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ORIGINAL ARTICLE

Powering life through MitoTechnologies: exploring the bio-objectification of mitochondria in reproduction

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Abstract Mitochondria, the organelles providing the cell with energy, have recently gained greater public visibility in the UK and beyond, through the introduction of two reproductive technologies which involve their manipulation, specifically 'mitochondrial donation' to prevent the maternal transmission of inherited disorders, and 'Augment' to improve egg quality and fertility. Focusing on these two 'MitoTechnologies' and mobilising the conceptual framework of "bio-objectification", we examine three key processes whereby mitochondria are made to appear to have a life of their own: their transferability, their optimisation of life processes and their capitalisation. We then explore the implications of their bio-objectification in the bioeconomy of reproduction. Drawing on publicly available material collected in two research projects, we argue that mitochondria become a biopolitical agent by contributing to the redefinition of life as something that can be boosted at the cellular level and in reproduction. Mitochondria are now presented as playing a key role for a successful and healthy conception through the development and promotion of MitoTechnologies. We also show how their "revitalising power" is invested with great promissory capital, mainly deriving from their ethical and scientific biovalue in the case of mitochondrial donation, and from the logics of assetisation, in the case of Augment.

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Introduction

Largely unknown only a few years ago, mitochondria[1] have recently gained greater public visibility in the UK and beyond. The existence of these cellular parts, whose metabolic functions are key to the growth and death of the cell, has long remained confined to the specialised domain of cytology. However, in recent years, they have become increasingly present in a large range of domains including clinical research, biomedicine, pharmaceutical and cosmetics industries. Mitochondria have also been popularised through genealogical searches and migration studies where mitochondrial DNA testing is used to trace maternal ancestry and population origins (Cannell 2011; Oikkonen 2015). Moreover, a large number of recently published papers have shown the crucial role mitochondria play in the development of cancers as well as Parkinson disease (Gómez-Sánchez et al. 2016; Kalyanaraman et al. 2018), generating high hopes in the biomedical field.

Mitochondria are especially becoming increasingly visible and significant in the field of reproduction. In the UK, the development and legalisation of new reproductive techniques, often referred to as 'three-parent IVF', brought them to the centre of public attention and ethical debates due to the use of genetic material from three distinct individuals in order to prevent the transmission of mitochondrial diseases. Mitochondria appeared again in the media at the beginning of 2016, when a clinical trial was requested for a new reproductive technique seeking to "boost" the "health" of old oocytes by changing their "batteries", i.e. their mitochondria (Connor 2016; Knapton 2016). In relation to this, fertility success increasingly seems to be related to the mitochondrial DNA itself, as suggested by the development of a new fertility test called MitoGrade which measures mitochondrial DNA levels in the embryo in order to select those with better chances of implanting in the womb and forming a pregnancy (Fragouli et al. 2015; Sample 2015).

The attributes granted to mitochondria have been highlighted and magnified in recent years through their circulation in these various domains. This is especially noticeable in the number of metaphors emerging to describe mitochondria, such as "powerhouse of the cells", "power generators", "energy convertor", "factories", "waste disposal and recycling centre", "cell battery", "micromanagers", "powerful liens", "power packs" or "elixir of life" (Connor 2016; Hamilton 2014; MacRae 2016; The Economist 2016). Describing metaphorically the roles mitochondria play in cellular and metabolic mechanisms, these terms evoke their 'power' in relation to life. This power seems to work as a double-edged sword, as both a power to support

[1] The term "mitochondria" designates, from a scientific perspective, the organelles situated in the cell cytoplasm, whose functions are to produce the energy necessary to its functioning and control the processes of cellular growth and death. They possess their own 37 genes which are maternally inherited and distinct from the DNA contained in the chromosomes of the cell nucleus.

life processes and contribute to the health of living organisms, and as participating in life's decay, as a cause of disease. Mitochondria are associated with both fertility and infertility, youth and ageing, and with two contrasted dimensions of inheritance; positive when it is a source of genealogical identity, and negative when it results in the transmission of serious diseases. This illustrates the double dimension of mitochondria: as a source of cellular power opening up prospects for regeneration and genealogical continuity, and as a vector of genetic malfunctions, disease and decline.

In order to explore the ways mitochondria have become manipulable and understood as source of power which can be used to boost life, we focus on the domain of reproduction, which is a unique site in which to question how social and cultural understandings of what life is, are transformed, and to explore how human intervention seeks to reconfigure life boundaries towards optimisation. We ask the three following questions: (1) Which processes have rendered mitochondria transferable and enable their circulation between bodies and domains as if they had a life of their own? (2) How does the increasing visibility of mitochondria in the public domain and their technologisation transform the understanding of reproductive processes and "life itself?" (3) What are the socio-political implications of their circulation in the bioeconomy of reproduction?

In order to tackle these questions, we turn to the conceptual framework of "bio-object" developed by Webster et al., "to refer to socio-technical phenomena where we see a new mixture of relations to life or to which 'life' can be attributed" (Webster 2012, p. 1). We examine how mitochondria become bio-objects by focusing our analysis on two reproductive technologies manipulating mitochondria, that we suggest calling MitoTechnologies. The first is the mitochondrial donation technique aimed at preventing the transmission of mitochondrial disorders that are caused by defects in mitochondrial DNA. The second technology is Augment, a reproductive technology developed by the US-based company OvaScience, which promises to revitalise older eggs by injecting mitochondria taken from immature egg cells. While they are both intended to improve conception, the first one targets hereditary disease by intervening in the fertilisation process and incorporating external mitochondria, while the second targets the aging process affecting the oocyte itself by using the woman's own mitochondria.

