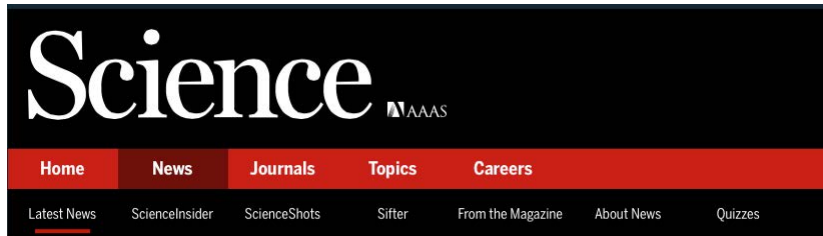


Developing a Pathway

- **Scientific imperative and limits of control**
- **Demand of unmet clinical need**
 - real or imagined
- **Poorly understood science and greed of some practitioners**
 - money or fame



Replacing the mitochondrial genome to overcome genetic disease & infertility



SHARE



Fertility specialist John Zhang holds the newborn baby (face blurred for privacy).

New Hope Fertility Center

Meet the world's first 'three-parent baby': Boy - delivered by US medical team in Mexico - carries a tiny piece of genetic code from a third donor 'parent' to avoid inheriting a disease from his mother

- Three-person baby technique lets parents with genetic mutations edit the mother's egg so they can have a healthy baby

First baby born using 3-parent technique to treat infertility

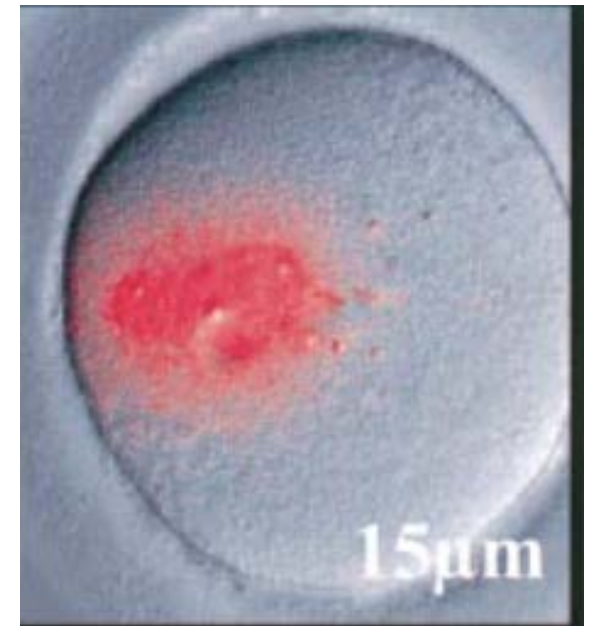
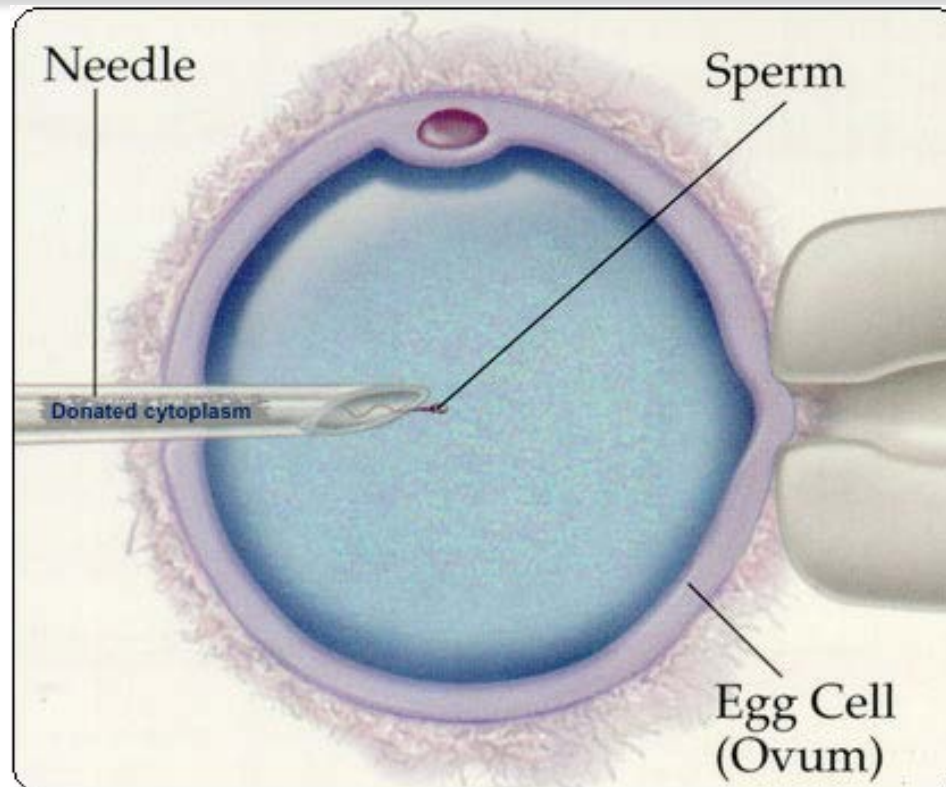


