

Three persons, three genetic contributors, three parents: Mitochondrial donation, genetic parenting and the immutable grammar of the ‘three x x’.

Abstract

In 2015 two novel in vitro fertilisation (IVF) techniques intended to prevent the inheritance of mitochondrial disease were legalised in the United Kingdom, following an intense period of inquiry including scientific reviews, public consultations, government guidance and debates within the Houses of Parliament. The techniques were controversial because (i) they introduced a third genetic contributor into the reproductive process and (ii) they are germ-line, meaning this genetic change could then be passed down to subsequent generations. Drawing on the social worlds framework with a focus on implicated actors and discursive strategies, this article explores key features of the UK mitochondrial debates as they played out in real time through policy documents and public debate. First of all it situates the technology within a repertoire of metaphors, emotional terminology and their politics. It then explores the immutable grammar of ‘three x x’ that formed a key component of the political debate, by focusing on how institutional reviews discursively negotiated uncertainty around genetic parentage and how beneficiaries were implicated and rendered distant. Following the 2016 announcement of the first baby born through mitochondrial donation (in Mexico) and several pregnancies (in the Ukraine), we close with a discussion about the specific nature of UK regulation within a global economy. Overall, this article contributes to a much needed sociological discussion about mitochondrial donation, emerging reproductive technologies and the cultural significance of genetic material and genetic relatedness.

Introduction

In 2015 the UK Parliament approved the clinical application of the novel in vitro fertilisation (IVF) procedures ‘maternal spindle transfer’ and ‘pro-nuclear transfer’ after an extensive process of scientific and ethical review, and public consultation. In this article we analyse the political debates in the UK that led to the first national regulations permitting mitochondrial donation as they played out in real time through policy documents and public debate. The techniques, known as ‘mitochondrial donation’ or ‘mitochondrial transfer’, used part of a donated egg to enable a woman with mitochondrial disease to have a healthy, genetically related child. Significant features of these techniques, and the reason why they have attracted such intense ethical enquiry are (i) they involved a third genetic contributor within the reproductive process in the form of the mitochondrial donor, and (ii) they are germline technologies in that the donor’s genetic material can be passed on through the generations.

Mitochondria are small structures in the cytoplasm of a cell which produce the cell’s energy and can cause mitochondrial disease when they fail to function (for an overview of the history of mitochondrial diseases, see DiMauro, 2011). Women with faults in their mitochondrial DNA will pass these on to their children, which means that both sexes can inherit the disease from their own mothers, but only women are at risk of having a child who also has the disease (Poulton et al., 2010). There is no cure for mitochondrial disease and as treatment options are currently limited, attention has turned to reproductive intervention.

Mitochondrial donation and the role of the donor

The two IVF technologies that have now been legalised in the UK could allow a woman with mitochondrial disease to have a child without the risk of passing on the disease. Maternal spindle transfer involved removing the nucleus of the egg and placing it into a donated, enucleated egg. Pro-nuclear transfer, which has been developed by the Wellcome Trust Centre for Mitochondrial Research in Newcastle (UK), involved a similar process but occurred after fertilisation (for a technical overview of the techniques see Amato et al., 2014; Herbert and Turnbull, 2015; for a review of the ethical distinction between the two techniques see Wrigley et al., 2015).

Mitochondria contain genetic material, so any child born through the techniques would inherit nuclear genes from the intended mother and father and mitochondrial genes from the mitochondrial donor. As Richards (2014) describes, the inclusion of others in the reproductive process, as a collaborative enterprise, is not necessarily a new phenomenon. Richards et al. (2012: 1) highlight that up to five progenitors had been possible: 'a social mother, a social father, a biological father (sperm provider), a biological mother (egg provider) and a surrogate (gestational mother)'. The mitochondrial donor can now be added as the sixth. However, the mitochondrial donor presents us with an interesting categorical challenge because along with the biological father and biological mother, she is also a *genetic* contributor.

The techniques were first developed more than ten years ago, and the law amended within the UK in 2008 to allow for the future possibility of legalisation (Jones and Holme, 2013). Across this period the presence and role of this 'third person' remained the primary focus of debate. Questions included the social and legal status of the relationship between child and donor (Bredenoord et al., 2008; McCanless and Sheldon, 2014) and the potential impact on the child and their sense of self (Baylis, 2013; McLean, 2015). Furthermore, this led to

ontological questions, including what is identity, what is a parent and what is genetic relatedness. In sum, much of the debates about mitochondrial donation can be characterised by competing perspectives about the biological and social significance of the mitochondrial donor and her imagined role in the life of the child.