Drawing on public material collected in two separate empirical research projects, we argue that mitochondria, through their bio-objectification, contribute to the redefinition of life as something that can be 'powered' which we understand both in a biological sense as 'generator of cellular energy', and in the analytical sense of a biopolitical agent of optimisation (Rose 2007). Taking into account these two levels of understanding allows us to grasp the political implications of these biological and technological transformations. In so doing, the bio-objectification of mitochondria, we suggest, challenges current understanding of reproductive processes by adding to the fragmentation of gametes and redefining reproductive ageing. Furthermore, we

argue that the power of mitochondria to optimise life processes at the cellular level is invested with great promissory capital and biovalue aiming at maintaining reproductive promises present in the bioeconomy of reproduction.[2] Characterised both by the great hopes and expectations associated with reproductive technologies (Kitzinger and Williams 2005; Martin et al. 2008; Mulkay 1993), the market for eggs, sperm and reproductive technologies has especially become a lens through which to explore the complex dynamics of capitalisation, technologies and the transformations of meanings and engagements with life itself (Clarke et al. 2010; Waldby 2002; Waldby and Cooper 2008).

After discussing the conceptual framework of bio-objectification and situating it in relation to the scholarship on bioeconomy and biovalue, we provide a description of our methodologies and the material analysed. Focusing on two MitoTechnologies, we then examine three key processes whereby mitochondria are made to appear to have a life of their own and become bio-objects: their transferability, their transformation into an agent of revitalisation in reproduction and their capitalisation. We end by discussing the implications of their bio-objectification for the bioeconomy of reproduction.

Analytical perspectives: bio-objectification and life itself

In the wake of the Human Genome Project in the nineties and the rapid expansion of molecular biology, social scientists have increasingly focused their attention on social understandings of 'what life is'. Expanding on Foucault's work on biopolitics, these authors have considered how understandings of life are transformed when it becomes open to technical intervention and reengineering. They have also shown how these transformations are part of the biomedicalisation process, characterised by a change of scale in medical gaze and types of interventions, from the "external nature" to the "internal one" (Clarke et al. 2010). In particular, Rose describes this shift as "molecularisation", defined as "the style of thought of contemporary biomedicine [which] envisages life at the molecular level, as a set of intelligible vital mechanisms among molecular entities that can be identified, isolated, manipulated, mobilised, recombined, in new practices of intervention, which are no longer constrained by the apparent normativity of a natural vital order" (Rose 2007, p. 15). The objective of these interventions on life is not only to treat pathologies or repair body damages but also to maximise body and biological capacities by technoscientific means, in a logic of "optimisation" (Rose 2007) or "enhancement" (Clarke et al. 2010). Biological processes thus become open to an ever-ending technological optimisation, blurring the distinction between disease and normality, but also between treatment and enhancement as the purpose of these techniques, as in the case of cosmetic surgeries or preimplantation genetic diagnosis (PGD), may become unclear and subject of discussion.

[2] The term "bioeconomy" has been used over the last decade to account for the key role economic and neoliberal logics play in the development of new biotechnologies, biomedical knowledge, products, and services, and in which life itself is a source of financial and health value (see Clarke 2010; Rose 2007; Waldby 2002; etc.).

Rose insists on the political dimension of these interventions, as they involve not only the transferability of molecular elements of life at a technical and biological level, but also their "standardisation, regulation, and even ethics" (2007, p. 15), which means that life itself becomes open to politics (cultural and social values, meanings and norms) in an unprecedented way. In other words, the normativity of a natural vital order tends to be substituted by social, cultural and political normativity. In the field of biotechnologies, ethics has become a pervasive normative domain shaping the production of new genetics knowledge and of biological entities. Debates on stem cells and nuclear transfer cloning techniques illustrate especially well how moral norms shape the development of biologically engineered entities, envisioned as technological solutions to political controversies about the frontiers of humanity and the value of life, encoding in this way moral values and desirable norms in biology itself (Beltrame 2013; Franklin 2001; Testa 2008).

The manipulation, circulation and transformation of the living more broadly take part in what has been described as the bioeconomy. This term refers to the capitalist logics at work in the transformation of biological tissues, body parts, molecular and cellular processes, into commodities. The bioeconomy rests on the production of value derived from these biological entities and processes through severing their link from their initial environment and capitalising on their biological properties (Mitchell and Waldby 2010). Waldby defines the resulting biovalue as "the yield of vitality produced by the biotechnological reformulation of living processes" (2002, p. 310). In this conceptualisation, the surplus of vitality produced in vivo may lead to the production of value through health use, under the form of therapeutic and preventive potential, but also through exchange, as it may be transferred into commercial profit, the "productivity of tissues [intersecting] with the productivity of markets entering into the circuits of national and transnational capital economies" (Waldby 2014, p. 2). The famous example she discusses is stem cells, a biological product turned from waste, like discarded embryos, into a valuable resource whose regenerative properties create biovalue (Waldby 2002).

Taking over and developing further this analytical framework, a number of scholars have explored, analysed and conceptualised the political economies of life itself visible in the biotech sector and health industry and their implications for medicine, health, and the making of identities, with a burgeoning of related notions such as "biocapital" (Rajan 2006), "life as surplus" (Cooper 2011), "promissory capital" (Thompson 2005), or "tissue economies" (Mitchell and Waldby 2006). The notion of biovalue and its associated concepts have been discussed critically by Birch (2017) who proposes a complementary approach. Departing from the importance granted to the biological and material, he argues for a better consideration of the political-economic actors, knowledges, and practices involved in the creation and management of value, such as the biotech firms and stock analysts. Trying to explain the apparent paradox of a biotech industry which generates high and rising income, even though constantly failing to deliver the services or products it promises to develop, he draws attention to the logics of assetisation which he distinguishes from the commodification logics favoured in analyses focusing on the biological side of the bioeconomy (Birch 2017).

Some Science and Technology Studies scholars have also attempted to grasp the contemporary technoscientific transformations of life through the concept of the "bio-object" (Holmberg 2012; Holmberg et al. 2011; Metzler and Webster 2011; Vermeulen et al. 2016). Although there is no definitive description of bio-objects or a list of their intrinsic properties (Metzler and Webster 2011, p. 648), bio-objects can be broadly defined as new forms of biological entities, created in the context of the laboratory or collected in the clinic, that are transposed into other domains, where they acquire new uses, meanings and values. This is the case, for instance, of genetically modified organisms or discarded tissues which are 'revitalised'. It also encompasses "entities that we are, by now, much more familiar with but that have been brought into new spaces", such as human gametes or tissue samples stored and frozen for future research purposes (Metzler and Webster 2011, p. 649).

