Q&A: Mitochondrial Donation

About 1 in 200 children in the UK carry a mitochondrial DNA mutation, while around 1 in 6500 children is thought to develop serious mitochondrial disease. The Wellcome Trust Centre for Mitochondrial Research are developing a technique known as mitochondrial donation, which can prevent mitochondrial DNA disease from being passed on from mother to child.

For the technique to be used in patients, the Government must pass new regulations, which are currently being drafted for public consultation. Following the consultation, the regulations will be considered by Parliament and there will be a debate and vote on whether to bring the regulations in. You can contact your local MP to ask them to represent your views on this. If the regulations are approved by Parliament, the intention is that they may be in place by the end of 2014, allowing mitochondrial donation to be used to help patients have healthy children once the science is ready.

What is mitochondrial DNA disease?

1. What are mitochondria?

Mitochondria are small structures found in our cells which generate the energy required to allow our bodies to function (see Figure 1)[1]. They sit outside the nucleus, which houses most of the cell's DNA. Mitochondria also have their own DNA, which makes up about 0.1% of the total cell DNA and does not affect the features that make each person unique, such as appearance and personality.

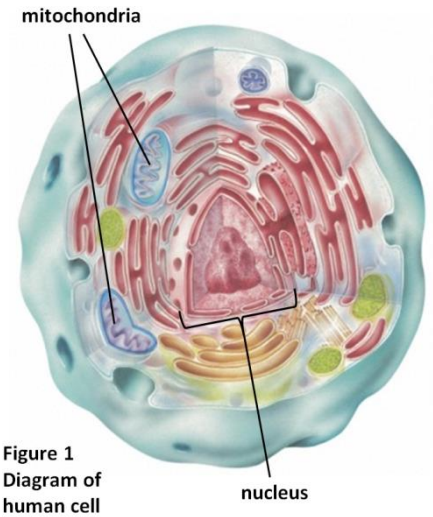

Figure 1
Diagram of human cell

2. What causes mitochondrial DNA disease?

When mitochondrial DNA contains genetic defects, the mitochondria do not work properly, so do not produce enough energy. This results in mitochondrial DNA disease.

Mitochondrial DNA disease is a genetic disease. There are many different genetic defects that can cause mitochondrial DNA disease and therefore symptoms and severity can vary considerably between mitochondrial DNA disease sufferers.

3. What are the symptoms of mitochondrial DNA disease?

Symptoms vary depending on which organs are affected. They can include loss of control over movement, muscle weakness and pain. It can result in heart disease, disorders of the stomach and intestines and disorders of the brain. The severity of mitochondrial DNA disease varies from mild to extremely debilitating, and it can result in death in childhood.

4. Can mitochondrial DNA disease be treated/cured?

[1]Figure 1: 'Diagram of human cell cutaway to show content'. **N0027743**, Miles Kelly Art Library, Wellcome Images. wellcomeimages.org

There is no cure for mitochondrial DNA disease at present. Current treatments aim to decrease the effect of the symptoms but do not change the course of the disease.

5. How is it passed on?

Mitochondrial DNA defects leading to mitochondrial DNA disease are often passed down from mother to child. Those who inherit faulty mitochondrial DNA can develop symptoms or be carriers of the condition without experiencing symptoms, and in both cases they are able to pass the defects on to their children.

What can be done to prevent it?

6. What is mitochondrial donation?

Faulty mitochondrial DNA from a mother's egg can be replaced with healthy mitochondrial DNA from a donor egg. This prevents mitochondrial DNA defects from being inherited, so the child that develops from the egg will not get mitochondrial DNA disease.

7. What techniques are used in mitochondrial donation?

Two techniques can be used for mitochondrial donation:

- **Maternal Spindle Transfer**

Maternal Spindle Transfer involves removing the nuclear DNA (which contains 99.9% of the total cell DNA) from the donor egg, leaving the part of the cell containing the healthy mitochondria. The nuclear DNA from the mother's egg is then inserted into this cell. The healthy egg is fertilised and is then implanted into the mother's uterus in the same way IVF is carried out already.

- **Pronuclear transfer**

Pronuclear Transferis similar to Maternal Spindle Transfer but involves fertilising the mother's egg first and then transferring the nuclear DNA to the fertilised donor egg containing healthy mitochondria, from which the original nuclear DNA has been removed. The healthy fertilised egg is then implanted

into the mother's uterus in the same way as in Maternal Spindle Transfer.

8. How safe are the techniques?

Maternal Spindle Transfer has been successfully performed in monkeys, leading to the birth of healthy offspring. Pronuclear Transferhas been performed in mice and is successful in preventing mitochondrial DNA disease in mice that carry a genetic defect in their mitochondrial DNA. There is no evidence to suggest that a mitochondrial donation pregnancy would be unsafe for the mother or child.

Maternal Spindle Transfer has been used on human eggs and Pronuclear Transfer on human zygotes (fertilised eggs), in both cases leading to the successful development of a bundle of cells (blastocyst). This suggests that they would develop as normal if implanted in the uterus.

It is impossible to say that any new technique would have zero risk. However, scientific reviews of the current research by an Expert Panel in April 2011 and March 2013 found that there was no evidence to suggest that the techniques were unsafe for clinical use. The Department of Health has also asked the HFEA to reconvene the Expert Panel to review the latest evidence of safety and efficacy and will consider their advice alongside the responses to the consultation.