Clinic director Valery Zukin holding the baby girl
Nadiya Clinic

Ooplasmic transfer in mature human oocytes

Jacques Cohen^{1,4}, Richard Scott¹, Mina Alikani¹, Tim Schimmel¹, Santiago Munné¹, Jacob Levron², Lizi Wu³, Carol Brenner¹, Carol Warner³ and Steen Willadsen¹

¹The Institute for Reproductive Medicine and Science of Saint Barnabas, Livingston New Jersey, USA, ²Department of Obstetrics and Gynecology, Tel Hashomer, Tel-Aviv, Israel, and ³Department of Biology, Northeastern University, Boston, Massachusetts, USA



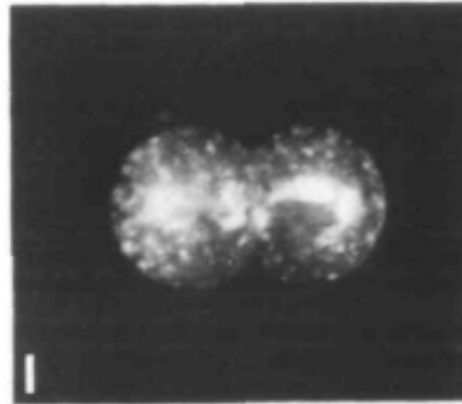
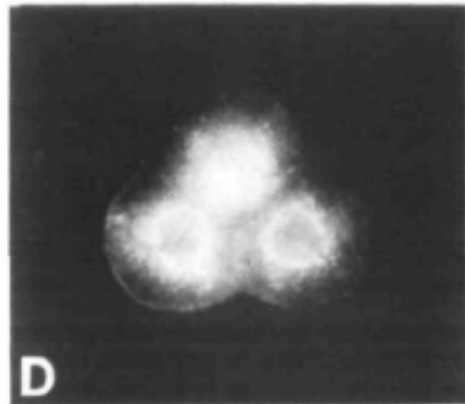
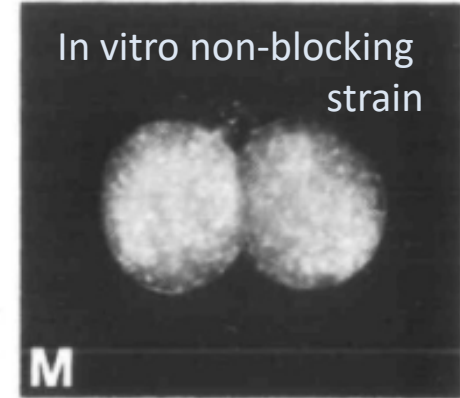
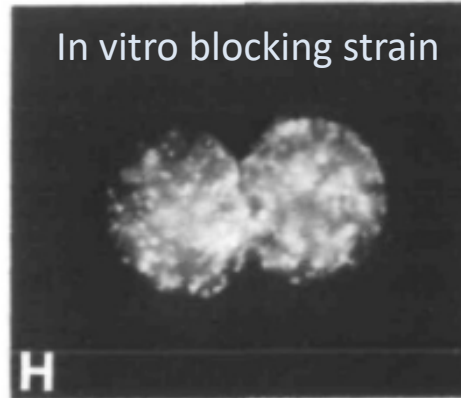
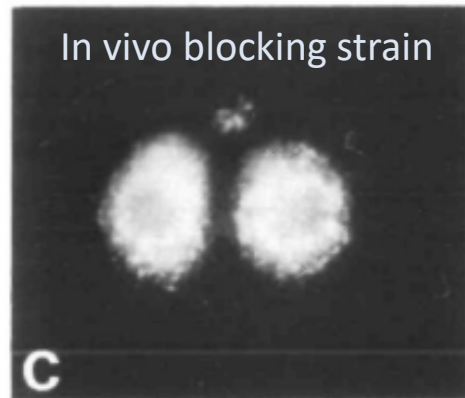
Outcome of 37 attempts of OI at St Barnabas (1996-2001)

