Ethics of modifying the mitochondrial genome

Annelien L. Bredenoord, PhD
University Medical Center Utrecht
Department of Medical Humanities
A.L.Bredenoord@umcutrecht.nl
1. Does mitochondrial donation entail germ-line modification?
2. Are there moral differences between germ-line modification of the nuclear DNA and modification of the mtDNA?
3. What are conditions for a responsible use?
Germ-line modification?

Several differences nuclear DNA and mtDNA:

(1) mtDNA is extremely small
(2) mtDNA has very specific function
(3) mtDNA has own transmission pattern

Not relevant!
Germ-line modification?

YES!

Germ-line modification refers to any biomedical intervention that modifies the genome that a person can transmit to his/her child and the child’s entire lineage

➢ Novel mtDNA can be transmitted to further generations

Modification of the *nuclear* genome is considered more controversial than modification of the *mitochondrial* genome. This is because only the nuclear DNA would contain the ingredients for our identity.

Tenable dichotomy?
Modification mtDNA less controversial?

Fear to alter ‘essential’ characteristics of a future person. As the nuclear DNA would contain our identity, modification of the mtDNA would be less controversial.

Human Fertilisation and Embryology Authority (HFEA, 2005): “mtDNA is not associated with identity or predetermined characteristics of the individual”

(1) Little is known about the exact role, significance and function of the mtDNA. Studies have questioned the assumption that mtDNA is not associated with essential characteristics (Nagao et al, 1997; Roubertoux et al, 2003; Moreno-Loshuertos et al, 2006; Waters, 2009 - cited in Frankel and Hagen, 2011)

(2) None of the key terms are defined. What constitutes ‘identity’, ‘essential’ or ‘predetermined’ characteristics?

- Does modification of the mtDNA alter the identity of the person born?
Does germ-line modification of the mtDNA affect the identity of the person born?

Qualitative identity:
two persons or objects are exactly alike

Numerical identity:
two persons or objects are one and the same

Does germ-line modification of the mtDNA affect the identity of the person born?

Even if the mtDNA has a basic cellular role then still it is meaningful to say that germ-line modification of the mtDNA will change the (qualitative) identity of the future person.

After the modification, the future person will no longer be exactly alike.

After all, without the mtDNA disease the child will have:
- A different life experience
- A different biography
- A different character(?)

Does germ-line modification of the mtDNA affect the identity of the person born?

This means that the dichotomy between modification of the nDNA and modification of the mtDNA is untenable from this perspective: no matter whether one modifies a (pathogenic) nuclear gene or a (pathogenic) mitochondrial gene, the identity of the future person will be changed.
Does germ-line modification of the mtDNA affect the identity of the person born?

This is not to say that the distinction may not be relevant from other perspectives.

But modification of the mtDNA cannot be considered substantively different to modification of the nuclear DNA in terms of its effects on the identity of the future person.

Is germ-line modification compatible with the right to an open future?

Habermas (2003): ‘genetic modification may entail a prejudgment of specific life projects, which may imperil autonomy. Choosing the genetic make-up of a child may violate its right to an open future’

In a pluralist liberal society, one should indeed allow people to be the authors of their lives.

- Does germ-line modification of the mtDNA potentially threaten the child’s right to an open future?
General purpose means

Only allow modifications that broaden ‘general purpose means’ (Buchanan et al, 2000): capacities that are useful and valuable for carrying out nearly all plans of life

Health is a *sine qua non* for many (though not all) plans of life
Modification of the mtDNA is not substantively different from modification of the nuclear DNA in terms of its effects on the identity of the future person.

Therefore, any conclusion regarding the moral acceptability of modifying the mtDNA applies *mutatis mutandis* to modification of the nuclear genome.

This means that modification of the nuclear genome is equally acceptable as long as, other things being equal, this does not violate the child’s right to an open future.

Conclusion

1. Modification of the mtDNA entails germ-line modification
2. Modification of the mtDNA has identity-altering potential
3. The dichotomy between modification of the mtDNA and nuclear DNA is untenable from this perspective: all germ-line modifications change identity
4. Germ-line modification could be morally acceptable under certain conditions.
Conditions for a responsible use

I. Germ-line modification should not violate the child’s right to an open future

II. Safety and efficacy: examine the ethics of first human use
Ethics of mitochondrial gene replacement: from bench to bedside

The prospect of using mitochondrial gene replacement to conceive children free of mitochondrial disease highlights the need for a sound ethical framework for reproductive genetic technology, say Annelien Bredenoord and Peter Braude.
Thank you

Annelien L. Bredenoord
University Medical Center Utrecht
The Netherlands
A.L.Bredenoord@umcutrecht.nl