

Emerging techniques

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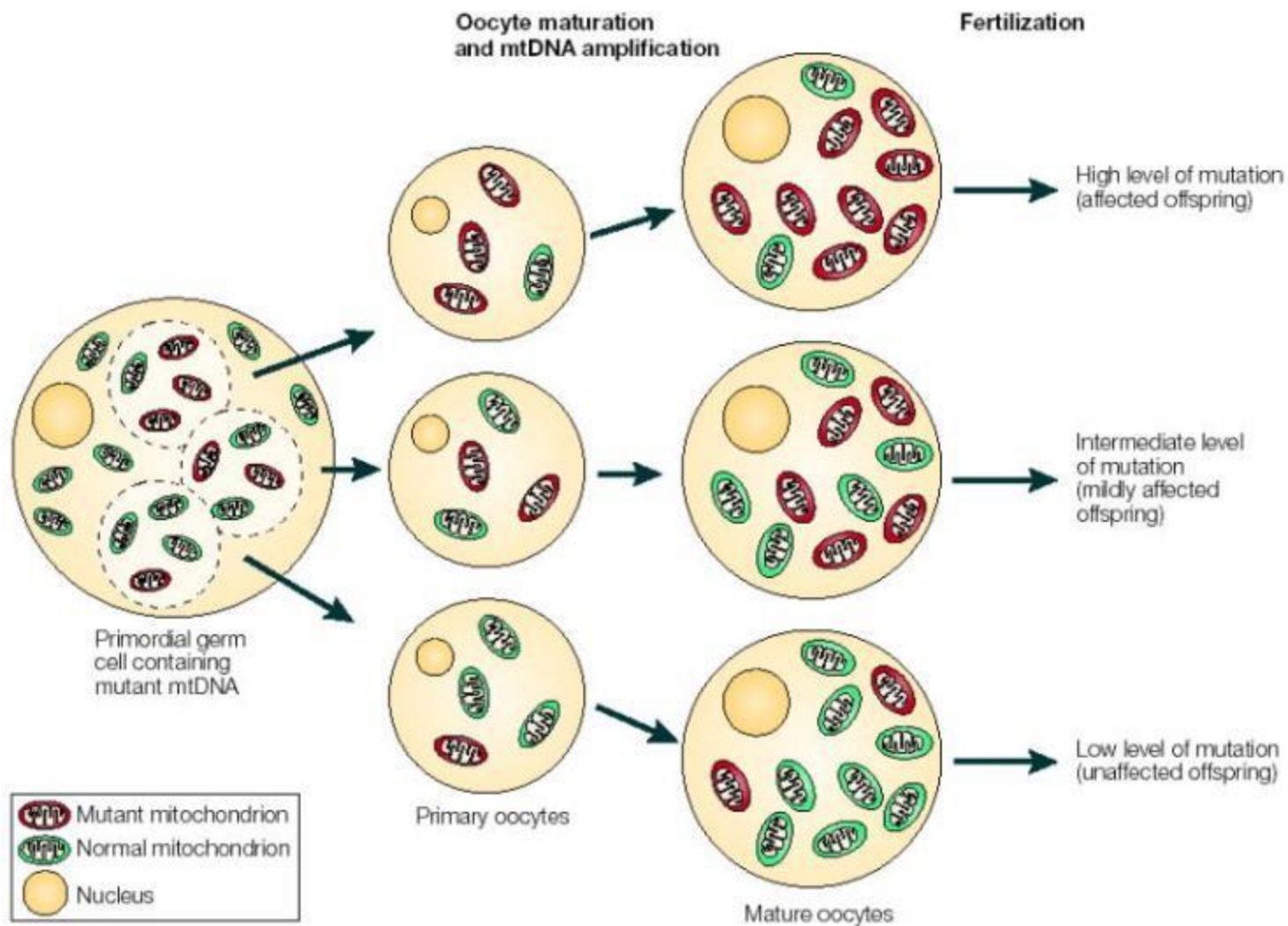
Professor of Clinical Genetics at King's College, London

Options for avoiding transmission (1)

- Remain childless
- Adopt – not genetically related to either parent
- Egg donation - not genetically related to mother

PGD

The problem of heteroplasmy



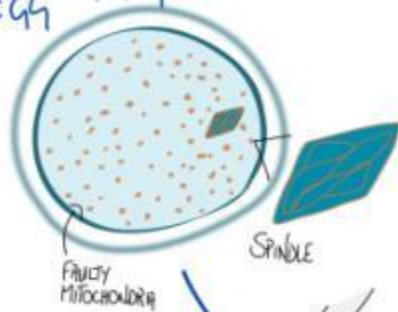
Clinical presentation dependent on proportion of 'bad' mitochondria and also a function of age

Options for avoiding transmission (2)

- Prenatal Diagnosis – possibility of terminating a pregnancy with a significant level of mutated mtDNA
- Preimplantation Genetic Diagnosis – selective transfer of embryo with low % of mutated mtDNA

