Mitochondrial Disease and Donation – Q&A

This document has been created to enable members of the mito community to prepare to answer questions that people are likely to ask about mitochondrial disease and mitochondrial donation.

This document is not intended to be handed out to anyone: it is an internal document intended to support the mito community in preparing to talk to stakeholders.

ABOUT MITOCHONDRIA

What are mitochondria?

Mitochondria are small structures found in our cells that generate the energy that powers every part of our body. Mitochondria are often called the 'powerhouses' that provide us with the energy our body needs to walk, talk, laugh, hear, digest food, function and breathe.

All cells in the human body have mitochondria, except for red blood cells. Mitochondria have their own DNA which controls their function and their role in energy production. This is separate from our *nuclear* DNA which informs who we are, our appearance and our personality.

What do mitochondria do?

Mitochondria take the fuel from food that we consume and, together with oxygen, transform this into the energy that our bodies need to function.

In people with healthy mitochondria, this process works smoothly but, in people with faulty mitochondria, this process is impaired.

Why do mitochondria have their own DNA?

Unlike the DNA in our nucleus which has 23 chromosome pairs inherited equally from our mother and our father, our mitochondria have only 1 chromosome and are inherited entirely from our mother.

Mitochondria and their DNA are believed to have evolved from primordial bacteria that entered into a symbiotic relationship with primordial cells that evolved into animal species (and ultimately humans). In this way, mitochondrial DNA has persisted as genetic material that is physically and functionally separated from DNA on chromosomes in the nucleus.

What percentage of our genes are in the mitochondria?

The DNA in our nucleus has 23 chromosome pairs inherited equally from our mother and our father and around 20,000 genes within them.

In contrast, our mitochondria have only 1 chromosome and only 37 genes. They are less complex and quite discrete in themselves.

ABOUT MITOCHONDRIAL DISEASE

What is mitochondrial disease?

Mitochondrial disease (known as mito for short) is a debilitating genetic disorder that robs the body's cells of energy, causing multiple organ dysfunction or failure and sometimes death.

Mitochondrial disease occurs when a person's mitochondria are not working properly and can develop at any age from birth onwards.

About half the time, mitochondrial diseases are caused by mutations in the separate mitochondrial DNA (mtDNA) that we inherit only from our mother. About 1 in 200 people (or approximately 120,000 Australians) carry a mutation in their mitochondrial DNA that could potentially cause disease and it is likely that mtDNA disease is much more common in the community than previously thought.

When do you get mitochondrial disease?

People can develop mitochondrial disease at any age, at any stage and in any organ or tissue.

Individuals with a significant burden of faulty mitochondria tend to develop mitochondrial disease earlier in life. However, we are aware of circumstances where adults develop the disease and later their parent also does.

What are the symptoms of mitochondrial disease?

The symptoms of mitochondrial disease can be debilitating. Depending on the person and the form of their mitochondrial disease, they may suffer a whole range of symptoms from loss of motor control, strokes, seizures, visual or hearing problems, cardiac and/or liver disease, developmental delay and intellectual disability.

How are you diagnosed with mitochondrial disease?

Mitochondrial disease can be difficult to diagnose as it often presents with symptoms common to other diseases or illnesses. As a result, it can take a long time to identify the specific mitochondrial disease that a person is experiencing.

Once mitochondrial disease is suspected, the traditional approach to diagnosis includes a test for common mtDNA mutations and a muscle biopsy to measure how an individual's cells are metabolising enzymes.

What treatments exist for mitochondrial disease?

There is no cure for mitochondrial disease and very few effective treatments.

For some symptoms, standard treatments already exist such as physical therapy for motor problems. Other treatments can include vitamin/cofactor supplements, anti-oxidants, dietary manipulations and structured exercise programs, however their effectiveness is inconsistent.

How many people in Australia have mitochondrial disease?

Approximately 1 in every 200 Australians or around 120,000 people carry the genetic mutation that could potentially lead to mitochondrial disease developing – although it is thought the number could be much higher. One in 5,000 babies are born with a severely disabling form of mitochondrial disease that can cause death in infancy, childhood or adulthood.

What is the impact of mitochondrial disease?