The authors in using this conceptual framework insist on the importance of focusing attention on the *processes* leading to the *making of life* in different settings in order to avoid essentialising biological entities and reducing life to its biological understanding. The aim is to trace what they call the "bio-objectification process", wherein "life-forms or living entities are first made into objects, become possible, through scientific labour and its associated technologies, and then come to be attributed with specific identities" (Holmberg et al. 2011, p. 740). This enables us to examine how these bio-objects are produced through socio-technical processes and are thus not fixed entities. On the contrary, they gain new meanings while they circulate in different domains. Furthermore, the manipulation of bio-objects tends to blur boundaries between categories—classification, taxonomies—whose distinctiveness is taken for granted. 'Cybrids', for instance, these embryos made of a human nucleus and animal cytoplasm through advanced nuclear transfer techniques, disrupt and modify current boundaries between human and non-human through their public and parliamentary discussions (Brown 2012; Holmberg 2012).

The study of the bio-objectification processes and their implications are of particular interest in the domain of reproduction. Indeed, a crucial site where cultural and social understandings of life itself have been produced, debated, and reconfigured is the biomedicalisation of reproduction (Franklin and Lock 2003; Strathern 1992; Thompson 2007). Egg, sperm and embryos not only contribute very materially to the making of life in the form of children-to-be, but also symbolise life itself in Western societies (Franklin et al. 2000). The centrality of reproduction to existence has turned this domain into a fertile ground to conceptualise how biological life becomes open to politics. The 'biological facts' have long been thought to provide a universal and stable ground to the social organisation of kinship and gender which in contrast is thought to be variable historically and culturally. However, the increasing technologisation of biology, especially in the realm of reproduction, has challenged this taken for granted fixity. It has transformed the common understanding of biology or of life itself, and has also opened up a space for public debates about the ethics as well as for new biotechnologies as well as for new legal regulation in unprecedented ways.

Franklin and Lock (2003), Clarke et al. (2010), Thompson (2005), and Waldby and Cooper (2008) have all shown how reproduction plays a central role in the bioeconomy. Indeed, specific properties of reproductive material, especially its (re)

generative properties are increasingly harnessed for profit, such as in the case of stem cells or cloning technologies. Reproduction therefore becomes productive (Thompson 2005), despite invisibilising new forms of reproductive labour (Waldby and Cooper 2008). The contrasting logics of donation and commodification, their tensions and overlapping, in the bioeconomy have been discussed in relation to reproductive cells and labour by various scholars (Almeling 2011; Curtis 2010; Haimes et al. 2012; Nahman 2013; Pollock 2003, etc.). However, the conceptual framework of bio-objectification as such, which is at the core of our analysis, has rarely been used in these works. In contrast, this framework has been used to analyse how reproductive material such as placenta (Kroløkke et al. 2018), umbilical cord blood (Beltrame 2014) or the embryo (Bock von Wülfingen 2012; Metzler 2012) changes ontological status and meaning when redirected into a new life domain, but few studies have focused on how reproductive material becomes bio-objectified when its purpose remains reproductive, in the sense of making babies and parents. Mitochondria provide therefore a unique lens through which to examine the implications of the "technologisation of life" (Franklin 2013a) in this particular domain. In other words, they are a useful and relevant "looking glass" (Franklin 2013b) to analyse what happens to life and reproduction, when inner parts of the reproductive cell—mitochondria—become transferable and acquire new potentialities within the realm of reproduction.

While all bio-objects result from specific and situated processes and are therefore singular, Metzler and Webster have pointed out a number of similarities which enable them to be considered together analytically to examine "how life enters into the picture in new ways and crossing boundaries" (2011, p. 648), opening up "novel socio-technical (including political) relations" (Webster 2012, p. 6). In what follows, we would like to highlight three key features shared by bio-objects, which we have identified as especially relevant and useful to track the ways mitochondria have become objectified in the field of reproduction.

A first important feature of these bio-objects is their *manipulation* or *technologisation* which allows their transferability. They often are "very tangible objects that can be leveraged and stored, as well as circulated and exchanged" (Metzler and Webster 2011, p. 649). This implies the capacity, at a material level, to make specific biological entities which become manipulated through their technologisation. The development of genetic editing or nuclear transfer techniques, for instance, has enabled the possibility of creating new or hybridised life forms such as transgenic crops, crispr/cas9 or human-animal chimeras, by transferring and combining distinct biological organisms or material in novel ways (Brown 2012; Chrupek et al. 2012; Hansen 2013; Pavone and Martinelli 2015).

Secondly, bio-objects are transposed into new domains or settings in order "to know and *enhance life*—that is bio(s)" by generating and using innovative knowledge (Metzler and Webster 2011, p. 649). Through their objectification, these biological entities acquire or optimise their potentiality to tame, redirect or control life processes, and by doing so challenge and transform the *understanding* of these processes. In other words, the social and cultural meaning, but also the ontology of biological material is transformed when they are used in new domains or when they acquire new potentialities for medical, research or consummation purposes.

For instance, human placenta, which is initially considered as waste, is collected and becomes a commodity with supposedly positive virtues for food and cosmetics (Brown and Williams 2015; Kroløkke et al. 2018).

A third key feature is the potential for bio-objects to become *valuable* through the promises and hopes they rise in terms of clinical applications or industrial outcomes (Beltrame 2014; Vermeulen et al. 2016). Through their manipulation and their circulation across domains, these living biological entities acquire new potentialities and uses which can be exploited to generate different types of capital and values, participating therefore in the bioeconomy. Hauskeller and Beltrame describe, for instance, how Umbilical Cord Blood (UCB), collected in the clinic and stored in bio-banks, is objectified and acquires present- and future-oriented biovalue by becoming material for stem cell research, a valuable life-saving tissue for possible transplants, as well as a property (Beltrame 2014: 68; Hauskeller and Beltrame 2016). These authors (2016, p. 230) emphasise that "the UCB banking sector is a hybrid of different bio-economic regimes where redistributive and market economy […], commodification and decommodification processes coexist and overlap in complex configurations". These process of value creation, notes Webster, raises specific ethical and legal issues and may require renewed regulation or standardisation measures (Webster 2012), which are necessary for their circulation and transferability, but also more broadly for their legitimacy and valuation.