MATERNAL SPINDLE TRANSFER

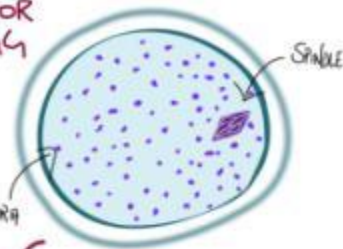
INTENDING MOTHER'S EGG



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

DONOR EGG

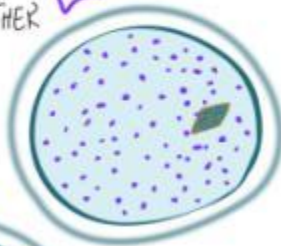
HEALTHY MITOCHONDRIA



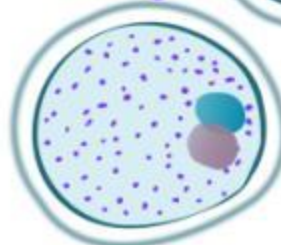
THE SPINDLE OF CHROMOSOMES IS REMOVED AND DISCARDED

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

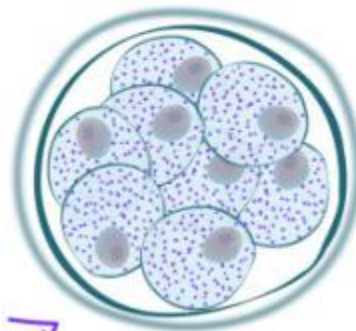
THE RECONSTRUCTED EGG CAN NOW BE FERTILISED WITH SPERM EITHER FROM THE INTENDING FATHER OR A DONOR



Two Pronuclei



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



Maternal spindle transfer (MST)

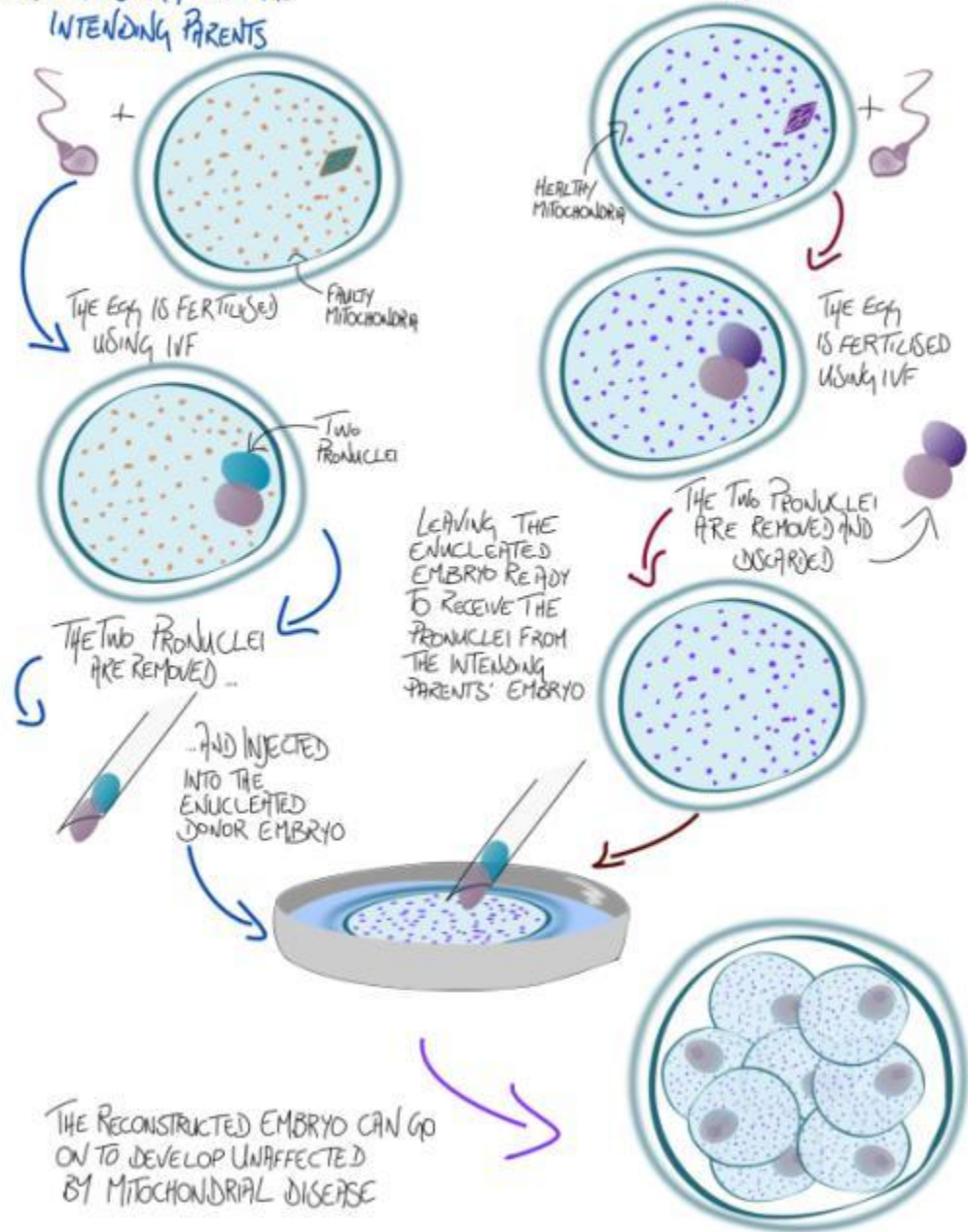
- 2009: Oregon researchers successfully conducted MST on primates, resulting in healthy offspring with no detected carryover of mother's mitochondria
- In collaboration with Oregon, Newcastle University researchers are currently testing MST on human eggs – results yet to be published



Pronuclear Transfer

SPERM AND EGG FROM THE INTENDING PARENTS

DONOR EGG AND SPERM FROM THE INTENDING FATHER



Pronuclear transfer (PNT)

- Experiments in mice since 1990s show reconstructed embryos continue developing after PNT
- 2008: Newcastle University researchers successfully transferred pronuclear DNA between day one single-celled human embryos
- Later experiments show embryos develop normally to blastocyst stage with minimal or no detectable carryover of mother's mtDNA

Other techniques

Important to distinguish PNT and MST from other *in vitro* techniques with germline effects, also unlawful in the UK, such as:

- Cytoplasmic transfer (CT) / ‘ooplasmic transfer’
- Human reproductive cloning and nuclear transfer