

“Three-parent Children”: Ethical questions

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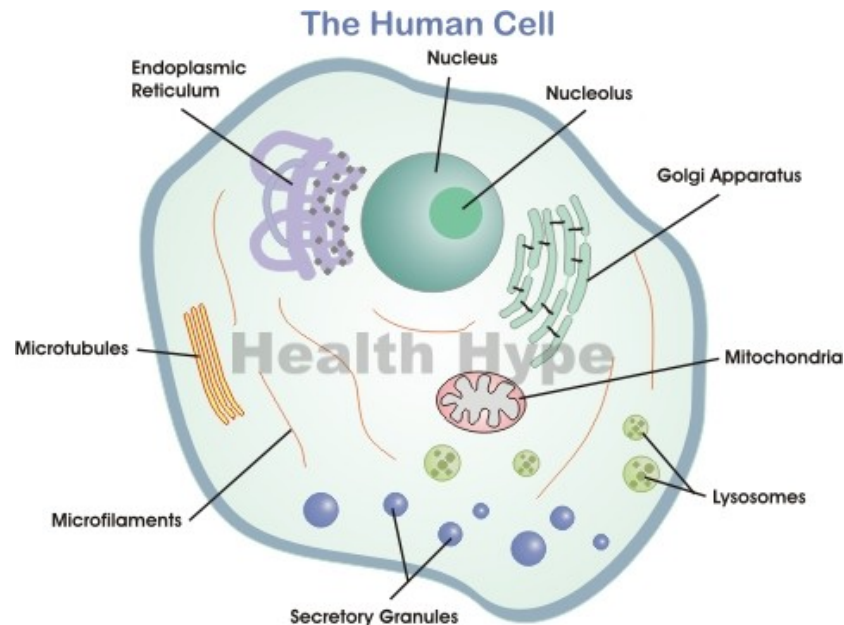


Overview

1. Background Biology
2. Mitochondrial replacement therapy and non-identity
 1. Why might it matter?
 2. Why might the techniques be different
3. Does the argument work?

Background: Biology

We are generally familiar with the DNA that resides in the nucleus of cells, but mitochondria, a cellular organelle, have their own genome





Background: Biology

The mitochondrial replacement therapies replace mitochondria (including mtDNA) from the ovum with diseased mitochondria with the mitochondria (including mtDNA) of a donor.

The resulting child thus inherits DNA from three individuals:

- Nuclear DNA from sperm
- Nuclear DNA from the ova of the person undergoing the treatment
- Mitochondrial DNA from an ova donor

This is where the media phrase ‘three parent’ babies comes from

Background: Biology

CNN

'Three-parent' babies: UK clinic gets OK for groundbreaking technique



By [Laura Smith-Spark](#) and Meera Senthilingam CNN

🕒 Updated 9:45 AM ET, Thu March 16, 2017



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By Mary Papenfuss

REPRODUCTIVE HEALTH

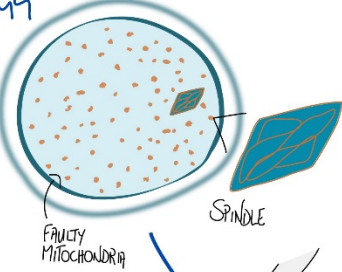
Controversial 'three-parent baby' fertility technique takes off in Mexico City

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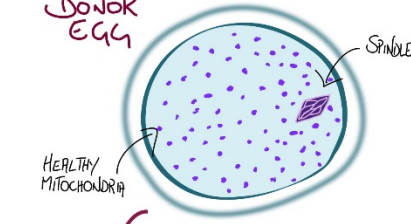
MATERNAL SPINDLE TRANSFER

INTENDING MOTHER'S EGG

DONOR EGG

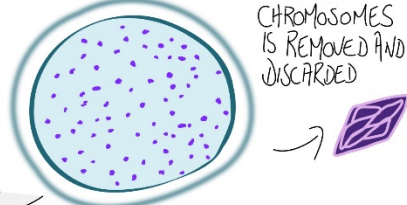


THE SPINDLE OF CHROMOSOMES IS REMOVED AND THE CHROMOSOME-FREE EGG IS DISCARDED



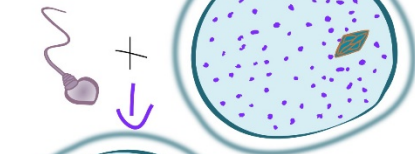
HEALTHY MITOCHONDRIA

THE SPINDLE OF CHROMOSOMES IS REMOVED AND DISCARDED



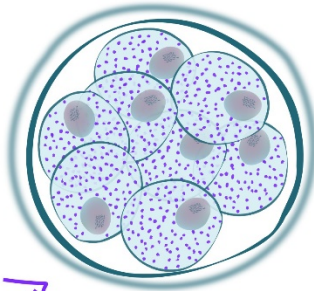
THE SPINDLE IS PLACED INTO THE ENUCLEATED DONOR EGG. IT NOW CONTAINS THE INTENDING MOTHER'S NUCLEAR DNA AND THE DONOR'S HEALTHY MITOCHONDRIA

