



BDF Bioethics Briefing

Three-Parent Embryos: Reproductive Human Cloning to Produce Genetically Modified Babies

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Scientific White Paper by Maureen L. Condic, PhD.

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- Overview

The UK government is seeking to legalize the creation of human embryos that will have DNA from three different people for the purported purpose of eliminating mitochondrial diseases. Babies born as a result, and their descendants, will have permanently modified DNA. All three of the possible procedures to effect “mitochondrial donation” involve the dangerous creation of genetically modified human beings. Two of the three procedures involve reproductive human cloning. This BDF Bioethics Briefing sets forth serious concerns of law, science, safety and ethics.

The attached white paper by Maureen L. Condic, PhD explains the science and sets forth illustrations of the three possible means of creating “three-parent” embryos. As explained by Dr. Condic, “all three procedures carry significant risks to the children intended to be born; and two of the procedures involve a eugenic form of reproductive cloning, in which a human being with a medical condition is killed and his or her parts are used to create a new human being with an intended improved biological state.”

Executive Summary

The attached BDF Briefing Paper (setting forth both a legal memo and a science white paper) focuses on an important yet seemingly overlooked reality in the UK debate surrounding the proposed regulations on mitochondrial donation, also known as “three-parent embryo” procedures.¹ In specific, the UK government’s proposal to allow the “pronuclear transfer” method is, in fact, a proposal to allow a eugenic form of **reproductive human cloning**, *i.e.* cloning to produce genetically modified children.

The proposed regulations also allow “maternal spindle transfer” to create human embryos intended to be transferred to a woman’s womb. While that particular method does not involve human cloning, it does cross bioethical and legal boundaries by allowing the genetic modification of human beings and the creation of designer babies.

- **Conclusion:** Unless the Parliament of the United Kingdom acts to reject the proposed “Mitochondrial Donation” Regulations, it is likely acting *ultra vires* to protect what is commonly known as reproductive human cloning in violation of the laws of the United Kingdom, European law, and the United Nations Declaration on Human Cloning (2005). It is also likely in violation of laws forbidding genetic modification of human beings.

The attached BDF Bioethics Briefing Paper includes two parts: (1) a legal and policy briefing by Bioethics Defense Fund (“BDF”), a public interest law and policy organization that provides legal consultation on bioethics policy issues in the United States and abroad; and (2) a scientific white paper prepared for the members of the United Kingdom’s Parliament by Maureen L. Condic, Ph.D., Associate Professor of Neurobiology and Anatomy at the University of Utah School of Medicine.²

(1) Law and policy briefing

The law and policy briefing sets forth a non-exhaustive survey of some of the legal provisions that seem to be contravened.

- In short, this memo concludes that the proposed regulations allow techniques that all involve the unlawful creation of genetically modified human beings, with some forms of the technique involving the unlawful cloning of human beings to produce children

¹ See The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015, *available at* <http://www.legislation.gov.uk/ukdsi/2015/9780111125816/contents> .

² This briefing paper is presented in collaboration with Dr. Maureen L. Condic in her individual capacity; it does not represent the views or opinions of the University of Utah or its employees.

(“reproductive human cloning”).

- The memo also raises issues regarding potential tort claims based on birth defects of live-born children, as well as ethical concerns surrounding the risk of coercive abortion of unborn children detected to have adverse health conditions.

(2) Science briefing

A scientific white paper prepared for the UK Parliament by Maureen L. Condic, Ph.D. is attached. It is respectfully submitted for the purpose of providing a resource to inform matters of law and policy with a clear and accurate description of the basic science (along with graphics and explanatory legends). As explained by Dr. Condic:

Whatever the purported justifications, public officials considering the legalization of these methods of genetic engineering should clearly understand the science showing that:

- all three procedures involve genetic modification, i.e. “modifications to the subject’s germ line genetic identity”;
- all three procedures carry significant risks to the children intended to be born; and
- two of the procedures involve a eugenic form of reproductive cloning, in which a human being with a medical condition is killed and his or her parts are used to create a new human being with an intended improved biological state.