The impact of mitochondrial disease can be devastating and virtually all forms have a significant impact on patients.

Babies and young children die of Leigh disease whilst other types of mitochondrial disease can impact sufferers in different ways. Repeated seizures and loss of motor control can mean that people of all ages have to stop working and may need full time care, further impacting their family and friends.

Many people with mitochondrial disease have repeated and/or prolonged visits to hospital. Symptoms can include vision loss, mitochondrial strokes, balance difficulties and digestive or eating

difficulties, all requiring significant treatment and care. Patients may rely heavily on the healthcare, and sometimes social services, systems.

Can we prevent mitochondrial disease from being passed on?

It is possible to significantly reduce the risk of some types of mitochondrial disease being passed on. Where mitochondrial disease is caused by mistakes or mutations in one of the nuclear genes involved in mitochondrial function, it may be prevented through prenatal testing or an IVF based procedure called preimplantation genetic diagnosis.

Where the mutation is in mitochondrial DNA inherited from the mother, mitochondrial donation can prevent the transmission from mother to child.

ABOUT MITOCHONDRIAL DONATION

What is mitochondrial donation?

Mitochondrial donation, also known as mitochondrial transfer or replacement, can occur in one of two ways, both involving IVF.

One technique involves transferring the nuclear genetic material from the affected mother's egg into a donor egg that has had its nuclear DNA removed and retains only its healthy mitochondrial DNA. This is called maternal spindle transfer.

The other technique, which is more common, **involves taking the nuclear DNA from** the mother's egg after the mother's egg is fertilised with the father's sperm but before it begins to develop further. The nuclear DNA is then transferred to the donor egg containing healthy mitochondria, which has had its nuclear DNA removed. The healthy fertilised egg is then implanted into the mother's uterus in the same way as in maternal spindle transfer. This is called pronuclear transfer.

How many people would mitochondrial donation help in Australia?

A simple extrapolation from the UK, where there has been significant work on mitochondrial disease, indicates that there are around 56 children born each year in Australia who would benefit from this technique. This number is based on our respective population sizes and assumes roughly the same age distribution and fertility.

Whilst this may seem a relatively low number, it represents a significant burden to our health system and a major burden and fear on behalf of families at risk. Conversely, eliminating this risk does not represent a significant cost or burden to the financial sustainability of the health system and would provide parents and families a choice in regards to the health risks facing their child.

Who would have access to mitochondrial donation?

Who would have access to mitochondrial donation would be a decision for Australian legislators to make. In the UK, we have seen legislation passed that limits access to mitochondrial donation to those people at significant risk of passing on mitochondrial disease to their children.

LEGAL SITUATION IN AUSTRALIA

Is mitochondrial donation legal in Australia?

Currently, Australian legislation does not permit mitochondrial donation.

The key federal laws governing research and clinical practice in relation to embryology are the *Prohibition for Human Cloning for Reproduction Act 2002* and the *Research Involving Human Embryos Act 2002.*

Whilst there are a few sections of the laws that are relevant, the clauses critical for mitochondrial donation currently prohibit implantation of a human embryo that contains more than two people's genetic material regardless of whether that material is simply transferred, as in mitochondrial donation, or where genetic modification is proposed.

What is the current situation with regards to potential legislation change?

In 2018, the Senate Community Affairs Committee undertook an inquiry into the *Science of mitochondrial disease and related matters.* Reporting in June that year, they made a series of recommendations including that a public consultation be undertaken about the introduction of mitochondrial donation and that 'the Australian Government prepare a consultation paper, including options for legislative change that would be required'. The Senate Committee further recommended that the NHMRC provide advice regarding any new findings about mitochondrial donation since the introduction of mitochondrial donation in the UK.

Following this, the Government tasked the NHMRC to bring together an Expert Working Committee to work on scientific and other matters raised by the Inquiry. In addition, public consultation was held in late 2019 with public forums, webinars, online submissions, a citizens' panel and other activities undertaken.

Subsequent to this, the Government issued a consultation paper outlining a two stage implementation process for the introduction of mitochondrial donation in Australia before, on 24 March this year, Minister for Health Hon Greg Hunt MP introduced the *Mitochondrial Donation Law Reform (Maeve's Law) Bill 2021* into the House of Representatives.