Mitochondrial donation and UK biomedical culture

The second feature of mitochondrial donation, and possibly the most important in terms of legal requirements, is that it involves modification of the germ line. This means that if the child is female, her children will also inherit the donor's mitochondrial DNA. Because of this, a positive vote was required in both UK Houses of Parliament before it could be legalised, as mandated in the 2008 Human Fertilisation and Embryology Act. The change in law was preceded by a lengthy process of inquiry including: scientific reviews (HFEA, 2014, 2016), a call for evidence on the ethical issues organised by the Nuffield Council on Bioethics (2012), public consultations (HFEA, 2013; DOH, 2014a) and government guidance on draft regulations led by the UK Department of Health (2014b). During the final debates of the Houses of Parliament, MPs in the House of Commons (2015) voted 382 in favour of legalising the techniques with 120 against while the House of Lords (2015) voted 280 in favour with 48 against. Mitochondrial donation was legalised and the UK began the process of conducting the final safety checks and establishing a licencing procedure to regulate the first pregnancies.

The UK was the first country to confirm a policy position on this issue, capitalising on the existing structures for regulating assisted conception technologies. The move was part of a broader UK project to continue the mobilisation of its highly regulated yet permissive human embryo research base, manifest in the work of the Human Fertilisation and Embryology Authority (HFEA)

(Lovell-Badge, 2008; Mikami and Stephens, 2016; Reubi, 2013). As such the mitochondrial donation debate can be mapped onto a historical lineage of public debates leading to early adoption of highly bureaucratic but essentially permissive regulatory forms on a set of embryology and assisted reproduction technologies beginning with IVF in the 1970s and 80s (Mulkay, 1993). More recent examples include human embryonic stem cells (Stephens, Atkinson and Glasner, 2008), hybrid embryos that combine human and animal material (Haran, 2013) and subsequent to the mitochondrial donation debates, human embryo research using gene editing techniques of CRISPR/cas9 (Authors).

At the time of writing no child has been born in the UK through the newly legalised procedures and no clinics have yet been licenced. However, in September 2016 the *New Scientist* revealed that a child had been born through mitochondrial donation by a US team operating in Mexico (Hamzelou, 2016; Zhang et al. 2016) and that the techniques had also resulted in two pregnancies in the Ukraine (Coghlan, 2016). Neither Mexico nor Ukraine had formal legal positions on mitochondrial donation, just as neither had pursued a programme of scientific and ethical consultation on the topic, as seen in the UK. These announcements of the world's first mitochondrial donation baby conceived in Mexico, and the Ukrainian pregnancies, highlight considerable differences in how reproductive medicine is practiced and regulated across the globe and situates the UK narratives reported here in a context of international innovation.

In this article we apply a much needed sociological lens to this controversial technology and its regulatory biography in the UK through the social worlds framework (Clarke and Star, 2008). We first of all describe how the social worlds theory and methods package, and the concept of implicated actors, can be usefully applied to the mitochondrial debates. Secondly, we examine how mitochondrial donation draws upon a familiar set of metaphors and emotive

terminology often used to describe new genetic technologies and their social implications. This is followed by an extended section specifically focusing upon the immutable grammar of 'three x x' that formed a key component of the political debate. We focus on the politics of the 'three x x', its institutional use and its implicated and silenced beneficiaries. Finally we close with a discussion and conclusion about the nature of UK regulation within the global economy.

Theory / methods package: the social worlds framework

We draw on a social worlds framework to understand the journey of mitochondrial donation from bench towards bedside, reflecting a long tradition of application in the context of embryo politics and assisted reproduction (Clarke, 1998; Ganchoff, 2004; Kitzinger et al., 2007; Timmermans and Shostak, 2016; Williams et al., 2008). The concept of social worlds was developed within the tradition of symbolic interactionism associated with pragmatism and the Chicago School of symbolic interactionism, and was initially described by Mead (1934) as a 'universe of discourse'. Social worlds are created through interaction, communication and negotiation. The framework is useful for highlighting how actors and groups can have different perspectives yet remain capable of working together, involving shared commitments, activities, materialities, work, performance and relationships (Clarke, 1997; Fujimura, 1992; Strauss 1978). Clark and Star (2008) linked several core ideas as 'sensitising concepts' (Blumer 1969) which can act as a guide for empirical analysis and form a conceptual tool box for theory building. Out of these, boundary objects is possibly the most recognisable and most frequently used to explain how objects can support co-operation between groups who otherwise experience an incommensurability of perspective, practice or language (Star and Griesemer, 1989). 'Implicated actors' is a less familiar concept, but it is useful for understanding political debates about new

technologies and is particularly relevant for this article. Clarke and Star (2008: 119) highlight two kinds of implicated actors, those who are “physically present but are generally silenced/ignored/made invisible by those in power in the social world or arena” and those who are “*not* physically present in a given social world but solely discursively constructed and discursively present” [emphasis in original].