Dr. Condic’s white paper sets forth the mechanics of the three procedures revealing that two involve reproductive human cloning (Section I), the serious health risks to the children intended to be born (Section II), and some of the serious ethical concerns that have not been adequately addressed (Section III). *See* Condic ML, *Mitochondrial Donation: Serious Concerns for Science, Safety and Ethics*, attached.



Law and Policy Briefing

Proposed “Mitochondrial Donation” Regulations in the UK contravene laws banning “reproductive” human cloning of genetically modified children

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Introduction

1. On February 3, 2015, the British House of Commons voted to approve so-called “three parent embryo” techniques under the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015, intended to come into effect as early as October of 2015.³
2. This submission is made to the House of Lords to provide a resource of law as informed by science that leads to the conclusion that the proposed regulations involve human experimentation techniques that are unlawful, dangerous and unethical.
3. This legal survey is informed by the attached white paper prepared for the House of Lords by Dr. Maureen L. Condic. Dr. Condic’s white paper sets forth the mechanics of the three procedures used in this form of human experimentation – (1) maternal spindle transfer, (2) pro-nuclear transfer, and (3) embryo cell nuclear transfer (Section I), the serious health risks to the children intended to be born (Section II), and some of the serious ethical concerns that have not been adequately addressed (Section III).
4. The three methods of mitochondrial donation all include genetic modification and fit the

³ “[I]f approved by Parliament, the Regulations will be entitled The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 and that they will come into force on 29th October 2015.” UK Department of Health, *The Draft Human Embryology and Fertilisation (Mitochondrial Donation) Regulations 2015, a guide on new regulations to enable the use of mitochondrial donation techniques in clinical practice* (January 2015), available at <http://www.legislation.gov.uk/ukdsi/2015/9780111125816/contents>.

EU Clinical Trial Directives prohibition in article 9(6) against “modifications to the subject's germ line genetic identity.”

5. Two of the techniques (pro-nuclear transfer and embryo cell nuclear transfer) are methods of reproductive human cloning. (*See* Condit, Section I, *attached*). They therefore violate reproductive human cloning bans of the United Kingdom and the European Union. *See* par. 13-15, *infra*.

Policy Concerns

6. Proponents of conducting human experiments to generate “three parent embryos” initially cast this procedure as a beneficent therapeutic approach, with the proposed regulations purporting to limit the procedure to treat women with mitochondrial disease to increase their ability to bear healthy children.
7. Yet, within a week of the House of Commons’ approval of the regulations, one of the techniques’ pioneers filed for permission from the United States FDA to use these techniques as a fertility treatment for women who find it difficult to get pregnant because of their age.⁴
8. Once approved for purposes of “disease prevention” or “age-related infertility,” there will be no principled reason to prevent this or similar techniques to be used to produce made-to-order designer babies, and no practical means to prevent commercialized designer babies (whether regulated or available on the black market).
9. Despite the asserted good intentions, the reality is that the proposed regulations raise profound ethical concerns by sanctioning genetic modification of human beings and a destructive, eugenic form of reproductive cloning, in which a human being with a medical condition is intentionally produced, only to be killed so that his or her parts can be used to create a new human being with an intended improved biological state.

Human Experimentation

10. As an initial matter, it is important to note that the proposed regulations sanction experimentation on human subjects, thus requiring the highest scrutiny of ethical concerns.

⁴ Connor, S. (8 Feb. 2015). Scientist who pioneered “three-parent” embryo technique now wants to offer it to older women trying for a baby. *The Independent* (available: <http://www.independent.co.uk/news/science/threeparent-embryos-an-ivf-revolution-or-a-slippery-slope-to-designer-babies-10031477.html>).

