

Origin, Incidence and Outcomes: Piecing Together the Patterns of Embryonic Mosaicism

PCRS 2024

Andrea Victor, PhD



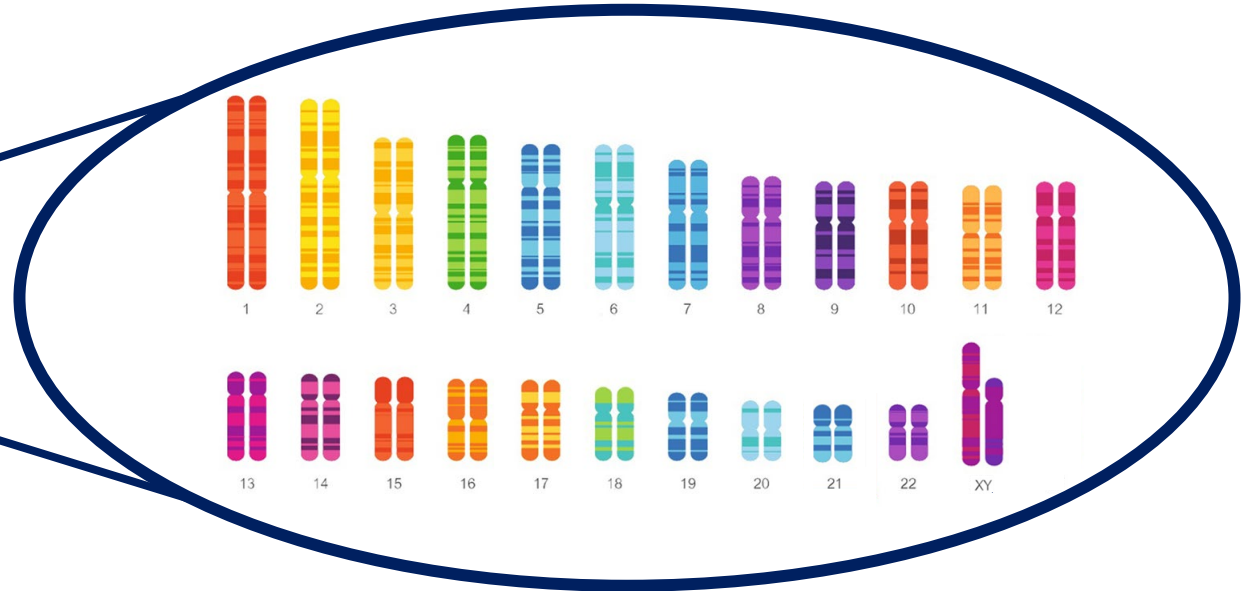
Nothing to disclose.

Learning Objectives

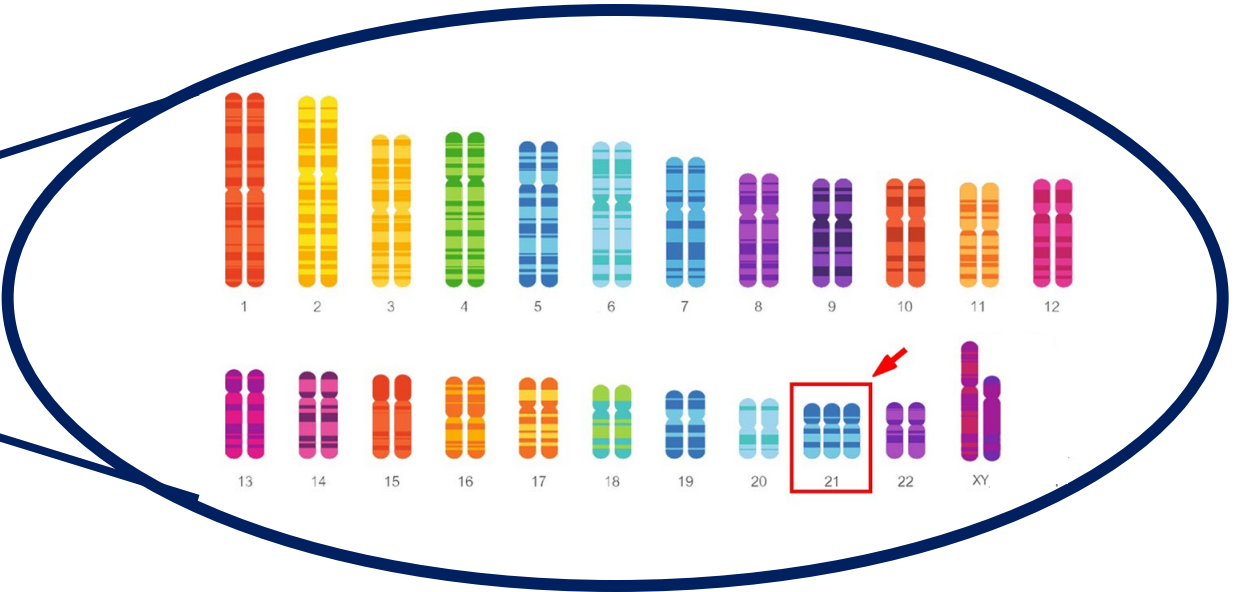
- Define the incidence of embryonic mosaicism.
- Review the cellular mechanisms by which embryonic mosaicism can arise
- Review outcomes of mosaic embryo transfers.

Cellular Ploidy

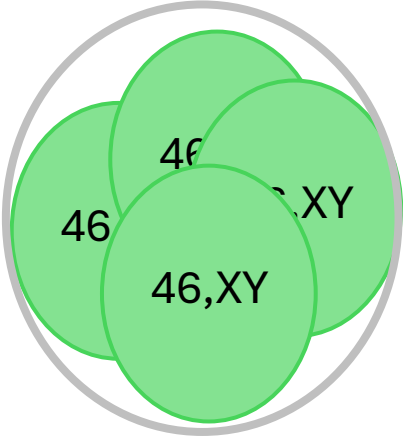
46,XY
Euploid or Diploid Cell



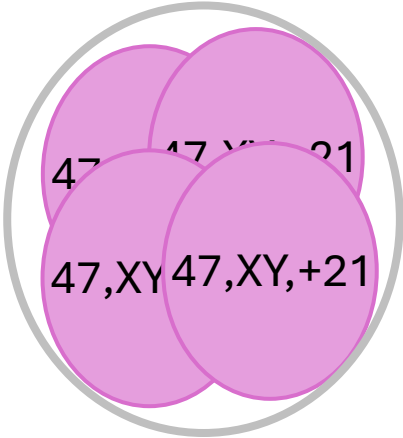
47,XY,+21
Aneuploid Cell



Embryo Ploidy

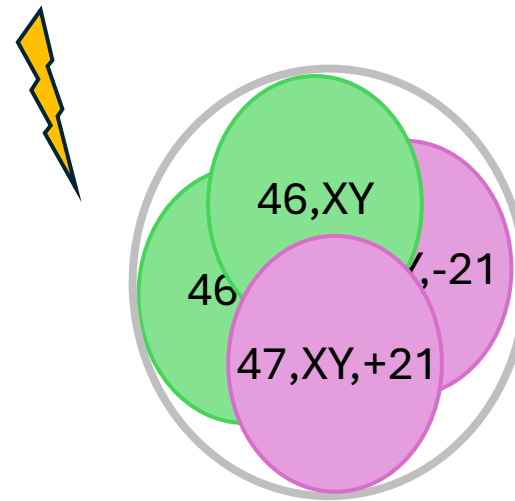


Euploid Embryo



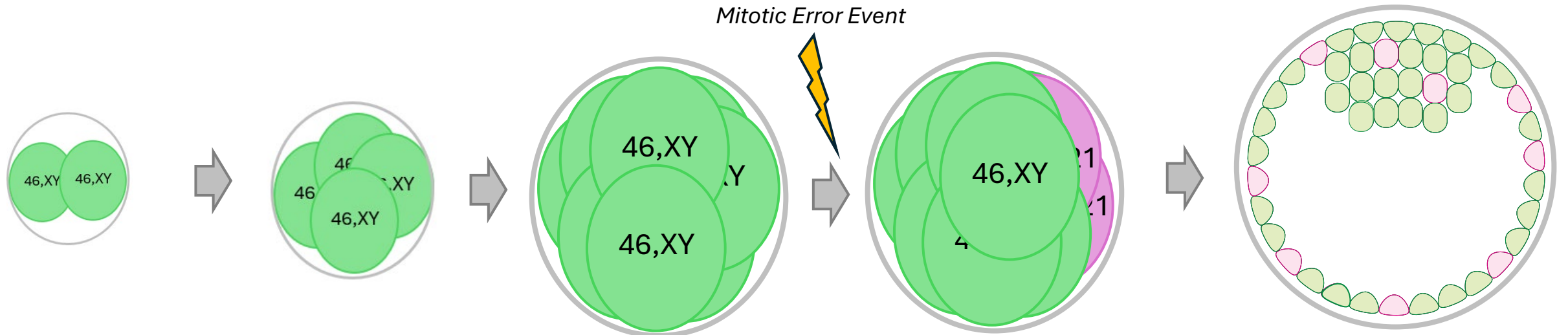
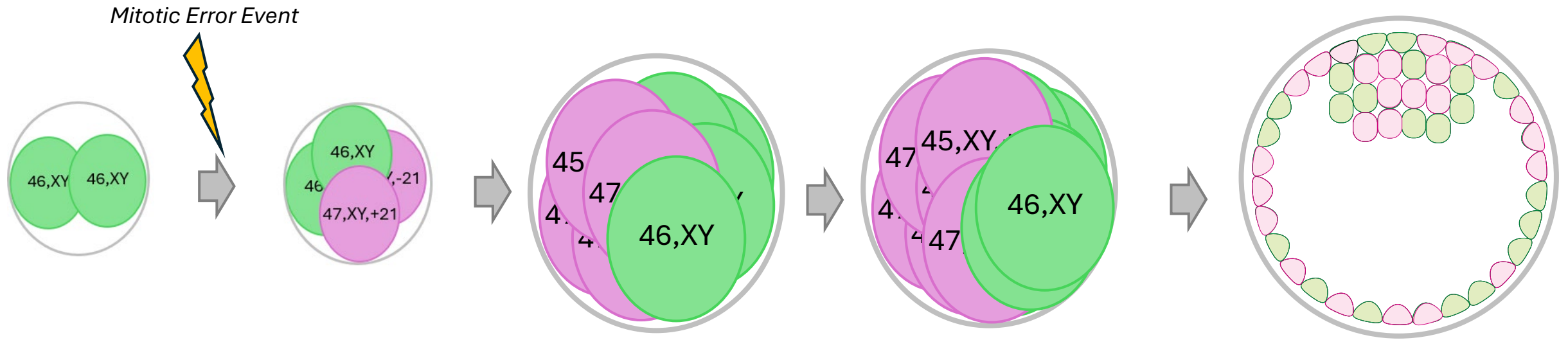
Aneuploid Embryo

Embryo Ploidy: Mosaicism



Mosaic Embryo

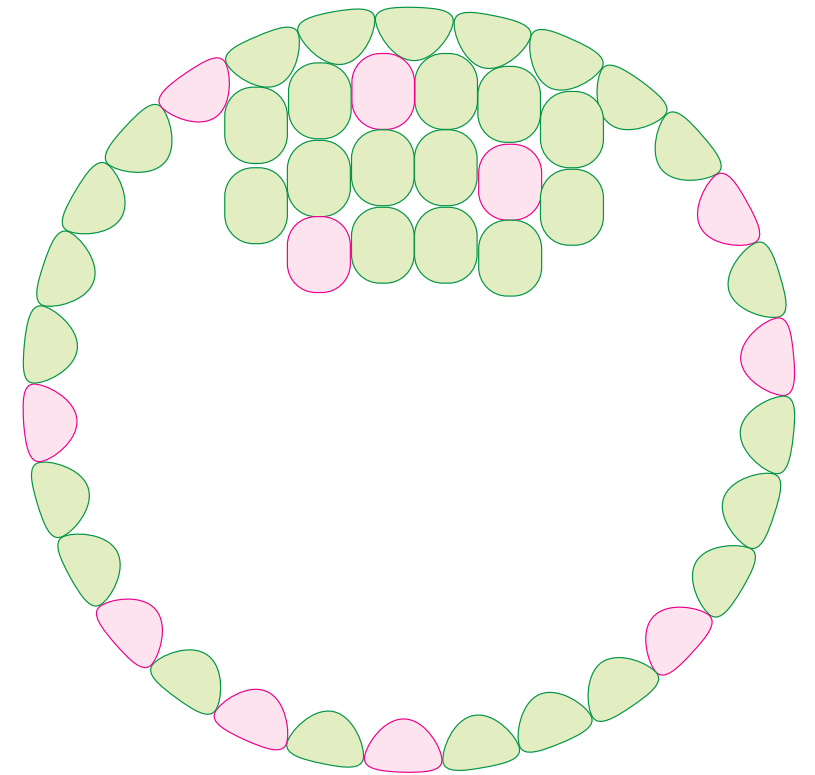
Embryo Ploidy: Mosaicism



Overview

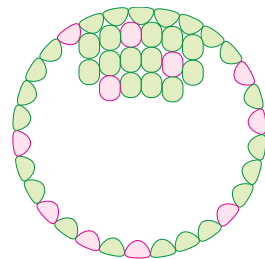
- Biological mechanisms of embryonic mosaicism

- Can mitotic errors be induced?
- Artifactual mosaic results
- Incidence of embryonic mosaicism
- Outcomes of mosaic embryo transfers



Embryonic Mosaicism: Biological Mechanisms

- First detected in human embryos by FISH
 - Griffin et al 1991
- Confirmed in cleavage and blastocyst embryos
- Many mechanisms that can cause a mitotic event and induce embryonic mosaicism



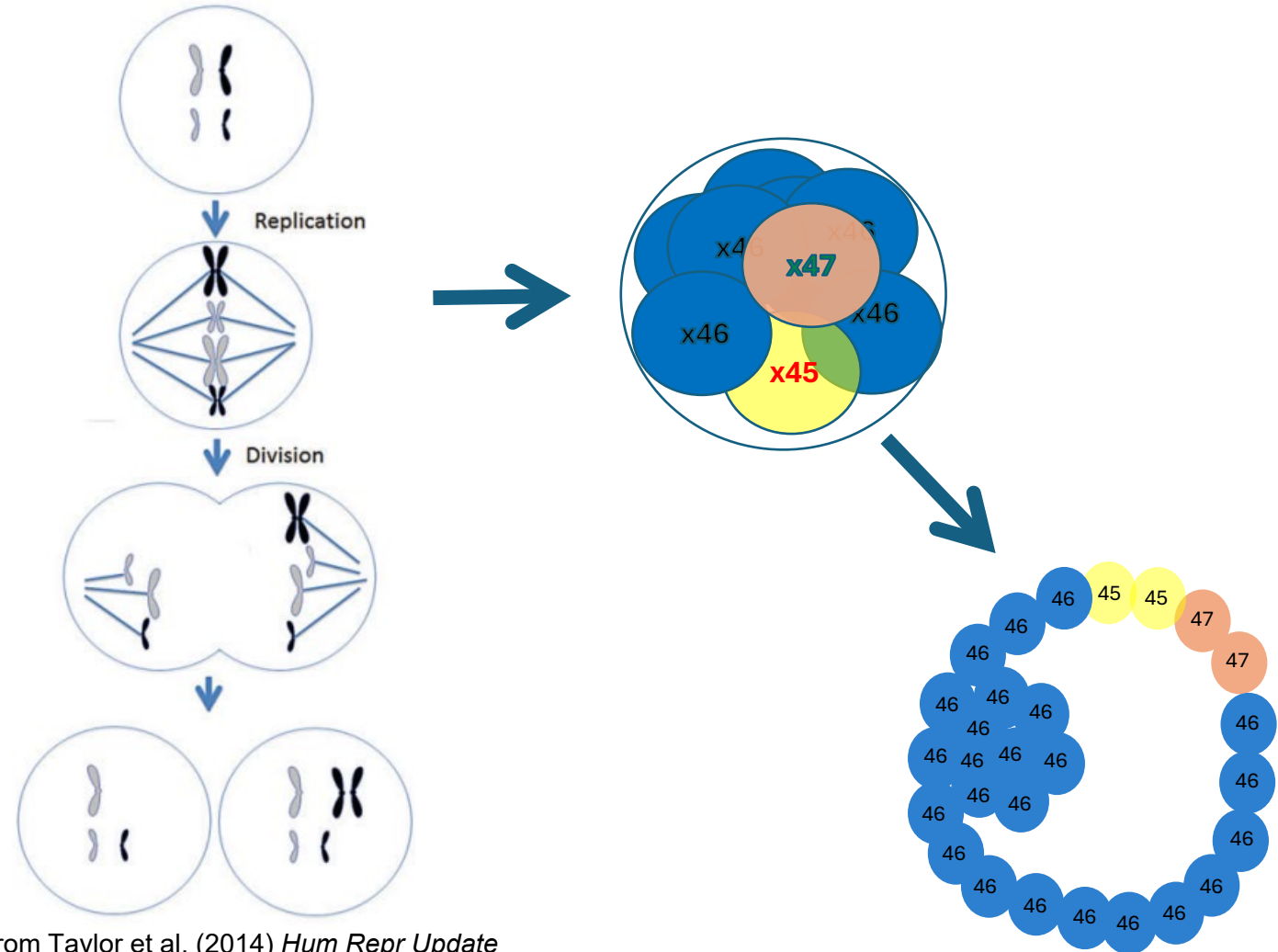
Biological Mechanisms:

How does mosaicism arise?