Mitochondrial donation proves a valuable contemporary case study because it challenged both the UK legal framework and prevailing cultural assumptions about the symbolic and biological significance of genetic material. But the concept of ‘implicated actors’ is particularly relevant because of the novelty of the technology. The mitochondria donor, the intended mother with mitochondrial disease and the future child are all new actors who were introduced and discursively produced through the public and policy debates. This article explores how this group of implicated actors were “conceived, represented, and perhaps targeted by the work of arena participants” (Clarke and Star, 2008: 119).

The social worlds framework also implies a methodological approach as part of its theory/methods package that draws upon the constructivist move in grounded theory (Clarke and Star, 2008; Charmaz, 2000, 2006). Grounded theory is a systematic approach to qualitative data analysis that can account for the complexity of social phenomena, allowing themes to emerge as the research progresses by constantly and consistently developing interpretations (Glaser & Strauss, 1967; Strauss and Corbin, 1998; Atkinson *et al.* 2003). We apply this to our analysis of a range of publically available documents, collected between 2012 and 2015, at a time when mitochondrial donation received significant parliamentary and media attention.

The documents were collected in 'real time', as the events unfolded under the public gaze (Jaspal and Nerlich, 2016). All policy relevant documents produced by key UK institutional actors (primarily the Department of Health, the HFEA and Nuffield Council on Bioethics) between 2012 and 2015 were analysed. This included statements of remit, calls for evidence for consultation (and those contributions where they were available), published reports by these institutional actors on consultation conclusions, and any other related formal documents released. We also analysed Hansard transcripts of parliamentary debates in both UK Houses of Parliament. Outside of the key governmental actors we also analysed reports and outputs from key groups campaigning for legalisation (for example, Muscular Dystrophy UK and the Progress Educational Trust) and those opposed to legalisation (for example Christian Medical Fellowship and Human Genetics Alert). We also draw upon newspaper reporting of the events as the media was an important forum for the rapid communication of personal and professional viewpoints. We recognise our reference to media sources through purposive sampling serves as illustrative examples rather than constitute a systemised and exhaustive analysis of media outputs as found in more detailed cultural studies research. Although content analysis of newspaper coverage during the process of public debate would produce interesting insights, intensive and detailed media analysis is beyond the scope of this article. Instead, our attention to media coverage which also includes television, radio and online content (for example the Progress Educational Trust's 'Bionews' archive of professional and expert views and commentary on genetics and assisted conception) forms one part of our real time following of the debate, alongside the extensive analysis of policy documents, parliamentary debates and institutional reports. Both authors analysed the data using thematic analysis, where themes emerged in real time as the political process progressed (Strauss and Corbin,

1998). Several key themes were identified including: the role of patients in the debates; discourses of hope and fear; histories and future imaginaries related to IVF technologies; national representations; risk; and appeals to expertise and evidence. In keeping with a grounded theory approach to generating thematic categories that span multiple years, the themes used were flexible and responsive to shifts in the data. For example data relating to patients was initially drawn from accounts of professionals who were speaking publically about or on behalf of patient groups. This theme later began to include more references to patients' own accounts as increased numbers of patients actively spoke about themselves and their families. Our thematic categories evolved to include the engagement and activities of patients to ensure this important dynamic was captured. Overall the primary focus on the multiple metaphors and descriptors used to portray mitochondrial donation and the role of the mitochondrial donor was a direct response to the prominence of this theme in the analysis across all sections of the data corpus.