11. The embryo created by mitochondrial donation techniques is a *human* subject. The woman and the fetus she may miscarry after uterine transfer of the genetically modified embryo are both *human* subjects. The live-born children produced using these techniques are *human* subjects who are subject to serious health risks, including increased incidence of birth defects, cancer and metabolic diseases (Condic, Section II, *attached*). Finally, the embryos that are deliberately destroyed in the cloning procedures themselves are *human* subjects. (Condic, Section I, *attached*).
12. Modern developmental biology establishes that at every phase of human embryonic and fetal development, the subject is **not** a “potential life,” but rather an individual human being. *See, e.g.,* William Larsen, HUMAN EMBRYOLOGY 4 (3rd ed. 2001)(explaining that male and female sex cells “unite at fertilization to initiate the embryonic development of a new individual.”); *see also* Maureen L. Condic, Ph.D., *When Does Human Life Begin? A Scientific Perspective*, Westchester Institute White Paper (October 2008), available at <http://bit.ly/1vBg6Nu> (the human zygote has “all the properties of a fully complete (albeit immature) human organism; it is ‘an individual constituted to carry on the activities of life by means of organs separate in function but mutually dependent: a living being.’” (citing NIH, Medical Dictionary of the National Library of Medicine, available at <http://www.merriam-webster.com/medlineplus/organism>)).

Violation of Bans on Reproductive Human Cloning to Produce Children

13. As set forth more fully in the attached white paper by Dr. Condic, two of the methods of mitochondrial donation (pro-nuclear transfer and embryo cell nuclear transfer) entail reproductive human cloning – also known as human cloning to produce children. This is because both procedures produce a human embryo by fertilization and then, just as in other forms of cloning, transfer a nucleus from this human being at the embryo stage to an enucleated donor egg to produce a clone, or genetic copy of the original human embryo. The proposed procedures are also *destructive* human cloning, because the original donor of the nucleus is killed after the nucleus has been transferred. Finally, these procedures are also *eugenic* human cloning, because an individual with a medical condition is intentionally produced, only to be killed so that his or her parts can be used to create a new, cloned human being with an intended improved biological state. (Condic, Section I(2)-(3), *attached*).
14. The human embryos created by the cloning methods of mitochondrial donation are “reproductive human cloning” because the cloned human embryo is transferred to the uterus of a woman for the purpose of gestation and childbirth. (Condic, Section I(2)-(3), *attached*).
15. Under the UK’s Human Fertilisation and Embryology Act 1990, as amended in 2008, embryonic stem cell research and cloning for the purpose of biomedical research

(“therapeutic human cloning”) are permitted, but cloning to produce children (“reproductive human cloning”) is banned. *See* HFEA sections 3(2) and 3ZA(4).

16. In specific, the sections 3-9 of the Draft Regulations violate current Section 3(2) of the HFEA 2008, which bans human cloning by providing “No person shall place in a woman— (a) an embryo other than a permitted embryo.” Section 3ZA(4) provides that “[a]n embryo is a permitted embryo if - (a) it has been created by the fertilisation of a permitted egg by permitted sperm, (b) **no nuclear or mitochondrial DNA of any cell of the embryo has been altered**, and (c) no cell has been added to it other than by division of the embryo’s own cells” (emphasis added).
17. The two cloning methods of mitochondrial donation do not meet the three requirements of placing a “permitted embryo” in a woman because (a) the embryo to be transferred is not created by fertilization of sperm and egg, but rather by nuclear transfer (human cloning) and (b) the embryo to be transferred was subject to the intentional altering of mitochondrial DNA in all cells of the embryo, including the germ line.
18. The EU Charter of Fundamental Rights, Article 3(2)(d), provides for “the prohibition of reproductive cloning of human beings.”
19. In March 2005, a non-binding United Nations Declaration on Human Cloning called for the ban of all forms of human cloning. The resolution expressed that the UN General Assembly is “[m]indful of the serious medical, physical, psychological and social dangers that human cloning may imply for the individuals involved, and also conscious of the need to prevent the exploitation of women,” and is “[c]onvinced of the urgency of preventing the potential dangers of human cloning to human dignity.”⁵
20. Some opponents of reproductive human cloning to produce children point to safety concerns. For example, the American Association for the Advancement of Science (AAAS) “endorses a legally enforceable ban on efforts to implant a human cloned embryo for the purpose of reproduction. The scientific evidence documenting the serious health risks associated with reproductive cloning, as shown through animal studies, make it unconscionable to undertake this procedure. At the same time, we encourage continuing open and inclusive public dialogue, in which the scientific community is an active

⁵ United Nations Declaration on Human Cloning, General Assembly Resolution 59/280.

