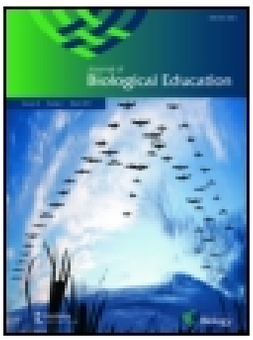

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Challenges to biology education from new reproductive technologies

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ABSTRACT

Teaching students about human reproduction is becoming increasingly daunting as assisted reproduction technologies challenge scientific, social and legal perceptions of parenthood. Mitochondrial replacement in particular forces us to re-examine established paradigms not only in the context of human reproduction but also with regard to the way in which we teach students about genetic modification, the nature of the eukaryotic cell, and eukaryote evolution.

KEYWORDS

Assisted reproduction; mitochondrial replacement; parent; eukaryotic cell; genetic modification

Introduction: teaching about human reproduction–more of a minefield than ever

Most school students know about 'the birds and the bees' long before a science teacher introduces the topic to them. At that stage, usually around age 13, they have the intricacies of human reproduction explained to them in traditional terms of sexual intercourse leading to fertilisation and pregnancy. But we live in a world where the traditional course of events is increasingly rivalled by reproductive technologies such as gamete donation, surrogacy and most recently, mitochondrial replacement (MR, also referred to as mitochondrial donation). All of these confound to some degree the conventional biparental model that has long been normative in biology, the law, and indeed society at large.

In the cases of gamete donation and surrogacy, there is no real scientific issue with regard to identifying parentage, but there are social and legal ones. For instance, a sperm donor relinquishes his claim to fatherhood for any resultant offspring, but it is the surrogate who is expected to relinquish her claim on the child even if she is the genetic mother (as she is in 'partial' surrogacy). In the case of 'full' surrogacy (where the surrogate has the commissioning couple's embryo implanted), the surrogate has no genetic claim to motherhood but continues to be regarded in English law as the mother simply because she bore the child. At this stage, science and the law–English law, at least–part company (*cf.* Ukrainian law which recognises the commissioning couple as the parents from conception).

2016 saw the birth of the first baby involving the revolutionary technique of MR which is aimed at eliminating hereditary diseases that arise from faulty genes in the mitochondrial DNA of the egg cell (mtDNA). A child thus produced has genetic material from three people–a man and two women, one of whom contributed the nuclear DNA whilst the other contributed mtDNA. The expression 'three-parent babies' caught on quickly with the popular press.

MR in particular is forcing bioethicists and law-makers to re-examine some of their fundamental assumptions concerning human reproductive biology. Emotions as well as the intellectual faculties are invoked and feelings run high about these issues in some sections of the community. Science/biology

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teachers are not strangers to socioscientific controversies and sometimes find themselves skating on thin ice when such issues arise in the classroom. The problem with socioscientific controversies is that they are not resolvable with sole resort to science as they involve premises based on opposing beliefs and values that, whilst being irreconcilable, are rational in their own right (Levinson 2007; Oulton, Dillon, and Grace 2004). In the case of sensitive issues such as human sexuality and its concomitants, teachers have to be doubly wary as they may not only upset some students but also inadvertently fall foul of legal maxims. Reproductive technologies bring with them their own distinct baggage of social, ethical and legal issues (Brezina and Zhao 2012; Briscoe 2013) which teachers at any level are well advised to thoroughly acquaint themselves with.

There are other implications for biology educators. MR poses a challenge to the way in which we teach upper secondary and lower tertiary students not only about human reproduction but also about genetic modification, the nature of cells and evolution.

Mitochondrial replacement: a new entrant to the brave new world of assisted reproduction

The UK was the first country to endorse the technique with the amendment of the Human Fertilisation and Embryology Act. The hitches had been the Act's prohibition on transplanting genetically modified embryos into a woman, and an EU petition calling upon the UK to not introduce MR techniques based on a general prohibition on genetic modification owing to its association with eugenics (Garasic and Sperling 2015). In a classic display of English legal wordplay, the UK Parliament acknowledged that MR 'represent(s) a *germline* modification but … does not represent *genetic* modification *(emphasis added)*', citing a 2014 Dept of Health report to the effect that a working definition of genetic modification applies to nuclear DNA only (House of Commons 2015). Biology instructors take note when teaching about genetic engineering!

The relatively small amount of total cellular DNA that mtDNA represents has typified the defence of MR. Professor Dame Sally Davies put it this way to Parliament:

> [We] need to make the distinction between nuclear DNA, which makes us who and how we are … and the 37 genes in the mitochondria which are about energy for the cell, and which we describe as the power pack. (House of Commons 2015, 21)

This approach does, however, gloss over the fact that most of the genes that control mitochondrial architecture and operation are located in the nucleus, not in the mitochondria themselves (Scarpulla 2002, 2005; Wanrooij and Falkenberg 2010). It also implies a purely quantitative mindset in which a certain mitochondrial percentage of cellular DNA would cross an arbitrary threshold between 'two-parent babies' and 'three-parent babies'. In contrast, the Dept of Health position noted above hints at a fundamental difference between nuclear DNA and mtDNA. Riley (2015) describes the contribution of a mitochondrial donor as 'materially different' from that of a gamete donor and points out that only the nuclear DNA has social significance as a determinant of parental status. Cohen and Alikani (2013) draw attention to the fact that individual mtDNA donors may be very difficult to identify given the maternal mode of inheritance of mtDNA. Appleby (2015) makes the useful distinction between 'genetic parents' and 'genetic contributors'.