Metaphors, meanings and mitochondrial donation

The UK mitochondrial donation debate regularly drew upon metaphorical and emotive language. Analysing such discourse has a long history in medical sociology and science and technology studies in general (cf. Hellsten and Nerlich, 2008; Hacking, 1999) and with reference to social worlds theory in particular (cf. Bowker and Star, 2000). Whereas Sontag (1979) highlighted how military metaphors– the body under attack and invaded – or the body as machine, are used to make sense of illness, the wider development and use of genetic technologies were accompanied by a new set of descriptive language. Computer metaphors and essentialist images enabled our genetic make-up to be described as a 'code', genes as part of the 'book of life' or a 'blueprint', with the quest to

map the human genome becoming the 'holy grail' (Nelkin, 2001). Metaphors can both constrain and facilitate our thinking (Nelson et al., 2015), and remain core topics for social science analysis.

In some regards the UK mitochondrial debate draws upon this familiar set of representations which are now an entrenched repertoire for describing new technologies. Writing at the time when mitochondrial donation first became a possibility, Haran et al. (2008) documented some of the early metaphors used in the UK, including the 2004 Daily Mail heading 'Science Seeks to Deliver a Baby with Three Parents' and from 2005, 'Designer Babies To Wipe Out Diseases Approved' (Haran et al., 2008: 127). More than ten years later, the mitochondrial debates continue to feature such vivid imagery including: dystopian predictions about 'slippery slopes' and 'crossing a line' (Le Page, 2015); 'designer babies' (Hills, 2012); 'Frankenstein science' (McKie, 2014); and emotive themes such as 'playing god' and stopping children suffering (Driscoll 2015).

One example of a metaphor specific to the mitochondrial debates is the description of mitochondria as a 'battery'. Jane Ellison MP, in her opening remarks at the House of Commons Debate, stated that 'Mitochondria are present in almost every cell in the body and produce the energy we need to function. This is why they are often referred to as "the battery pack" of the cell.' (Hansard, 3rd February 2015, column 160). Ellison went on to state that the techniques 'are about replacing the battery pack that contains a small number of unhealthy genes with a healthy battery pack' (column 161). Based on competing perspectives about the biological significance of mitochondrial DNA, the battery metaphor can be recognised as an accurate representation of complex science, an over simplification or a misrepresentation. Reducing the complexity of mitochondrial function enabled those supportive of legalisation to represent mitochondrial donation as the equivalent of 'simply' changing a laptop battery (Muir et al.,

2015). In contrast the different analogy of comparing it to replacing one of the CPUs in a laptop might lead to a very different understanding of the contribution of the biological material to the child's identity (Gemmell and Wolff, 2015).

The mitochondria as battery metaphor reveals how language and representations matter, and that their use can be political. Representing mitochondria as a battery is an important component of the discourse surrounding mitochondrial donation, as it performs the important work of enabling the technology to be positioned as unproblematic. Further examples within the mitochondria debates include the cultural relevance and implications of describing the third person as donor or provider (Haines and Taylor, 2015); whether the techniques should be classified as donation, transfer or replacement and whether it is appropriate to talk about reproductive technologies as a treatment or cure (Rulli, 2016). For the remainder of this paper we focus upon perhaps the most visible and contested metaphors used, the immutable grammar of the 'three x x'. After introducing it and articulating its affordances in terms of the politics of genetic relatedness and kinship significance, we focus upon its denial in institutional reviews and the implicated actors it casts as beneficiaries and those beneficiaries distanced.

Genetic parentage and the immutable grammar of 'three x x'

As mitochondrial donation increasingly moved into the public gaze it was accompanied by a varied linguistic repertoire of terms referring to the mitochondrial donor as a 'third person' in one form or another (Ravitsky et al., 2015). Mertes and Pennings (2008: 8), referring to the work of Robertson (1999), suggest 'a major genetic mother' and a 'minor genetic mother' as a way of distinguishing the intended mother from the mitochondrial donor. Other terms

include 'mito mum' (as reported in *The Economist*, 2014) and 'shadow mum' (McGee, 2012). However, none of these phrases attracted the profile of what we term the 'three x x' set which became a key trope around which genetic relatedness was contested during the period of the policy debate. This set of metaphors are a family of terms with multiple reconfigurations across what has become an immutable grammar of 'three x x'. It includes 'three person IVF', 'three person DNA', 'three person babies', 'three person IVF', 'three-parent embryo', 'three parent family', 'three parent children' and 'three-parent baby'. Applying the social worlds theory perspective to the actors implicated in the multiple variants of the 'three x x' grammar reveals multiple networks of kinship and genetic relatedness contested and enacted within the set. The first 'x' in the grammar is typically either 'person' or 'parent'. 'Three person' variants imply less direct kinship and limited biological or social connectedness compared to 'three parent' variants. 'Parent' or 'mother' suggest more significance and relationality in the role of the third person – always understood to be the donor woman – to the family unit. The second 'x' typically denotes either the technique, biological material, the child or the child in a kinship context. We see all these as on a continuum that suggests the process of bringing into being a new life free of mitochondrial disease, but affording different notions of relationality to that life. At either end of this continuum, 'three person IVF' implies less relatedness and less kinship significance to the donor mother. In contrast, 'three parent baby' and 'three parent family' both invoke strong biological, and possibly social, significance to the mitochondrial donor.

