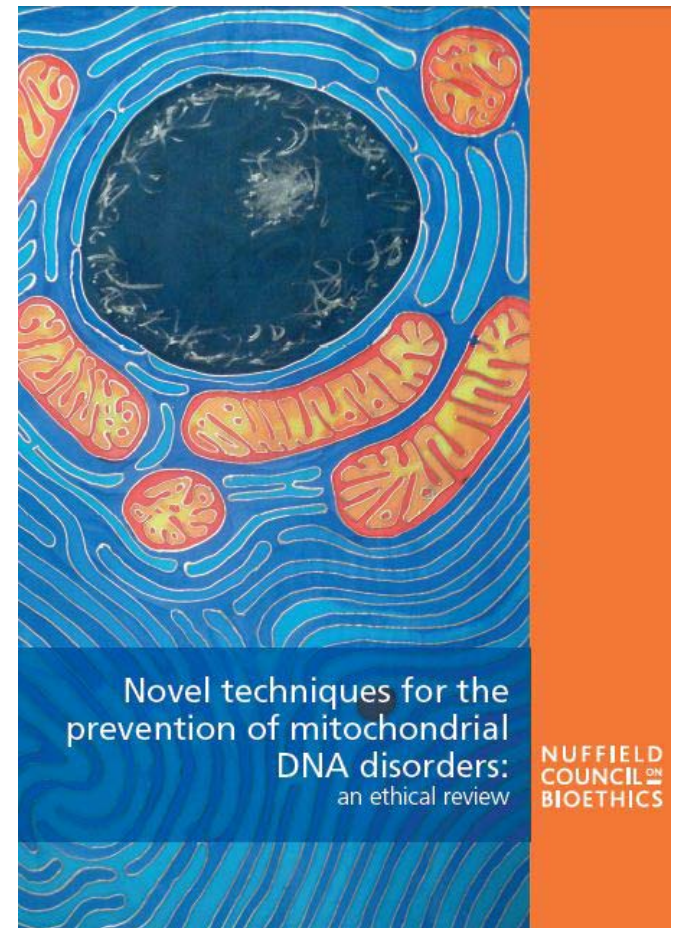


# Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review

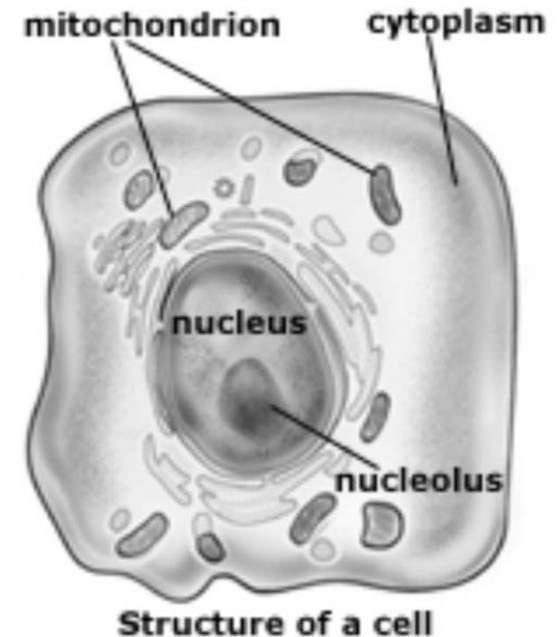
**Dr Tim Lewens**

Member of Council and  
Member of the Working Party  
on mitochondrial donation



# Mitochondria

- **Mitochondria: the ‘batteries of a cell’**
- Contain their own DNA system (mtDNA)
- Maternally inherited
- Mutation rate about ten times that of nDNA



# Mitochondrial DNA disorders

- Inherited genetic disorders caused by mutations in mitochondrial DNA
- Progressive disorders can onset from any age from birth and there is currently no cure
- Can cause debilitating and disabling health problems including heart failure, stroke, blindness, deafness, muscle weakness
- Severe forms can lead to death in early infancy and affect approximately one in 6,500 infants.

