicism: to transfer or not to transfer?

Worldwide web-based survey

102 IVF units, 32 countries, 108900 IVF cycles, 87% performing PGT-A

**FIGURE 1**

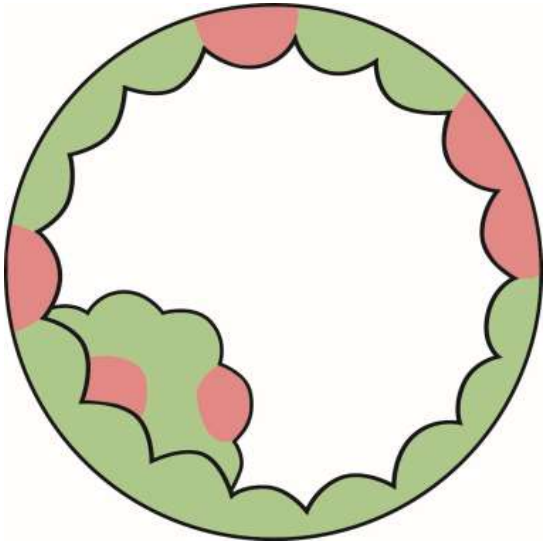



Should mosaic embryos be stored for potential therapeutic use or discarded? *Black bars*: centers performing preimplantation genetic screening (PGS). *Gray bars*: centers not performing PGS.

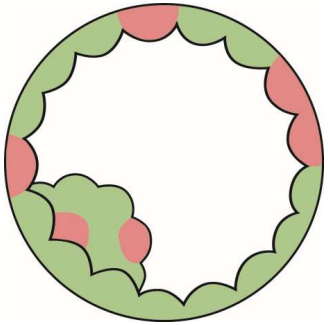
*Weissman. Survey on chromosomal mosaicism in PGS. Fertil Steril 2017.*

Dexeus mujer

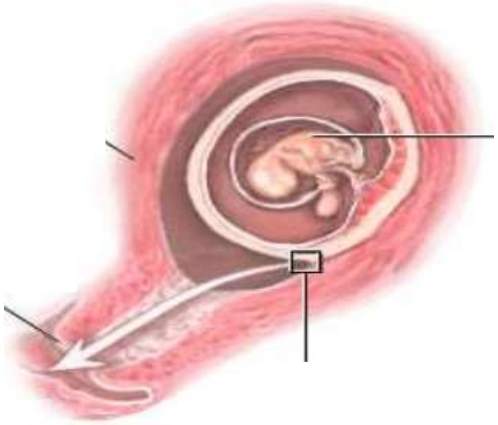
# Evidence supporting the transfer of mosaic blastocysts



# Mosaicism: to transfer or not to transfer?



**PGT-A**
10-30%



**CV**
1-2%

**AF**
0,2%

*To date, no abnormalities detected in newborns from mosaic embryos*

# Mosaicism: to transfer or not to transfer?

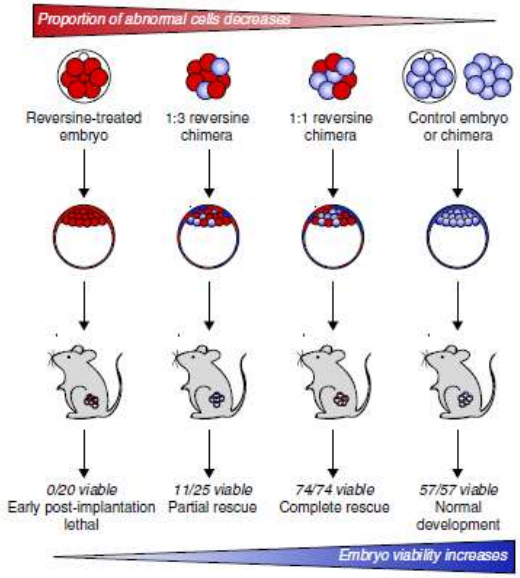
ARTICLE

Received 10 Jun 2015 | Accepted 26 Feb 2016 | Published 29 Mar 2016

DOI: 10.1038/ncomms11165 OPEN

## Mouse model of chromosome mosaicism reveals lineage-specific depletion of aneuploid cells and normal developmental potential