It is possibly not surprising in the context of cultural privileging of genetic information, genetic identity and genetic parentage, that mitochondrial donation has become synonymous with 'three parents', at least in popular discourse. Representations of the 'three parent' family, along with various images of one

man, two women and a baby or child in different forms of embrace and configurations have dominated media stories for some time. In one example the BBC radio programme 'Mum and Dad and Mum', broadcast in February 2015, followed the story of a child born thirteen years previously through cytoplasm injection. This was a related technology which resulted in the birth of 17 children in 2000 in the US (Barritt et al., 2001)¹. The radio programme was advertised with a striking image of four silhouettes, one behind each other at equal distance - a child, a woman, a man and then last in line, but remaining close, another female, presumably the mitochondrial donor.

The strong imagery of the 'three parent family' and the language of the 'three parent baby' has itself become the focus of public debate as well as the technology which they represent. The media have sometimes been blamed by pro-legalisation groups for putting a negative spin on the idea of the 'three parent baby' (Johnson, 2013). The role of the 'three x x' grammar as a political tool was noted during the debate and identified as potentially detrimental to garnering public support. Viscount Ridley in the Lords debate stated that the phrase was 'wildly misleading' and the term three parents as a 'misuse of the English language' (House of Lords, 2015: 1587). Lord Robert Winston, renowned fertility expert and IVF pioneer wrote in his self-penned newspaper article (2015) that the 'three parent child' idea was 'nonsense' and that it was used to court controversy before the parliamentary vote. Explicit attempts were subsequently made to encourage a move away from this term, including requests by prominent spokespeople at a public conference (Progress Education Trust Annual Conference, 2015), yet the term prevails in popular and political discourse.

Throughout the debates, campaigners against legalisation continued to use the 'three x x' grammar and assert its appropriateness. Philippa Taylor of the Christian Medical Fellowship wrote in an information leaflet titled 'three-parent

embryos for mitochondrial disorders' that "the outcome of the technique is the creation of an embryo with two 'mothers' and one father" (2013). Like Taylor, Christian advocacy group CARE (2014) used a more kinship orientated variant of the 'three x x' set in their campaign materials, notably including statements such as "No other nation in the world has legalised the creation of three-parent children" in their commissioned survey of public attitudes (finding "just four per cent of those surveyed said they were more likely to support changing the law" based on this statement), and directing readers keen to support their campaign towards the no longer operative url www.stopgm3parentbabies.com. The affordance of discomfort in the 'three x x' set was also explicitly used as a strategy to discredit legalisation, for example Tim Stanley (2015), in the Telegraph newspaper, wrote: "'Three parent babies.' Run that phrase through your head. Doesn't it sound a little wrong?... I would suggest... [y]our instinct is probably that 'three parent babies' sounds like a step too far. Your instinct is entirely correct." In all these cases the use of the kinship displaying variants of the 'three x x' asserts the moral and technical accuracy of emphasising the genetic relatedness of the egg donor to any progeny born.

The 'three x x' grammar can be powerful for a number of reasons. Haran et al. (2008) highlighted how the 'three parent baby' threatens normative assumptions about society, as evidenced in headlines such as 'Three-parent babies 'threat to humanity'' (The Sunday Times, 2014). Despite ever increasing possibilities of family forms (see for example, Franklin, 2013; Lock and Nguyen, 2010) and a greater awareness of difference (Palacios-González et al., 2014), the spectre of the 'three parents' can seem 'monstrous' (Johnson, 2013), a danger to the 'traditional' nuclear family (Appleby and Karnein, 2014) and a threat to society. Thus the conceptualisation of, and metaphorical language surrounding the three contributors becomes much more symbolic than a question of biological

accuracy. The prominence of the 'three x x' language, as with the battery metaphor, suggests it has become an integral part of the 'interpretive package' (Gamson and Modigliani, 1989) of metaphors, images and justifications which give meaning to mitochondrial donation. The significance, and novelty, of the inclusion of a third person's DNA, has meant that the 'three x x' set was unavoidable as an immutable grammar that became a vital vehicle for expression, or a problematic, which needed to be addressed whatever one believed about the role of the donor.