- Altered recombination pattern
- Anaphase lag
- Cell cycle control breakdown
- Centriole dysregulation
- Chaotic divisions
- Chromosome loss
- Chromosome gain
- Chromothripsis
- Cohesin depletion
- Cohesion exhaustion
- Embryo correction
- Endoreplication
- Insufficient crossover maturation
- Inter-chromosomal effect
- Mitotic non-disjunction
- Precocious sister chromatid/dyad separation
- Reverse segregation
- Trisomy rescue
- Weakened centromere cohesion
- Etc, etc, etc.....

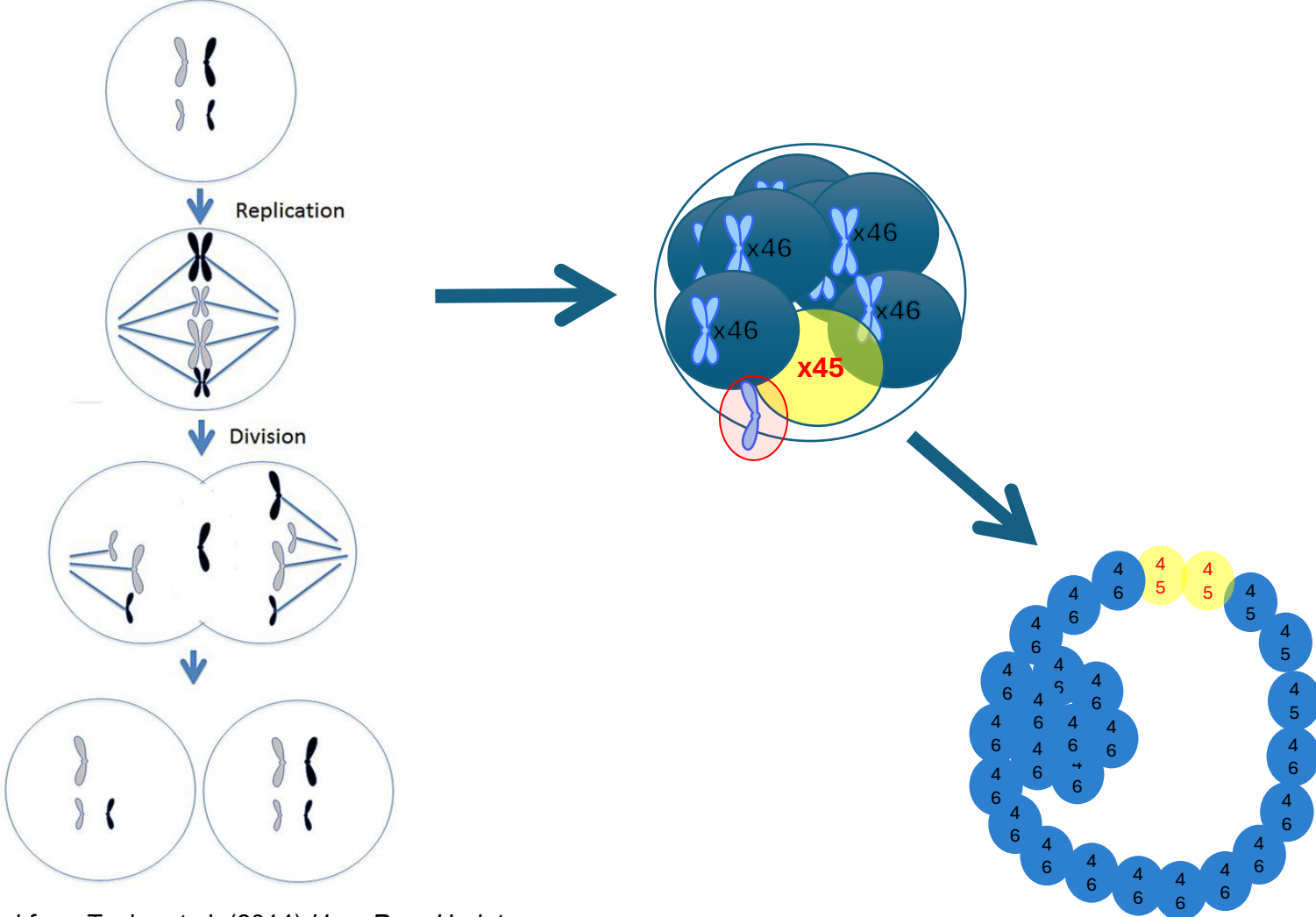
Biological Mechanisms: How does mosaicism arise?

Mitotic Non-Disjunction



Biological Mechanisms: How does mosaicism arise?

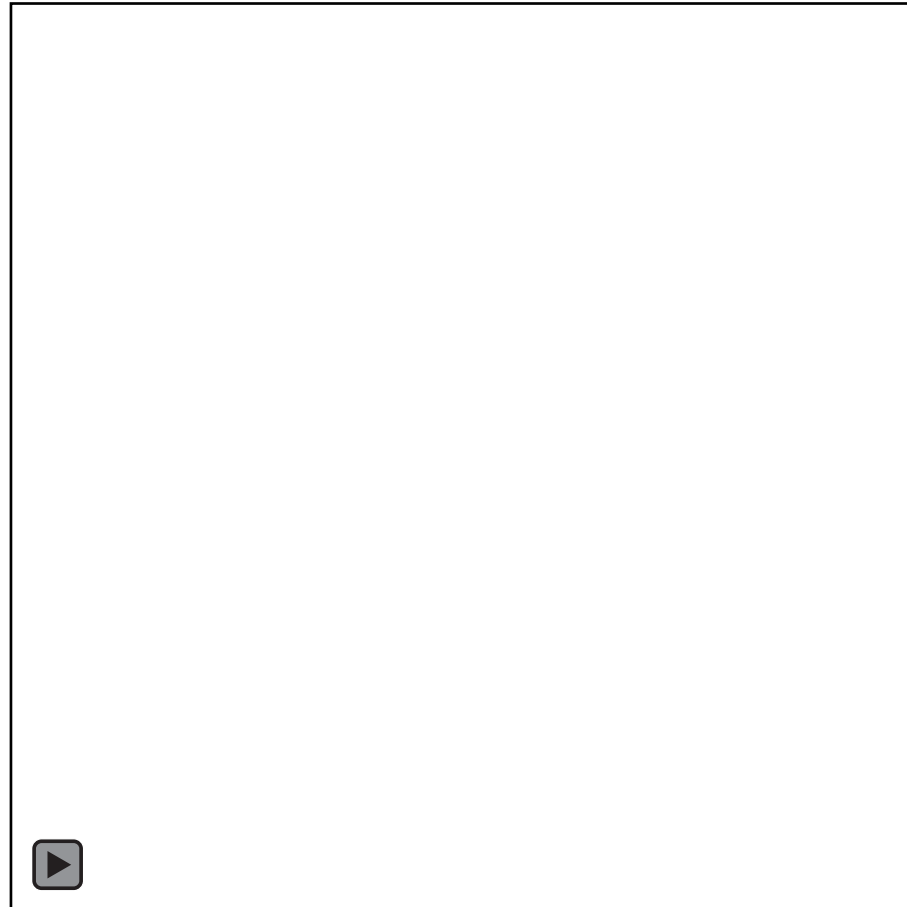
Anaphase Lag



Adapted from Taylor et al. (2014) *Hum Repr Update*

Biological Mechanisms: How does mosaicism arise?

Anaphase Lag



Biological Mechanisms: How does mosaicism arise?

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10 APRIL 2015 • VOL 348 ISSUE 6231

Common variants spanning **PLK4** are associated with mitotic-origin aneuploidy in human embryos

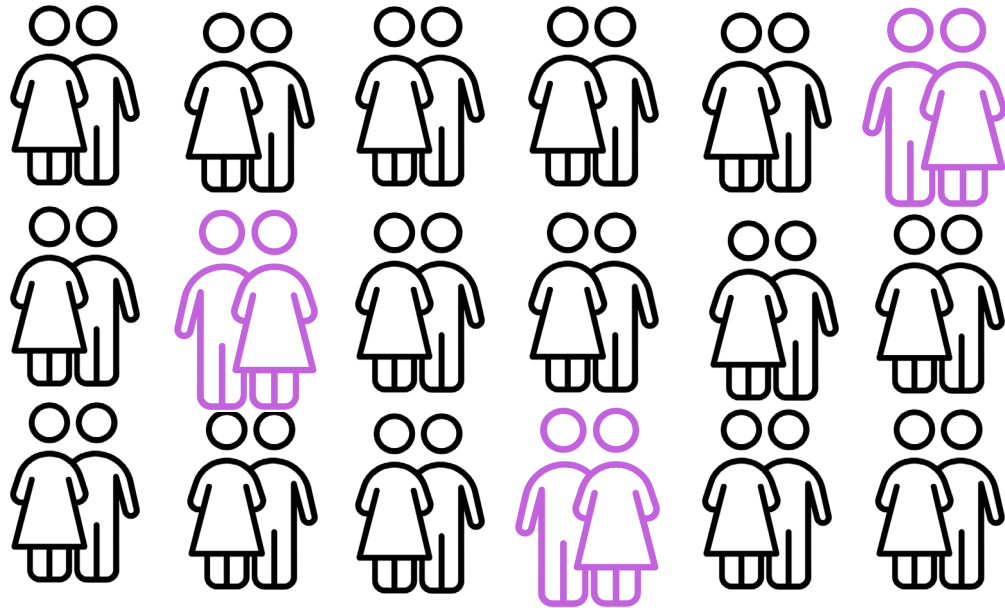
Rajiv C. McCoy¹, Zachary Demko², Allison Ryan², Milena Banjevic², Matthew Hill², Styrmir Sigurjonsson², Matthew Rabinowitz², Hunter B. Fraser¹, and Dmitri A. Petrov¹

¹Department of Biology, Stanford University, Stanford, California, USA

²Natera, Inc., San Carlos, California, USA

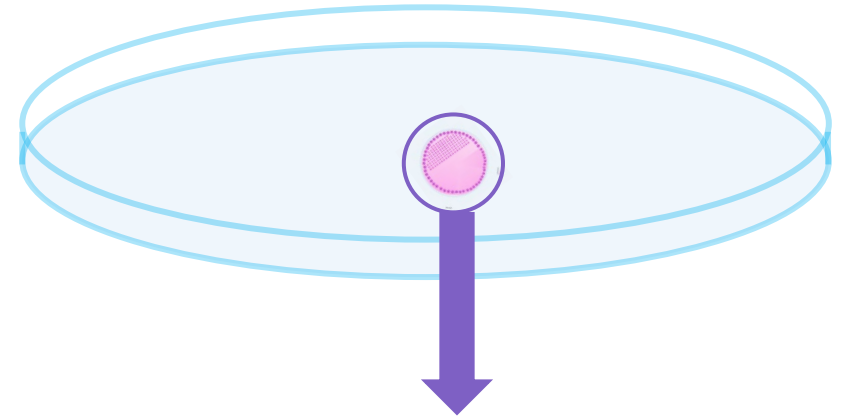
Biological Mechanisms: How does mosaicism arise?

Endogenous



Page, Fertility and Sterility 1989

Exogenous



Overview

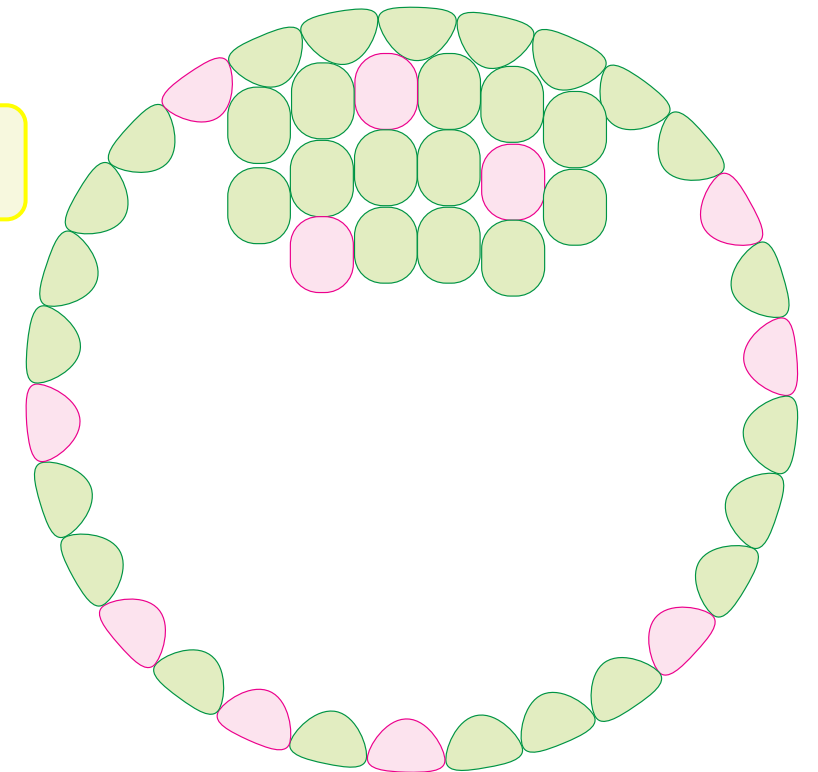
- Biological mechanisms of embryonic mosaicism

- Can mitotic errors be induced?