Helen Bolton[1], Sarah J.L. Graham[1], Niels Van der Aa[2], Parveen Kumar[2], Koen Theunis[2], Elia Fernandez Gallardo[2], Thierry Voet[2,3] & Magdalena Zernicka-Goetz[1]




≤50% cells affected → Similar viability compared to uniformly euploid

>66% cells affected → Lethal

Aneuploid cells in foetal lineage → Apoptosis

Aneuploid cells in placental lineage → Proliferation defficiencies

*"Mosaic embryos have full developmental potential provided they contain sufficient euploid cells"*

# Mosaicism: to transfer or not to transfer?

**Healthy Babies after Intrauterine Transfer of Mosaic Aneuploid Blastocysts**

E. Greco & MJ. Minasi The New England Journal of Medicine. November 2015.

↓ CPR
↓ LBR (33%)

**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**

Susan M. Maxwell, M.D.,[a] Pere Colls, Ph.D.,[b] Brooke Hodes-Wertz, M.D.,[a] David H. McCulloh, Ph.D.,[a] Caroline McCaffrey, Ph.D.,[a] Dagan Wells, Ph.D.,[c] Santiago Munné, Ph.D.,[b] and James A. Grifo, M.D., Ph.D.[a]

↑ MR

**Extent of chromosomal mosaicism influences the clinical outcome of in vitro fertilization treatments**

Francesca Spinella, Ph.D.,[a] Francesco Fiorentino, Ph.D.,[a] Anil Biricik, Ph.D.,[a] Sara Bono, Ph.D.,[a] Alessandra Ruberti, B.Sc.,[b] Ettore Cotroneo, Ph.D.,[a] Marina Baldi, Ph.D.,[a] Elisabetta Cursio, B.Sc.,[b] Maria Giulia Minasi, B.Sc.,[b] and Ermanno Greco, M.D.[b]

Aneuploidy detected in < 50% of the biopsied cells: similar clinical outcomes compared to euploid.

# Mosaicism: to transfer or not to transfer?

(Preimplantation Genetic Diagnosis International Society)

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

1. Recommendations for the laboratory (if reporting mosaic aneuploidies)
2. Recommendations for the clinician
3. Suggested guidelines to prioritize mosaic embryos for transfer

**Suggested guidelines to prioritize mosaic embryos for transfer**

Based on our current knowledge of the reproductive outcomes of fetal and placental mosaicism from prenatal diagnosis, the following can be used as a guide by the clinician (or a genetic counselor if available) when a mosaic embryo is being considered for transfer:

1. Embryos showing mosaic euploid/monosomy are preferable to euploid/trisomy, given that monosomic embryos (excepting 45, X) are not viable
2. If a decision is made to transfer mosaic embryos trisomic for a single chromosome, one can prioritize selection based on the level of mosaicism and the specific chromosome involved

a. The preferable transfer category consists of mosaic embryos trisomic for chromosomes 1, 3, 4, 5, 6, 8, 9, 10, 11, 12, 17, 19, 20, 22, X, Y. None of these chromosomes involve the adverse characteristics enumerated below

b. Embryos mosaic for trisomies that are associated with potential for uniparental disomy (14, 15) are of lesser priority

c. Embryos mosaic for trisomies that are associated with intrauterine growth retardation (chromosomes 2, 7, 16) are of lesser priority

d. Embryos mosaic for trisomies capable of liveborn viability (chromosomes 13, 18, 21) are of lowest priority, for obvious reasons