Defining genetic parentage in institutional reviews

The debate over the 'three x x' grammar was a recurrent theme of the institutional reviews supporting the public dialogue on mitochondrial donation. In 2012 the Nuffield Council on Bioethics, in one of the first public calls for evidence about the ethical implications of the techniques, identified genetic relationships as a key issue. The Nuffield Council on Bioethics is the technically independent group who in practice come closest to a UK national bioethics committee in that they represent the UK at international meetings and broadly align with the politically dominant view in the UK on evidence-based scientific practice and the regulated permissibility of human embryo research (Jasanoff, 2005). Their consultation was based on a rapid response model to the emerging technology, creating the capacity for them to set the terms of the debate. In their call for evidence they asked: What might the use of these techniques signify for the relationships of the resulting child to the three adults with whom it shares a genetic connection? When subsequently reporting conclusions on the assembled submission to their call for evidence, internal hearings and discussion, the Nuffield Council on Bioethics (2012: xvi) declared "it is the view of the Working Group that

mitochondrial donation does not indicate, either biologically or legally, any notion of the child having either a ‘third parent’, or ‘second mother’”.

The initial question and concluding statement are important for several reasons. Firstly, they highlight the possibility of genetic relatedness initiated by the introduction of a third genetic contributor. Secondly, they demonstrate how the role of the mitochondrial donor as parent or non-related donor is contestable, dependent on a particular perspective or ‘view’ rather than biological fact. Thirdly, they highlight the requirement to resolve the uncertainty surrounding the relationship between donor and child. This pattern of mentioning genetic relatedness but then ‘undoing’ kinship (Edwards, 2014) by ruling out the possibility of identifying the donor as a ‘parent’ remained a key feature of the government policy documents that we analysed.

Another central institution of UK biomedical regulation, the Department of Health, conducted their own public consultation in an explicit attempt to move forward plans to legalise the technique under HFEA inspection (DoH, 2014a). The report also drew the conclusion that the mitochondrial donor was not a ‘second mother’ and regarded the term ‘three parent families’ as ‘completely inappropriate’. The report states:

In using these techniques, the resulting child will have nuclear DNA (99.9 per cent) from their father and mother and healthy mitochondrial DNA (0.1per cent) from a female donor. Genetically, the child will, indeed, have DNA from three individuals but all available scientific evidence indicates that the genes contributing to personal characteristics and traits come solely from the nuclear DNA, which will only come from the proposed child’s mother and father. The donated mitochondrial DNA will not affect those characteristics. (DoH, 2014b: 15)

Finally on institutional responses, in their document explaining the regulatory process around licencing mitochondrial donation, the HFEA stated:

A key reason for encouraging clinics to disclose non-identifying donor information to patients and parents of donor-conceived people is to help parents share information about their child's genetic origins, and to prepare them for potentially meeting their donor once they can receive donor identifying information at 18. These Regulations introduce a different system for mitochondrial donor-conceived children because it is recognised that a mitochondrial donor does not determine the characteristics of a child in the same way as with gamete donation and will not be the genetic parent of any child born. The Regulations specify that mitochondrial donors cannot be identified, reflecting the policy view that mitochondrial donation is more akin to organ donation than egg or sperm donation. (HFEA 16/09/2015: 47)

While attempting to draw conclusions and thereby reduce the complexity of genetic relationships, this extract serves to highlight the ambiguity of genetic information in relation to the child and donor. Significantly, while the regulations around mitochondrial donation declare that the donor is not a genetic parent, it remains possible that the child might want to have information about the mitochondrial donor if it concerns 'their genetic origins'. This reveals the social significance of genetic relatedness as a strong cultural influence. Yet it also reveals how mitochondrial donation disrupts established classificatory systems and legal frameworks around reproductive technologies; both the child and the mitochondrial donor are positioned in relation to a technology that is

ambiguously represented as similar to both solid organ and gamete donation, but not the same.