We mobilise these three features for the analysis of our two cases in order to describe and examine how the bio-objectification of mitochondria occurs in the use and promotion of two particular MitoTechnologies, and what their implications are.

Methods

This paper draws on data collected in two distinct research projects. The first one focuses on the use of reproductive technologies in the context of mitochondrial disorders and the other on the production of knowledge on reproductive ageing and reproductive technologies aiming at extending fertility. The former project, led by Cathy Herbrand, used mitochondrial donation as a lens to explore the interactions between scientific progress, policies and patients' lives. The study involved interviews in the UK with women affected by mitochondrial disorders and with key stakeholders, including genetic counsellors, clinicians and support group representatives. It also drew on the analysis of various political and media documents, as well as on the observation of numerous public and parliamentary debates surrounding mitochondrial donation which have taken place between 2013 and 2016 in the UK (Herbrand 2017; Herbrand and Dimond 2017). Ethics approval was granted from De Montfort University and the London NRES Committee. The second research project, led by Nolwenn Bühler explored how knowledge of reproductive ageing is produced, shifts, and materialises in reproductive science and medicine, as well as the socio-political implications of extending fertility medically in Switzerland. The material for this project was collected via in-depth interviews with women or couples undergoing reproductive treatment and with experts involved in the field, ethnographic observations and a corpus of scientific and medical articles collected

through the data bases PubMed, Web of Science and Google Scholar, as well as legal and media texts relevant to the Swiss context (Bühler 2016). Ethical approval was obtained in September 2011 from the Cantonal Commission of Ethics of Research on Humans Beings.

In this paper, only the research data derived from textual sources and public debates directly relating to mitochondrial donation and Augment were shared and discussed by both researchers. This mainly comprised analysis of a corpus of scientific articles, newspaper articles and opinion pieces, as well as public reports and information published online between 2010 and 2016. In addition to initial data collection, further thematic analysis of material available in the public domain before 2010 and between 2016 and 2018 was jointly conducted in order to trace back and follow up recent developments around both techniques.

New MitoTechnologies: powering life?

Drawing on the three key features of bio-objects described above, we trace and analyse the bio-objectification of mitochondria through their technologisation, their reconfiguration, and their valuation, by examining two specific MitoTechnologies. We show how mitochondria (1) become a transferable element 'powering life', (2) enter into and circulate within the domain of reproduction to become an agent of revitalisation, and (3) acquire increasing biovalue in the reproductive bioeconomy.

Transferring mitochondria's vitalising power

One of the key elements in the bio-objectivisation of mitochondria has been the possibility, at a practical level, to use what is perceived as their vitalising power in other human cells by rendering mitochondria transferable. While the role of mitochondria in the cell energy production, notably as the site of cellular respiration, has already been identified in the 1930s (Ernster and Schatz 1981) and their functioning has increasingly become a central object of medical research over the twentieth century, new MitoTechnologies and the research which has led to their development have taken a major step further by changing the way mitochondria are approached scientifically and by opening up new potential clinical applications. They have enabled the manipulation of mitochondria and the exploitation of its vitalising power in unprecedented ways, by making them *transferable* and thus, usable in other body parts.

Early manipulations involving the transfer of mitochondria in humans started in the late 1990s when an experimental reproductive procedure called 'cytoplasmic transfer' was developed in the US to improve the quality of eggs, based on the assumption that mitochondria might play a crucial role in fertility (Cohen et al. 1997). Although the notion of mitochondria was not explicitly mentioned at that time, this technique involved mitochondria transfer through the injection of cytoplasm donated by young woman into the patient's egg, which resulted in the coexistence of two different types of mitochondria within this egg. After being used to help

a few dozen of women with infertility problems conceive, this technique was banned in 2002 by the FDA when genetic or clinical abnormalities were detected in two children (Castro 2016). Whilst this experimental procedure was not so successful in terms of reproduction, it enabled a better understanding of infertility and reproductive ageing mechanisms, as it oriented research to the role mitochondria may play in the decline of oocyte quality with age (Pru and Tilly 2001; Tilly 2001). While research has continued in this area, public attention waned and interest remained confined to the domain of basic research in order to understand the fundamental mechanisms of reproductive ageing and somatic ageing more generally.

A few years later however, the existence and the transferability of mitochondria were again highlighted in the UK debates on the creation of transspecies hybrids, i.e. embryos made of human and animal parts through nuclear transfer. The debates taking place around 2007 about the status to give to these hybrids questioned the significance and the role of mitochondria and their specific DNA in genetic identity (Brown 2009). These questions re-emerged and gained even more attention from 2012, with the discussion and media coverage round a new reproductive technique involving mitochondrial transfer as a means to prevent inherited disorders (Connor 2014; Gallagher 2015). In this case, the procedure consists of transferring the nucleus of the affected mother's egg into a healthy enucleated donor egg. In other words, the nucleus of the donor egg is replaced by that of the intending mother. The newly reconstructed egg containing the mother's nuclear DNA and the donor's mitochondrial DNA is then fertilised by the chosen sperm in order to create an embryo with non-affected mitochondria.