# Current options

- **Preventing transmission**
  - Transmission is complex and hard to predict
  - Only definite option is to avoid using own eggs (egg donation, surrogacy or adoption)
- **Minimising risk**
  - Preimplantation genetic diagnosis (PGD)
  - Prenatal diagnosis (PND)

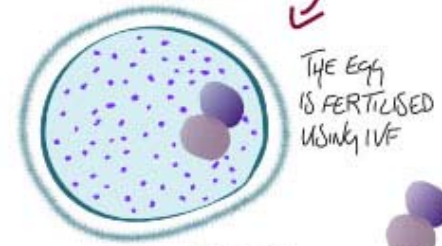
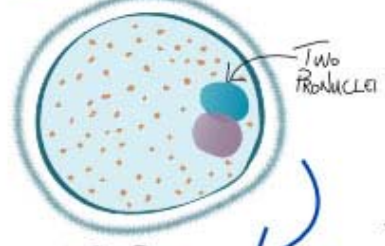
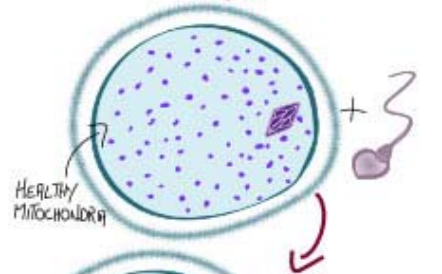
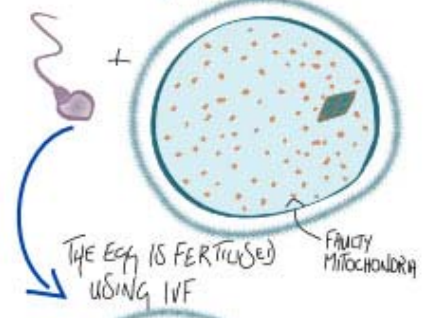
# Novel techniques: the context

- The UK is at the forefront of research on new techniques to prevent transmission
- The techniques are currently unlawful but regulatory-making powers exist that could enable the Secretary of State to permit these techniques in future
- The HFEA started a public dialogue on the issues shortly after we published our report, they will report findings in 2013
- A possible debate in Parliament?

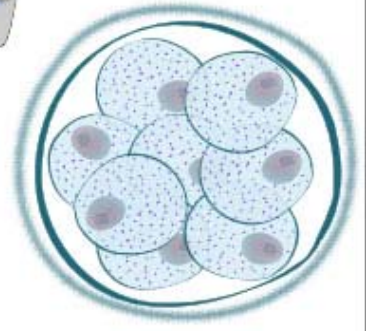
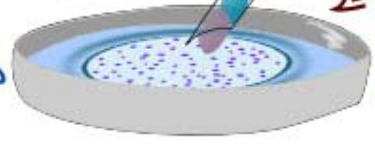
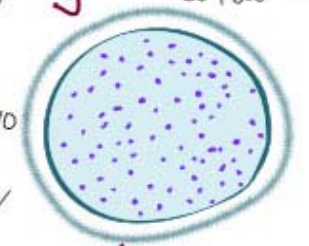
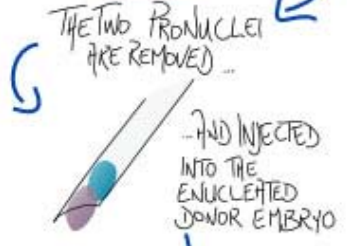
# Pronuclear Transfer