- Artifactual mosaic results

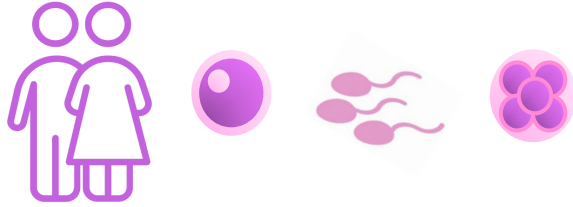
- Incidence of embryonic mosaicism

- Outcomes of mosaic embryo transfers



Mosaicism: What causes mitotic errors?

Endogenous



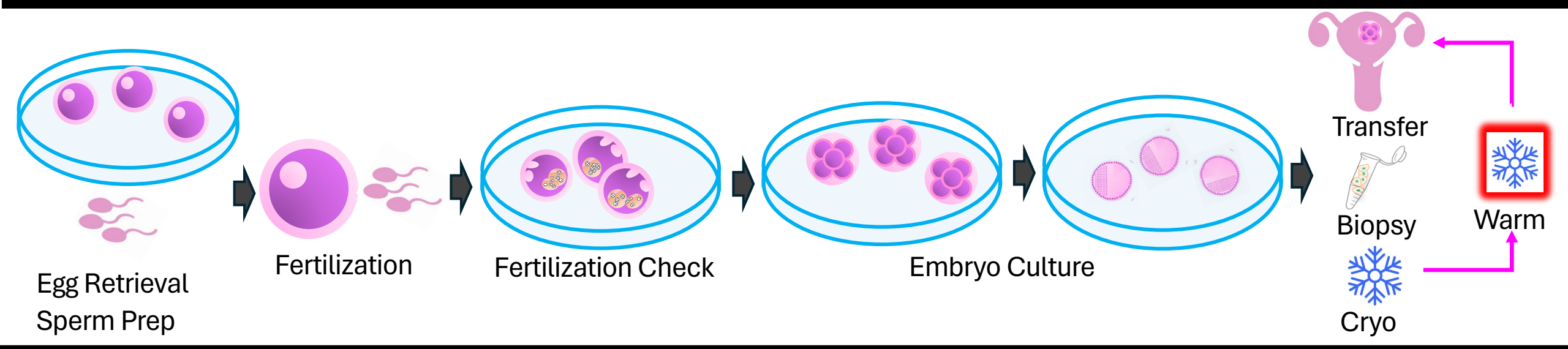
Exogenous

Mosaicism: What causes mitotic errors?

Day 0

Day 1

Day 5/6/7

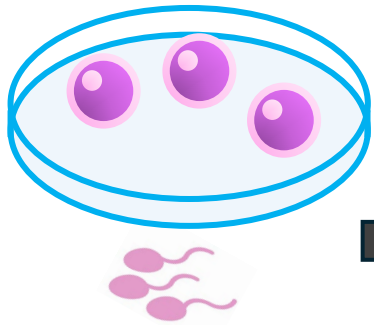


Mosaicism: What causes mitotic errors?

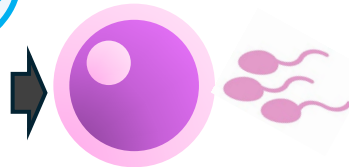
Day 0

Day 1

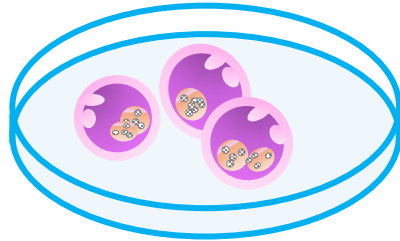
Day 5/6/7



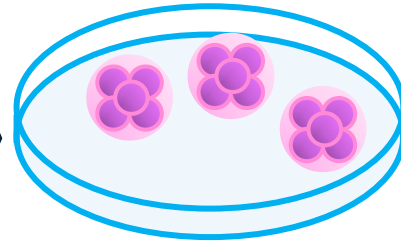
Egg Retrieval
Sperm Prep



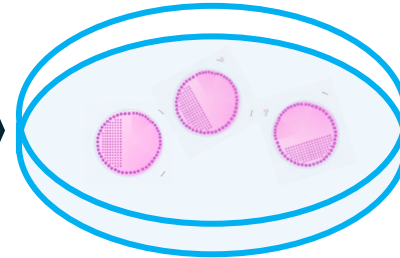
Fertilization



Fertilization Check



Embryo Culture



Transfer



Biopsy



Cryo



Warm

Retrieval Technique
Fresh/Frozen sperm
Sperm prep (microfluidics/gradient)



Minimizing mosaicism: assessing the impact of fertilization method on rate of mosaicism after next-generation sequencing (NGS) preimplantation genetic testing for aneuploidy (PGT-A)

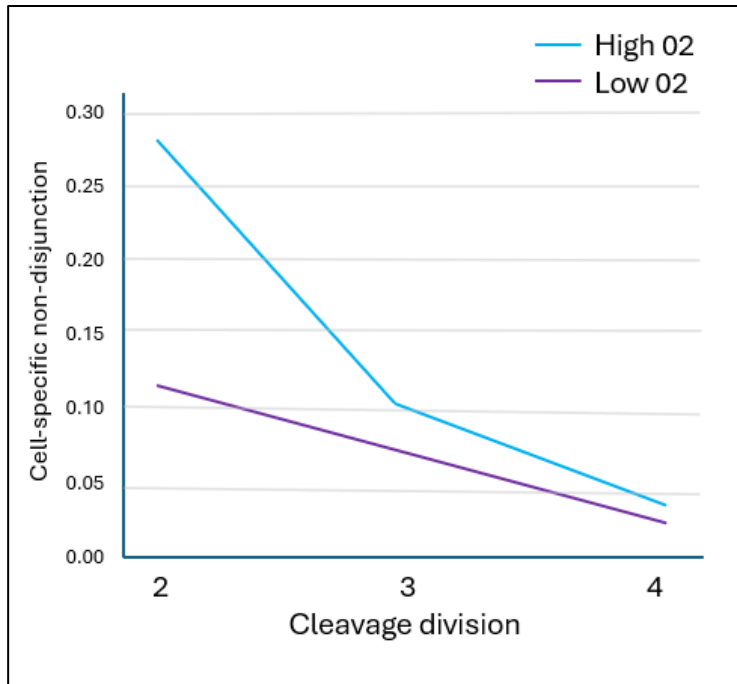
Katherine L. Palmerola^{1,2} · Sally F. Vitez² · Selma Amrane^{1,2} · Catha P. Fischer³ · Eric J. Forman¹

Received: 27 July 2018 / Accepted: 16 October 2018
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ICSI cases resulted in fewer mosaic embryos than insemination cases.

Primary outcome			
NGS PGT-A diagnosis	Conventional insemination (251 blastocysts)	ICSI (724 blastocysts)	<i>p</i> value*
Euploid	70 (27.9)	217 (30.0)	0.59
Aneuploid	104 (45.4)	312 (43.1)	0.70
Mosaic	65 (25.9)	151 (20.9)	0.12
No result	11 (4.4)	45 (6.2)	0.36
Secondary outcomes			
Mosaic subtypes	Conventional insemination (65 blastocysts)	ICSI (151 blastocysts)	<i>p</i> value*
Simple	35 (53.8)	106 (70.2)	0.03
Double	15 (23.1)	25 (16.6)	0.35
Complex	15 (23.1)	20 (13.2)	0.11
Aneuploid subtypes	Conventional insemination (104 blastocysts)	ICSI (312 blastocysts)	<i>p</i> value*
Simple	49 (47.1)	125 (40.1)	0.25
Double	13 (12.5)	46 (14.7)	0.69

Mosaicism: What causes mitotic errors?



Adapted from Bean et al, Human Reproduction 2002

Human Reproduction Vol.17, No.9 pp. 2362–2367, 2002

Fertilization *in vitro* increases non-disjunction during early cleavage divisions in a mouse model system

Christopher J.Bean, Terry J.Hassold, LuAnn Judis and Patricia A.Hunt¹

Department of Genetics and the Center for Human Genetics, Case Western Reserve University and University Hospitals of Cleveland, Cleveland, OH, USA

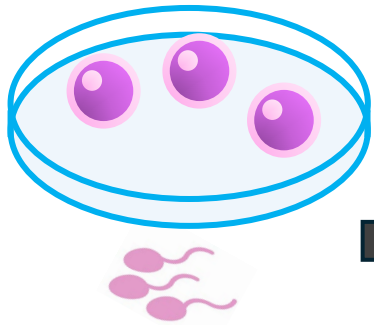
¹To whom correspondence should be addressed at: Department of Genetics, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, OH 44106, USA. E-mail: pah13@po.cwru.edu

Mosaicism: What causes mitotic errors?

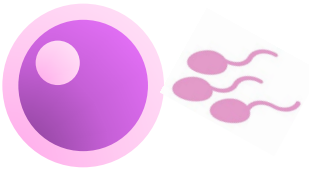
Day 0

Day 1

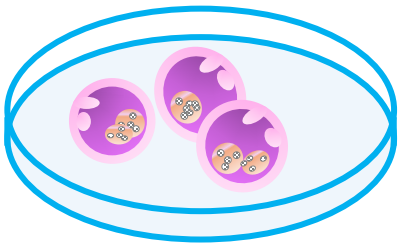
Day 5/6/7



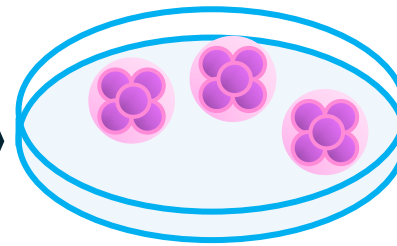
Egg Retrieval
Sperm Prep



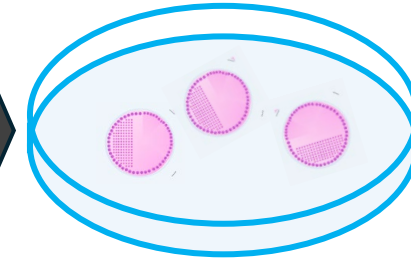
Fertilization



Fertilization Check



Embryo Culture



Transfer



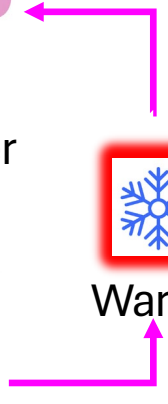
Biopsy



Cryo



Warm



Mosaicism: What causes mitotic errors?

Cell Systems
Brief Report

ROS and Oxidative Stress Are Elevated in Mitosis during Asynchronous Cell Cycle Progression and Are Exacerbated by Mitotic Arrest

Jesse C. Patterson,^{1,2,3,4,5} Brian A. Joughin,^{2,3,4,5} Bert van de Kooij,^{1,2,3,4} Daniel C. Lim,^{1,2,3,4} Douglas A. Lauffenburger,^{2,3} and Michael B. Yaffe^{1,2,3,4,6*}

¹Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139, USA
²Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA
³David H. Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology, Cambridge, MA 02139, USA
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⁵These authors contributed equally
⁶Lead Contact
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<https://doi.org/10.1016/j.cels.2019.01.005>

CellPress

Article

Replication stress impairs chromosome segregation and preimplantation development in human embryos

Katherine L. Palmerola,^{1,7} Selma Amrane,^{1,7} Alejandro De Los Angeles,^{2,7} Shuangyi Xu,^{2,3,7} Ning Wang,^{2,7} Joao de Pinho,¹ Michael V. Zuccaro,² Angelo Tagliatela,² Dashiell J. Massey,² Jenna Turocy,² Alex Robles,² Anisa Subbiah,¹ Bob Prosser,¹ Rogério Lobo,¹ Alberto Ciccia,² Amnon Koren,² Timour Baslan,^{4,7} and Dieter Egli^{1,2,3,6*}

¹Department of Obstetrics and Gynecology, Columbia University, New York, NY 10032, USA
²Department of Pediatrics and Naomi Berrie Diabetes Center, Columbia Stem Cell Initiative, Columbia University, New York, NY 10032, USA
³Masters of Biotechnology Program, Columbia University, New York, NY 10027, USA
⁴Department of Genetics and Development, Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY 10032, USA
⁵Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY 14853, USA
⁶Cancer Biology and Genetics Program, Memorial Sloan Kettering Cancer Center, New York, NY 10065, USA
⁷These authors contributed equally
 *Lead contact
 *Correspondence: de2220@cumc.columbia.edu

Free Radical Biology and Medicine

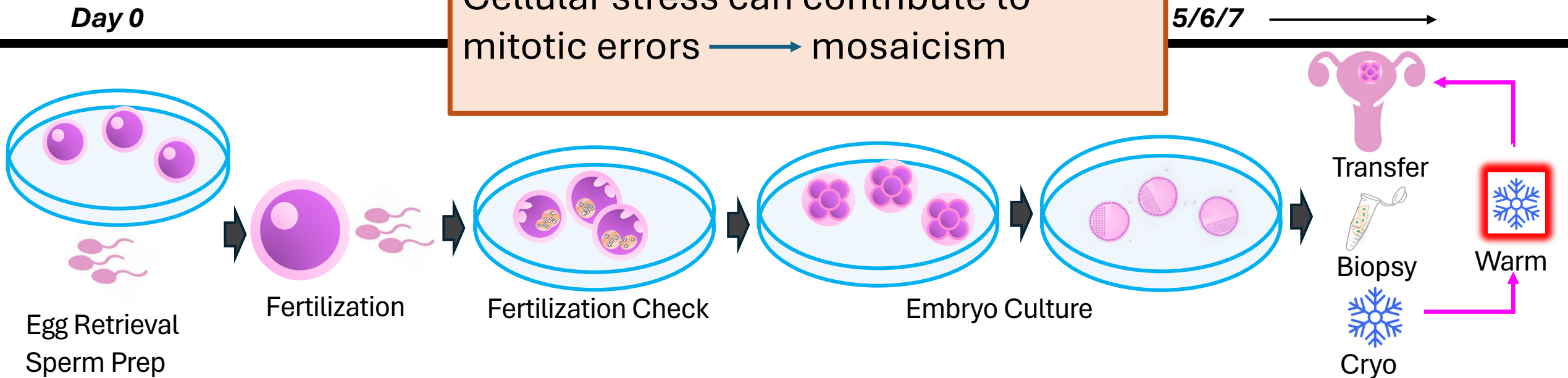
Volume 103, February 2017, Pages 177-187

Original article

Oxidative stress induces mitotic arrest by inhibiting Aurora A-involved mitotic spindle formation

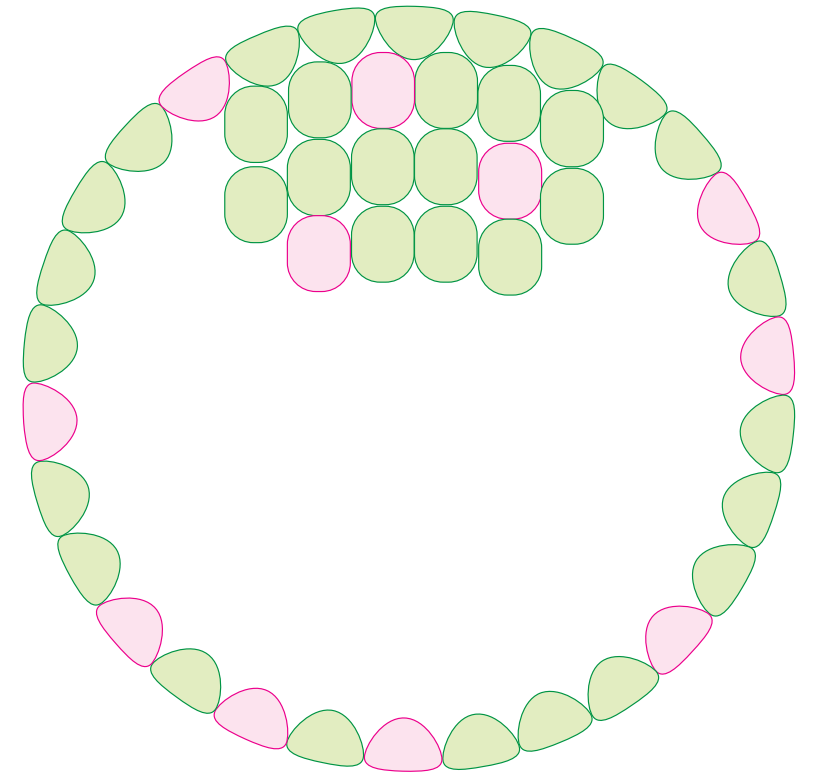
Guang-Fei Wang,^{a,1} Qincai Dong,^{b,1} Yuanyuan Bai,^b Jing Yuan,^c Quanbin Xu,^b ...
 *Correspondence: ...