<i>Maternal age at cytoplasmic transfer cycle (years)</i>	<i>Number of previous cycles</i>	<i>Number of embryos transferred/fetal heartbeat after cytoplasmic transfer</i>	13 patients pregnant
39.5	4	3/1	17 babies born + 1 preclinical loss (XO)
38.4	6	6/1	
37.6	9	5/1	
30.5	3	4/1	
37.2	3	2/1	
35.7	4	5/2 (1) XO TOP: (2) XX	
31.6	3	4/1	
34.1	6	3/1	
36.5	6	5/2 (1) OI; (2) OD	
33.8	4	6/4	
34.8	10	4/1	
36.6	3	4/1	
36.3	3	4/2	

Control of events during early cleavage of the mouse embryo: an analysis of the '2-cell block'

By MARTIN J. GODDARD AND HESTER P. M. PRATT¹

From the Department of Anatomy, University of Cambridge

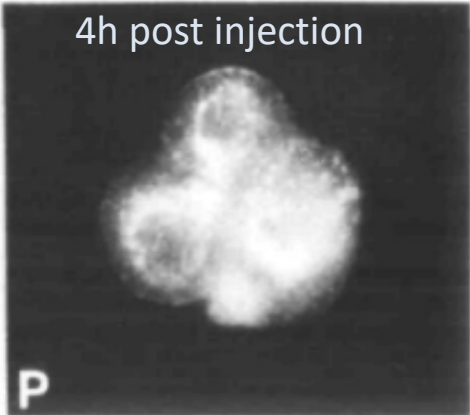
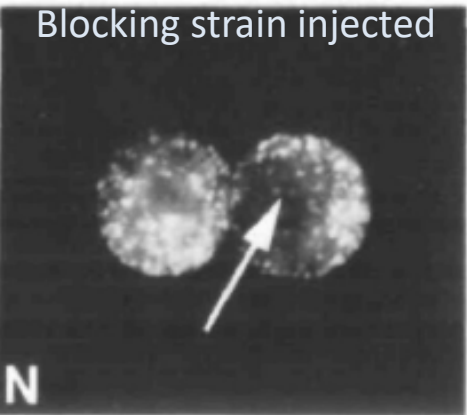
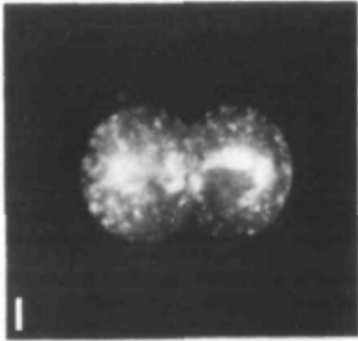
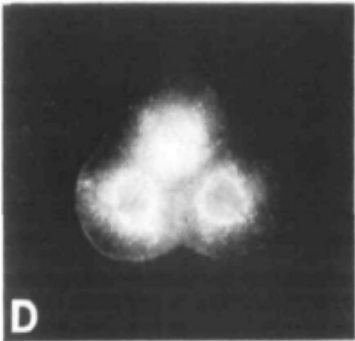
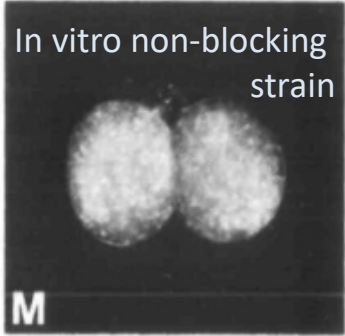
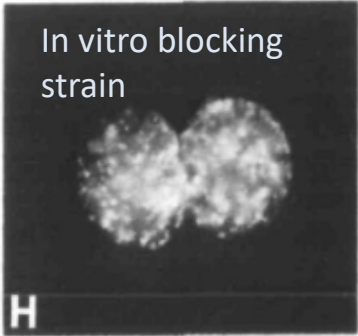
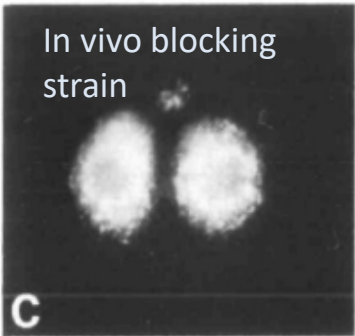