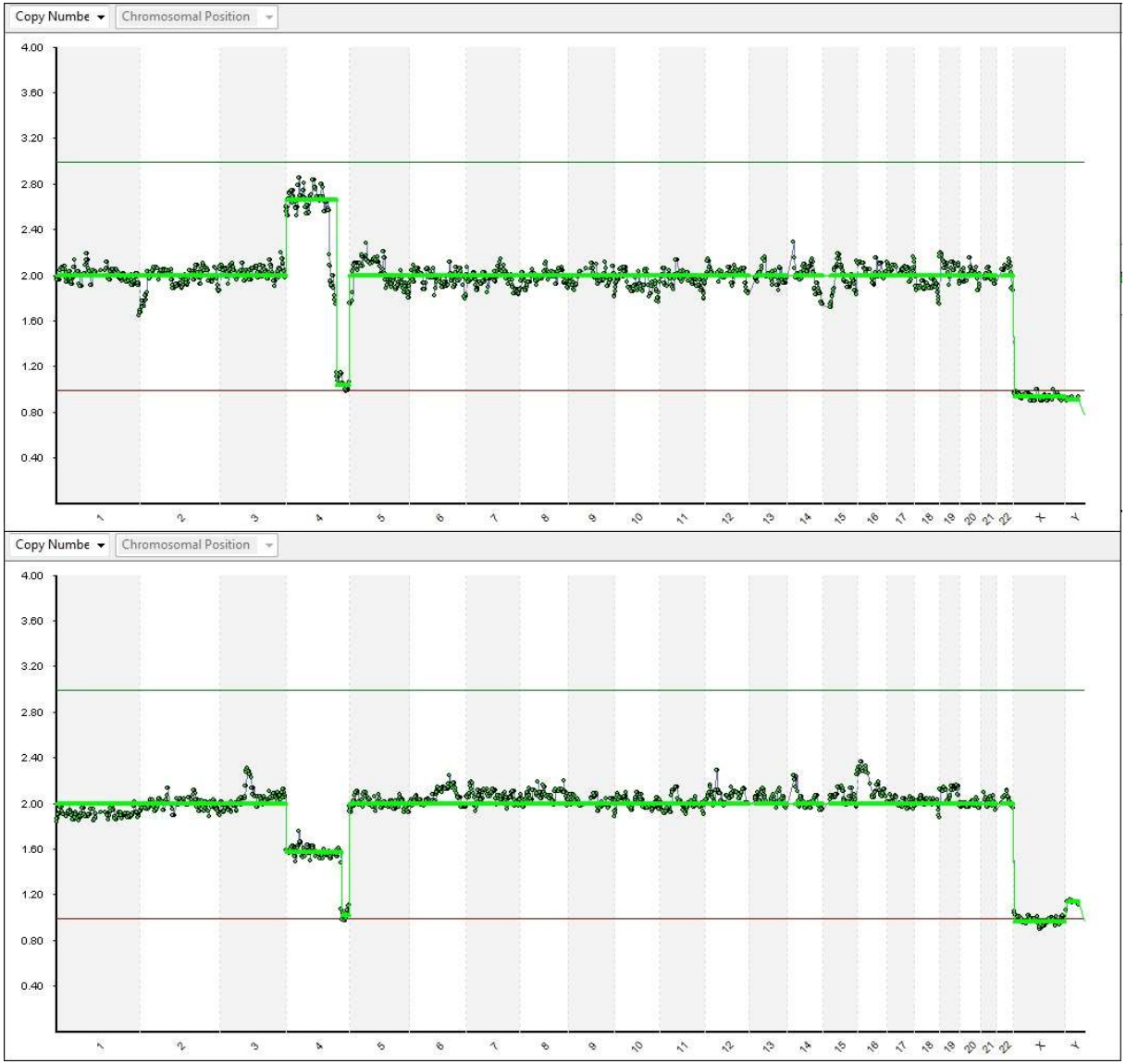
# Mosaicism: to transfer or not to transfer?