Why does the law need to be changed?

The law does not currently allow an egg or an embryo which has had its mitochondrial DNA altered to be used in treatment in humans. In 2008 when this law was written the Government did, however, foresee that techniques such as those described above were being developed to prevent mitochondrial DNA disease. It therefore provided the Government of the day the power to make regulations to enable techniques which avoid 'serious mitochondrial disease' to be used for patients in the clinic. The Government proposes to now exercise its power under the existing law to bring new regulations into force (which will be debated and voted on by Parliament). This would then allow a very few specialist doctors to apply for a licence to do this work once it is seen as sufficiently safe and effective.

What are the principles behind the new regulations?

9. What are the ethical arguments in favour of the techniques being allowed?

Although mitochondrial DNA disease affects a small number of individuals, its effects on them and their family can be devastating. Mitochondrial donation will enable mothers to choose to have children who are genetically related to them and free from a potentially debilitating or fatal disease.

10. Should we be creating 'three-parent' babies?

Scientists estimate that our DNA is made up of 20,000-30,000 genes. Using this new technique, almost all of the child's genes will come from its parents; the mitochondrial donor will only contribute 37, which enable the mitochondria to produce energy. The donor mitochondrial DNA will not affect the child's appearance, personality or any other features that make a person unique – it will simply allow the mitochondria to function normally and the child to be free of mitochondrial DNA disease. Furthermore, the Nuffield Council on Bioethics conducted an ethical

review which concluded that, “by the societal norms, [mitochondrial] DNA does not confer genetic identity”. As a result, there is no reason why the techniques should affect the child’s sense of identity.

11. Could allowing mitochondrial donation be the start of a ‘slippery slope’ towards allowing other techniques, such as nuclear genetic modification, which could be used to create ‘designer babies’?

Mitochondria are separate structures from the nucleus (see Figure 1) and the regulations will only allow the techniques to be used on mitochondrial DNA, not on nuclear DNA. The ban on altering nuclear DNA will remain in place, and there is no intention of changing this. Mitochondrial donation is totally different to altering nuclear DNA and allowing mitochondrial donation will not lead to the acceptance of genetic modification in the nucleus, nor give us the capability of doing this.

12. Mitochondrial donation involves ‘germ-line modification’ (changes to sperm or egg cells), which enables DNA modifications to be passed on to children. Should we be changing future generations in this way?

These techniques replace the mitochondria, and involve reconstruction (where nuclear DNA is moved from one cell to another) but do not involve any modification of the DNA sequence itself. New combinations of mitochondrial DNA and nuclear DNA occur in nature every time an egg is fertilised. Mitochondrial donation will have the hugely beneficial effect of future generations being born without mitochondrial DNA disease and will not enable the selection of other traits.

How will the regulations work in practice?

13. How will doctors be licensed to offer the techniques?

Once Parliament has passed regulations allowing mitochondrial donation, doctors will still need to obtain approval from the Human Fertilisation and Embryology Authority (HFEA) in order to use the techniques. The HFEA will assess each application to use the techniques on a case by case basis, so doctors will need to get approval for each patient and it will only be provided at specialist clinics.

14. What legal status will the mitochondria donor have?

Although women donating mitochondria would also be egg donors, only the mitochondria-containing part of their eggs would be used for the procedure. The HFEA report and recommendations to the Government after a large public consultation in 2013 advised that mitochondrial donors should have a similar status to that of tissue (organ) donors and that the children born after mitochondrial donation should not have a right to access identifying information about the donor.

What happens next?

The regulations are currently being drafted by the Department of Health who plan to run a public consultation in early 2014. This will be a chance for patients and the public to have their say on the possibility of the new techniques. Subject to that, the regulations would be put to Parliament for debate and approval.

If the regulations are approved by Parliament, the Government's intention is to bring them into force by the end of 2014. This will allow more reproductive choice for parents at risk of having a child with mitochondrial DNA disease, and the possibility to have a healthy child.

How can I get involved?

There are two big opportunities to make a difference.

1. **Write to your MP**

   You can write to your MP and let them know this is happening and express your views on this issue. To find your local MP look at: http://findyourmp.parliament.uk/

2. **Respond to the public consultation**

   Public consultations are there to find out what the public thinks. Anyone can respond and it is important that patients' views are represented. For a simple guide on how to respond to a public consultation, have a look at this guide.

Links to further background information

Wellcome Trust Policy Spotlight on Mitochondrial Disease
http://www.wellcome.ac.uk/About-us/Policy/Spotlight-issues/Mitochondrial-diseases/index.htm

Video from the Human Fertilisation and Embryology Authority: Mitochondrial Replacement -Some facts.
http://vimeo.com/49147390

HFEA advice to Government on the ethics and science of mitochondria replacement
http://wellc.me/HFEAmito

Nuffield Council on Bioethics report 'Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review'
http://www.nuffieldbioethics.org/mitochondrial-dna-disorders

Mitochondria: Nuts and bolts – What are mitochondria?
http://wellc.me/MitoBolts

Healing Broken Batteries – A short film about mitochondrial disease and the new techniques being developed at Newcastle University.
http://wellc.me/brokenbatteries