Cellular stress can contribute to mitotic errors → mosaicism



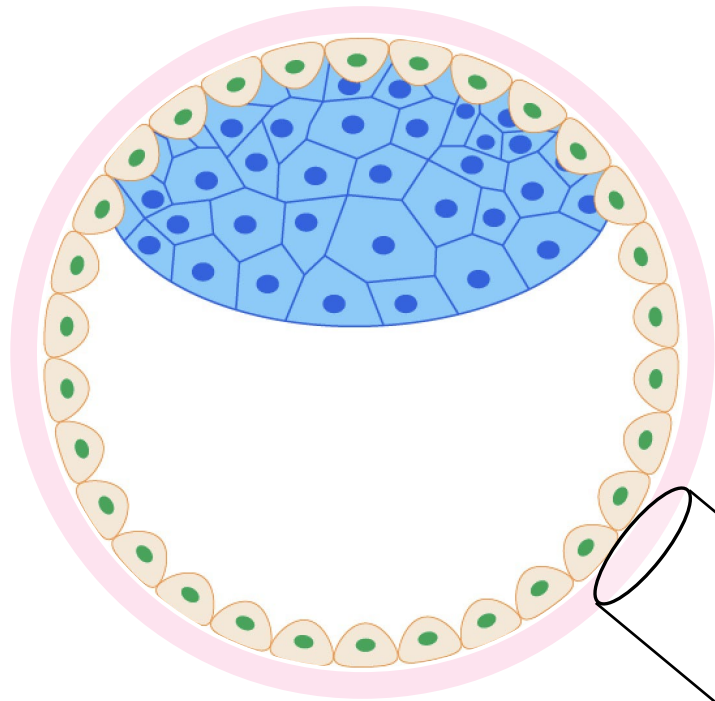
Overview

- Biological mechanisms of embryonic mosaicism
- Can mitotic errors be induced?
- Artifactual mosaic results
- Incidence of embryonic mosaicism
- Outcomes of mosaic embryo transfers

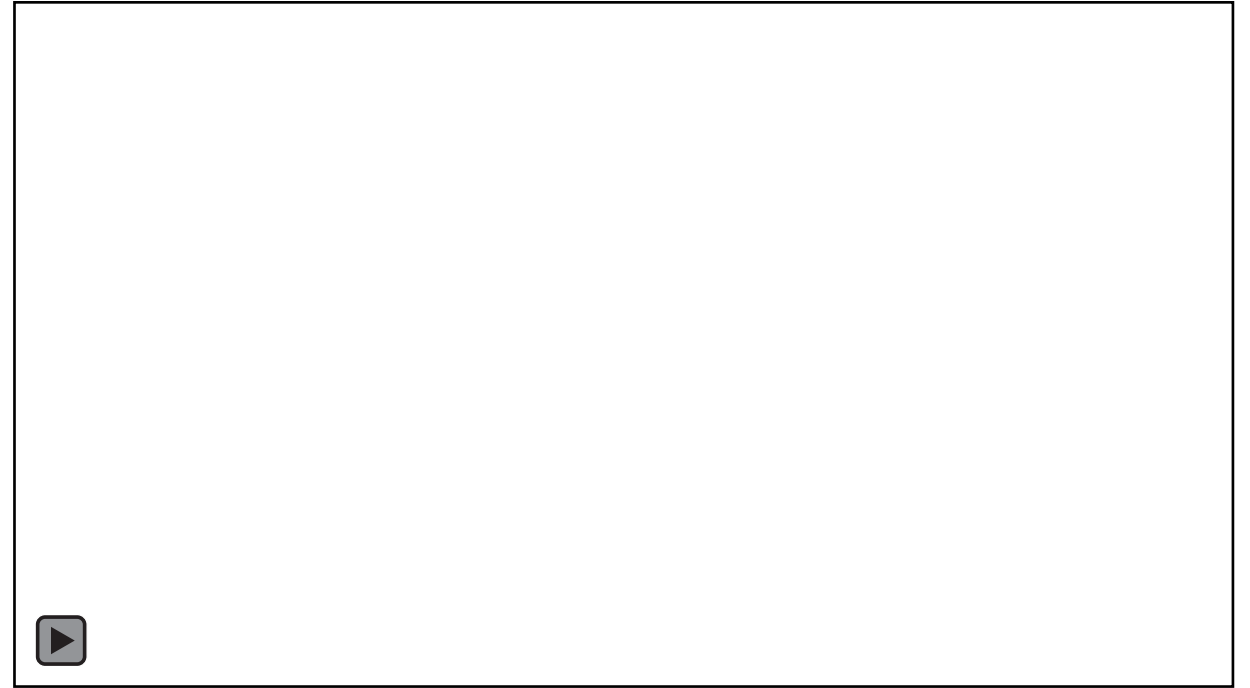
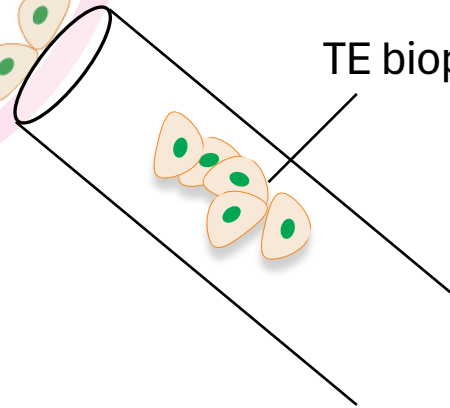


Identifying Mosaic Embryos:

Artifactual mosaic results

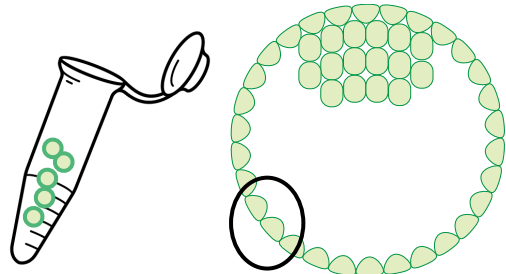


TE biopsy

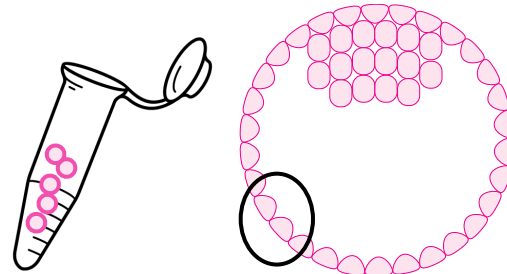


Identifying Mosaic Embryos:

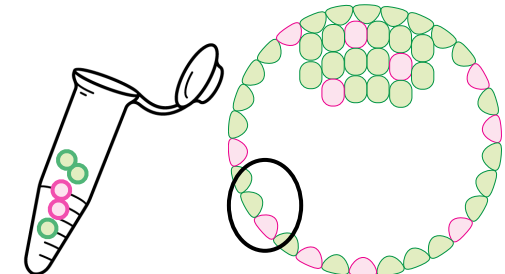
Artifactual mosaic results



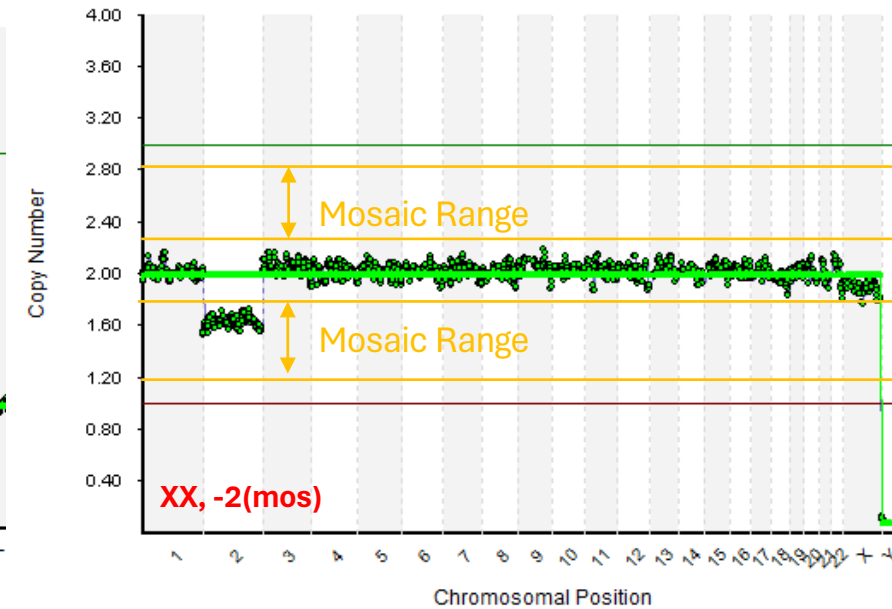
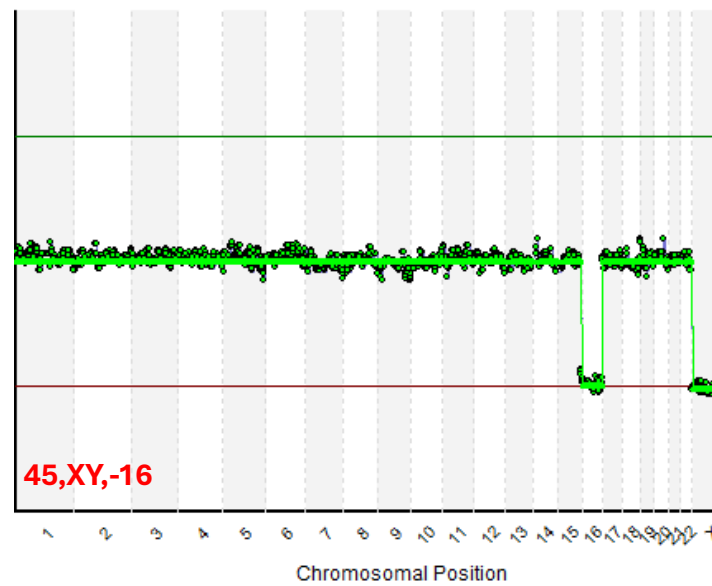
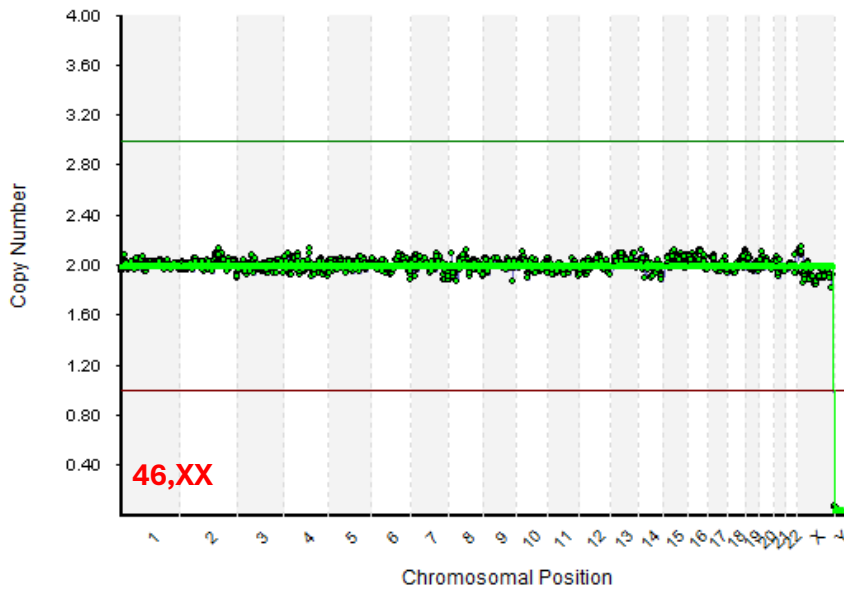
Euploid



Aneuploid



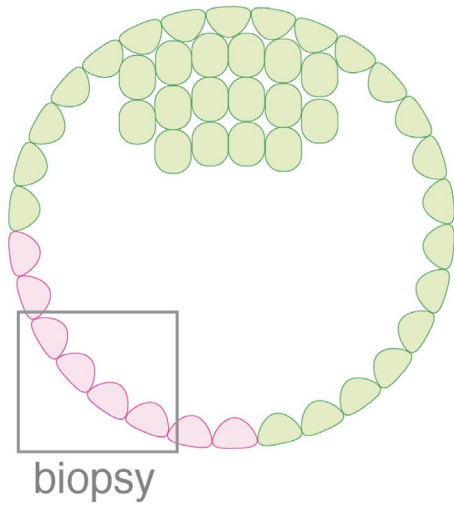
Mosaic



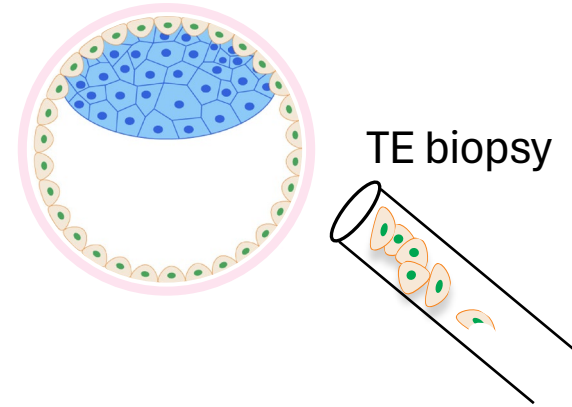
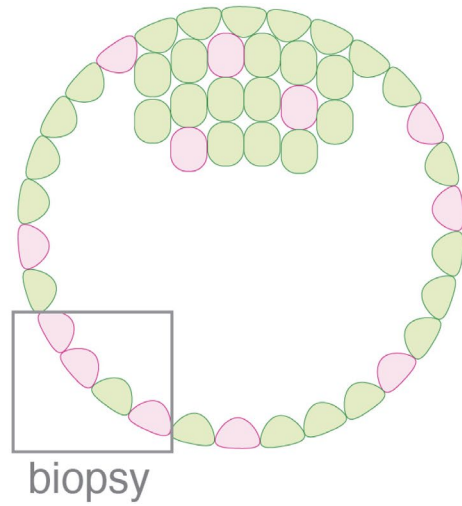
Identifying Mosaic Embryos:

Artifactual mosaic results

Global Mosaicism

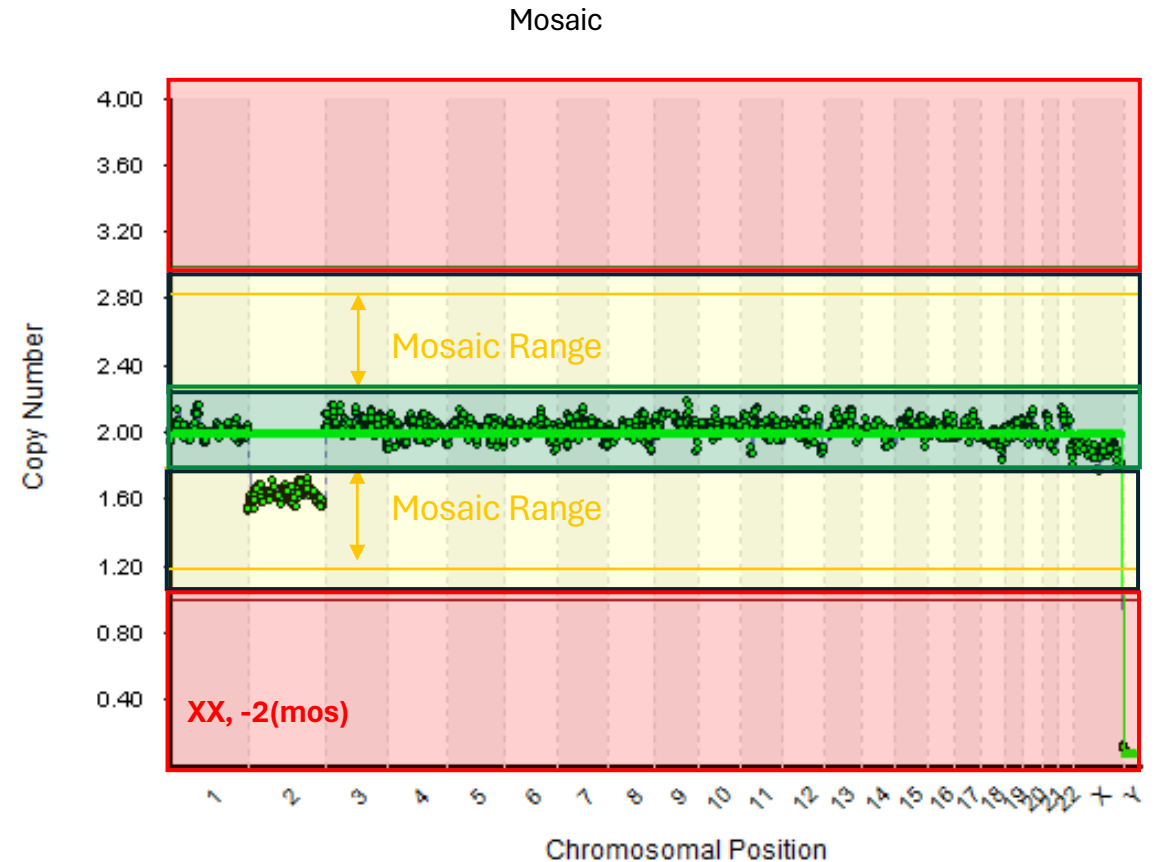
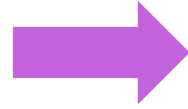
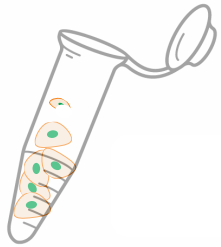


Intra-biopsy Mosaicism



Identifying Mosaic Embryos:

Artifactual mosaic results



Euploid
Mosaic
Aneuploid

Identifying Mosaic Embryos: Artifactual mosaic results

Human Reproduction Open, pp. 1–18, 2022
<https://doi.org/10.1093/hropen/hoac044>

human
reproduction
open

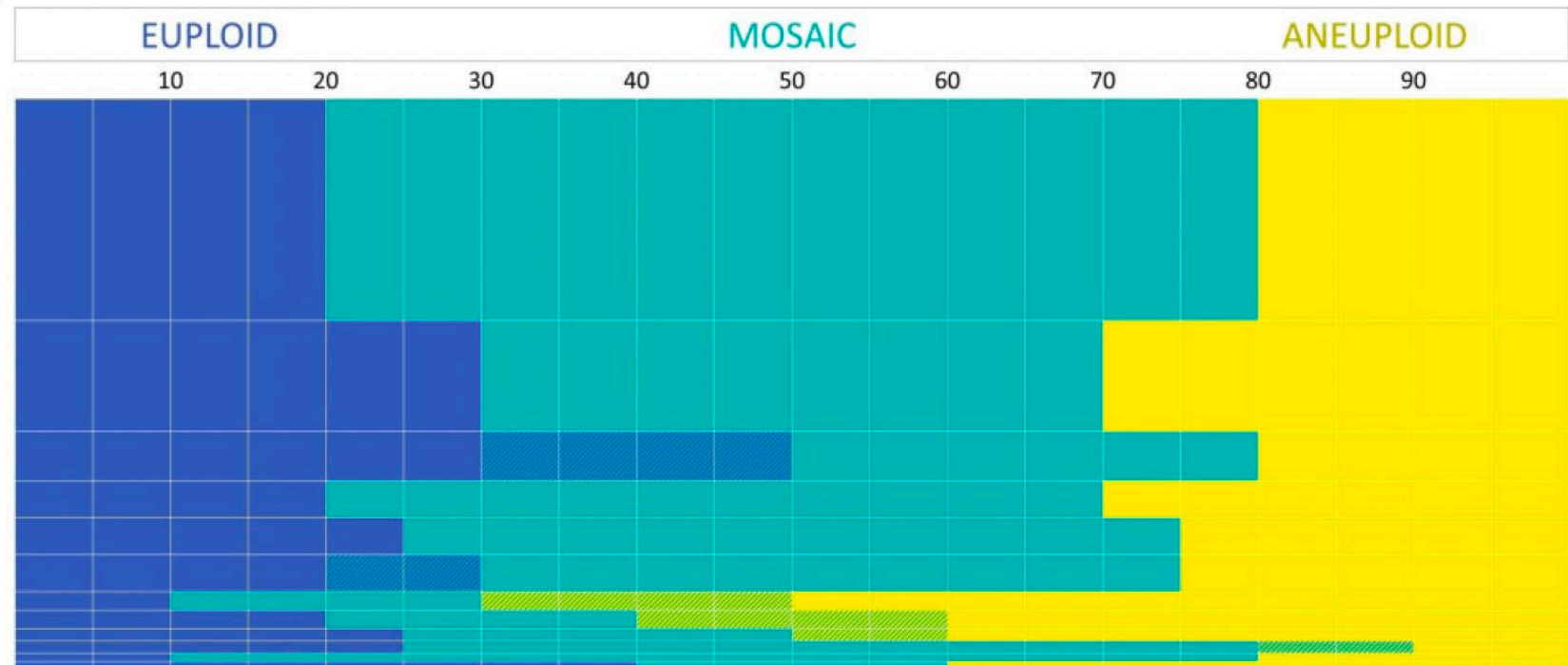
ESHRE PAGES

ESHRE survey results and good practice recommendations on managing chromosomal mosaicism†

ESHRE Working Group on Chromosomal Mosaicism, Martine De Rycke ^{1,*}, Antonio Capalbo ², Edith Coonen ^{3,4}, Giovanni Coticchio ⁵, Francesco Fiorentino ⁶, Veerle Goossens ⁷, Saria Mcheik ⁷, Carmen Rubio ⁸, Karen Sermon ⁹, Ioannis Sfontouris ¹⁰, Claudia Spits ⁹, Joris Robert Vermeesch ¹¹, Nathalie Vermeulen ⁷, Dagan Wells ^{12,13}, Filippo Zambelli ¹⁴ and Georgja Kakourou ¹⁵

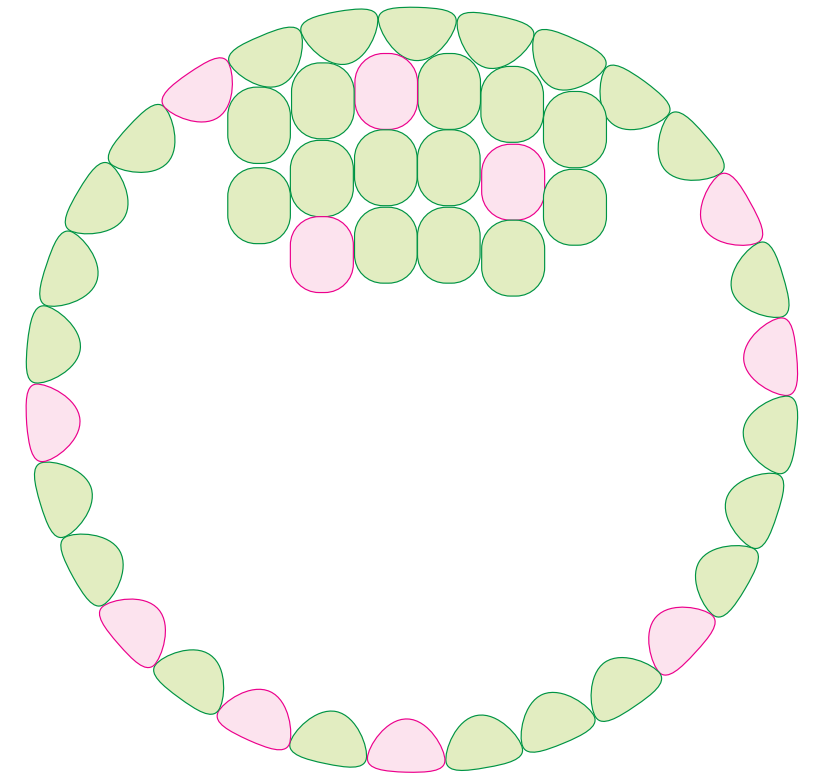
¹Centre for Medical Genetics, UZ Brussel, Reproduction and Genetics, Vrije Universiteit Brussel (VUB), Brussels, Belgium ²JUNC Genetics, Rome, Italy ³Departments of Clinical Genetics and Reproductive Medicine, Maastricht University Medical Centre, Maastricht The Netherlands ⁴GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands ⁵Baby, Generalife IVF, Bologna, Italy ⁶Rome, Italy ⁷ESHRE Central Office, Strombeek-Bever, Belgium ⁸PCTA Research Igenomix, Valencia, Spain ⁹Research Group Reproduction and Genetics, Vrije Universiteit Brussel, Brussels, Belgium ¹⁰Hygeia IVF Embryogenesis, Athens, Greece ¹¹Laboratory for Cytogenetics and Genome Research, Department of Human Genetics, KU Leuven Leuven, Belgium ¹²Nuffield Department of Women's & Reproductive Health, John Radcliffe Hospital, University of Oxford, Oxford, UK ¹³Juno Genetics, Oxford, UK ¹⁴Eugin Group, Barcelona, Spain ¹⁵Laboratory of Medical Genetics, National & Kapodistrian University of Athens, Choremio Research Laboratory, "Aghia Sophia" Children's Hospital, 11527 Athens, Greece

Range of mosaicism (% abnormal cells) considered diagnostically indicative of an aneuploid, euploid or mosaic embryo.

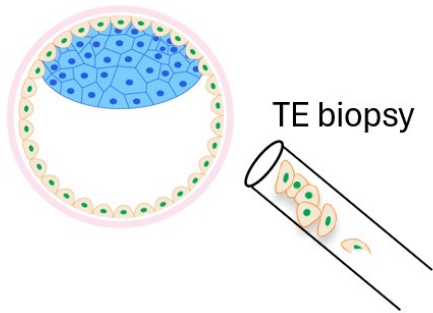


Overview

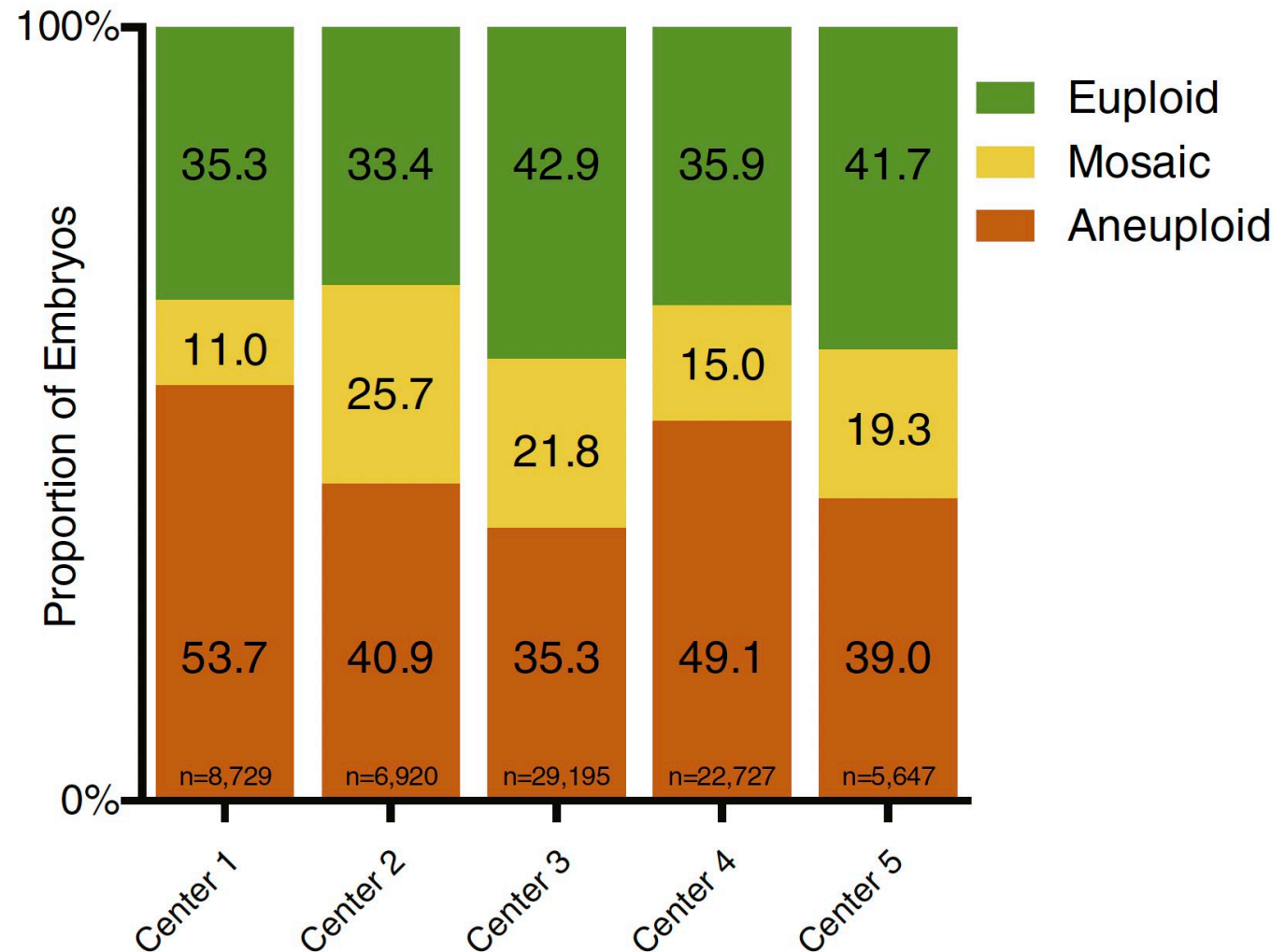
- Biological mechanisms of embryonic mosaicism
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Incidence of Embryonic Mosaicism: Clinical mosaicism rates by Biopsy and PGT-A



