Science Media Centre Fact Sheet

Mitochondrial DNA

Mitochondrial DNA (mtDNA) is DNA contained in the mitochondria in our cells - these are the energy-generating structures commonly referred to as the 'batteries' or 'powerhouses' of the cells

Mitochondria have their own genome which is separate from that contained within the cell nucleus - this consists of a circular molecule of DNA, containing the genes necessary for mitochondrial formation - the mitochondria The mitochondrial genome contains around 16,500 base pairs (the nuclear genome contains over 3 billion base pairs) and 37 genes (compared to around 23,000 genes in the nuclear genome).

It is thought to have evolved separately from nuclear DNA, when bacteria containing circular DNA became part of the precursors to cells that exist today - this is shown by the observation of similarities between mitochondrial and bacterial genomes.

Mitochondrial DNA is inherited solely through the maternal side (i.e. from the mother).

Mitochondrial diseases

Mitochondrial diseases are a group of disorders caused by damage to the mitochondrial DNA, or to nuclear DNA that contributes to mitochondrial components. A number of these conditions are associated with mitochondrial myopathy, which feature neuromuscular disease symptoms resulting from failure of the mitochondria to function properly.

Examples of mitochondrial diseases include:

- **Neuropathy, Ataxia, and Retinitis Pigmentosa (NARP)** - a condition consisting of various symptoms affecting the nervous system, including numbness or pain in the limbs (sensory neuropathy), muscle weakness, and problems with balance and coordination (ataxia) as well as deterioration of light-sensing cells I the retina (retinitis pigmentosa).
- **Leigh syndrome** - a progressive degenerative disorder affecting the brain and nervous syndrome which mainly appears in infants during their first year of life.
- **Myoclonic Epilepsy with Ragged Red Fibres (MERRF)** - a rare type of progressive epilepsy characterised by 'ragged red' muscle fibres.
- **Leber's hereditary optic atrophy (LHON)** -- the onset in midlife (average age 30) of painless central visual loss that progresses over a period averaging 4 months, resulting in blindness in both eyes.

They can affect either single or multiple organs, and can appear at any age and with variable frequency. The defects that cause them are transmitted by maternal inheritance, in accordance with the maternal pattern of mtDNA inheritance.

It's important to note that these are not always clearly distinguishable conditions - there may be various symptoms present than can be attributable to more than one disorder, and careful examination may be required to make a diagnosis.

In most cases, the possibilities of treatment are limited, although there are options for managing the conditions.