If, technically, the mitochondria remain in their own cytoplasm and the nucleus is the one moved, there is a transfer of mitochondria in practice with respect to the final outcomes, as the mitochondria of the intending mother's egg have been replaced. This transfer of mitochondria not only occur at a material level but has been explicitly emphasised at a discursive level through various visual and rhetorical mechanisms mobilised in the media coverage and the public debates. First, the procedure has often been compared to a device whose battery is replaced; the 'battery' being the frequent metaphor used to designate the mitochondria. These were, for instance, the term and the image used by the Wellcome Trust and depictured in a short online video to explain what mitochondrial diseases were (Wellcome Trust 2012). Furthermore, naming these techniques 'mitochondrial donation' has clearly contributed to constructing mitochondria as transferable. Using the term of 'donation' is significant here, as it refers to organ donation in public imaginary, which involves the collection and replacement of one body part by another, rather than an intervention at the molecular level. This term simultaneously avoid the connotation of commodification which could have been perceived as ethically problematic. Overall, these messages confirm and reinforce the notion of mitochondria's transferability at a discursive level. Consequently, through the debates and media coverage of this new reproductive technique, mitochondria have gained a significant visibility in public imaginary and been represented not only as a crucial source of power but also as independent biological entities which could easily be used and moved around: i.e. establishing their *transferability* as a key characteristic. At the same time, it is noticeable how ethics was already 'built in' to this technique by constructing it as an altruistic

donation aimed at preventing inheritable diseases, side-lining potentially controversial issues linked to the need for egg provision and the mixing of different types of DNA.

One year after the legalisation of mitochondrial donation in the UK, mitochondria made the headlines again, as the authorisation for a clinical trial for the technology Augment was asked for by a medical team based in Nottingham (Knapton 2016; MacRae 2016). Augment promises to boost old oocytes or to re-establish their efficiency by injecting mitochondria taken from immature eggs, found in the ovarian lining and rich in good quality mitochondria, into the cytoplasm of mature eggs together with the sperm (ICSI). In newspapers, one could read that a new kind of IVF described as "turbocharged" could help older women conceive (MacRae 2016), some commentators insisting on the pioneering dimension of the technique as "the next IVF revolution" (Connor 2016).

The technique itself was developed and tested by OvaScience, an American-based company. In media articles, the 'battery' metaphor and the boosting or energising role mitochondria might play to remediate the age-related loss of quality of eggs are put forward such as in the following quote:

> Augment aims to revitalise old and poor quality eggs by giving them a power boost. An egg's energy comes from mitochondria, tiny 'battery packs' that weaken with age. OvaScience believes these can be supplemented with young, healthy mitochondria taken from a bank of very immature eggs that lurk on the edges of a woman's ovaries. These extra 'batteries' should give the egg the energy it needs to develop into an embryo (MacRae 2016).

In this case again, the transferability of mitochondria as a source of power is put forward, but the origin of the mitochondria is different. While donation from a third body is highlighted with mitochondria donation/transfer, it is rather the autologous dimension of mitochondria which is emphasised in the case of Augment, meaning that they come from the same individual. Their transferability is presented as a solution that women have *inside their body*. Indeed, the boosting power and regenerative properties of mitochondria come here from the biology of the women themselves, their own 'bank' as mentioned in the previous quote. According to the first couple who have used Augment to conceive a child, this was reassuring: "We thought that it was something that was safe, and it was almost like the body treating and healing itself. We were very, very excited about the opportunity to try it" (Weintraub 2017). Moreover, the regenerative power of mitochondria is doubly underlined as one speaks from immature eggs or stem cells, already source of new life and regeneration in public imaginary and from mitochondria described as the powerhouse and extracted from these immature cells. As a consequence, these discourses represent the whole reproductive and regenerative process as internal to one woman's biology, with an empowering tint. However, the emphasis on women's bodies own capacities contributes also to counter the ethically controversial potential of the technology in avoiding both the mixing of different individuals' genetic material, and the use of egg donors.

These new Mitotechnologies have made possible the collection of mitochondria as well as their transposition into other cells, which was not previously the

case. In other words, mitochondria, through their technologisation, have been 'disentangled' from the cell to which they belonged and can be reincorporated in other cellular or body environments. Mitochondria have therefore become both 'manipulable' and 'manipulating', in the sense that they are themselves the object of a technical intervention and are used to intervene on other cells or bodies. These biological entities, through their transferability, are thus enacted (Mol 2002) in different ways, opening up the possibility for them to acquire new uses, potentialities and meaning.

Revitalising cells, reconfiguring reproduction?

With the development and the promotion of new technologies involving the transfer of mitochondria, these biological entities have publicly entered the domain of reproductive medicine, from which they were previously absent. In this section we question the effects of this integration into a new domain, by showing that these MitoTechnologies construct gametes and embryos as reproductive cells which can be 'revitalised' through a transfer of mitochondria, while simultaneously the cell boundaries and 'wholeness' are challenged. By introducing new ways of boosting fertility and preventing inherited diseases, these transfers of mitochondria contribute to transform current understanding of reproductive processes at two levels: the mechanisms of fertilisation themselves, and reproductive ageing limits.

Firstly, mitochondrial donation *complicates* current understandings of fertilisation by adding new sequences to the conception of a child. This technique involves the *fragmentation* of the egg or embryo to remove its nucleus and the *reconstruction* of a new egg or embryo. It thus adds a very novel step with respect to processes of both IVF (which enables conception outside female body) and with respect to PGD (which involves the selection of an embryo but maintains conceived embryos as intact). With mitochondrial donation, the egg is divided and reconstructed with an external biological component which is supposed to repair it from a medical point of view, by replacing the faulty mitochondria with functional and 'powerful' ones. This provision of mitochondria brings life itself to the egg or embryo. The development of mitochondrial donation therefore has implications at the material level, by making reproductive mechanisms more complex and transforming reproductive cells, but also at the conceptual level, by shifting general understanding of fertilisation mechanisms and reproductive cells in public imaginaries. Through the media coverage of mitochondrial donation, it has indeed been repeated frequently that faulty mitochondrial leading to miscarriages or ill children are replaced by 'good quality' or 'powerful' mitochondria, enabling a successful pregnancy and a healthy child. The egg, and by extension the individual it will constitute, appears to be in need of this crucial living energy represented by mitochondria.

The development of Augment introduces another important change in the understanding of reproduction, in particular of reproductive ageing, that is the decrease of the fertility potential of eggs over a woman's life time. By adding mitochondria from 'younger' immature eggs to the 'older mature egg', Augment is intended to rejuvenate the latter. Underlying this technological development, is the assumption

that some eggs and their mitochondria would age, but that some reproductive cells – the ovarian stem cells, also called 'egg precursor cells', and their mitochondria, would be protected from ageing processes and hold a development potential which might be redirected towards reproductive purposes. It is the regenerative quality of these cells, and especially of their mitochondria, which would be used to rejuvenate the former. In other words, a specific spatial and temporal configuration of women's biology emerges, where some kinds of cells situated in a specific location of the body would be a source of renewing vitality, while others would be subjected to the ineluctable process of ageing, a heterogeneity of times, already identified by Waldby (2002) in her work on stem cells.