## COGEN Position Statement on Chromosomal Mosaicism Detected in Preimplantation Blastocyst Biopsies

III. RECOMMENDATIONS FOR PRIORITIZING MOSAIC EMBRYOS FOR TRANSFER

a. If a decision is made to transfer a non-complex, low-level mosaic embryo, one can prioritize selection based on the specific chromosome involved.
b. Embryos mosaic for trisomies capable of live born viability (chromosomes 13, 18, 21, 22) are of lowest priority.
c. Embryos mosaic for trisomies associated with uniparental disomy (chromosomes 14, 15) are low priority.
d. Embryos mosaic for trisomies associated with intrauterine growth retardation (chromosomes 2, 7, 16) are low priority.
e. Mosaicism involving chromosomes 1, 3, 4, 5, 6, 8, 9, 10, 11, 12, 17, 19, 20, have not been associated with the aforementioned adverse outcomes; only adverse outcomes have been observed when mosaicism is present in the fetus.
f. Mosaic monosomies seem to implant with a similar incidence to mosaic trisomies. They may contain trisomic cell lines, and should be considered to have similar risk as their counterpart trisomies.

# Mosaicism: to transfer or not to transfer?



## Mosaicism: Prioritizing mosaic embryos to transfer

# Detailed investigation into the cytogenetic constitution and pregnancy outcome of replacing mosaic blastocysts detected with the use of high-resolution next-generation sequencing

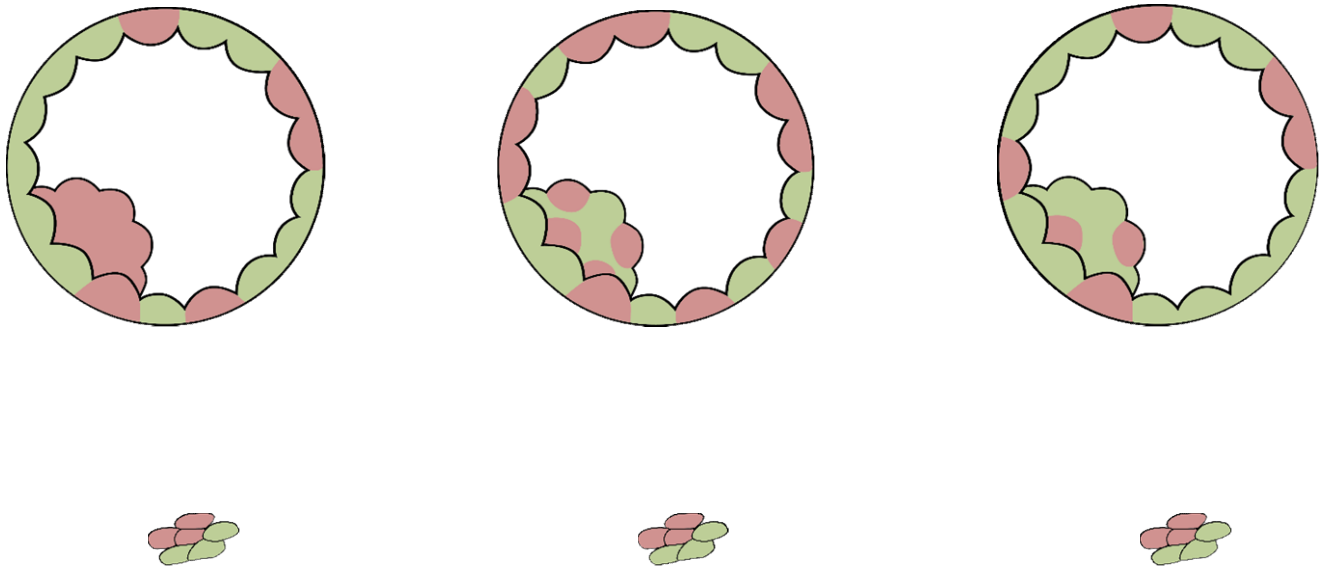
Santiago Munné, Ph.D.,[a] Joshua Blazek, Ph.D.,[b] Michael Large, Ph.D.,[b] Pedro A. Martinez-Ortiz, Ph.D.,[c] Haley Nisson, B.S.,[a] Emmeline Liu, M.Sc.,[a] Nicoletta Tarozzi, Ph.D.,[d] Andrea Borini, M.D.,[d] Amie Becker, M.Sc.,[e] John Zhang, M.D.,[e] Susan Maxwell, M.D.,[f] James Grifo, M.D., Ph.D.,[f] Dhruti Babariya, M.Sc.,[g] Dagan Wells, Ph.D.,[g] and Elpida Fragouli, Ph.D.[g]