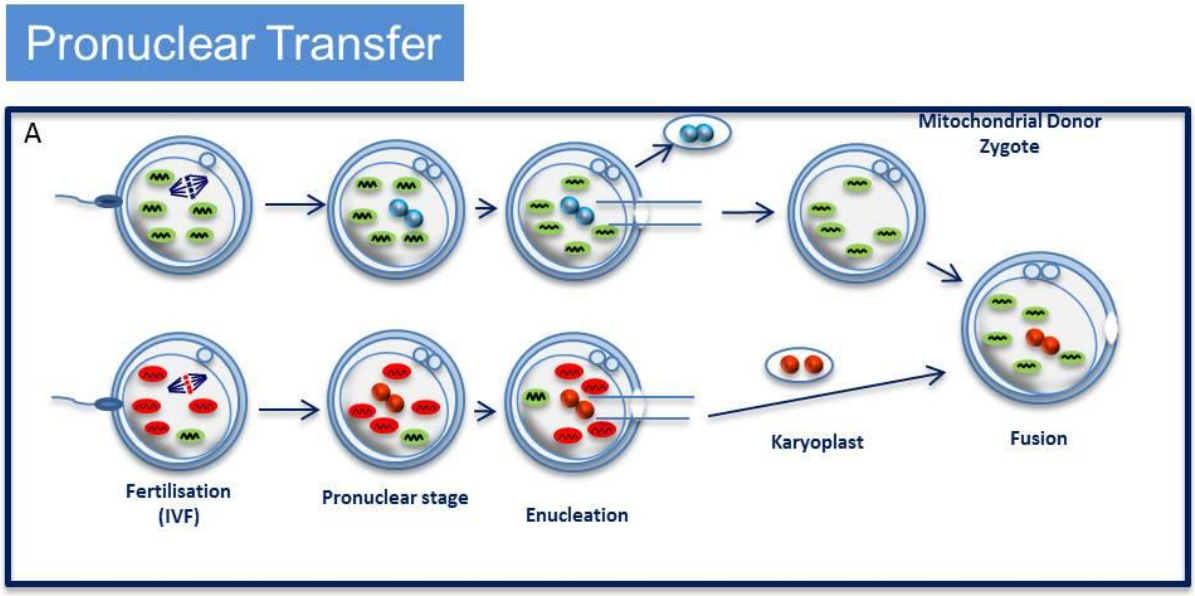
Emerging research on mtDNA

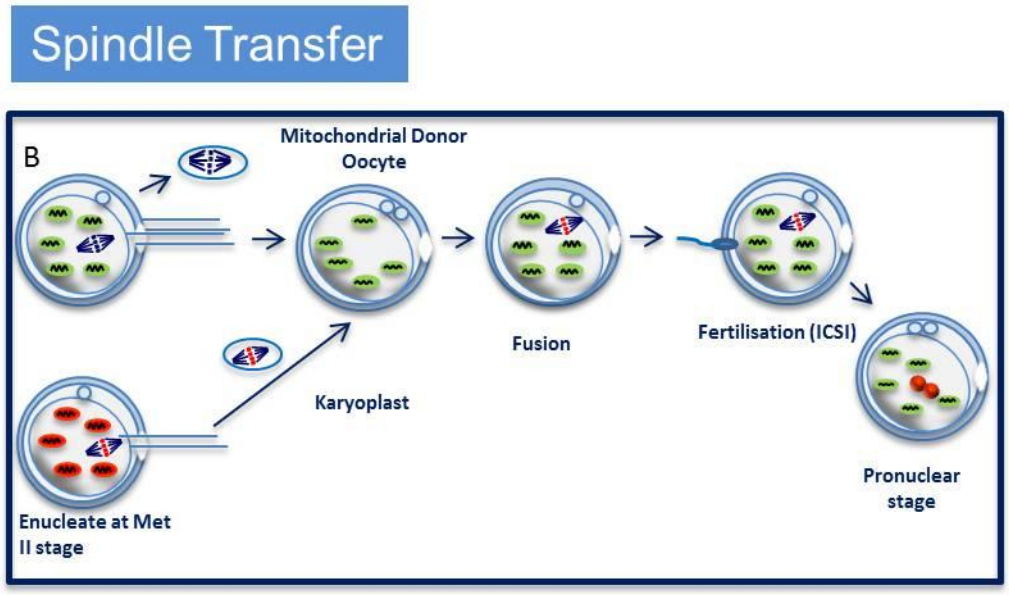
Researchers are working on ways to replace damaged mitochondrial DNA in cells as a means of preventing mitochondrial disease being passed on to the next generation. Research in this area is at a stage where treatments could be offered to parents, although it is tightly controlled. It is permitted by the most recent Human Fertilisation and Embryology Act (2008) and is subject to licensing by the Human Fertilisation and Embryology Authority.

The idea is to be able to extract genetic material (nuclear DNA) from the fertilised egg in which the mitochondrial DNA is damaged, and to insert it into another unfertilised egg obtained from a donor in which the mitochondria are undamaged. The DNA is in the form of two pronuclei - one from the egg and one from the sperm that fertilised it - which exist separately before they fuse to form the nucleus with the full set of chromosomes (one set each from mother and father).

The egg is then allowed to develop *in vitro* with normal mitochondria, as per the (simplified) diagram below.

An alternative emerging technique is **maternal spindle transfer**, whereby the mother's nuclear genetic material (the spindle with the chromosomes attached) is transferred from an unfertilised egg into a donor egg which has had its own nuclear material removed; the reconstituted egg is then fertilised with sperm from the patients partner. This is not dissimilar from **pronuclear transfer** (described above) in that both techniques require donated eggs and involve the transfer of genetic material; but with spindle transfer the extraction of the genetic material takes place prior to fertilisation, whereas pronuclear transfer involves the transfer of the pronuclei after fertilisation has taken place.





Diagrams courtesy of Newcastle University

Sources / further information

HFEA Scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception (2011)
http://www.hfea.gov.uk/docs/2011-04-18_Mitochondria_review_-_final_report.PDF

(the techniques are discussed in Chapter 4, and page 15 has a useful diagram comparing the two techniques discussed above)

Further information about the review is available at http://www.hfea.gov.uk/6372.html

Genetics Home Reference page at the US National Library of Medicine:
http://ghr.nlm.nih.gov/chromosome=MT

Information on NARP:
http://ghr.nlm.nih.gov/condition=neuropathyataxiaandretinitispigmentosa

Wellcome Trust Human Genome page:
http://genome.wellcome.ac.uk/doc_WTD020740.html

US National Institute of Neurological Disorders and Stroke:
http://www.ninds.nih.gov/disorders/mitochondrial_myopathy/mitochondrial_myopathy.htm

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