While still controversial at the scientific level (Bühler 2016), this idea challenges one of the most entrenched beliefs about reproduction. Indeed, it is generally taken-for-granted that age-related fertility decline is irreversible both in quality and quantity and that the ovarian reserve, i.e. the quantity of oocytes contained in ovaries, reaches exhaustion a few years before menopause. However, the new understanding applied by the Augment technique implies that there would be some renewal or regeneration process taking place in the ovaries at the adult age (Johnson et al. 2005) and that this regenerative power could be used to optimise reproductive processes through the transferability of mitochondria (White et al. 2012), participating in this way to their bio-objectification.

Significantly, the notion of age itself tends to disappear in the marketing discourse of this MitoTechnology as reproductive aging is reframed as 'egg health'. While Augment is the result of research on the understanding of the molecular biological mechanisms of ageing, it becomes a matter of health that can be optimised through a transfer of mitochondria. This generates the possibility of no longer speaking and thinking of age limit, but rather only of a 'ever better health optimisation' of the reproductive biological material. Like mitochondrial donation, Augment aims at restoring the level on energy of a damaged egg by transforming it into a 'healthy egg', contributing more broadly to blur further the distinction between treatment and enhancement (Clarke et al. 2010).

Both technologies construct mitochondria as a key ingredient for a successful and healthy conception in ways that were not previously apparent. In this respect, the introduction of a new human biological entity in the reproductive process generates a new relationship to reproduction, which becomes understood as being 'powered up'. The MitoTechnologies create a new hybrid: the 'mito-enhanced egg', that is an egg made of mitochondria of different origins or at different ageing stage, which has been 'revitalised' or 'boosted with life' thanks to the input of good quality mitochondria.

These 'powering up' processes are highly gendered, at least in two different ways, in relation to women's bodies and their biologies. First, these MitoTechnologies convey a negative connotation associated to women's reproductive bodies and cells in need of being 'powered up' by technological means. As Martin has shown (1987), women' bodies and cells are often encapsulated in the metaphor of the 'machine' and compared to 'production systems', 'mechanical factories', etc., converting energy into particular products which play a role in the economy of the organism as a whole. Second, the agent of this 'powering up'

process is itself associated to female attributes as mitochondria and their DNA are exclusively transmitted through the maternal line. Both techniques, but also by extension women's bodies, require women's body material itself to be (re) boosted but in the case of Augment, this logic is used to promote the technique by insisting on the supposed empowering capacity of women's own mitochondria, enabling them to take control of their 'faulty reproductive mechanisms'.

Mito-enhanced eggs in the reproductive bioeconomy: a form of promissory capital

Once simple organelles described in biology textbooks, mitochondria, when transferred and manipulated in MitoTechnologies, become imbued with much promissory capital (Thompson 2005). Like other reproductive technologies, they are constructed socially and culturally as a desirable solution and promise to repair the disruption in the life course created by infertility and to increase the control over reproductive processes while maintaining some biological connection to the child (Becker 1994; Franklin 1997). MitoTechnologies indeed generate hope: to have a healthy and genetically-related child in the case of mitochondrial donation, or a biological child in spite of age-related fertility decline in the case of Augment, both technologies thus reinforcing social expectations of biological parenthood. But beyond providing hope for individuals and promising to improve health and fertility in society, MitoTechnologies also raise scientific and economic expectations and investments. By increasing the number of reproductive technologies available on the market and fuelling their promissory potential, they also nourish the growing business of IVF "which is projected to expand from about $10 billion today to $22 billion globally by 2020" (Weintraub 2017) and expand the scope of the reproductive bioeconomy. Indeed, far more than being increasingly visible in the public imaginary, MitoTechnologies become an important stake in the competition for the prestige and the financial benefits associated with new scientific discoveries and innovative technologies. This transformation of a publicly inexistent organelle into a capitalised object is a crucial part of their bio-objectification, as we show in this section.

In the case of mitochondrial donation, although public discourses were dominated by a narrative of hope promising to prevent and cure mitochondrial diseases, the technologisation of mitochondria has been primarily associated with scientific prestige, and less directly with the prospect of improving public health and generating wealth. Indeed, the prevention of mitochondrial diseases concerns only a limited number of persons (Herbrand 2017) and therefore is a niche in the market of reproductive technologies which is unlikely to create important profit.[3] What is expected from this MitoTechnology is more the valorisation of the national scientific capital and the promotion of the UK ethical model, than a financial value as such.

The development and mastering of this cell reconstruction technique by the Newcastle research team has turned this centre into *the* main pole of expertise in this

[3] Except if mitochondrial donation is used in the future for broader purposes. Some clinicians would indeed like to use it, and in some cases said they already have used it, in cases of infertility to increase pregnancy rates (Gallagher 2019).

field. It has therefore enabled the UK to maintain its position as a leader in cutting-edge scientific and technological innovations. The vote for legalisation of mitochondrial donation reflected the recognition and legitimation of this technology, which was celebrated as a British scientific accomplishment (Connor 2015). The success of mitochondrial donation—e.g. the birth of the first non-affected baby conceived via this technique in the UK—would align with previous reproductive achievements pioneered by UK scientists (Ridley 2016), such as the first IVF baby or the first cloned mammal, and allow the country to stay competitive in the academic market, by helping research teams attract further funding, scientific prestige and international recognition.

