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Human Genetics Society of Australasia

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Senate Community Affairs References Committee
Parliament House
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Inquiry into the Science of mitochondrial donation and related matters

The Human Genetics Society of Australasia's response to a request for comment

Thank you for asking the Human Genetics Society of Australasia (HGSA) to provide a written submission around issues being considered by the Senate's Community Affairs References Committee inquiry into the science of mitochondrial donation and related matters. As you will be aware the HGSA is the peak professional body representing Clinical Geneticists, Genetic Counsellors, Genetics Laboratory Scientists and Genetic Pathologists in Australia and New Zealand. Our *Society* represents the health, ethicist and legal professionals who deliver genetic diagnosis, testing and counselling to Australian patients who have, or are at risk of inheriting genetic conditions and syndromes including the mitochondrial disorders that are currently being considered by the Committee.

With regard to the specific issues where the committee sought a response:

(a) the science of mitochondrial donation and its ability to prevent transmission of mitochondrial disease

Extensive preclinical studies have provided high confidence that mitochondrial donation will prove to be a safe and effective way of enabling women carrying these devastating disorders to have children who are both genetically their own and without the mitochondrial disorder. There has been an immense body of high quality translational genetics research undertaken in the United Kingdom by the Newcastle-upon-Tyne research group, supported by the Wellcome Trust, and in Oregon in the United States that has clearly demonstrated the clinical utility of mitochondrial donation for carefully considered cases.

(b) the safety and efficacy of these techniques, as well as ethical considerations

Technology: Mitochondrial donation is not a 'life saving' technology in that it will not save the life of anyone born with mitochondrial disease. It is not a 'magic bullet' to cure all mitochondrial disease. This point is important to recognise in public deliberation; taking care not to over-hype the potential of this technology. That said, the safety and efficacy of mitochondrial donation has been demonstrated by programs in

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Newcastle-upon-Tyne and in Oregon. These teams have provided as much evidence for safety and efficacy as is practical in studies based on primate models and human embryos. The Director of the Wellcome Trust, Dr Jeremy Farrar stated publically in early 2015 that "I don't think there's been any more rigorous look at any scientific endeavour coming into humans".

The technology is in essence a modification of standard IVF with the donor egg providing the cytoplasm containing the mitochondria, the mother providing the nucleus (nuclear DNA), and the father providing sperm. Ethical reviews in the UK and USA have also recognised that there mitochondrial donation is distinct from germline genetic modification and should not be prevented based on false equivalency arguments.

The HGSA is not aware of any evidence to suggest that there would be significant risks to the children who would be born following mitochondrial donation. Mitochondrial DNA transferred as a consequence of this technique will only affect the capacity to generate cellular energy, and there is no evidence to suggest that it would have any significant impact on physical appearance, behaviour, intelligence or other individual characteristics. Children born from similar techniques (in the early 2000's) appear well.

The HGSA notes that two past-Presidents of the *Society*, Professors John Christodoulou and David Thorburn who are experts in the science, translational research and medical care of people and families with mitochondrial disorders will both be making their own submissions to this inquiry and have been invited to provide evidence at the Inquiry's hearings.

Ethics: Mitochondrial donation gives rise to a large range of ethical considerations; all of which have been extensively considered in the literature and in policy reports in other countries (e.g. Nuffield Council on Bioethics, US National Institute of Medicine). Issues include:

- Determining the point at which a technology is deemed 'safe enough' to proceed with human trials
- The moral significance of genetic relatedness (having a genetic connection; genetic kinship). Some couples may use mitochondrial donation when their other choice may have been to not have children at all.
- Whether the inheritability of the alteration to the oocyte or early embryo has ethical significance
- Resource allocation aspects
- The place and value of the '3 parent' analogy: A significant part of the controversy of this technique centres on the concept of a "three parent family". However, IVF has often involved techniques which have resulted in three parents. Does the genetic nature of the parent as opposed to the social nature of the parent differ so significantly? The HGSA's view is that while biology makes a contribution to the concept of a family, it not the fundamental issue that matters as families with adopted children will overwhelmingly attest to.
- What constitutes a 'need' for this technology
- The kind of life that those born of mitochondrial donation lead, for example the media exposure they may endure; and how any possible harm from this can be managed
- The place of oocyte donors; notably whether they should remain anonymous and whether the child born should have access to information about the donor (including whether mitochondrial donation is more analogous to gamete donation or organ donation; which have very different approaches to anonymity)
- The importance of access to counselling and a thorough discussion-based consent process for any couples seeking to use mitochondrial donation



The HGSA notes that the co-chair of its Education, Ethics and Social Issues Committee, A/Prof Ainsley Newson is an expert in the ethics of mitochondrial donation; and that she will both make her own submission to this inquiry and has been invited to provide evidence at the Inquiry's Sydney hearing.

(c) the status of these techniques elsewhere in the world and their relevance to Australian families;

Internationally mitochondrial donation is being made available on a case-by-case basis, with individual licenses being approved for each case after very careful evaluation. Legislation enabling mitochondrial donation was passed in the UK in 2015 and couples are now undergoing the procedure in the UK. There is one report of an apparently successful outcome from a US team that performed the technique in Mexico to avoid regulatory oversight. That is a very poor precedent that could be avoided in Australia by instituting a proper regulatory framework.

If this technology were not available in Australia, it should be recognised that some families may choose to travel to a jurisdiction where it is permitted. Planning for ongoing support for any such families would be prudent.