The Senate Standing Committee on Bills has now reviewed the Bill and the Senate Community Affairs Legislation Committee undertook an inquiry into it. As this is a conscience matter, their report summarise the views put forward in submissions and to the hearing held

Next Steps

On 24 March this year, Minister for Health Hon Greg Hunt MP introduced the ***Mitochondrial Donation Law Reform (Maeve's Law) Bill 2021*** into the House of Representatives. This Bill will give women who carry these genetic mutations the choice to eliminate the risk of their children inheriting this devastating and life-threatening disease by legalising mitochondrial donation.

It is expected that the Bill will be debated in late 2021 or early 2022. Liberal, National and Labor MPs and Senators will be allowed a conscience vote on the Bill and we are asking for your support when the Bill comes before Parliament.

GLOBAL EXPERIENCE

Is mitochondrial disease legal elsewhere in the world?

After many years of consultation, the use of mitochondrial donation was approved by the UK Parliament in 2015. In March 2017, the first clinical mitochondrial donation licence was granted to the Newcastle Fertility Centre at the International Centre for Life in Newcastle-upon-Tyne, United Kingdom.

In February 2018, the first licences were granted to two women to undergo mitochondrial donation at the Newcastle Fertility Centre. The first child born via mitochondrial donation in the UK may well have already been born but, due to privacy issues, the births will not be announced.

How did it become legal in the UK?

Newcastle University in the UK has undertaken many years of research and work in relation to mitochondrial disease and, together with the Wellcome Trust, worked with UK politicians, scientists and the community to raise awareness of mitochondrial disease and the choice that mitochondrial donation offers parents.

Australia, likewise, undertakes a significant amount of research in this area and is home to a number of world leading scientists. Given this and the impact of mitochondrial disease on Australian families and society, it is logical for us to seek to replicate the UK experience.

What rules govern mitochondrial donation in the UK?

The legislation introduced in the UK regarding mitochondrial donation is comprehensive and covers a number of issues including:

- Tight eligibility for mitochondrial donation
- The need for the eggs to be used in mitochondrial transfer to be donated
- Clear definitions of the legal relationships between the parents of a child born as a result of mitochondrial donation and the individual who donated the egg
- Clear definitions around mitochondrial donation and genetic modification to exclude mitochondrial donation, recognising it as a ‘transfer’ rather than a ‘modification’.

Why is it legal in the UK?

Like Australia, UK scientists have been significantly involved in research in this area for many years and, together with the Wellcome Trust, affected parents and patients, worked with the UK Government to change the laws regarding mitochondrial donation. This recognises the significant impact of mitochondrial disease on families and society as well as the fact that there are few treatments and no cures for these diseases.

I think I’ve seen news articles about children being born elsewhere in the world from mitochondrial donation. Is that right?

Yes. In the last couple of years, there have been reports of children being born in other countries from mitochondrial donation.

In 2016, a child was born in Mexico from mitochondrial donation whilst this year a child was born in Greece. In the Mexican situation, the child was at risk of developing mitochondrial disease and its parents had lost previous children due to this. The situation in relation to the birth in Greece was different and the technique was used in order to avoid fertility issues experienced by the mother.

The Mito Foundation is not advocating that mitochondrial donation is used for any purpose other than to avoid parents passing on mitochondrial disease to their children and to help save those children's lives.

We are also concerned about situations in which mitochondrial donation is used in countries where no regulations govern its use and one of our reasons for advocating legal change in Australia is to ensure that the technique is available to Australian families in their own country in a safe and well-regulated environment.

ETHICAL ISSUES

What are the ethical issues involved in mitochondrial donation?

As with IVF more broadly, there are some ethical issues involved in mitochondrial donation. These range from concerns about a child being born carrying three people's DNA to the safety of those individuals choosing to donate their eggs and the issues of selecting against disease and what the implications of that might mean.

Equally, mitochondrial donation offers the only choice for parents at risk of passing on mitochondrial disease to have a child genetically related to them both, who would have a significantly reduced risk of developing the condition. Mitochondrial donation would avoid the distress of having a child experience mitochondrial disease and save the lives of those children.

How are these issues dealt with in the UK?