participant, on the scientific and ethical aspects of human cloning as our understanding of this technology advances.”⁶

21. Others base opposition to reproductive human cloning on possible abuses such as the generation of humans from whom organs and tissues would be harvested.⁷
22. Many oppose human cloning to produce children and all forms of artificial reproduction and genetic manipulation based on the status of the human being at the embryonic stage and onward that entitles them to inherent dignity and worth. As such, the dignity of the human being is violated when commodified as a product to be manipulated, discarded, or made the subject of dangerous experimentation and financial transactions.
23. The proposed methods of mitochondrial donation that involve the destruction and cloning of human embryos – pro-nuclear transfer and embryo cell nuclear transfer – are therefore subject to the same concerns of safety, abuse and human commodification in violation of the inherent dignity of each individual human life.

Violation of the EU Ban on Eugenic Genetic Modification

24. As more fully set forth in the opinion of Lord Brennan QC, the attorney general for Northern Ireland as well as by legal counsel for Alliance Defending Freedom⁸, this legislation sanctions research that is unlawful under the EU Clinical Trials Directive (2001).
25. Article 9(6) of the Directive states that “No gene therapy trials may be carried out which result in modifications to the subject's germ line genetic identity.”
26. As set forth more fully in the attached white paper by Dr. Condic, all three techniques

⁶ American Association for the Advancement of Science, Statement on Human Cloning, available at: <http://www.aaas.org/page/american-association-advancement-science-statement-human-cloning>.

⁷ McGee, G. (October 2011). “Primer on Ethics and Human Cloning.” American Institute of Biological Sciences; *see also* Article 11, "Universal Declaration on the Human Genome and Human Rights". UNESCO. 1997-11-11 (“Practices which are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted. States and competent international organizations are invited to co-operate in identifying such practices and in taking, at national or international level, the measures necessary to ensure that the principles set out in this Declaration are respected.”)

⁸ Alliance Defending Freedom, Opinion on the legality of the draft Mitochondrial Donation Regulations (UK) (5 Feb. 2015), available at <http://www.adfmedia.org/files/UKMDRmemo.pdf>

involve “modifications to the subject’s germ line genetic identity.” This is because all of the proposed procedures are intended to produce a live-born individual with mitochondrial DNA that has been permanently altered by an experimental manipulation. The proposed manipulations therefore would produce a “modification to the subject’s germ line genetic identity” that would be inherited by all future generations. (Condic, Section II(5) and III(A), *attached*).

Potential Tort Claims Based on Resulting Birth Defects and Abortion

27. Some commentators have pointed out that human beings born as a result of cloning techniques could pursue actions in tort against their creators for “wrongful life” because of birth defects or other health conditions. “Creators” could include the government authority, the scientists and physicians, and/or the parents and other who contributed gametes to the production of the cloned human embryo ultimately transferred to a woman’s body under an asserted, but non-existent “right to procreate.”⁹
28. The claim in a so-called “wrongful life” cases is that a child (or his parents) would rather that the child would not have been born than have been born with a particular disability. Cases have found breaches of duties to the child’s parents. For example, in *Curlender v. Bio-Sciences*, the parents were told by a genetic testing laboratory that the father did not carry the gene for Tay-Sachs, which was erroneous, leading to the creation of a child with Tay-Sachs, who successfully sued the laboratory for wrongful life.¹⁰
29. The court in the *Culender* case said in dicta that the child would also have had a cause of action against her parents for not aborting her. Under that logic, parents are seen as having a duty to future offspring not to give birth to a child with serious disabilities. Some commentators argue similarly that choosing to give birth to a child with a serious disability should be analogized to the parent maiming a child through child abuse.¹¹
30. As explained in Dr. Condic’s white paper, the proposed techniques of mitochondrial donation carry significant risks that the resulting live-born child may still carry the mitochondrial disease, or suffer from some other health condition as a result of the genetic manipulation.

⁹ Andrews, L., *Is There a Right to Clone?*, 11 Harvard J. of Law and Technology 3, 643 (Summer 1998); see also Forsythe, C.D., *Human Cloning and the Constitution*, 32 Valparaiso 469 (Spring 1998).