Moreover, the adoption of the law meant that for the first time ever, some type of germline modifications on human embryos and gametes were democratically authorised and regulated in a permissive but controlled way following a number of expert and public consultations (Department of Health 2014). The UK henceforth appeared, at the international level, as a pioneer with respect to mitochondrial donation regulation and its ethical deliberations. This was apparent in the talk of the Chair of the Human Fertilisation and Embryology Authority, Sally Cheshire, when she claimed, at a well-attended public conference in London a few months after the adoption of the law, that "the UK was the best place for mitochondrial donation" as its infrastructures and institutional system "gives people confidence in allowing innovation to take place" (Herbrand 2016). More broadly and above all, the 2015 law confirmed, in line with previous successful liberal IVF and embryo policies, the UK position as an ethical model for the discussion and regulation of complex biomedical technological innovations through the processes and frameworks which were put in place. As Dimond and Stephens show, by "making the technology knowable, desirable, ethical and sanctionable", the UK enacted "ethical futures" which contribute positively to society in terms of health and economy (2018, p. 132).

The case of Augment is different. While the pioneering dimension of the technique was also put forward, the altruistic dimension was absent. This MitoTechnology was developed by a "global fertility company dedicated to improving treatment options for women around the world"—Ovascience,[4] which is listed on the stock market. Like the other treatments created and commercialised by OvaScience, Augment is based on the use of the controversial oogonial stem cells identified by Jonathan Tilly and his team (see among others Johnson et al. 2005, Johnson et al. 2005, Skaznik-Wikiel 2009). Tilly, a reproductive biologist, has worked since the end of the nineties to understand the molecular mechanisms of reproductive ageing (Tilly 1996, Morita and Tilly 1999). After more than a decade marked by a controversy around the oogonial stem cells he claimed to have identified (Johnson et al. 2005),[5] he founded the company in 2013. The technological process identifying these cells, now called Egg Precursor Cells (EggPCSM), were patented, along with treatments using them, such as Augment, the "autologous germline mitochondrial energy transfer", in 2012 under several exclusive licenses from the Massachusetts General

[4] See their website: https://ovascience.com/ (consulted in December 2017).

[5] For an analysis of the controversy, see Bühler (2016).

Hospital where Tilly worked as chief of research (Woods and Tilly 2015). The patenting of these techniques and the change of the cells' name marked an important step in their bio-objectification at two levels.

First, it enabled Ovascience to move away from the controversial connotation of oogonial stem cells. Their renaming into 'egg precursor cells' makes them less ethically problematic with respect to the debates and legal regulations about genetic manipulation and thus increases their financial value by making them more likely to be invested by shareholders. Secondly, the patenting of the egg precursor cells, which transforms scientific knowledge and methods into property, capitalises on their promissory potential and of the associated treatments, in a for-profit logics. The biovalue of these cells results also from OvaScience's communication strategies. Indeed, the company is listed on the stock exchange and on their website, a specific section is intended for investors, showing the importance of the financial investments made in these promissory technologies. Financial reports for shareholders are published online on a regular basis, as well as other relevant news possibly impacting on the future of the company, such as the publication of scientific articles presenting promissory results or the availability of the technique in a new country (McNeely 2015; Waltham 2016).

This bio-objectification of mitochondria in the case of Augment and its promissory capital result from two different kinds of valuation processes. In addition to the expected revenue income derived from the prospective reproductive treatments, a process of assetisation (Birch 2016) is at play in the creation of these cells' biovalue. While the biological properties of these cells 'boosted by younger mitochondria' feed into the promissory capital of treatments which are still in development, what is also decisive in raising a significant stream of income are the financial strategies of value creation. For instance, the strategic management of information which impacts the value of the shares on the stock market, as well as the taking over of Ovascience by financial analysts and corporate managers, instead of technoscientific actors, reflect these processes.

However, while patenting was necessary to the production of biovalue in the assetisation logic, it also raised mistrust in the world of reproductive biology and had the effect of maintaining the scientific controversy around these cells. In particular, the lack of transparency around the technology is considered problematic, as it is not possible to reproduce the procedure. Scientific evidence is also still missing (Gosden and Johnson 2016; Heindryckx et al. 2015). In addition to the financial issues and the several scientific, methodological problems which are regularly criticised by experts in the domain (Powell 2007, 2005), the promissory dimension of the technology itself has become an ethical problem (Heindryckx et al. 2015). The promissory bubble generated by this MitoTechnology is especially criticised by Johnson and Gosden, two prominent UK-based figures in reproductive medicine and biology, as possibly misleading women wanting their own genetically-related child instead of turning to egg donation (Gosden and Johnson 2016). In a way, what makes the technology such a profitable investment, and plays an essential role on its stock market value—its promissory potential in terms of treatment possibilities—might also be what tarnishes and diminishes its biovalue, as it lacks the scientific and ethical approval necessary for it to be taken seriously in the scientific community.

It is interesting to observe that the company has met important financial difficulties as the promissory capital of Augment did not meet the investors and shareholders' financial and medical expectations. This led to internal restructuration and a resizing of the company leading it to cut half of its workforce at the beginning of 2018 (Elvidge 2018). In November 2018, OvaScience was then absorbed, through a reverse merger,[6] by another biotech company Millendo Therapeutics Inc. specialised in rare endocrine diseases (Waltham et al. 2018). Even though OvaScience failed to fulfil its promise in terms of treatment success and financial growth, this company and the technology it developed, like many other IVF technologies, has nevertheless played an important role in the reproductive bioeconomy. Augment enabled OvaScience to enter the stock market which turned out to be worth of investment by another biopharmaceutical company independent of the value of the technology itself. It illustrates well the paradox of the life sciences sector which is financially rising in spite of its failure to deliver the services and treatments it promises (Birch 2017). More generally, it also illustrates the considerable financial potential of a market for reproductive technologies targeting reproductive ageing in societies anxious about the postponement of family building and related fertility decline.

Conclusion

While the bio-objectification of regenerative stem cells has been thoroughly studied, this analysis adds to this body of scholarship by documenting how the process of bio-objectification occurs in the case of mitochondria and more broadly in the field of reproduction. Focusing on two reproductive technologies using mitochondria, we have shown how these organelles are built and perceived as 'powering life' or as a 'life booster'. Their technologisation renders them transferable and gives them the status of an autonomous bodily entity. Moreover, through their transferability, they become technologies themselves used to enhance, optimise or revitalise reproduction. Unlike other bio-objects, such as aborted foetal tissue or umbilical cord blood, mitochondria are not part of a waste circuit and their bio-objectification does not depend on the regenerative properties of discarded tissue, transforming it into a valuable good. Their bio-objectification rests rather on their physiological properties in regard to cellular metabolism—their function as 'batteries'—which, when transferred to another body or another body part, potentialise fertility and reproductive cells by playing a repairing and enhancing role.

