**Mitochondrial replacement therapy and identity – A comment on an exchange between
Inmaculada de Melo-Martin and John Harris**

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In the January 2017 issue of the Cambridge Quarterly of Healthcare Ethics there is an exchange between Inmaculada de Melo-Martin and John Harris about the ethics of mitochondrial replacement therapy (MRT) occasioned by John Harris' January 2016 article in the journal^{1 2 3}.

The debate between de Melo-Martin and Harris is wide ranging, but in this comment I want to focus on their disagreement about whether MRT is affecting the identity of the child which is born after MRT. Both de Melo-Martin and Harris seem to assume that this question has a straightforward answer, 'Yes' for de Melo-Martin and 'No' for Harris. More specifically de Melo-Martin argues that "susceptibility to disease and suffering"¹ (p. 160) is an identity-conferring trait, and that it is affected by MRT; and Harris counter argues that this entails that "all therapy and all disease is identity altering"² (p. 166-7) which he takes to be absurd. In his 2016 paper he argued that "no identity conferring features are transmitted by the mitochondria"³ (p. 11). In this comment I hope briefly to show 1) that the question is significantly more complicated than both seem to assume, and 2) that because they overlook important distinctions in relation to identity, they actually write at cross purposes.

In this short comment I will not discuss when, if ever questions about identity matter ethically.

The creation of identity

The first problem in the de Melo-Martin v Harris exchange is that both participants elide an important distinction, i.e. the distinction between changing an already existing identity, and creating or generating a specific identity. The question 'is the identity of entity A that has been created by MRT determined by MRT?' is a different question than 'is the identity of entity A, which already has an identity of the relevant kind, changed by entity A undergoing or having undergone MRT?'. This is perhaps most clearly seen if the identity in question is personal, psychological identity, e.g. Parfit's account of personal identity as overlapping, psychological continuity. On this account embryos do not have an identity, because they do not have a psychology, so MRT cannot change their identity, but it can still determine it. Some mitochondrial diseases lead to intra-uterine death, so simply prevent the foetus from ever developing a Parfitian personal identity. And even in cases where the child is born MRT can determine its psychological identity. For example, if a child can either be born with or without maternally transmitted Leigh Syndrome, the psychological and therefore personal identity of that child will be determined by MRT, since Leigh Syndrome is characterised as being:

"... a progressive neurodegenerative condition, which particularly affects the brainstem, diencephalon, and basal ganglia. There are characteristic neuropathological features, but

newer neuroimaging techniques can now easily detect these lesions in life. Clinically, these infants and children have signs of brainstem and basal ganglia dysfunction and often deteriorate in a stepwise manner.”⁴

It is also plausible that some conditions which may determine which psychological identity an entity will develop, do not change the identity of an entity that already has one. Let us imagine a condition which lowers cognitive ability by 50%, but does not change memories. It is plausible that a child born with that condition will develop a different psychological identity from the child that had been treated with something like MRT, but equally plausible that a 30 year old adult who is struck by the condition will not change identity because the adult preserves psychological continuity.

Identity of what?

The second problem in the de Melo-Martin v Harris exchange is that neither of the participants defines which type of identity they are discussing. There are at least five different kinds of identity that could be in play (see Table 1), and whereas MRT does not affect some of these, it does affect others.

The first and most basic type of identity is numerical identity. Here we simply ask whether an entity is the same physical entity over time. What is important is the physical continuation of the entity, not its characteristics. Numerical identity plays a role in one important philosophical argument related to assisted reproduction. Am I numerically identical to the embryo that gave rise to me? Many would answer ‘Yes’, but that is a potentially problematic answer because of the possibility of monozygotic twinning. If twinning occurs the numerical identity relation is broken because numerical identity is transitive. Numerical identity between an embryo and a later child is only secure about 14 days after fertilisation when there is no longer a possibility of monozygotic twinning. It should be uncontroversial that MRT changes the numerical identity of the unfertilised or fertilised egg depending on which MRT technique that is used. Parts of two prior ‘things’ are brought together to create a new thing. The numerical identity of the child is therefore also changed. Against this it could be argued that the mitochondria are only auxiliary to the entity, just as batteries are auxiliary to an electrical toy, and that no change in numerical identity takes place when the mitochondria are replaced⁶. The problem with this argument is that when we look at the actual techniques for MRT they involve the replacement of all the cellular cytoplasm and machinery except for the nucleus or spindle, and the donor egg contributes by far the largest part of the resulting entity. We might then say that it is never the less the nucleus that is the important part, but that seems to involve an

implicit reliance not on considerations of numerical identity, but on considerations of genetic identity. Here it may be worth noting in passing that the very same technique we here discuss as Mitochondrial Replacement is called Nuclear Replacement in discussions of cloning.

The second type of relevant identity is genetic identity. It is trivial that MRT works because it changes the genetic makeup of the egg, and thereby the zygote, embryo, fetus, child and adult that emerges without mitochondrial disease as a result of the treatment. But does that constitute a change of genetic identity? This seems, as with many questions about genetic identity to be a question of threshold that is susceptible to *sorites* considerations. It is difficult to say that changing one base pair in the genome changes genetic identity, and two still does not seem enough, neither does three and so on and so forth. One of the relatively common MtDNA mutations is a 5kBase deletion, but it is still a threshold question whether a change of 5000 base pairs, in this case by addition is enough to say that MRT affects genetic identity⁴⁵. Compared to the whole human genome 5kBase is not much, but the mitochondrial genome is only about 14kBase in total, so the change is about 35% of the mitochondrial genome. It might also be noted that MRT does change the detectable maternal mitochondrial lineage, and that might be sufficient to claim an effect on genetic identity.