¹⁰ *Curlender v. Bio-Science Lab.*, 165 Cal. Rptr. 477 (Ct. App. 1980).

¹¹ See, e.g., Shaw, M., *Conditional prospective rights of the fetus*, 5 J. L. Med. 63, 99 (1984).

31. Potential litigation over “wrongful life” based on disabilities or failure of the parents who have received poor prenatal diagnoses to abort the imperfect child promote an eugenic duty to use abortion to prevent the birth of children with genetic anomalies or health conditions.
32. For the above stated reasons, Bioethics Defense Fund submits that the proposed methods of human experimentation by genetic modification and human cloning subvert human dignity into human commodification, where human children are treated as products to be perfected, rather than human beings to be respected.



Science Briefing

Mitochondrial Donation: Serious Concerns for Science, Safety and Ethics

Maureen L. Condic, Ph.D.

February 19, 2015

Scientific White Paper by Maureen L. Condic, PhD, mlcondic@neuro.utah.edu

Related **Law and Policy Briefing** by Bioethics Defense Fund, Nikolas T. Nikas, Esq., ntnikas@bdfund.org, and Dorinda C. Bordlee, Esq., dbordlee@bdfund.org,

Three-Parent Embryos: Reproductive Human Cloning to Produce Genetically Modified Babies, available at: <http://www.BDFund.org/3parent>

Mitochondrial Donation: Serious Concerns for Science, Safety and Ethics

*Maureen L. Condic, Ph.D.**

The governments of the United Kingdom and the United States are currently considering regulations that would allow an artificial reproductive technology that creates so-called “three-parent” embryos via a process known as mitochondrial replacement therapy or mitochondrial donation. Three separate procedures have been proposed, yet in all three cases, a human being is produced using essential components from three parents: nuclear DNA from the two intended parents and egg cytoplasm from a donor.¹

Proponents of conducting human experiments to generate “three parent embryos”² initially cast this procedure as a beneficent therapeutic approach to treat women with mitochondrial disease and allow them to bear healthy children. But close on the heels of the approval of the techniques by the British House of Commons, one of its pioneers has reportedly filed for permission from the United States FDA to use these techniques as a fertility treatment for women who find it difficult to get pregnant because of their age.³

Whatever the purported justifications, public officials considering the legalization of these methods of genetic engineering should clearly understand the science showing that all three procedures involve genetic modification, i.e. “modifications to the subject’s germ line genetic identity.”⁴; all three procedures carry significant risks to the children intended to be born; and two of the procedures involve a eugenic form of reproductive cloning, in which a human being with a medical condition is killed and his or her parts are used to create a new human being with an intended improved biological state.

The scientific, safety, and ethical questions raised by this practice are profound and are in need of deeper consideration. Section I of this paper will set forth the mechanics of the three methods proposed for mitochondrial donation (Maternal Spindle Transfer, Pro-nuclear Transfer and Embryo Cell Nuclear Transfer), all of which pose unacceptable risks for the intended offspring and constitute unethical experimentation on human beings. Section II will set forth the serious

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¹ This text is a modified and expanded version of an article that first appeared in Public Discourse: Condic, M.L. (2014). We Are Not Just Our DNA: The Ethical Dangers of Three-Parent Embryos. Public Discourse (available: <http://www.thepublicdiscourse.com/2014/03/12897/>).

² Mitochondrial replacement therapy in reproductive medicine. Wolf DP, Mitalipov N, Mitalipov S. Trends Mol Med. 2014 Dec 10. pii: S1471-4914(14)00215-9.

³ Connor, S. (8 Feb. 2015). Scientist who pioneered “three-parent” embryo technique now wants to offer it to older women trying for a baby. The Independent (available: <http://www.independent.co.uk/news/science/threeparent-embryos-an-ivf-revolution-or-a-slippery-slope-to-designer-babies-10031477.html>).

⁴ Article 9(6) of the EU Clinical Trial Directives states that “No gene therapy trials may be carried out which result in modifications to the subject's germ line genetic identity.”

health risks to the children intended to be born, including increased incidence of birth defects, cancer and metabolic diseases. Section III will raise serious ethical concerns that have not been adequately addressed.