THE RECONSTRUCTED EGG CAN NOW BE FERTILISED WITH SPERM EITHER FROM THE INTENDING FATHER OR A DONOR



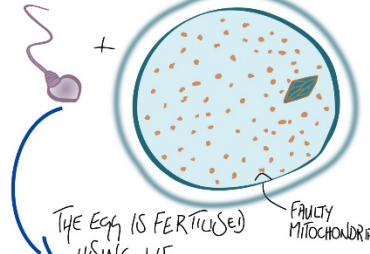
TWO PRONUCLEI

THE RECONSTRUCTED EMBRYO CAN GO ON TO DEVELOP UNAFFECTED BY MITOCHONDRIAL DISEASE

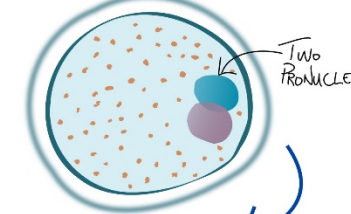


Pronuclear Transfer

SPERM AND EGG FROM THE INTENDING PARENTS

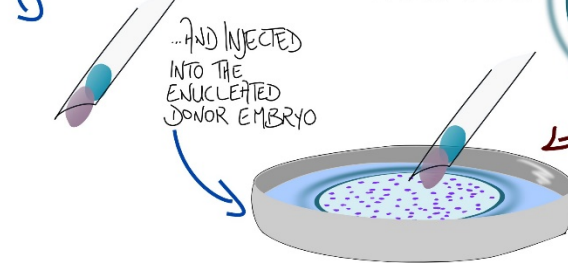


THE EGG IS FERTILISED USING IVF



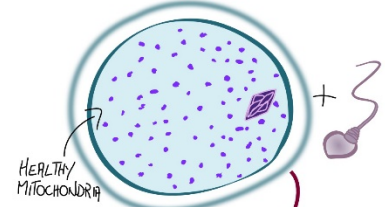
THE TWO PRONUCLEI ARE REMOVED ...

...AND INJECTED INTO THE ENUCLEATED DONOR EMBRYO



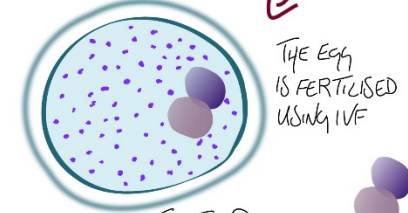
THE RECONSTRUCTED EMBRYO CAN GO ON TO DEVELOP UNAFFECTED BY MITOCHONDRIAL DISEASE

DONOR EGG AND SPERM FROM THE INTENDING FATHER



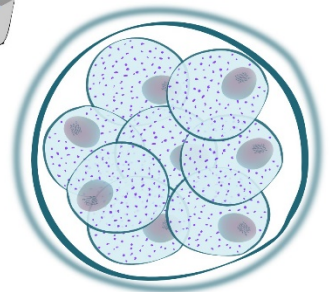
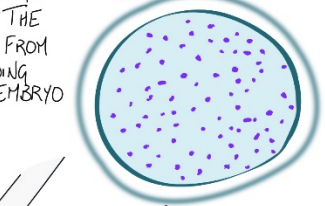
HEALTHY MITOCHONDRIA

THE EGG IS FERTILISED USING IVF



THE TWO PRONUCLEI ARE REMOVED AND DISCARDED

LEAVING THE ENUCLEATED EMBRYO READY TO RECEIVE THE PRONUCLEI FROM THE INTENDING PARENTS' EMBRYO



Background: Biology

Key differences:¹

	nDNA	mtDNA
Size/location	Nucleus, 20,000 – 30,000 genes	Mitochondria, 37 genes
Ubiquity of gene products	Universal	All but one constrained to mitochondria ²
Copies per cell	1	1000s
Inheritance	Paternal and maternal	Strictly maternal*
Variation within organism	Almost none	Universal heteroplasmy ³

1. Taylor, Robert W., and Doug M. Turnbull. "Mitochondrial DNA mutations in human disease." *Nature Reviews Genetics* 6.5 (2005): 389-402
2. Kariya, Shingo, et al. "Effect of humanin on decreased ATP levels of human lymphocytes harboring A3243G mutant mitochondrial DNA." *Neuropeptides* 39.2 (2005): 97-101.
3. Payne, Brendan AI, et al. "Universal heteroplasmy of human mitochondrial DNA." *Human molecular genetics* 22.2 (2013): 384-390.



Some questions

- Is there an obligation to use a mitochondrial replacement technique?
- Is one form of the techniques more preferable to the other?



Why non-identity might matter

- Duty to treat illness vs select a child that is better off
 - It is uncontroversial that reproducers have a duty to treat illness!
 - If one form of treatment preserves identity, then we might think of it as prenatal *treatment* → Obligation
- Worries about genetic selection
 - If one preserves identity, then it isn't selection! It's treatment!



Are the two different with respect to non-identity?

- According to Wrigly, Apleby and Wilkinson, YES!
- PNT preserves identity!
 - We can choose to go through with the treatment or not
 - In either case the resulting person develops from the same chromosomes
 - Thus identity is preserved
- MST
 - Choice to use the treatment determines which gametes fuse, so we have a different person

But wait, there's more

- Lewens argues that matters are not so straightforward
- Think back to Parfit – why is the time dependency claim 30 days?
 - Indeterminate cases!
- Why think that it is chromosomes that matter?
 - Parfit's origins view is about gametes
 - Wrigley et al assume *chromosomal essentialism*
 - There are more to gametes than nuclear chromosomes
 - What about the other features of the donor ova in PNT?
 - → maybe both are identity-affecting!



But wait, there's more

- Lewens argues that matters are not so straightforward
- We can construct MST cases that are similar to PNT cases in terms of preservation of chromosomes
- So what is the takeaway?

“A better line of argument, mindful of what we might call philosophical risk, goes like this. A philosophical conclusion with potential practical import should ideally be robust, in the sense that it follows from any of a variety of plausible premises. Failing that, if a conclusion with practical import follows only from one very specific set of premises, it is important to establish those premises to an adequate level of confidence.”



Some other questions?

- Should we permit the treatment?
 - Is it an effective use of resources?
 - Does it overvalue genetic ties?