(d) the current impact of mitochondrial disease on Australian families and the healthcare sector;

Mitochondrial DNA diseases are diverse and severe conditions, with some affected children dying in childhood after devastating illness. They are in other words, significant, severe conditions with profound psychosocial and medical impacts on affected individuals, their families and the healthcare system. Based on Gorman et al (NEJM 372, 885-7, 2015) there are about 60 women at risk of transmitting a mtDNA disorder to their baby each year in Australia. Clinical experience of HGSA members suggests that mothers who have transmitted these disorders are often plagued with guilt as there is a lack of effective treatments for these disorders. Some assisted reproduction technologies are possible (e.g. prenatal diagnosis and preimplantation genetic diagnosis), despite the uncertain correlation between the abnormal mitochondrial content of an embryo (heteroplasmy) and the ultimate outcome in the child. Mitochondrial donation will restore the reproductive confidence of these families (about 60/year as above) and potentially offers the opportunity to have children at much reduced risk of mitochondrial disease.

(e) consideration of changes to legal and ethical frameworks that would be required if mitochondrial donation was to be introduced in Australia;

We note that some research may be currently permitted under license, in all states and territories with the exception of Western Australia. Clinical use is not currently permitted in any Australian jurisdiction.

HGSA supports changes to legislation to enable mitochondrial donation with the intention of providing additional reproductive options for women and families with mitochondrial disease. If clinical use of mitochondrial donation is to be introduced, multiple pieces of legislation will require amendment, at both commonwealth and state/territory levels

We would strongly advocate for a flexible and adaptive system of governance, to help avoid the problems that have come from the existing regulatory regime; in particular there being no further reviews required to the cloning/embryo laws. This and similar areas of reproductive science are fast-moving; and regulation needs to be similarly flexible and adaptive.



HGSA proposes that Australia does not need to 're-invent the wheel' of what is required for the necessary enabling legislation, but should develop a regulated process based on the UK model whereby any centre seeking to offer the procedure and any couple seeking access should require a license/approval. This will ensure couples are provided appropriate counselling about the potential benefits, safety & efficacy, other potential options and any degree of uncertainty.

Regulation/licensing is also known to be a robust tool that could be used to ensure appropriate implementation of mitochondrial donation, and can also be used to appease any community/public unease; and foster trust in provision

HGSA has a preference that only a small number of such licenses be granted to provider organisations in the initial period in order to aggregate relevant clinical experience, provide training, patient follow-up and clinical audit so as to support the greatest possible benefits to patients and healthy outcomes for children.

(f) the value and impact of introducing mitochondrial donation in Australia;

Mitochondrial donation is likely to be a relevant choice for only a few Australian families each year. But the significance of this choice for those families to whom it is relevant is likely to be large. Despite their small numbers mitochondrial disorders place significant burdens on families and on the healthcare system. There are no effective pharmaceutical treatments for these disorders.

Health economic studies have repeatedly demonstrated that the cost of care for severely disabled children is in the millions of dollars per life-time, substantial components of which are provided by parents. The care provided by parents to one child risks creating poverty both material and emotional for other members of the family.

(g) other related matters.

The HGSA welcomes further community engagement on mitochondrial donation to enable informed and transparent debate, increasing awareness of mitochondrial disease and sharing of views

HGSA notes that language has been shown to change the framing of a public discussion and its media, so would urge the Inquiry to consider the terminology they use carefully. In the existing literature, researchers have suggested more neutral terminology such as mitochondrial/nuclear transfer rather than the emotive "three-parent babies", "mitochondrial gene therapy" or "mitochondrial donation", others have suggested the emotion is less of an issue, when the term is accurate. As such, the Inquiry might like to consider nomenclature and what the best name for this intervention is.

HGSA would like to highlight that there is a dichotomy of views amongst its own membership regarding the status of the ethical review of mitochondrial donation performed in other jurisdictions and its applicability to the Australian environment.

- The majority of responses, including all responses from specialist medical practitioners involved in the care and management of children and families with mitochondrial disorders believe that further scientific or ethical reviews are not necessary, and that Australia can learn from the experiences in the UK to make mitochondrial donation a reality for the Australian public.



- An alternative opinion, represented by highly regarded ethicists and legal scholars among the Society's membership, is that further ethical review would be very appropriate in Australia (citing, for example that the UK's position on the anonymity of donors may not reflect Australian norms).
- HGSA notes that these views are not intrinsically incompatible, but both sets of expectations could be met by setting a clear timeframe for any further consideration of ethical issues so as to not represent a significant delay in any recommended changes to legislation.

HGSA suggests that this issue would be most appropriately explored by the Committee during face to face discussions with individuals making oral submissions to the Inquiry.

The HGSA also notes that the Genetic and Rare Disease Network is currently undertaking a survey of its members regarding attitudes to mitochondrial donation. The response times may not fit with this Inquiry, but it would be appropriate for the secretariat to contact them for follow-up in the future.

Overall, HGSA contends that given the work that has been done to get to this point in the UK, and the scientific rigor that was applied during the course of this body of work, the Senate Community Affairs References Committee should have sufficient information to be able to make recommendations for any modifications to existing legislation to facilitate the rapid integration of mitochondrial donation for specific primary mitochondrial DNA disorders.

Thank you once more for this opportunity to provide commentary to the Committee.

Yours sincerely,

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President

The HGSA recognises with gratitude input from the following members of the *Society* into this document,

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