Cytoplasmic factors influence mitochondrial reorganization and resumption of cleavage during culture of early mouse embryos

A.L.Muggleton-Harris and J.J.G.Brown

MRC Experimental Embryology and Teratology Unit, Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey SM5 4EF, UK

Outcome for
Blocking and
Non-Blocking mouse strains



Ooplasmic transfer in mature human oocytes

What factors might be added in OT

Cohen et al MHR 1988

1. Mitochondria from the donor supplement pool of mitochondria
2. Internal pool of inherited (maternal) mRNAs may be boosted
3. Other organelles (ribosomes, proteins, spindle organizing units)
4. Specific consequences by altering a single mechanism
e.g. change in the polarization of mitochondria

“The transfer of small amounts of donor ooplasm (5–15%) probably includes mRNAs, proteins, mitochondria, as well as other factors and organelles”.

Cytoplasmic Transfer Abroad - Medical Tourism Guide

Details of leading clinics and hospitals performing Cytoplasmic Transfer to foreign patients.



Successful Parents Ukraine

Surrogacy & Egg Donations Agency, Ukraine

An agency that coordinates egg donors, surrogacy and fertility treatments in the Ukraine. Provides European egg donors, Ukraine surrogacy services, PGD, and many other services relevant for couples looking to have a child.

[View profile](#)[Request Info](#)

Instituto Bernabeu

Fertility Clinic, Spain

Instituto Bernabeu is staffed by recognised fertility and assisted reproduction specialists. Thousands of patients from over 60 different countries have entrusted Instituto Bernabeu with their dream of becoming parents

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Bahceci IVF Centers, Istanbul, Turkey



Location

Istanbul, Turkey

[Contact Hospital](#)

Bangkok Hospital Pattaya

Private Hospital, Thailand

JCI Accreditation Thai HA Accreditation

This multi-specialty tertiary hospital offers various medical services as well as dental procedures to local and overseas patients. It serves over 100,000 international patients every year.

[View profile](#)[Request Info](#)

Lived fertility specialist:



Dr. Bancho Kankuan

Gynaecology and Obstetrics, Reproductive Medicine

Prices

Procedure	Prices
Cytoplasmic Transfer	upon request



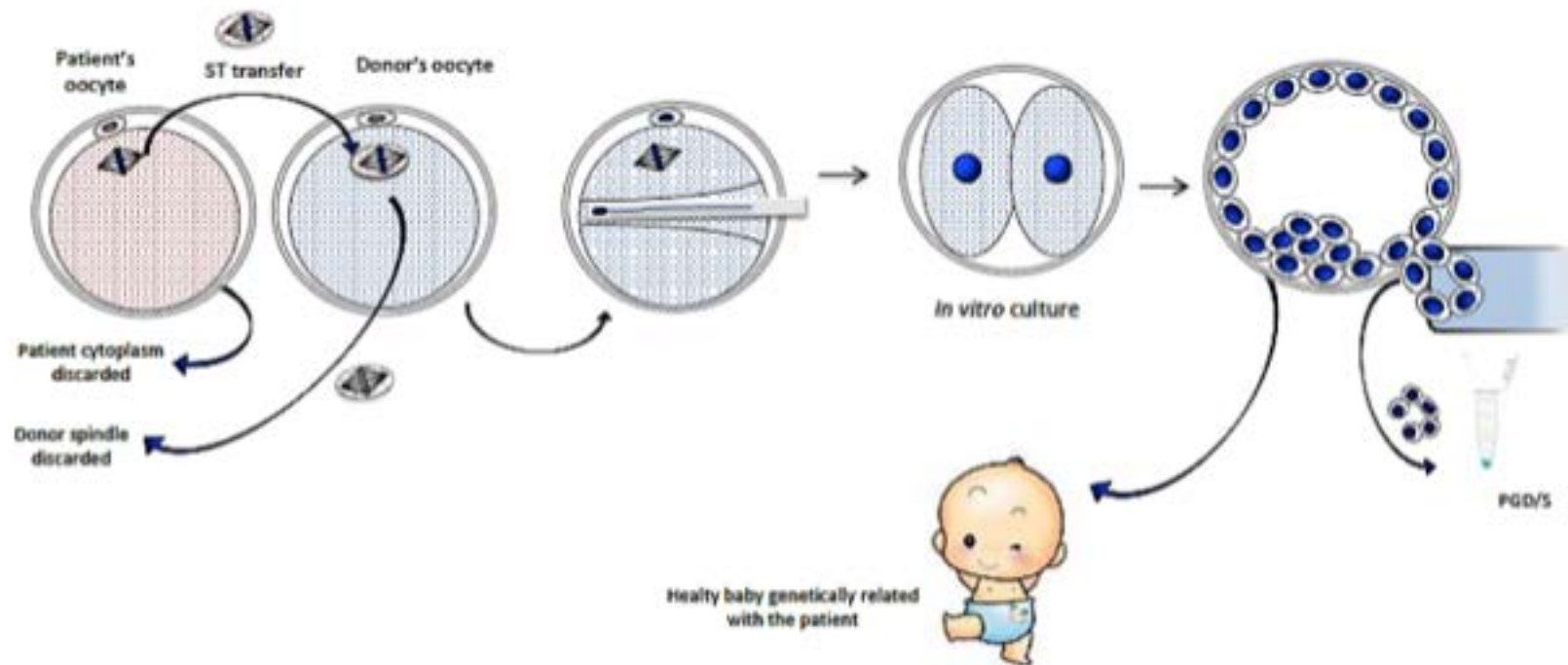
Cytoplasmic Transfer FOR INFERTILE COUPLES

Published on November 23, 2015

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Best IVF treatment in Chennai, Fertility Doctors in Chennai at Pras...



Spindle transfer (ST)



17.01.2019

Researchers from the Spanish centre [Embryotools](#) –with headquarters in the Barcelona Science Park (Parc Científic de Barcelona, PCB) – are participating in a landmark scientific event in Greece that will shape the future of assisted reproduction. In a pilot clinical trial conducted on women, which is being sponsored by the assisted reproduction centre [Institute of Life](#) in Athens, Spanish scientists have achieved the world's first pregnancy that uses the Maternal Spindle Transfer technique to solve problems of infertility.

MITOCHONDRIAL REPLACEMENT THERAPY GIVES NO BENEFITS TO PATIENTS OF ADVANCED MATERNAL AGE



DARWIN LIFE
NADIYA

KYIV, UKRAINE

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YEREM VESELOVSKIY, MD,
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PROMETHEUS MEDICAL,
Kyiv,
CHIEF OF REPRODUCTIVE MEDICINE
"NADIYA"
Kyiv, Ukraine



1. OBJECTIVE:

To determine if mitochondrial replacement therapy (MRT) could increase blastulation rates, euploidy rates and pregnancy rate in infertile patients of advanced maternal age (AMA).