Proportion of PGT-A Categories in Participating Centers



ORIGINAL ARTICLES: ASSISTED REPRODUCTION



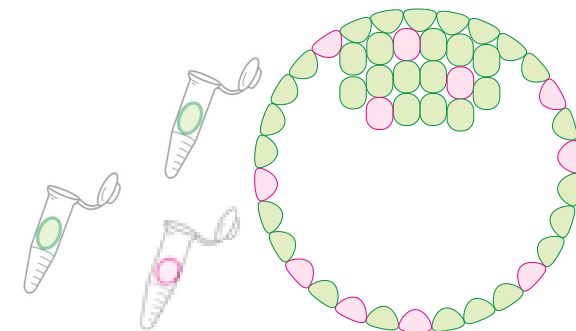
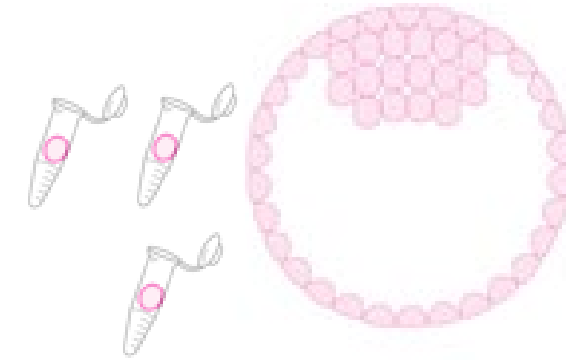
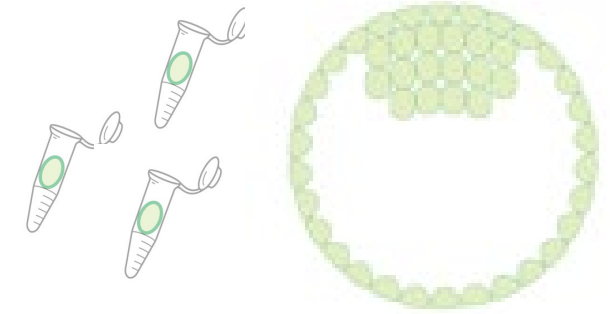
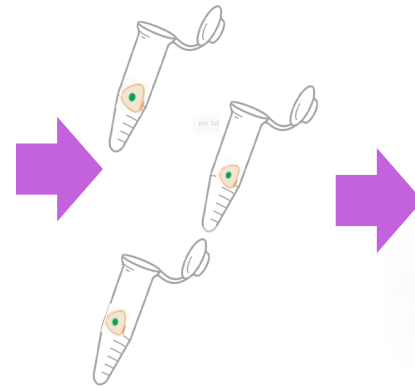
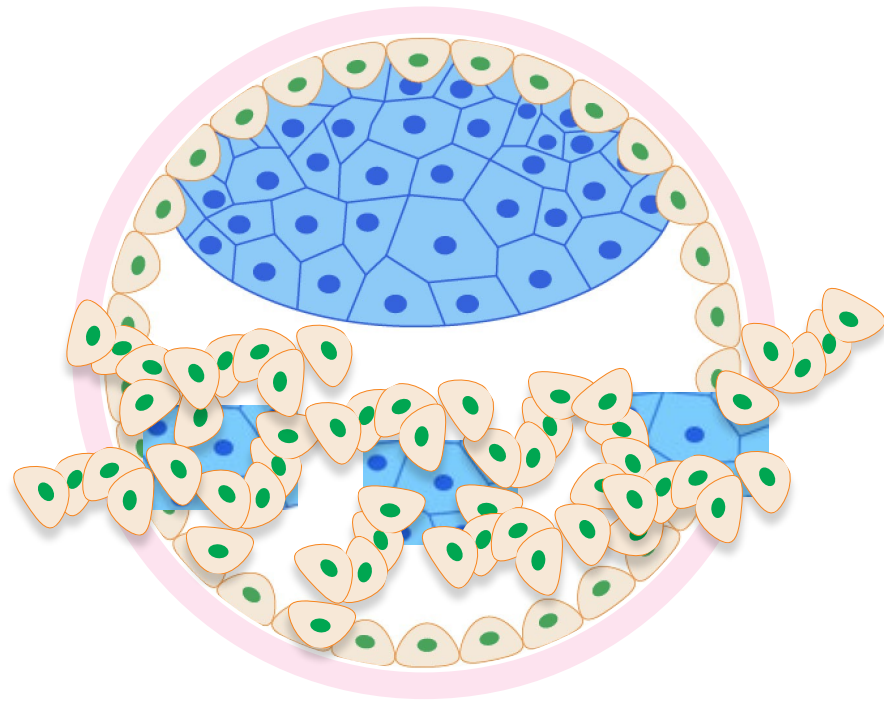
Using outcome data from one thousand mosaic embryo transfers to formulate an embryo ranking system for clinical use

Manuel Viotti, Ph.D.,^{a,b} Andrea R. Victor, M.S.,^a Frank L. Barnes, Ph.D.,^{a,b} Christo G. Zouves, M.D.,^{a,b} Andria G. Besser, M.S.,^c James A. Grifo, M.D., Ph.D.,^c En-Hui Cheng, Ph.D.,^d Maw-Sheng Lee, M.D., Ph.D.,^{d,e} Jose A. Horcajadas, Ph.D.,^f Laura Corti, M.Sc.,^g Francesco Fiorentino, Ph.D.,^h Francesca Spinella, Ph.D.,ⁱ Maria Giulia Minasi, M.Sc.,^j Ermanno Greco, M.D.,^k and Santiago Munne, Ph.D.^k

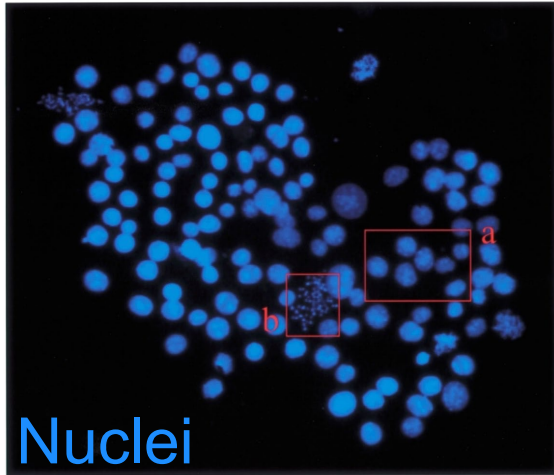
^a Zouves Foundation for Reproductive Medicine, Foster City, California; ^b Zouves Fertility Center, Foster City, California; ^c New York University Langone Fertility Center, New York, New York; ^d Lee Women's Hospital, Taichung, Taiwan; ^e Chung Shan Medical University, Institute of Medicine, Taichung, Taiwan; ^f Overture Life, New York, New York; ^g IRCCS San Raffaele Scientific Institute, Milan, Italy; ^h Eurofins Genoma Group, Molecular Genetics Laboratories, Rome, Italy; ⁱ European Hospital, Centre For Reproductive Medicine, Rome, Italy; ^j Villa Mafalda, Center For Reproductive Medicine, Rome, Italy; ^k Cooper Genomics, Livingston, New Jersey

Incidence of Embryonic Mosaicism:

Whole embryo analysis



FISH Studies In Whole Embryos Identify Mosaicism



Sandalinas et al. 2001 Hum Rep

Reference	Number of chromosomes analysed	Number of embryos in sample	Method	Euploidy Rate (%)	Aneuploidy Rate (%)	Mosaicism Rate (%)	No result (%)	Re-analysis
Munne et al., 1998	6	67	Methanol: acetic acid, 3:1	29.9	23.9	46.2	n/a	Yes
Gianaroli et al., 1999	9	148	Methanol: acetic acid, 3:1	5.4	71.0	23.6	n/a	Yes
Magli et al., 2000	6	143	Methanol: acetic acid, 3:1	49	51.0	n/a	n/a	No
Sandalinas et al., 2001	9	215	Methanol: acetic acid, 3:1	14.9	47.0	38.1	n/a	Yes
Bienlanska et al., 2002	9	216	Tween 20	29.6	22.2	48.1	n/a	Yes
Ziebe et al., 2003	7	103	Tween 20	31.1	8.70	55.3	4.90	No
Abdelhadi et al., 2003	13	426	Methanol: acetic acid, 3:1	23.2	44.1	32.6	n/a	Yes
Munne et al., 2003	9	1071	Methanol: acetic acid, 3:1	29.7	45.4	25.0	n/a	Yes
Jones et al., 2004	7	411	n/a	34.8	62.5	n/a	2.70	No
Ying-hui et al., 2004	5	54	Tween 20	44.4	50.0	n/a	5.60	No
Baart et al., 2005	10	196	Tween 20	35.7	33.2	31.1	n/a	Yes
Li et al., 2005	5	660	Tween 20	55.6	42.6	n/a	1.80	Yes
Cooper et al., 2006	8	51	Methanol: acetic acid, 3:1	31.4	33.3	35.3	8.10	Yes
Mantzouratou et al., 2007	6	354	Tween 20	0.28	5.37	94.9	9.00	Yes
DeUgarte et al., 2008	5	241	Tween 20	24.5	68.0	7.50	n/a	Yes
Hanson et al., 2009	7	149	Tween 20	4.00	65.8	30.2	n/a	Yes
Alegretti et al., 2009	9	75	n/a	30.7	69.3	n/a	n/a	No
Barbash-Hazan et al., 2009	8	83	Tween 20	0.00	79.5	18.1	2.40	Yes
Mir et al., 2010	9	2477	Methanol: acetic acid, 3:1	42.7	56.8	0.60	n/a	Yes
Ebrahimian et al., 2020	8	68	Methanol: acetic acid, 3:1	67.6	17.7	14.7	n/a	Yes

adapted from Darren Griffin and Lauren Kelly

Incidence of Embryonic Mosaicism: Whole embryo analysis

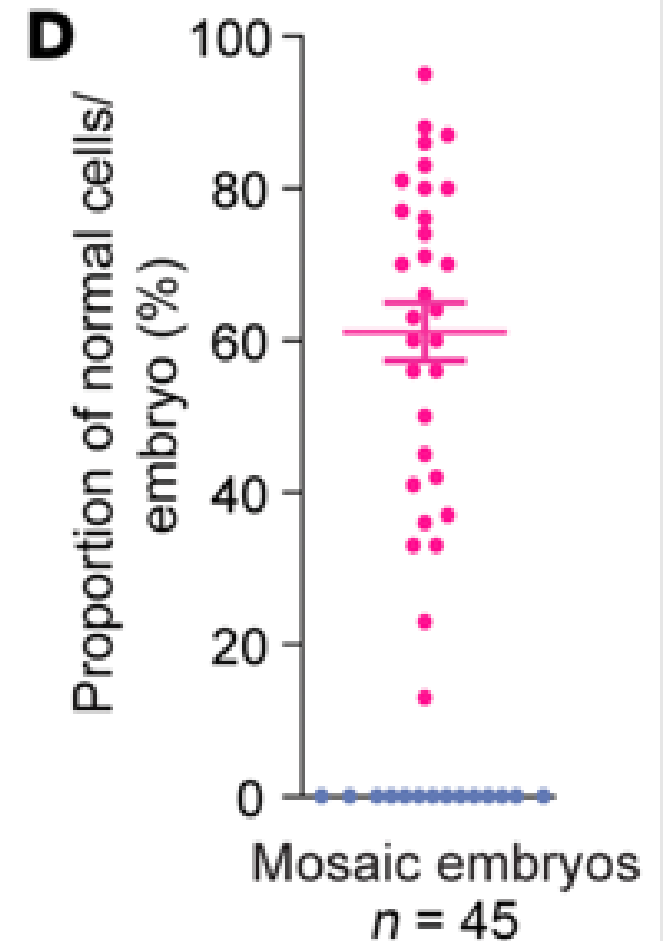
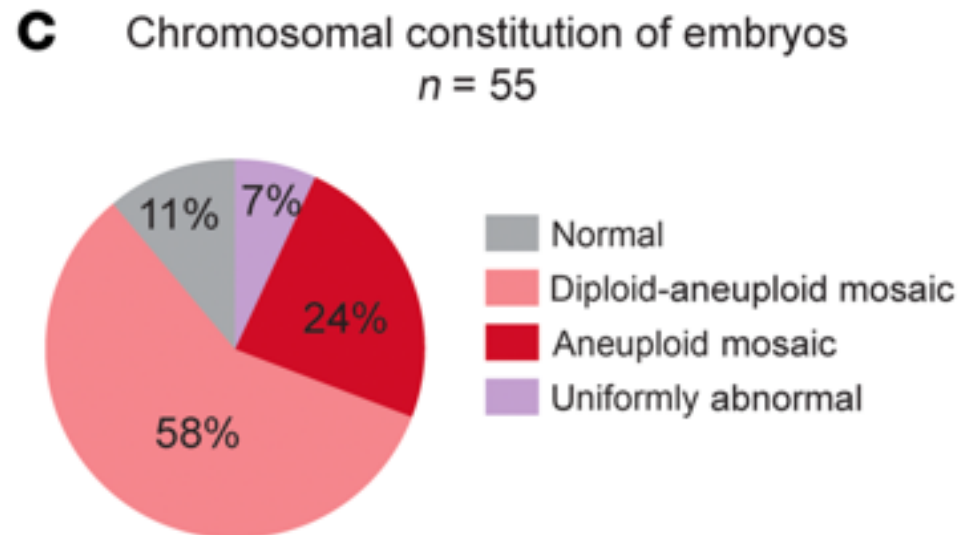
The Journal of Clinical Investigation

RESEARCH ARTICLE

Single-cell DNA sequencing reveals a high incidence of chromosomal abnormalities in human blastocysts

Effrosyni A. Chavli,¹ Sjoerd J. Klaasen,^{2,3} Diane Van Opstal,⁴ Joop S.E. Laven,¹ Geert J.P.L. Kops,^{2,3} and Esther B. Baart^{1,5}

¹Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands. ²Hubrecht Institute-KNAW (Royal Academy of Arts and Sciences) and University Medical Center Utrecht, Utrecht, Netherlands. ³Oncode Institute, Utrecht, Netherlands. ⁴Department of Clinical Genetics and ⁵Department of Developmental Biology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands.