The UK has had to manage a number of ethical issues in establishing its legislation on mitochondrial donation. These issues have included:

- Eligibility for those participating in mitochondrial donation
- The requirement for eggs being used in mitochondrial transfer to be donated
- Clear definitions of the legal relationships between the parents of a child born as a result of mitochondrial donation and the individual who donated the egg
- Clear definitions around mitochondrial donation and genetic modification, recognising mitochondrial donation as a 'transfer' rather than a 'modification'

Fundamentally the UK legislation recognises the impact on families and society of mitochondrial disease and the fact that there are few treatments for these diseases and no cures.

I've heard the term '3 parent babies' used in relation to mitochondrial donation. What do you think of this?

The term '3 parent babies' is not a term that the Mito Foundation uses in relation to mitochondrial donation. It sensationalises something that is scientifically based and tries to drive an emotive

response. Whilst this is an emotive topic, sensationalising the issue does not help those of us who have day to day experience with mitochondrial disease.

Having said that, it is true that children born as a result of mitochondrial donation will carry three people's DNA. This would also occur if they received a lung or other organ donation or a bone marrow transplant.

Mitochondria are discrete components within our cells and play a specific role in our body - to power us. They do not form part of the nuclear DNA that determines who we are, what we look like or our personality.

Is this simply the thin end of the wedge of people choosing their babies' sex and hair colour?

As has been recognised in the UK, mitochondria are discrete components within our cells and have a clear and limited function within our bodies – they transform fuel and oxygen into energy.

As such, the mitochondrial DNA are different from our nuclear DNA which influences who we are, our looks and our personality. Mitochondrial donation both acknowledges that difference and allows parents to choose whether to use mitochondrial donation to avoid their children inheriting the risk of mitochondrial disease.

How do you stop this from becoming the slippery path to eugenics?

Given that mitochondria are discrete components within our cells and have a clear and limited function within our bodies, mitochondrial donation can be viewed more as a transfer or transplant than the type of genetic modification that would alter how an individual would look, what their personality would be like or who they are.

The recognition of this, together with the impact of mitochondrial disease on families and society, is one of the reasons that the UK has legalised mitochondrial donation and has defined that it is not genetic modification.

FUNDING

How much would mitochondrial donation cost the Australian public?

International modelling has shown such significant savings across the health system from preventing mitochondrial disease that the Foundation has not commissioned any Australian-specific economic modelling.

Overseas experience indicates that the cost of the technique involved in mitochondrial donation is only minimally more than traditional IVF whilst, at the same time, there are significant and ongoing costs involved due to a person experiencing mitochondrial disease. These tend to involve significant use of hospital care, pathology and other diagnostic testing, doctor and specialist visits, and other needs depending on the type of mitochondrial disease suffered.

Given this, any costs involved with mitochondrial donation will be offset by the costs of the health and social services needed to support a person with mitochondrial disease.

What is the cost implication to government for mitochondrial donation?

Given that that costs of mitochondrial disease are significantly more than the cost of the technicque used in mitochondrial donation, the overall savings to the health system are substantial.

MITO FOUNDATION

Who set up the Mito Foundation?

The Mito Foundation was established by a group of concerned individuals and scientists, many of whom work in the area of mitochondrial disease or have family members impacted by it.

How is the Mito Foundation funded?

The Mito Foundation is a registered Australian charity and does not receive ongoing Government funding. It is heavily reliant on donations from the community and our corporate partners who participate in a range of fundraising and other activities. Every year the Mito Foundation holds a series of Bloody Long Walks around Australia in which thousands of people participate to raise money to fund research and support for those impacted by mitochondrial disease. The Mito Foundation also hosts Stay in Bed Day to highlight the impact of mitochondrial disease and raise funds.

What is the Mito Foundation trying to achieve?

The Mito Foundation supports sufferers and their families, funds essential research into the prevention, diagnosis, treatment and cures of mitochondrial disorders, and increases awareness and education about this devastating disease.

Driving legislative change to enable parents to choose whether to use mitochondrial donation to avoid their children inheriting the risk of mitochondrial disease aligns with those activities and is a key goal of the Foundation.

In 2019, the Mito Foundation marked 10 years since incorporation.