[a] Reprogenetics (Cooper Genomics), Livingston, New Jersey; [b] Genesis Genetics (Cooper Genomics), Houston, Texas; [c] Universidad de Alicante, Alicante, Spain; [d] Tecnobios Procreazione, Bologna, Italy; [e] New Hope, New York, New York; [f] New York University, New York, New York; and [g] Reprogenetics (Cooper Genomics), Oxford, United Kingdom

- 143 mosaic blastocysts transferred from 6 different IVF clinics.
- Maternal age: X=35.8.
- 53% IR, 24% FLR, 41% OIR (↑FLR compared with euploid control group).
- Pregnancy outcomes stratified according to:
  - · Type of mosaic abnormality → OIR mosaic monosomies ~ OIR mosaic trisomies
  - · Number of chromosomes involved → ≥3 chromosomes involved: ↓ OIR
  - · Percentage of abnormal cells → No differences according the % of abnormal cells
  - · Chromosomes involved →No correlation regarding the chromosome affected

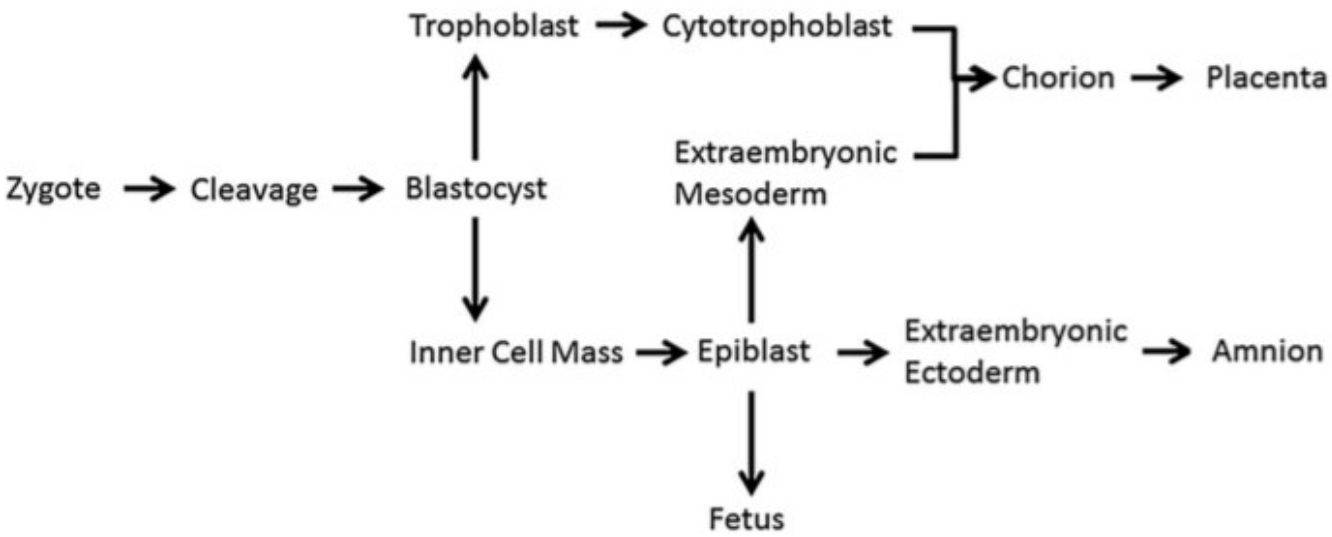
# Mosaicism: to transfer or not to transfer?