2. MATERIALS AND METHODS:

30 infertile patients (37-47 years old, mean age was 42±2 years) participated in this study. Five types of MRT (germinal vesicle transfer (GVT), MI spindle transfer (MIST), MI spindle transfer (MIIST), polar body 1 genome transfer (PB1GT) and pronuclear transfer (PNT)) were assisted by HVJ-E cell fusion kit. Intracytoplasmic sperm injection (ICSI) had been performed for all cases. If possible, reverse reconstitutions were done. Embryos obtained after reconstitution were cultured until blastocyst stage in time-lapse incubator, were biopsied for array comparative genomic hybridization (aCGH) or next generation sequencing (NGS) analysis and then were vitrified.



3. DESIGN:

The study period was from December 2015 to November 2018. Patients were informed and consent to possible risks and the experimental protocol was approved by ethics committee of local association of reproductive medicine. Inclusion criteria were: (1) no less than two failed previous IVF attempts, (2) low blastulation rates or recurrent embryo arrest, (3) low number or absence of euploid embryos, (4) age ≥ 37 years.



4. RESULTS:

After performing various types of MRT (efficiencies of NT types were different), 109 zygotes were obtained, that resulted in 34 blastocysts; 3 of which (one per patient) were euploid. One try of elective single embryo transfer (eSET) of thawed embryo was done for each of three patients. Positive hCG level (>100 mIU/mL) and following heartbeating were confirmed only for one patient (42 y.o., PNT group). The healthy baby boy was born on 15th of March 2018 by Caesarean section. After unsuccessful attempt of MRT, one of 30 patients (41 y.o.) had an euploid embryo from conventional aCGH cycle using donor sperm and the other patient (45 y.o.) became spontaneously pregnant and gave birth to a healthy baby at full term.

Contrary, zygotic cytoplasm of woman of AMA were competent enough to support normal embryo development when carry young karyoplasts: there were 47% blastulation rates and 70% euploidy rates for reversely reconstituted zygotes.



CONCLUSION:

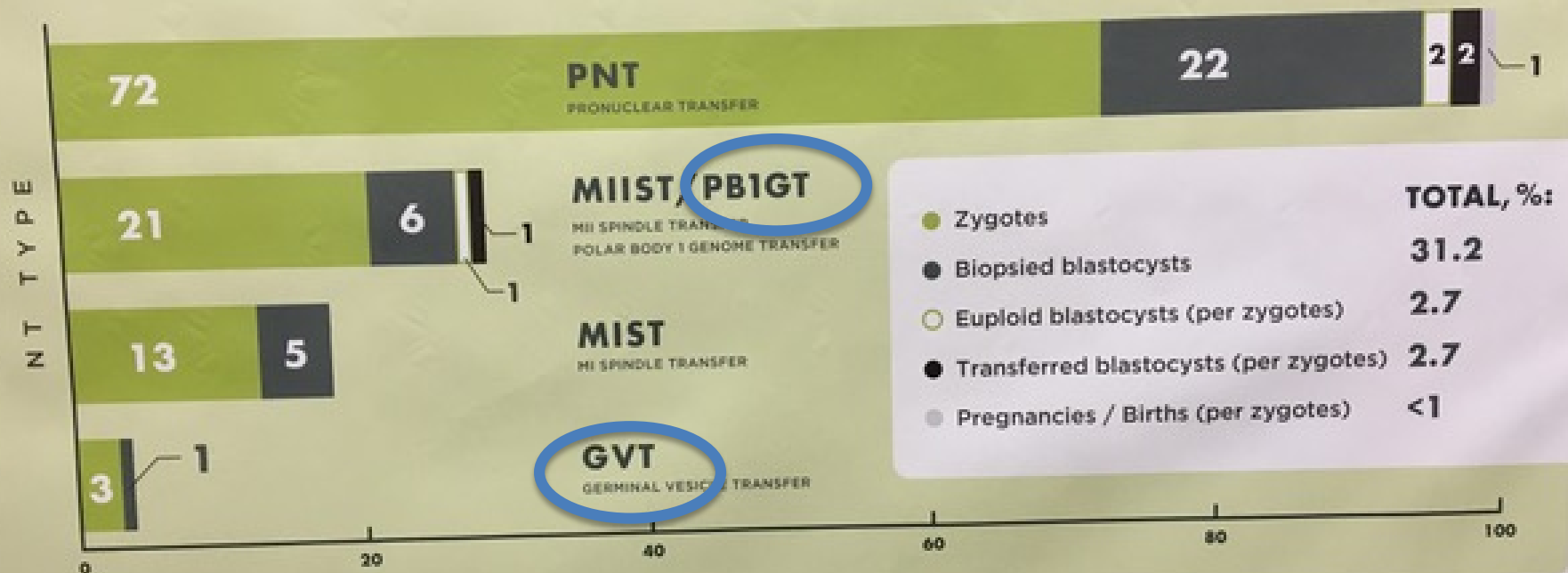
CONCLUSIONS: Although the investigation is limited to obtained zygotes, numbers of euploid embryos and ongoing pregnancies after applying MRT were dramatically low, thereby infertile patients of AMA should be advised not to undergo such procedures in order to increase the number of euploid