I. Three proposed methods of treating mitochondrial disease

Mitochondria are small structures within cells that supply the energy required for life. They are unusual in that they have their own DNA that produces some of the molecules required for energy metabolism. And when this mitochondrial DNA (mtDNA) has a mutation, medical conditions affecting energy production (i.e. metabolic disease) can result. A curiosity of mammalian biology is that unlike nuclear DNA (nDNA) that is inherited equally from both parents, all of the mitochondria are inherited from the mother. So, if the mother carries a mutation in her own mtDNA, her children will have the same mutation (Figure 1). It is in the context of this biology that three methods have been proposed to avoid the birth of children with certain mitochondria based diseases or health conditions.

1. Maternal Spindle Transfer

The procedures under consideration fall into three general classes. The first, known as Maternal Spindle Transfer (Figure 2), would use an egg from the mother with the mitochondrial disease

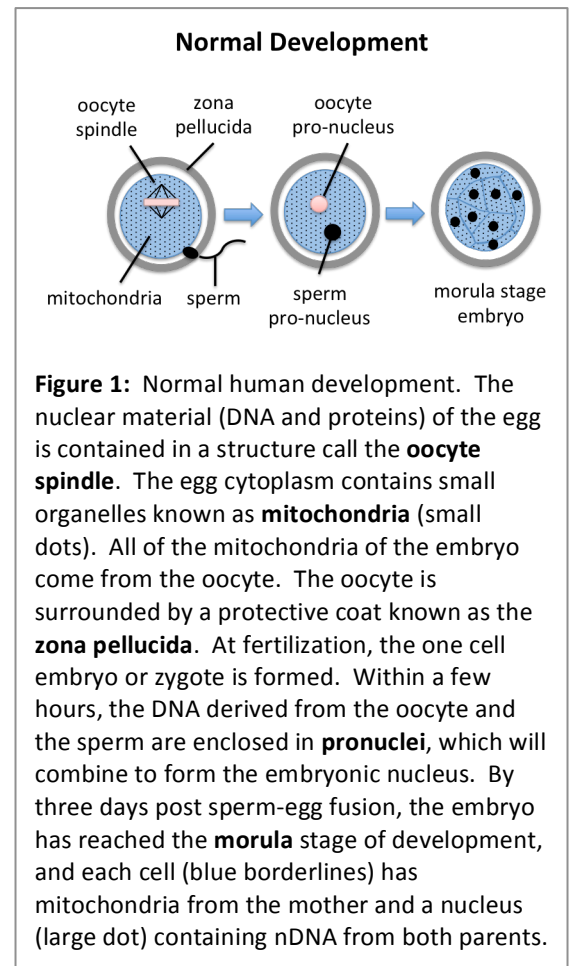


Figure 1: Normal human development. The nuclear material (DNA and proteins) of the egg is contained in a structure call the **oocyte spindle**. The egg cytoplasm contains small organelles known as **mitochondria** (small dots). All of the mitochondria of the embryo come from the oocyte. The oocyte is surrounded by a protective coat known as the **zona pellucida**. At fertilization, the one cell embryo or zygote is formed. Within a few hours, the DNA derived from the oocyte and the sperm are enclosed in **pronuclei**, which will combine to form the embryonic nucleus. By three days post sperm-egg fusion, the embryo has reached the **morula** stage of development, and each cell (blue borderlines) has mitochondria from the mother and a nucleus (large dot) containing nDNA from both parents.