- The % of abnormal cells in a TE sample does not necessarily represent the whole embryo.



# Mosaicism: to transfer or not to transfer?

- Unknown distribution of the abnormal cells.




(Taylor *et al., 2014)*

# Mosaicism: to transfer or not to transfer?

- All trisomies can be viable in mosaic form
- Mosaicism is proven to be related to several conditions

Am J Med Genet A. 2017 Jun;173(6):1681-1686. doi: 10.1002/ajmg.a.38194. Epub 2017 Mar 27.

**Clinical features of trisomy 12 mosaicism-Report and review.**

Hong B[1,2], Zunich J[3], Openshaw A[2], Toydemir RM[1,2,4].

⊕ Author information

**Abstract**

Trisomy 12 mosaicism is a rare condition. Herein, we report a patient with mosaic trisomy 12 who was conceived by in vitro fertilization. She presented with mild dysmorphic features at birth, including down-slanting palpebral fissures, a depressed and creased nasal bridge, and mild rhizomelic shortening of the limbs. She had age-appropriate development at 6 months of age, but displayed slightly more dysmorphic features than at birth. Chromosome analysis on peripheral blood revealed a normal female karyotype in 50 metaphases. A concurrent genomic microarray analysis showed trisomy 12 in about 25% of the specimen, which was also confirmed by fluorescence in situ hybridization analysis with the CEP12 probe. Our findings further delineate the clinical features in trisomy 12 mosaicism in liveborns and demonstrate the utility of genomic microarray analysis in identification of mosaic aneuploidies.

**Unknown clinical implications of mosaicism**

*"…The type of mosaicism and its clinical consequence is dependent upon a variety of aspects including when and where […] is generated.*

*"…the consequences of mosaicism are widespread and unique for each incident."*

(Taylor *et al., 2014)*

# Mosaicism: transfer track

1. Prioritise euploid embryos.

2. Individualised reproductive and genetic counselling.

**NO TRANSFER**

A. Repeat PGT-A cycle.

B. Gamete/embryo donation.

C. Abandon IVF.

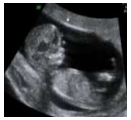
**TRANSFER**

A. Individualised informed consent.


B. Transfer of a single mosaic embryo.

C. Exhaustive pregnancy follow-up + PNT.

- Exhaustive sonographic control.
- Karyotype (50 metaphases) + aCGH (+ UPD testing).



# Mosaicism: to transfer or not to transfer?

## PROFESSIONALS INFORM

PGT-A embryologist → Reports

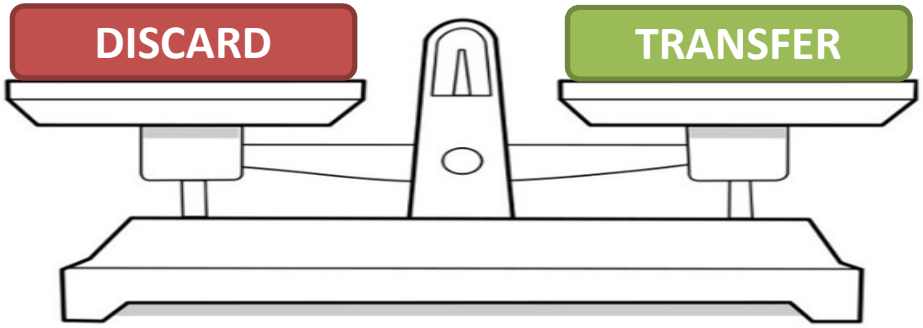
Clinician → Explains possibilities

Genetic counsellor → Informs on genetic risk

## PATIENTS DECIDE

Potential reduction of CLBR
Repeat PGT-A / Others

Potential genetic risk
Healthy live births reported



Ayer, hoy y siempre

Dexeus mujer

# Thank you very much for your attention

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