Incidence of Mosaic Embryos: Biological

McCoy et al. *Genome Medicine* (2023) 15:77
<https://doi.org/10.1186/s13073-023-01231-1>

Genome Medicine

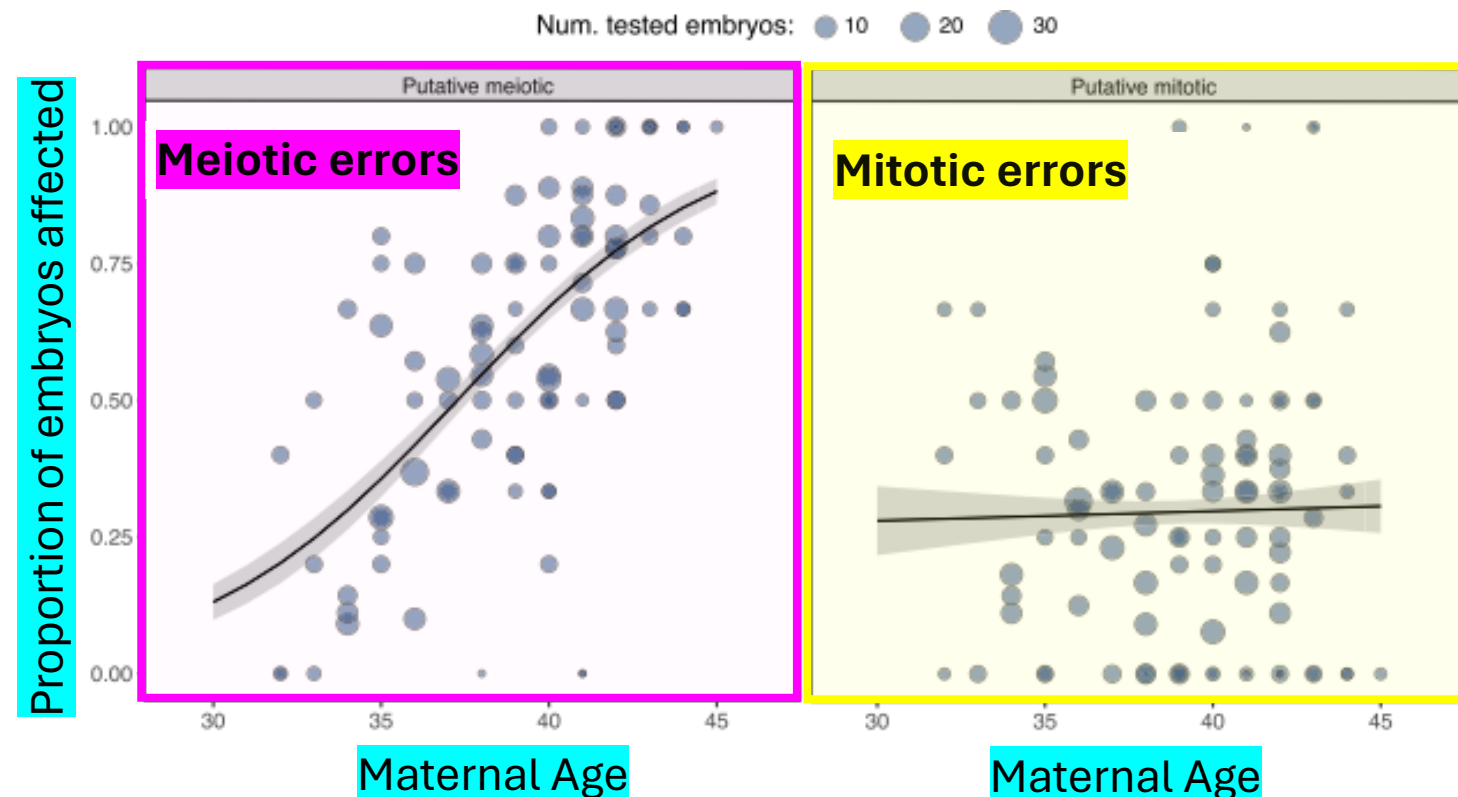
RESEARCH

Open Access

Meiotic and mitotic aneuploidies drive arrest of in vitro fertilized human preimplantation embryos

Rajiv C. McCoy^{1*}, Michael C. Summers^{2,3,4}, Abeo McCollin^{2,3}, Christian S. Ottolini^{2,5,6}, Kamal Ahuja² and Alan H. Handyside³

Incidence of mitotic error not associated with maternal age.



Adapted from McCoy et al, *Genome Medicine* 2023

Incidence of Mosaic Embryos: Biological

McCoy et al. *Genome Medicine* (2023) 15:77
<https://doi.org/10.1186/s13073-023-01231-1>

Genome Medicine

RESEARCH

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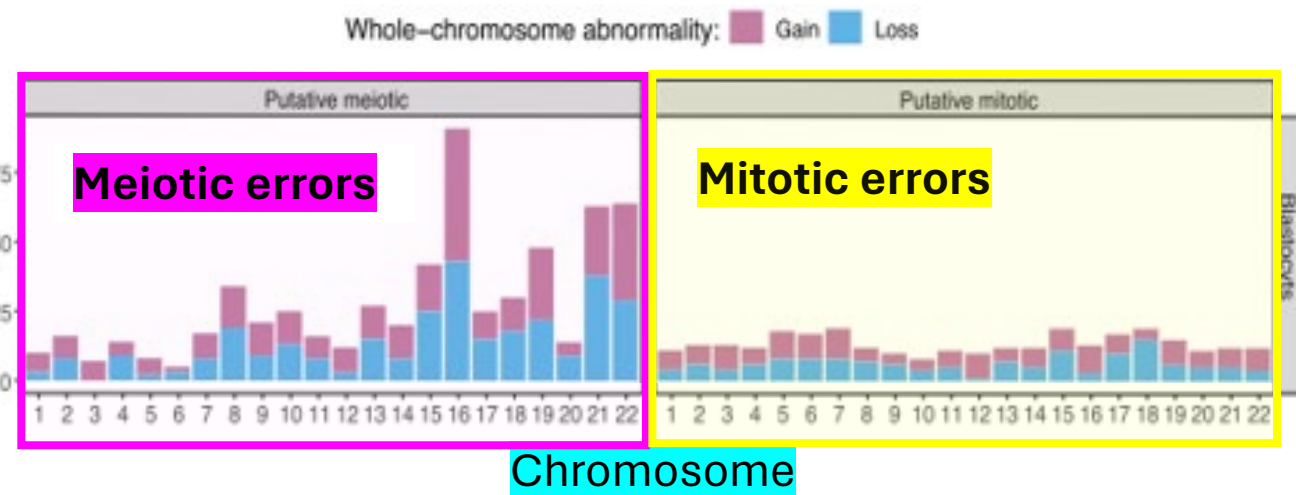
Meiotic and mitotic aneuploidies drive arrest of in vitro fertilized human preimplantation embryos



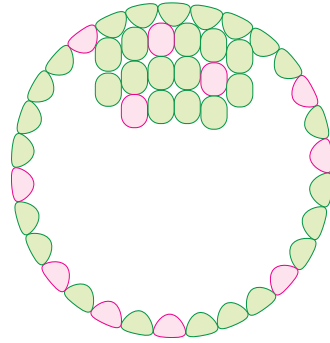
Rajiv C. McCoy^{1*}, Michael C. Summers^{2,3,4}, Aboe McCollin^{2,3}, Christian S. Ottolini^{2,5,6}, Kamal Ahuja² and Alan H. Handyside³

Mitotic errors affect all chromosomes at similar frequencies.

Number of samples affected



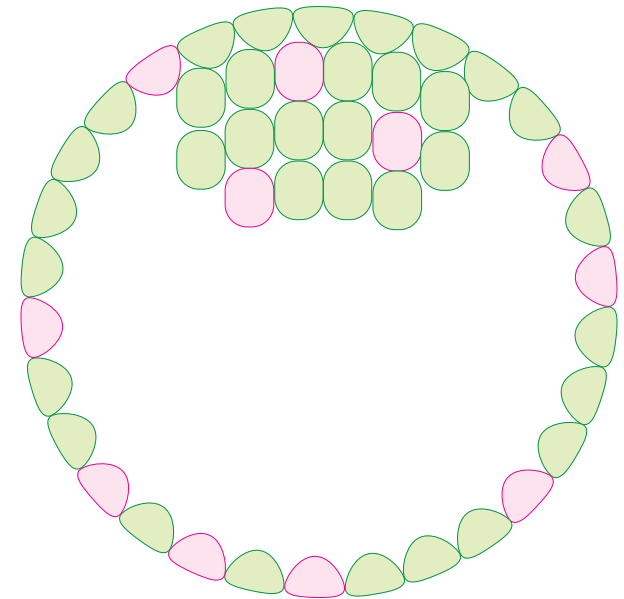
Incidence of Mosaic Embryos



$\sim \leq 100\%$

Overview

- Biological mechanisms of embryonic mosaicism
 - Can mitotic errors be induced?
 - Artifactual mosaic results
 - Incidence of embryonic mosaicism
- Outcomes of mosaic embryo transfers

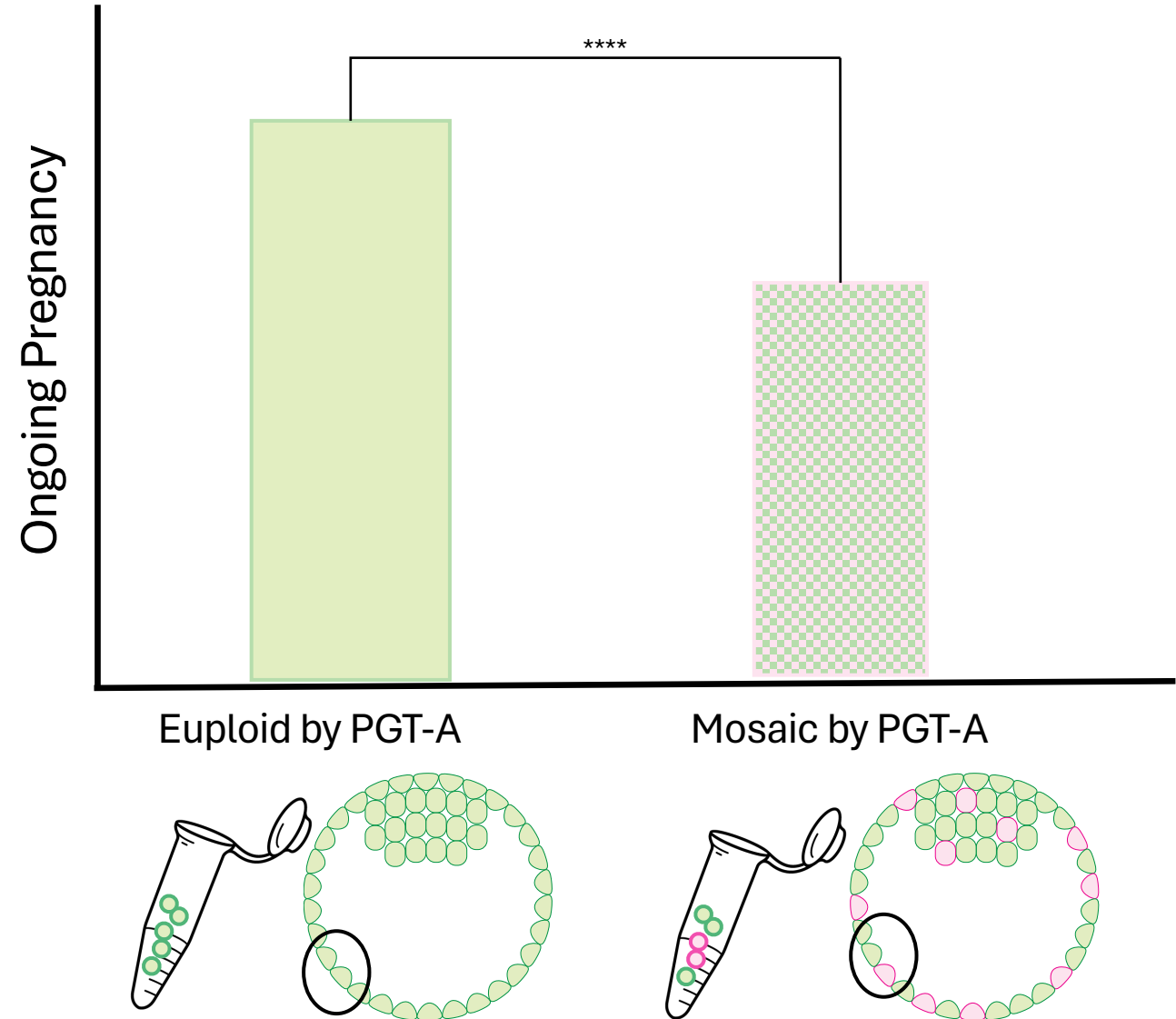


Mosaic embryo transfer

Healthy Babies after Intrauterine Transfer of Mosaic Aneuploid Blastocysts

TO THE EDITOR: Chromosomal aneuploidy is recognized as a factor that contributes to unsuccessful embryo implantation and spontaneous abortion. It provides an explanation for the relatively low success rate of in vitro fertilization (IVF) treatments. Preimplantation genetic screening is widely used to identify chromosomally normal (euploid) embryos and select them for intrauterine transfer in order to improve the clinical outcome of IVF.¹

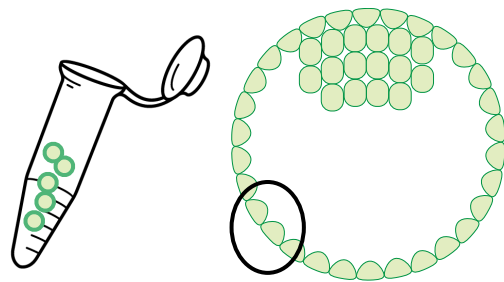
Greco et al NEJM 2015



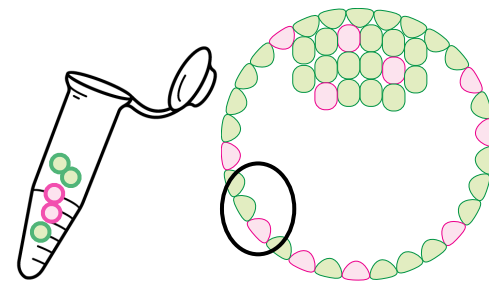
Mosaic embryo transfer



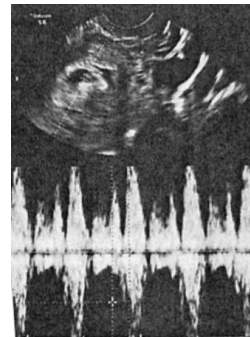
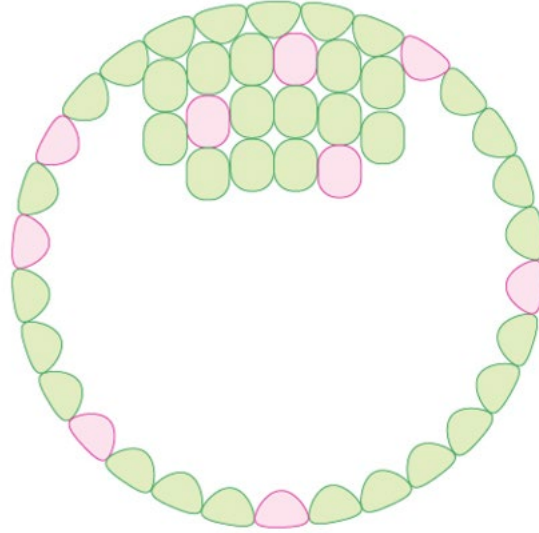
Euploid by PGT-A