The third type of relevant identity is phenotypical or physiognomical identity. Does the entity look the same or does MRT change the way the entity looks. When Harris writes in 2016 that “no identity-conferring features are transmitted by the mitochondria”³ it is most likely this type of identity that is referred to, and similar statements have been made by the UK Medical Research Council and the Wellcome Trust in reply to a call for evidence from the Nuffield Council on Bioethics:

“We do not believe the transfer of mtDNA raises issues around identity, since it does not carry any genetic data associated with the normally accepted characteristics of identity. An analogy could be drawn with replacing the battery in a camera – the brand of the battery does not affect the functioning of the camera.”⁷

It is true that the mitochondrial DNA does not contain any genes that determine physiognomy in the normal child, i.e. no genes for skin color, size of nose, curliness of hair, height or any of the many other characteristics that together decide how someone looks. This does, however not mean that mitochondrial mutations cannot affect physiognomy. On the more trivial side a number of the myopathy (muscle weakness) related mitochondrial mutations cause ptosis (droopy eyelids), but some cause more significant changes in looks. Kearns-Sayre syndrome is, for instance associated with short stature²³.

The fourth type of identity is psychological identity, as discussed in the previous section. It is undoubtedly the case that MRT determines psychological identity in those cases where the particular mitochondrial disease has a significant neurological component that impact on cognitive and psychological development. But there are also types of mitochondrial disease that do not affect psychological identity.

The final type of identity to mention is social and narrative identity. What kinds of relationships does the entity have, and in which stories is it inscribed and becomes a participant? Some kinds of social relationships and thereby social identity are conserved in MRT (at least where a child is born whether or not MRT had been used). The child will still, after MRT be 'the first son of X and Y, a little brother to Z', it will still be born into the same particular ethnic, social and linguistic community etc. etc. But, its social identity and narrative identity might diverge radically from the non-MRT identity over time. The child after MRT may become 'the husband of A, and the father of B, C and D' or 'the graduate from Berkeley', whereas the child without MRT might have become 'the child that X and Y tragically lost at age 4'.

Why does precision about identity matter?

Considerations about identity are prominent in a range of bioethical debates. They are raised in relation to reproductive technologies including MRT and reproductive cloning, but also play a role in end of life debates concerning persons with dementia. But, given that there are many different types of identity that may be ethically relevant (the five outlined above is not an exhaustive list) and given that there are a number of different identity questions there is great scope for elision between different types of identity and different identity questions. There is even greater scope for basing argument on one conception of identity in one context, and another in a different context. Many authors who deny that MRT affects identity, have previously argued that a child born after reproductive cloning is not identical to the person who is cloned. The argument that MRT does not affect identity can most plausibly be sustained on the basis of a genetic conception of identity. But, accepting a genetic conception of identity would entail that the clone is identical with the cloned person. The argument that cloning is not identity preserving is most plausibly made on the basis of a psychological and/or social and narrative conception of identity. It is perhaps too much to expect perfect consistency in peoples' arguments over time, but using fundamentally different conceptions of identity in arguments within the same area of discourse (reproduction) to sustain the desired conclusion should raise some concern.

Notes

1 de Melo-Martín I. When the Milk of Human Kindness becomes a Luxury (and Untested) Good. *Cambridge quarterly of healthcare ethics: CQ: the international journal of healthcare ethics committees*. 2017; 26(1):159-65.

2 Harris J. How To Welcome New Technologies: Some Comments on the Article by Inmaculada de Melo-Martin. *Cambridge Quarterly of Healthcare Ethics*. 201; 26(1):166-72.

3 Harris J. Germline modification and the burden of human existence. *Cambridge Quarterly of Healthcare Ethics*. 2016; 25(1):6-18.

4 Tuppen HA, Blakely EL, Turnbull DM, Taylor RW. Mitochondrial DNA mutations and human disease. *Biochimica et Biophysica Acta (BBA)-Bioenergetics*. 2010; 1797(2):113-28. p. 117

5 Schapira AH. Mitochondrial disease. *The Lancet*. 2006; 368(9529):70-82.

6 I owe this argument to Iain Brassington

7 Nuffield Council on Bioethics. Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review. London: Nuffield Council on Bioethics; 2012. p. 53

Table 1 Types of identity

Type of identity	Identity question	Conserved in Mitochondrial Replacement Therapy?
Numerical identity	Is it the same entity that is born?	No, if we think that changes to the numerical identity of the egg changes the numerical identity of the embryo
Genetic identity	Does the entity that is born have the same genetics?	Depends on threshold for genetic identity
Phenotypical / Physiognomical identity	Does the entity that is born look the same (and will it continue to look the same)?	Yes, for some mitochondrial disorders No, for other mitochondrial disorders
Psychological identity	Does the entity that is born have the same psychology (and will it continue to have the same psychology)?	Yes, for some mitochondrial disorders No, for other mitochondrial disorders
Narrative / social identity	Is the entity that is born inscribed in the same social / familial narrative?	Yes, but...