3rd May 2018

Ms Jeanette Radcliffe
Secretary
Senate Community Affairs Committee
Parliament House
PO BOX 6100
Canberra 2600

Re: Senate Inquiry: The science of mitochondrial donation and related matters

Dear Ms Radcliffe

I would like to make a submission to the Senate Committee investigating mitochondrial donation and its potential utility. I would like to begin by commending this Committee for considering this very important issue. I would also like to congratulate the Embryo Research Licensing Committee for its recent discussion paper, which is an excellent distillation of issues relating to advances in scientific and medical research in a number of areas, including mitochondrial transfer (aka mitochondrial donation or mitochondrial replacement therapy).

I am a clinical geneticist with over 30 years experience in the diagnosis and management of children with inborn errors of metabolism including mitochondrial disorders, and so have been witness to the devastating consequences of the disorder. I have also been involved in mitochondrial disease research for over 20 years, primarily focused on understanding the genetic bases and biological consequences of this group of disorders. One of my current research activities in this area is as Co-Lead of the Australian Genomics Health Alliance Mitochondrial Diseases Flagship, which has as a primary aim the acquisition of the evidence to support the use of genomic technologies early in the diagnostic odyssey of patients suspected of having a mitochondrial disorder. I wish to also declare that I am a member of the Board of the Australian Mitochondrial Disease Foundation, which has published its position on mitochondrial donation (https://www.amdf.org.au/mitochondrial-donation/). In addition, I am the approved pathology provider for the Victorian Clinical Genetics Service Laboratories, which among other things offers genetic testing for mitochondrial disorders.

To better understand what has led to the Senate Inquiry into mitochondrial donation, I imagine that the Senate Committee will have been briefed on the basic biology behind the mitochondrial disorders, and the rationale as to why mitochondrial donation is relevant to a subset of families with mitochondrial disorders. Working under this assumption, I will not elaborate on this here,

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but would be very happy to do so if required by the Senate Committee.

There are currently very few effective treatments for this group of disorders, and so prevention is the main approach that can be currently offered to families. For nuclear-encoded gene mutations traditional prenatal testing or pre-implantation genetic diagnosis techniques are very effective and have a long and established track record. However, apart from a few specific exceptions, for primary mitochondrial DNA disorders these approaches are generally not as definitive for a number of reasons. It is for this latter group of disorders where mitochondrial donation is particularly relevant.

As the Committee will no doubt be aware, there has been an immense high quality body of translational research undertaken in the UK by the very reputable and internationally very highly regarded Newcastle-upon-Tyne group, supported by the Wellcome Trust, and with very strong consumer engagement by the Lily Foundation, that has clearly demonstrated the clinical utility of mitochondrial donation for carefully considered cases. Their work, spanning more than a decade, and which included a very significant community engagement/education program, and which has been very carefully evaluated by the UK Human Fertilisation and Embryology Authority, ultimately led to laws in the UK being changed to permit this technology to be used within strict medical, ethical and legal parameters in an IVF setting. Mitochondrial donation is being made available on a case-by-case basis, with individual licenses being approved for each case after very careful evaluation. It is expected that the first babies will be born in the next 12 months through the Newcastle-upon-Tyne mitochondrial donation IVF program. This will be a ground breaking achievement in dramatically reducing, if not avoiding altogether, the risk of couples having affected children.

There has been some theorizing that mitochondrial donation through proposed epigenetic mechanisms, or as a consequence of not using mtDNA haplogroup matched donor egg cells for the procedure, could lead to untoward effects on the health of the embryo or the child after birth. However, I am aware of no such evidence supporting the notion that there would be any significant risks to children born following mitochondrial donation. Mitochondrial DNA transferred as a consequence of this technique will only affect the capacity to generate energy, and there is no evidence to suggest that it would have any significant impact on physical appearance, behaviour, intelligence or other individual characteristics.

I suggest that given all the work that has been done to get to this point in the UK, and the great scientific rigor and ethical scrutiny that was applied during the course of this body of work, the Senate Committee has all the information it needs to be able to make a determination on recommendations for modifications to the two relevant Australian Acts to facilitate the rapid integration of mitochondrial donation for **specific** (ie not all) primary mitochondrial DNA disorders. I personally do not feel that further significant scientific or ethical reviews are necessary, and that Australia can learn from the experiences in the UK to make mitochondrial donation a reality for the Australian public.

I note that in its reports, the Human Fertilisation and Embryology Authority made a number of recommendations including:

1. Centres offering mitochondrial donation should be licensed, having demonstrated satisfactory capability in all of the IVF methods to be used. ***I strongly endorse this recommendation. I understand that the Newcastle-upon-Tyne group would be prepared to provide instruction/guidance to centres in Australia wishing to establish mitochondrial***

donation services. It would be highly desirable, if not mandatory, for the Reproductive Technology Accreditation Committee to be responsible for issuing licenses to IVF facilities demonstrating the necessary level of expertise in the requisite IVF technologies. In addition, it would be expected that a molecular genetic testing laboratory associated with the IVF facility would have NATA/RCPA accreditation for the supportive molecular genetic testing.

2. In determining the eligibility for application of mitochondrial donation, there should be a case-by-case evaluation by an expert committee. ***I strongly endorse this approach, and would suggest that membership of such a committee should include paediatric and adult mitochondrial disease clinical specialists, a clinical geneticist, an IVF specialist and a community representative.***
3. mtDNA carryover rates should not on average exceed 2% and should be no greater than 10% per embryo. ***I agree with this suggestion.***
4. Follow-up prenatal testing should be offered to couples who have undergone mitochondrial donation. ***I agree that this is a logical approach.***
5. Whilst there is currently no evidence at this point to suggest that differences in mtDNA haplogroups between donor and recipient eggs is of clinical relevance, the mtDNA haplogroup of the recipient and donor eggs should be recorded for future possible evaluation. ***I also agree with this suggestion.***
6. There should be long-term clinical follow up of a child born as a consequence of mitochondrial donation to capture information about potential long-term adverse effects. ***I strongly support this recommendation, and suggest that the expert panel would be in the best position to determine a protocol for this.***

I wish the Senate Committee well in its deliberations.

Yours sincerely,

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