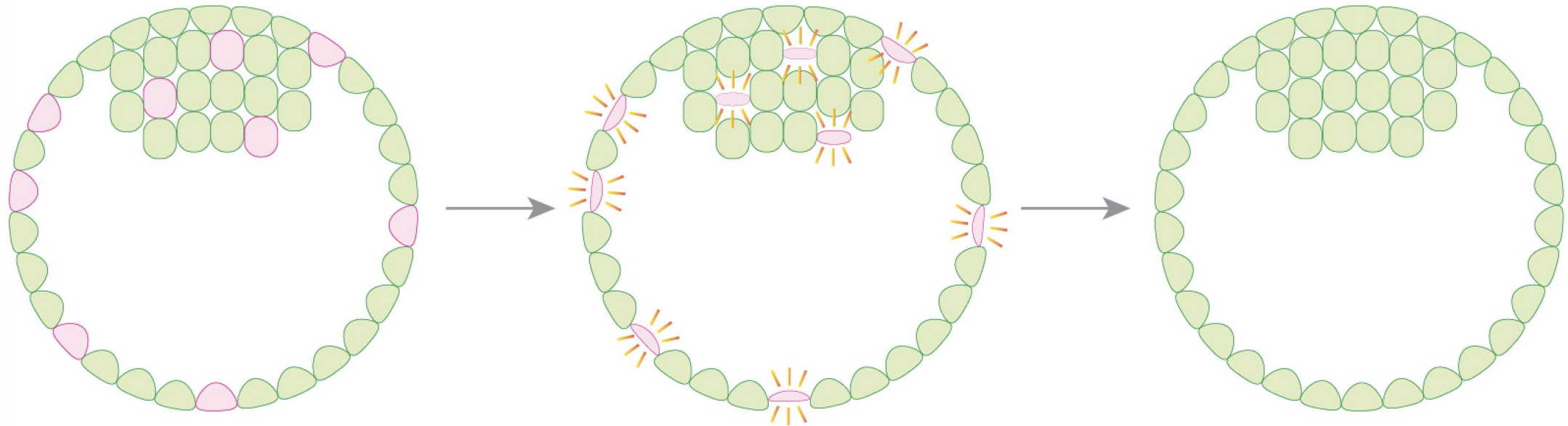
Mosaic by PGT-A



Mosaic embryo transfer



Mosaic embryo transfer: Self correction



Trends in Genetics

Supports open access

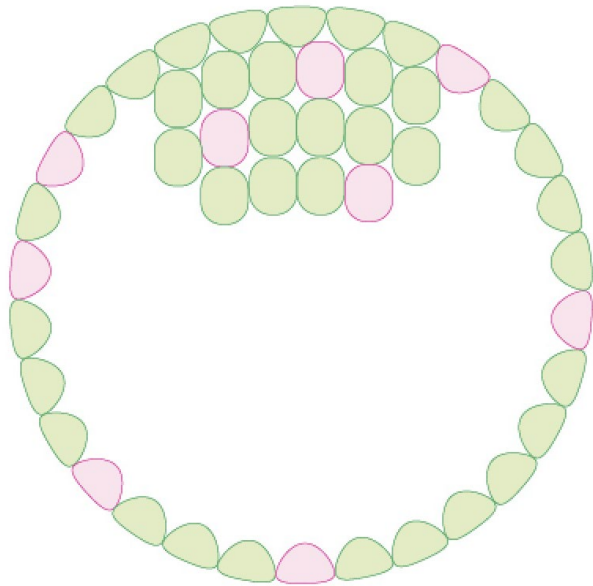
REVIEW | VOLUME 27, ISSUE 11, P446-453, NOVEMBER 2011

The aneuploidy paradox: costs and benefits of an incorrect karyotype

Jason M. Sheltzer • Angelika Amon [✉](#)

Published: August 29, 2011 • DOI: <https://doi.org/10.1016/j.tig.2011.07.003>

Mosaic embryo transfer: Self correction



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 Bolton¹, Sarah J.L. Graham¹, Niels Van der Aa², Parveen Kumar², Koen Theunis², Elia Fernandez Gallardo², Thierry Voet^{2,3} & Magdalena Zernicka-Goetz¹



ARTICLE

<https://doi.org/10.1038/s41467-020-16796-3> OPEN

Autophagy-mediated apoptosis eliminates aneuploid cells in a mouse model of chromosome mosaicism

Shruti Singla¹, Lisa K. Iwamoto-Stohl¹, Meng Zhu¹ & Magdalena Zernicka-Goetz^{1,2}

In mixed euploid-aneuploid embryos:

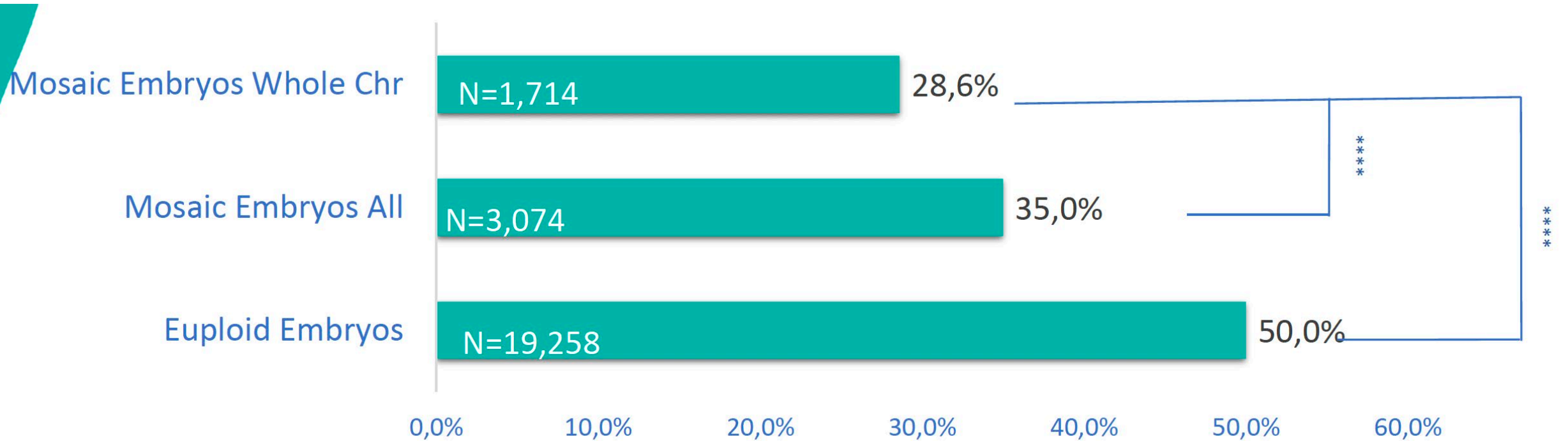
- aneuploid cells undergo preferential cell death or attenuated proliferation
- euploid cells compensate by increasing proliferation
- if the initial load of aneuploid cells is too high, embryo dies

Mosaic embryo transfer: Outcomes

Updated data from

IRMET (International **R**egistry of **M**osaic **E**mbryo **T**ransfers)

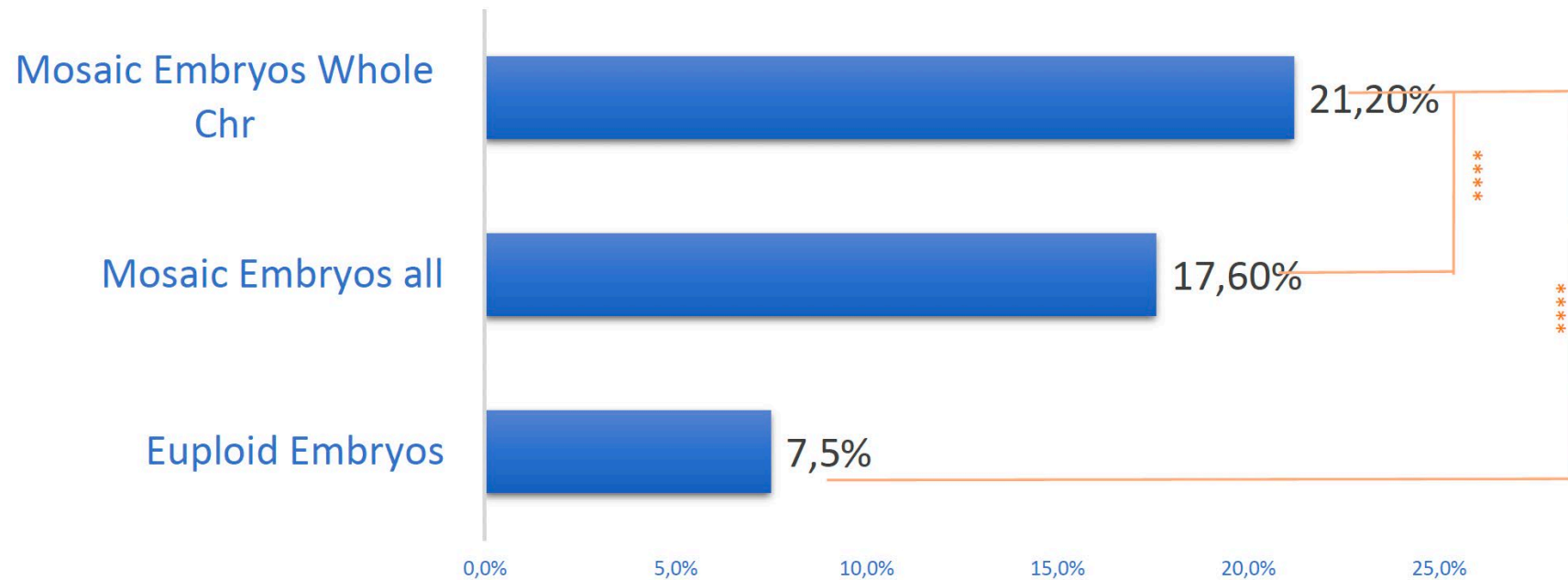
Mosaic embryo transfer: Outcomes



Ongoing Pregnancy/Birth rate

Mosaic embryo transfer: Outcomes

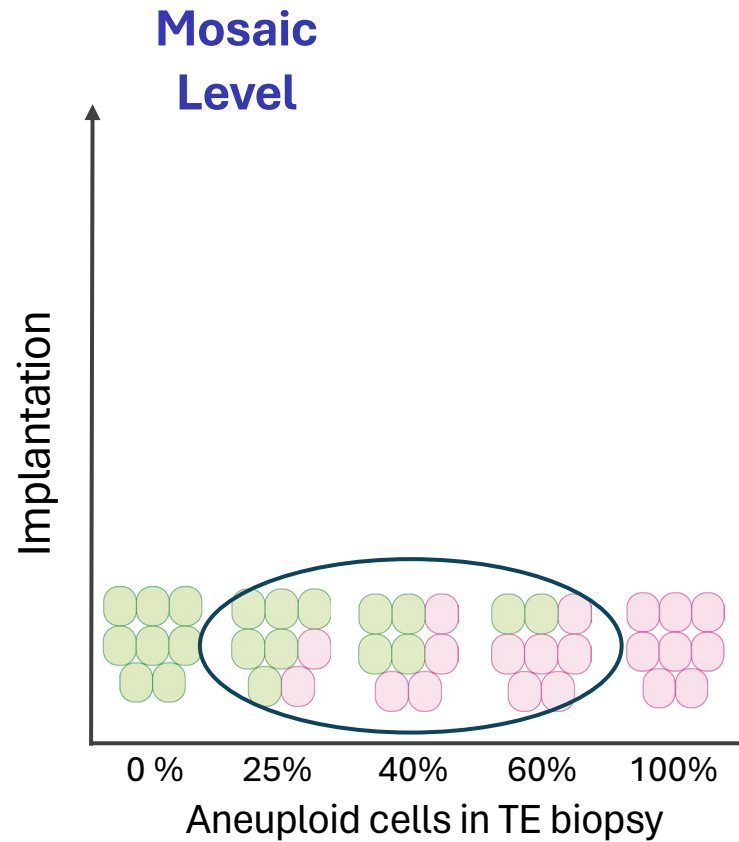
Clinical Outcomes of Euploid vs. Mosaic Embryos



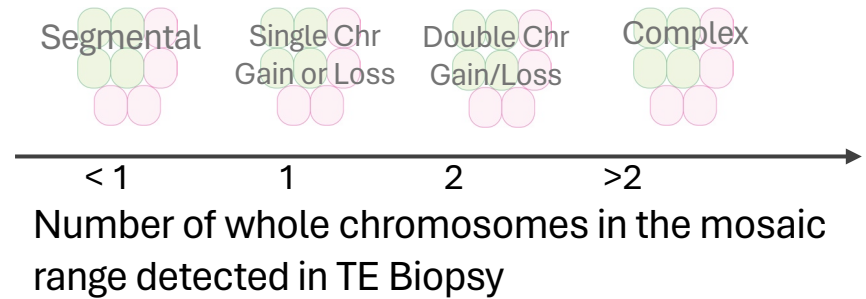
Spontaneous Abortion rate

Mosaic embryo transfer: Outcomes

Mosaic Features



Mosaic Type



Mosaic embryo transfer: Outcomes

Mosaic Level

Low is <50%

High is ≥50%

Mosaic Type

Segmental

One Whole Chromosome

Two Whole Chromosomes

Complex (>2 Chr)

High Complex

N=128

17%

HighOne/Two Chr

N=277

18%

Low Complex

N=268

25%

LowOne/Two Chr

N=1022

34%

High Segmental

N=290

36%

Low Segmental

N=1051

45%

Euploid Embryos

N=19,258

50%

0%

10%

20%

30%

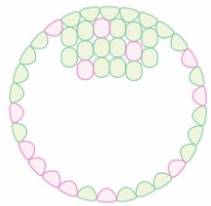
40%

50%

60%

Ongoing Pregnancy rate

Mosaic embryo transfer: Persistent Mosaicism



**Mosaic Embryo
Transfers
~3000**

?



**Persistence
of Mosaicism**

human
reproduction

CASE REPORT *Reproductive genetics*

The birth of a baby with mosaicism resulting from a known mosaic embryo transfer: a case report

Semra Kahraman*, Murat Cetinkaya, Beril Yuksel, Mesut Yesil, and
Caroline Pirkevi Cetinkaya

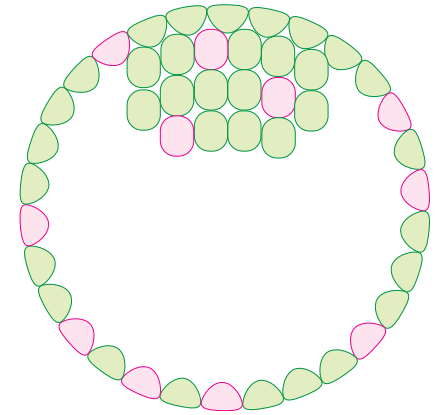
Istanbul Memorial Hospital, Assisted Reproductive Technologies and Reproductive Genetics Center, Piyale Pasa Bulvari 34385, Sisli, Istanbul, Turkey

*Correspondence address. Istanbul Memorial Hospital, Assisted Reproductive Technologies and Reproductive Genetics Center, Piyale Pasa Bulvari 34385, Sisli, Istanbul, Turkey. E-mail: semkahraman@gmail.com

Submitted on November 25, 2019; resubmitted on December 18, 2019; editorial decision on December 29, 2019

ABSTRACT: Mosaic embryos have the potential to implant and develop into healthy babies. The transfer of mosaic embryos is now considered to be a possible option for women undergoing ART with preimplantation genetic testing for aneuploidies and in the absence of euploid embryos, particularly those with diminished ovarian reserve and/or advanced maternal age. It can aid in avoiding the discard of potentially viable embryos, which might otherwise result in healthy babies. In over 500 studies on mosaicism, there have been no reports of mosaicism in babies born following the transfer of mosaic embryos. Here, we present a case report of a 39-year-old woman with diminished ovarian reserve with only one blastocyst available for trophectoderm biopsy. The transfer of the embryo, which showed 35% mosaicism of monosomy 2, resulted in pregnancy. Amniocentesis revealed a mosaic trisomic $\text{mos}46,XX(98)/47,XX,+2(2)$ karyotype. There were no pathological findings in detailed ultrasonography, and the fetus showed a normal fetal growth with no evidence of intrauterine growth retardation. A healthy female baby was born at Week 37. The peripheral blood chromosome analysis validated with fluorescence *in situ* hybridization showed 2% mosaic monosomy 2 [$\text{mos}45,XX,-2(2)/46,XX(98)$]. This is the first reported case of true fetal mosaicism resulting in a live birth following the transfer of a known mosaic embryo. Worldwide, prenatal diagnosis has shown the depletion of mosaicism in embryos transferred after they have been reported as mosaics. Our case demonstrates the need for close prenatal monitoring and diagnosis by early amniocentesis, preferably at > 14 weeks gestation.

Review



THANK YOU



Andrea Victor
avictor@rmaliivf.com