Made possible at a technical level, their transferability was also put forward in public discourses about mitochondrial donation. Mitochondria were inscribed in a narrative of donation from a healthy donor to couples and families struggling with genetic disorders and wanting to prevent transmission of disease to their child. In

[6] A financial operation which allows Millendo to access the stock market. It is therefore not the patented technologies by OvaScience, the MitoTechnology Augment, which is valued by this new company, but the entry into stock exchange Augment allowed to make (for more information, see: DeAngelis 2018 or Meiling 2018).

contrast, in the case of Augment, we have shown that it was the internal nature of mitochondria's transferability which was highlighted, the idea that mitochondria can easily be transferred between different cells and tissues within the same body. Instead of an altruistic transfer from one person to another, in the second case, it is the genetic continuity and the idea that the whole process, though mediated technologically, takes place inside one women's body which is highlighted. While the processes differ, in both cases MitoTechnologies are developed and presented as technological solutions which are ethically neutral or positive. In this respect, mitochondrial donation was contrasted as an ethical project in itself in the UK context, whereas augment development is inscribed in a search to circumvent legal and ethical constraints. In other words, they both exemplify how the development of bio-objects is shaped by ethical concerns, what is considered morally good and desirable becoming very materially inscribed in biology itself as shown in our analysis.

Through the development and promotion of MitoTechnologies,—technologies which both use mitochondria and transform them in technologies—these organelles have entered the domain of reproduction as appearing to play a key role for a successful and healthy conception. Not only have their existence and presumed functions become visible and praised, but mitochondria can now also be actively manipulated in order to optimise reproduction in highly novel ways. While other reproductive technologies have been developed to improve the fertilisation process or avoid inherited diseases, MitoTechnologies are characterised by another type of intervention. Unlike PGD, PGS, ICSI or medical abortion, which are about selecting (or discarding) particular gametes, embryos or foetuses, MitoTechnologies intervene directly on the cellular processes themselves in order to optimise fertilisation. Moreover, these technologies are characterised by seeking to act on reproduction as far upstream as possible. Indeed, they intervene directly on the reproductive gametes or immediately after fertilisation takes place. Thus, in contrast with other pre-conception, preimplantation or prenatal technologies, the temporal dimension of MitoTechnologies, combined with the microcellular site of intervention, is what makes MitoTechnologies unique.

Mitochondrial donation aims to restore the cell power and make it work correctly through the transfer of 'healthy' mitochondria, in order to increase the chances of having a child whose metabolism and body functions work correctly. In the case of Augment, instead of mitigating age-related fertility decline by substitution—egg donation—or time suspension—egg freezing—Augment intervenes directly on the ageing process rather than on its result. Both MitoTechnologies seek to optimise the cells and the cellular processes, and more broadly, the reproductive process itself (fertility), through the transfer of good mitochondria, this 'life fuel'. Through their technologisation, transferability and ability to 'power life', mitochondria reconfigure the notion of life, particularly as it relates to reproduction. Bio-objectification in reproduction is especially significant as it affects life at different levels: cellular, individual, and population. Mitochondria become thus a revitalising and biopolitical agent by 'powering life' not only inside the cells themselves but also by promising to assist the development of new human lives, in response to biopolitical concerns about the health and size of the population.

More than that, the bio-objectification of mitochondria reconfigures social and cultural understandings of reproduction. Firstly, mitochondria complicate scientific and popular understandings of fertilisation by challenging the cell boundaries and the wholeness of the egg, which can now be decomposed and recomposed by assembling its different parts. Secondly, they transform the current understandings of reproductive ageing as an ineluctable decline, into 'egg health', which, in contrast, conveys the idea of a technologically ever-optimisable biology. As part of this bio-objectification process, a new hybrid entity made of mitochondria from a different genetic origin and state of maturation (or ageing) is created, an entity that we call the mito-enhanced egg. In contrast with regular oocytes, these eggs are expected to function as 'better' or 'healthier' reproductive cells reinforcing in this way their revitalising role.

Finally, our analysis has shown how the 'life powering' properties of mitochondria and the promise of optimisation become part of the bioeconomy of reproduction. The two cases show how the promissory potential of these MitoTechnologies play not only a key role in creation of economic capital, but also of a scientific and ethical capital, illustrating the embedded character of related financial, knowledge and moral economies. While both technologies have seen investments as innovations, the first reflects the public service and the use of bioethics to increase its legitimacy as well as to reinforce the UK's leading position in the biotech sector; the second illustrates the functioning and dynamics of private (for profit) sector interests where in addition to the future-oriented commodity-based value of the technique, an asset-based value is created through its patenting. As new reproductive technologies of hope, they also contribute to the expansion and maintenance of a market in reproduction, by increasing the range of reproductive technologies available and promoting the idea that reproduction is biologically and technologically optimisable.

Overall, the bio-objectification of mitochondria contributes to disconnecting these cell organelles not only from their body environment but also from their social and political dimensions. The effort put into the development of these technologies and the attention they have attracted reflect, more broadly, how social, medical and ethical problems are increasingly addressed by intervening at the cellular level, rather than in the social and political sphere. Focusing on mitochondria and singling them out as both a source of fertility problems and their technological solution present a convenient and profitable way of responding at the individual level to much broader complex social, political and moral questions. MitoTechnologies and the discourses which promote them tend to obscure other interrelated complex ethical and economic issues; this includes the material and human resources needed for their development (e.g. the need for significant egg provision), their cost-effectiveness compared to existing alternatives, the emphasis put on biological relatedness, and the potential to improve health in society, or to increase health disparities by benefiting only a small group of privileged individuals. A detailed and critical analysis of their development and applications is therefore significant and timely.

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