Senate Inquiry into mitochondrial donation

RE: Australian Government announces Inquiry into legalising mitochondrial donation

May 8, 2018

My name is Charles Mohan Jr, and I am the Founder and Executive Director of the United Mitochondrial Disease Foundation (UMDF).

My wife and I lost our 15 year old daughter to a mitochondrial disease which motivated us to help support other families navigate this devastating and incurable disease.

The UMDF is the world's largest patient advocacy group for mitochondrial disease and is represented in every state in the USA and over 152 countries.

The mission of the UMDF is to promote research and education for the diagnosis, treatment and cure of mitochondrial disorders and provide support to affected individuals and families. To that end, we have personally supported over $13 million in research grants that have in turn generated over $100 million of additional government supported research.

We are professionally guided by a prestigious Scientific and Medical Advisory Board consisting of the top researchers and scientists in the field of mitochondrial function and dysfunction.

As the world's largest Patient Advocacy Group for mitochondrial disease we maintain that individuals with mitochondrial disease should have access to all current therapeutic innovations for the alleviation and prevention of mitochondrial diseases. To that end, we are pleased to submit the following position statement as a letter of support for further scientific investigation of oocyte mitochondrial replacement therapy as well as constructive debate towards the clinical approval of this therapy in women with mtDNA-related diseases.

Sincerely,

Charles A Mohan Jr
CEO United Mitochondrial Disease Foundation

UMDF POSITION & CLINICAL STATUS OF MITOCHONDRIAL REPLACEMENT THERAPY TO PREVENT TRANSMISSION OF mtDNA DISEASES

September 2016

The United Mitochondrial Disease Foundation (UMDF) maintains that every individual has the right to safe and effective health care as well as access to all current therapeutic innovations for the alleviation and prevention of mitochondrial diseases.

Mitochondria are cellular components that contain their own DNA (mtDNA) and are responsible for generating more than 90% of the body's energy. About one in 200 people is born with a pathogenic mtDNA mutation and one in 5,000-10,000 people develop a symptomatic mitochondrial disease. However, the incidence rates may be higher considering the difficulty of accurate diagnosis and the diversity of clinical presentations.

Most pathogenic mtDNA mutations affect children, who frequently suffer catastrophic organ failure. In adults, the symptoms worsen with age and often become debilitating. Mitochondrial dysfunction typically damages cells of the brain, heart, liver, skeletal muscles, kidney and the endocrine and respiratory systems. Currently, treatment is limited to symptomatic management using vitamins and supplements.

There is an important unmet clinical need to reduce the risk of transmitting mtDNA diseases to offspring. The mtDNA makes up only 0.1% of the entire human DNA and contains 37 genes, distinct from the nuclear DNA, which accounts for 99.9% of a person's genetic makeup and determine one's physical appearance and personality. As mitochondria are transmitted exclusively through mothers, a woman with defective mtDNA could potentially use her and her partner's own nuclear DNA in combination with the healthy mitochondria of a female donor and have a child who is 99.9% genetically identical to her and her partner.

Mitochondrial replacement therapy (MRT) uses healthy mitochondria coming from a donor's egg whose nucleus has been removed and into which the mother's nucleus is transferred. In vitro fertilization (either before or after MRT) produces an embryo that contains nuclear DNA from the father and the mother with healthy mtDNA from the donor. This procedure gives women with mtDNA mutations an excellent chance of having their own children, who will be free of the mitochondrial disease.

MRT is NOT genetic manipulation, but rather a technological innovation and an expansion of in vitro fertilization, a clinically-approved technique used for four decades. The latest evidence from leading mitochondrial research institutions in the US and the UK indicate that mitochondrial replacement techniques are safe and effective in primates, although further research will be necessary to fully understand the long-term effects of MRT.

We strongly support further scientific investigation of oocyte MRT as well as constructive debate towards the clinical approval of this therapy in women with mtDNA-related diseases. If demonstrated to be safe and efficacious, this technique should be made available with proper regulatory oversight as an option to families who carry mtDNA point mutations.

Clinical Status

In 2013, the Human Fertilization and Embryology Authority (HFEA) in the UK completed an extensive public consultation on mitochondrial replacement therapy and found widespread support for it. In 2015 the UK Parliament voted to allow mitochondrial donation, and the HFEA is now charged with issuing licenses to practice MRT at UK fertility clinics on a case by case basis.

In the US the FDA commissioned the National Academies of Science to convene an esteemed panel of experts to review the scientific, ethical and policy considerations of MRT. In a report issued in February 2016 the committee concluded that it was, on both a scientific and ethical basis, permissible to proceed with clinical testing of MRT with certain limitations. Importantly, the committee emphasized in their final report that concerns about genetic manipulation warrant significant caution and the imposition of restrictions rather than blanket prohibition of MRT to prevent transmission of serious mtDNA disease. Despite this position, the FDA has been prevented from further evaluating clinical applications of MRT by language included in the 2016 congressional spending bill banning the agency from evaluating clinical trials involving genetic modifications that affect the next generation.

In September 2016 it was publically announced that a male child was born earlier in the same year as a result of an MRT technique carried out by a US doctor in a Mexican fertility clinic for the purpose of preventing the transmission of Leigh Syndrome, a form of mitochondrial disease. Per the announcement, the child is doing well with a very low level of mutant mtDNA.