embryos or pregnancy rates. Sporadic pregnancies could appear after unsuccessful IVF treatment even in infertile patients of AMA. Further investigations of the efficiency of GVT (and sequential nuclear transplantation GVT-MIIST) and MIST are needed.

assisted by HVJ-E cell fusion kit. had been performed for all cases. If done. Embryos obtained after cyst stage in time-lapse incubator, genomic hybridization (aCGH) or next d then were vitrified.

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embryos or pregnancy rates. Sporadic pregnancies could appear after unsuccessful IVF treatment even in infertile patients of AMA. Further investigations of the efficiency of GVT (and sequential nuclear transplantation: GVT->MIIST) and MIST are needed.

What will users stick to?



Human Fertilisation and Embryology Act 1990

CHAPTER 37

**Forbids
any creation, storage or
use of human embryos
outside the body except
under licence**

LONDON: HMSO

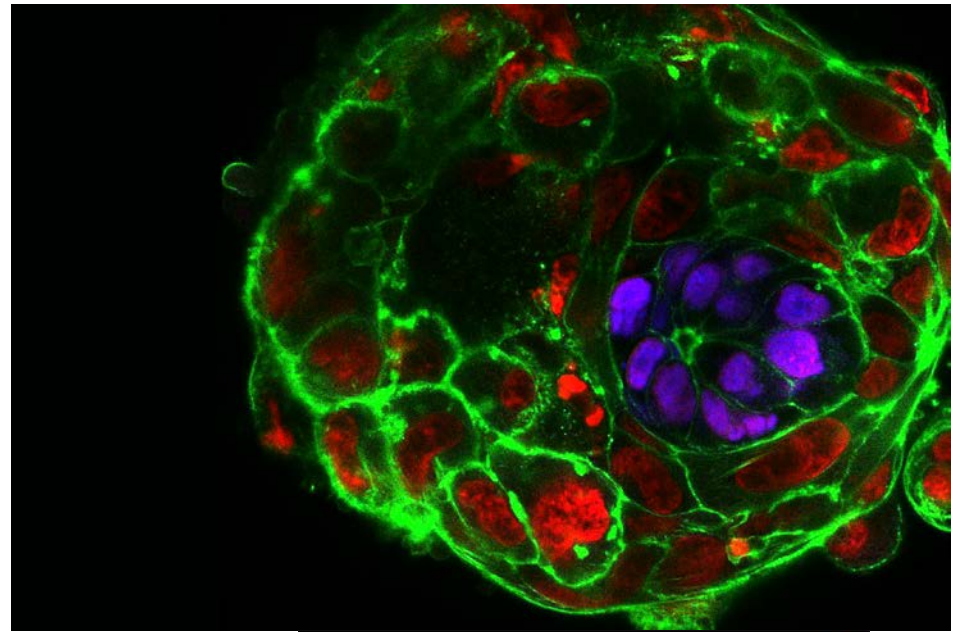
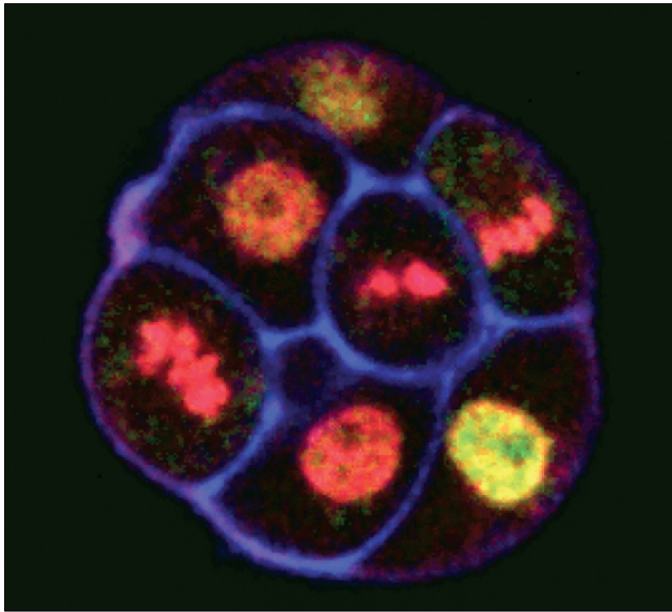
£5.85 net