Implicated actors invoked as beneficiaries

Those supporting the legalisation of the techniques, and typically denying the relevance of all but the least kinship orientated variants of the ‘three x x’ grammar, articulated a clear set of beneficiaries from the legalisation: families with a mother carrying mitochondrial disease and their as yet unborn progeny. Women currently carrying mitochondrial mutations, and thus at risk of giving birth to children who may have mitochondrial disease, were physically present and highly visible in the public debates. Their emotionally powerful stories, particularly around the devastating effects of severe disease on a child, were used as evidence in support of the techniques and enabled this group to be projected as future beneficiaries of the technologies. In addition to producing healthy children, one of the points of persuasion in the mitochondrial debate is that despite alternative reproductive options, including egg donation, mitochondrial donation offers these women the opportunity to have their own, *genetically related* children. This was highlighted as one of the key arguments in favour of supporting the techniques, as mentioned in the opening speech of the House of Lords debate:

The techniques provided for by these regulations offer the only hope for some women who carry the disease to have healthy, genetically related children who will not suffer from the devastating and often fatal consequences of serious mitochondrial disease. (The Parliamentary Under-Secretary of State for Health, Earl Howe, House of Lords, February 2015: column 1569)

This is a succinct account of why the techniques might be supported, with the possibility of a genetically related child alongside offering reproductive hope and a child in good health. The actors involved are the mothers carrying mitochondrial mutations and the entirely implicated and as-yet unborn children of these mothers who would live without mitochondrial disease or risk of transferring it to their own children. In the presentation of these techniques as a public good, genetic relatedness of the mother to her child is prioritised: we celebrate because the child is her biological progeny free from mitochondrial disease, as opposed to a child free from mitochondrial disease and brought into the family through adoption, for example. However, there is a discrepancy in how those contributing to the debates valued genetic relatedness and in the next section we ask for whom genetic relatedness is rendered important and how other potential beneficiaries of the technologies were positioned.

Actors rendered distant and beneficiaries denied

For those supporting legalisation the genetic relatedness of the mother was positioned as central to the benefit of the technique, while in contrast the genetic relatedness of the donor woman was distanced, in part through denying the 'three x x' grammar or using kinship reducing variants like 'three person IVF'. The donor woman is an example of Clarke and Star's (2008) second type of implicated actor: discursively constructed and represented in the debate by the voice of others. At the time of the debates donor women did exist in the UK but their kinship relation to a child was not yet a lived issue: their eggs had only been used in experimental procedures to produce embryos for research that were destroyed and were not implanted into a womb (Craven et al., 2010). This given, donor women did not personally feature in the public debates, but instead as

implicated actors were spoken for by others. Haimes and Taylor (2015) highlight how the donor had become an absent presence, where her role was minimised, distanced and rendered invisible as part of a political strategy. They suggest one layer to this is the terminology of 'mitochondrial donor', which implied that it was only mitochondria she provided, rather than the other cellular structures in the egg.

We suggest that positioning the mitochondria as a battery also performs this work of underplaying the social meaning of the donor's genetic contribution. The replicability, and with it disposability, of a battery that only powers, but does not alter the form of that which it powers, creates a disconnect between mitochondrial DNA and the identity of the child, just as the choice of the 'x' in the 'three x x' grammar configures the donor as parent or person. According to UK law now in place, even though she donates an egg she is not considered an egg donor; and even though her genes will be passed on to the child and future generations, she is not considered a parent.

There are another set of implicated actors who were distanced from the debate by those supporting the techniques. In the UK, mitochondrial donation will legally be available only to those at risk of having a child with mitochondrial disease, meaning that other user groups who could benefit from the potential of mitochondrial genetic relatedness could not be configured as future users or beneficiaries. For example, mitochondrial donation could be a way for a lesbian couple to have a child who is genetically related to both parties (one contributing nuclear DNA, the other contributing mitochondrial DNA). Older women with lower levels of fertility are another group who have been ruled out as potential beneficiaries. Mitochondrial donation might improve their chances of having a child (as reported in Smyth, 2015) and would be a clear successor to cytoplasm injection (mentioned previously) which was initially designed to combat infertility.

Thus older and lesbian women who had the potential to contribute to the debate, were implicated, but silenced, by being positioned outside the realm of noted beneficiaries. While the internal relationships of the 'three' in the 'three x x' was frequently debated and contested, the fact that the three did not include a lesbian couple or an older women seeking fertility treatment was not a prominent feature.