SPERM AND EGG FROM THE INTENDING PARENTS

DONOR EGG AND SPERM FROM THE INTENDING FATHER

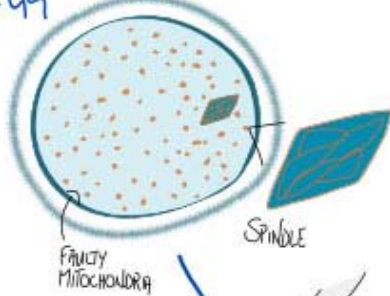


LEAVING THE ENUCLEATED EMBRYO READY TO RECEIVE THE PRONUCLEI FROM THE INTENDING PARENTS' EMBRYO



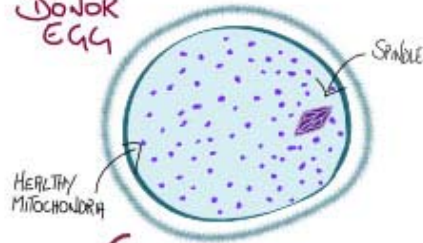
# MATERNAL SPINDLE TRANSFER

INTENDING MOTHER'S EGG

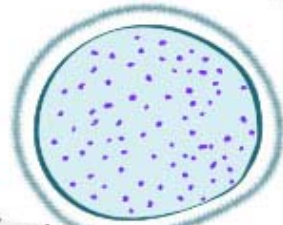


THE SPINDLE OF CHROMOSOMES IS REMOVED AND THE CHROMOSOME-FREE EGG IS DISCARDED

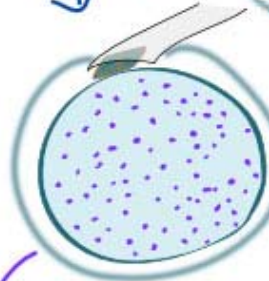
DONOR EGG



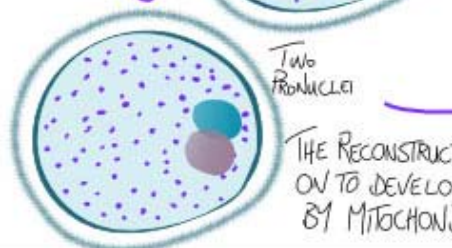
THE SPINDLE OF CHROMOSOMES IS REMOVED AND DISCARDED



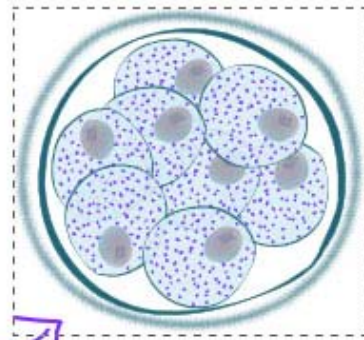
THE SPINDLE IS PLACED INTO THE ENUCLEATED DONOR EGG. IT NOW CONTAINS THE INTENDING MOTHER'S NUCLEAR DNA AND THE DONOR'S HEALTHY MITOCHONDRIA



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



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



# Ethical considerations

## Potential benefits

- Opportunity for parents to have genetically related children
- Children potentially born free from mitochondrial disorders, and descendants of any women born via these therapies

## Ethical questions

- PNT and MST are forms of germline therapy  
→ ‘slippery slope’?
- Uncertainty– potential harm?
- Issues of identity: confused self-image?
- Novel social and family relationships



# Working group conclusions

- If proved safe and effective, and if appropriate information and support is offered, **it would be ethical for families to use these techniques as treatment**
- Subject to appropriate oversight, **it is ethical to gather further information about these techniques** for them to be considered for treatment use

# Further conclusions

## Parentage of the child

- Not legally or biologically accurate to refer to as ‘mother’ or ‘third parent’

## Status of the donor

- Mitochondrial donors should not have same status as donors of egg or embryo for reproduction – e.g. be mandatorily identifiable

## Further conclusions (cont.)

If these techniques are approved for treatment in future:

- **Information and counselling** must be provided
- **Follow up and evaluation** is crucial, could be supported by centrally funded register of all UK procedures
- Should only be offered as part of a clinical trial in **specialist centres**

# Further issues for discussion

- We consider this to be a form of germline therapy
- The wider policy debate could benefit from a fuller discussion of the ethics of the different kinds of prospective and theoretical germline therapies than was possible within the remit of this report

[www.nuffieldbioethics.org/mitochondria](http://www.nuffieldbioethics.org/mitochondria)