The UK Human Fertilisation and Embryology Authority treats MR/donation much as it does organ donation rather than gamete donation; even in the case of the latter, no 'parental' rights are conferred to the donor, and the same reasoning applies to MR (House of Commons 2015; Riley 2015).

The strict distinction between nuclear DNA and mitochondrial DNA may nevertheless be seen to fly in the face of the high level of interaction between them (Baylis 2013; Bredenoord, Pennings, and de Wert 2008; Reinhardt, Dowling, and Morrow 2013). However, whilst Riley (2015) presents the majority consensus by referring to the expression 'three-parent babies' as 'a misnomer', Baylis (2013) reminds us of a case to be made for the three-parent model. The conundrum can be resolved by turning to the evolution of the eukaryotic cell and its organelles.

From primordial orgies to snug domesticity

Early life on Earth was dominated by a teeming variety of prokaryotes engaged in 'a global orgy of gene swapping' (Sterrer 2002, 392). Prokaryotic sex is generally unilateral and defies species boundaries, involving little more than the transfer of 'bits and pieces' (Sterrer 2002, 388).

The *Eukaryota* appear to have descended from a phagocytic Protozoan-like ancestral form that was nucleated, possessed a cytoskeleton and endomembranes, and was already carrying out mitosis. The endosymbiotic model posited by Margulis in 1970, which posits various organelles including the mitochondrion and the chloroplast as having originated from prokaryotes that took up residence in protoeukaryotic hosts, has since become standard doctrine in biology. The evolution of organelles with their own genomes occurred alongside the subsequent development of the eukaryotic nucleus and meiotic sex and involved intracellular coevolution (Cavalier-Smith 2010; Dacks and Roger 1999; Emelyanov 2003; Sterrer 2002).

The progenitor of the mitochondrion was an α-proteobacterium that, in typical prokaryote 'bits and pieces' manner, donated segments of its DNA to the host's non-reciprocating nucleus, and in so doing within the confines of the intracellular environment, lost much of its genome (Lang, Gray, and Burger 1999). With this loss also came about a surrender of autonomy with the host cell nucleus gradually taking control over mitochondrial replication and functioning (Scarpulla 2002; Sterrer 2002; Wanrooij and Falkenberg 2010). The replication of mitochondria remains poorly understood, especially for Mammals, but is vegetative and reminiscent of that of bacteriophages (Birky 2001; Holt and Reyes 2012). The mitochondrial genetic code does not conform to the 'universal' code and has to be read by specific tRNAs (Wanrooij and Falkenberg 2010). In the process of what Emelyanov (2003, 1599) called the 'domestication' of the mitochondrial symbiont, the eukaryotic host effectively sectioned off the mitochondrial genome, much of which it had captured in its nucleus. Thus, the nucleus emerged as by far the dominant partner in the relationship. This provides an evolutionary rationale for the emerging biolegal maxim that genetic parenthood is defined by nuclear DNA contributions alone.

MR pointers for biology education

There are profound implications arising from MR for the way in which we teach secondary and undergraduate students about the cell. We need to abandon the view of the eukaryotic cell as a unitary entity and present it as a composite one the evolutionary history of which is, in effect, polyphyletic. Whilst it may be acceptable at junior secondary level to speak of the nucleus being directly in charge of all goings-on in the cell by means of the 'universal' genetic code, more advanced students need to be made to realise that it is not as simple as that. The evolution of the eukaryotic cell is often glossed over in biology courses at upper secondary and introductory tertiary level but needs to become a central theme in the depiction of the history of life. The distinction between prokaryotes and eukaryotes needs to be softened as the eukaryotic cell contains organelles–mitochondria and chloroplasts–that in some ways still behave like prokaryotes.

With regard to sexual reproduction in humans and other eukaryotes, the reticence of either science or law to accommodate more than two parents suggests that the biparental model is quite secure and will remain so providing the nuclear DNA continues to be regarded as the sole arbiter of parental status. The process of fertilisation needs to be redefined in terms of the merging of nuclear DNA from two parents as opposed to the fusion of a sperm cell and an egg cell. The 'three-parent babies' concept as it applies to both full surrogacy and MR should be critically examined in class, an exercise that will be of considerable benefit to students' understanding not only of biology but also of the ways in which science intersects with social perceptions and law. In the current writer's view, teachers of biology are 'safe' in adhering to the biparental model, but they need to bear in mind that the term 'parent' has social and legal connotations that may not always sit comfortably with the strictly genetic definition.

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