Discussion and conclusion

The legalisation of mitochondrial donation represents a significant moment in UK biomedical political history. In this article we have focused on the discussions which took place in the UK prior to the change in law. The debates brought different kinds of genetic material into the public imagination. The introduction of a third *genetic* contributor in collaborative reproduction confronts our understanding of the biological and social significance of genetic material and genetic relatedness. Categorising genetic material on the basis of form, function and location has challenged previous ideas about the primacy of the gene as a 'cultural icon' (Nelkin and Lindee, 1995).

The social worlds theory provides an important framework to extend our analysis. The public debates about mitochondrial donation have been an inherently political process, legitimising particular kinds of discourse (for example, mitochondria as a battery; and the mitochondrial donor as a 'third' person) and implicating certain groups of people as natural beneficiaries (women at risk of having a child with mitochondrial disease). Social worlds theory also recognises the importance of context, which is particularly important for examining scientific controversies and newly emerging technologies (Clarke and Star, 2008). We have shown that the biography of mitochondrial donation and its journey from bench

towards bedside via public consultations and parliamentary debates can only be situated within the current political, cultural and social context.

Importantly, social worlds theory recognises the power of collective action, in order 'to get work done and to produce relatively (and temporarily) stable facts' (Fujimura, 1992: 168). Members of the social world who supported mitochondrial techniques shared a common goal (the legalisation of mitochondrial donation) where their primary activities involved the emotional and practical work of persuading others of its value (Strauss 1978). The overwhelming majority vote in favour of legalising the technologies in the Houses of Parliament attests to the success of this work; a group of scientists, parents and policy makers who were able to persuade others of the future value of mitochondrial donation. One of the reasons for their success was that they were able to draw upon cultural priorities of health and genetic relationships. The dominant representation of mitochondrial donation was as a technological solution for children and families and this offered a collective and powerful vision of hope (Mulkay, 1993; Novas, 2006).

A remarkable feature of the mitochondrial debates within the UK was that there has been little room for exploring the wider significance of the terminology in use and it has featured minimal talk about progression and wider benefits of the developing science. In fact it was the opposite, and unusually for a novel technology, part of its promise (within the UK) was that its use would be restricted to a defined population and that it would remain closely controlled and regulated.

Despite there being potentially expansive uses for different groups of people, mitochondrial donation was presented as a restricted technology that would only benefit a specific group of patients defined through their health status and reproductive risk. Those with the power to concentrate the discourse upon

the disease state of heterosexual families with mitochondrial disease were able to render others invisible. Despite having the potential to be discussed as a transformative technology, in many ways the terms of the mitochondrial debates and the conclusions of key UK institutions remained within conservative boundaries.

The UK decision to legalise the two techniques of maternal spindle transfer and pro-nuclear transfer could have global implications (Ishii, 2014) and debates are currently happening alongside gene editing in the US and elsewhere (Rulli, 2016). But it is now clear that although the UK was celebrated as the first to legalise mitochondrial donation, two important moments in the mitochondrial donation timeline might also prove to have a significant impact on its future global trajectory. While scientists in the UK were conducting further experiments to satisfy the requirements of the HFEA, a US team delivered a baby boy born via maternal spindle techniques, circumventing the as yet unresolved US legal position by conducting the procedure in Mexico. And while the UK has restricted use to only those at risk of mitochondrial disease, the two pregnancies in the Ukraine resulted from the techniques used by women with fertility issues rather than those at risk of passing on an inherited condition. If these pregnancies result in healthy babies, then we might witness a potentially large and powerful population initiate their contribution to the debate by demanding access to the technology within or outside UK boundaries. This could lead to more expansive debates about the social value of the technology, paralleling those currently taking place about social egg freezing for example, where the focus is on freezing eggs for social reasons such as a lifestyle choice rather than health reasons (see for example, Baldwin et al., 2014).

Overall this article has highlighted why mitochondrial donation and its related debates are sociologically interesting. Greater attention to the political

nature of science debates, the context in which they take place and how social worlds operate as powerful collectives can help us understand the different logics at play. Following the unexpected announcement of the birth of the first baby and with the new technology of gene editing also on the horizon (Nuffield Council on Bioethics, 2016), it is important that social science researchers are in a position to respond to these challenges and opportunities.

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¹ Whereas mitochondrial donation involves the transfer of the nucleus into an enucleated donated egg, this previous technology injected cytoplasm from the donated egg (which contained healthy mitochondria), in the hope that the healthy mitochondria would out-perform the faulty mitochondria. The children born were not enrolled in any kind of follow up study and the technique was subsequently discouraged by the FDA (Food and Drug Administration) due to fears about safety.