THE LICENSING AND REGULATION OF HUMAN EMBRYO USE IN THE UK

- for therapy (IVF/DI)
- for cryostorage of gametes and embryos
- for research using embryos in vitro up to 14 days

Breach of the Law is a
criminal offence

Punishable by
2 years imprisonment
a £20,000 fine or both



nature

in

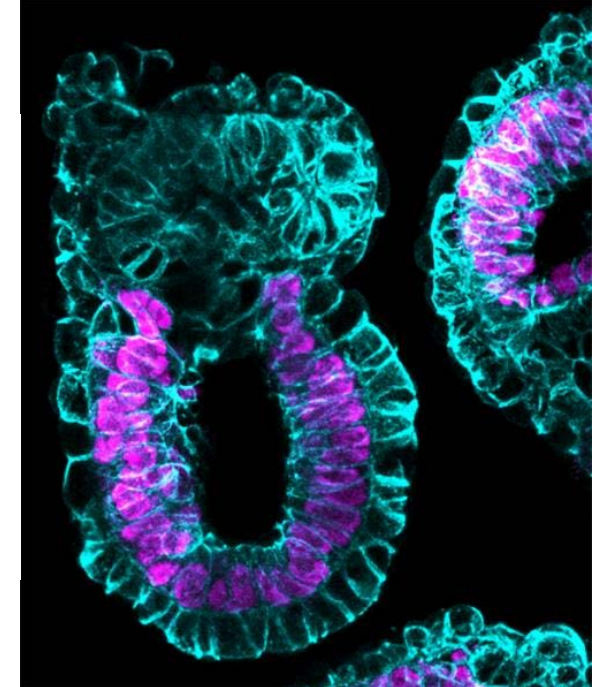
Letter | Published: 04 May 2016

Self-organization of the *in vitro* attached human embryo

Alessia Deglincerti, Gist F. Croft, Lauren N. Pietila, Magdalena Zernicka-Goetz, Eric D. Siggia & Ali H. Brivanlou ✉

Nature 533, 251–254 (12 May 2016) | Download Citation ⌵

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Consistency of approach

1. Why do we want/need to do GGE? What is the goal?
2. How does the commission provide advice when there is already so much variation between states/countries about acceptable ART technology – Embryo research MRT?
3. If we are really concerned about GGE, why is ART unregulated in so many countries (e.g. USA) when ART manipulations may cause epigenetic effects transmissible to the next generation?

What is doable now? What is practical? What is honest?