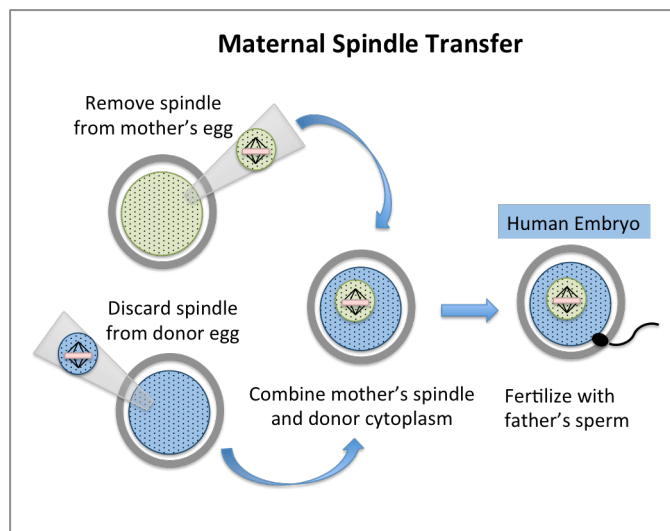


Figure 2: Maternal Spindle transfer. The spindle containing the oocyte DNA is discarded from a donor egg with healthy mitochondria (**blue**). The spindle from an egg of the intended mother is also removed, along with a small number of disease-causing mitochondria (**green**). The spindle from the intended donor egg, and the resulting "reconstituted" oocyte is fertilized by sperm of the intended father to produce a one-cell **human embryo** or zygote where the nuclear DNA is derived from the intended parents and most mitochondria from the donor. Having two types of mitochondria is known as **heteroplasmy**.

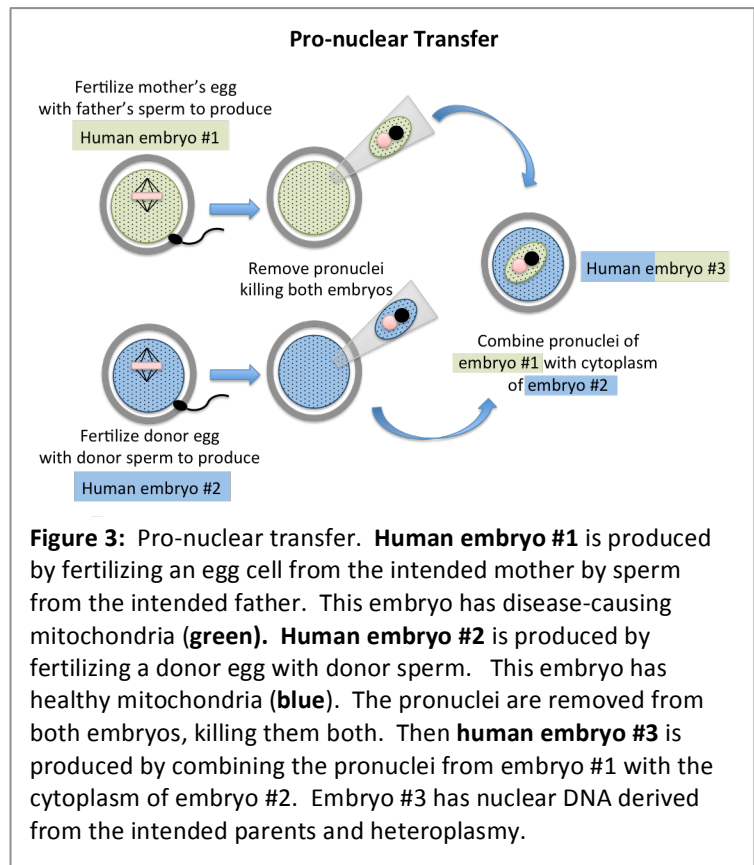
and a donor egg from a woman with healthy mitochondria. The nucleus of the donor's egg would be replaced by the nucleus of the mother's egg. This would create a "hybrid" egg, with the nDNA from the mother and the cytoplasmic elements of the egg cell (including healthy mitochondria) from the donor. This hybrid egg would then be fertilized by the father's sperm to create a "three-parent" human embryo: nDNA from the mother, nDNA from the father, and non-nuclear components (including mtDNA) from the donor.

Maternal Spindle Transfer is a risky experiment with an uncertain outcome. If either the mother's nucleus or the donor's egg is damaged, the embryo resulting from fertilization of this experimentally reconstructed cell will develop abnormally or die. Indeed, the success rate for this procedure in animals very low (see below; *Serious Medical Risks*), raising the important question of how many human "casualties" we are willing accept in the hope of producing one human who survives and is free of disease.

Despite this serious safety concern, Maternal Spindle Transfer is essentially a manipulation of human *cells*, not human *beings*. Consequently, it is the least ethically problematic of the three proposals. By contrast, the two other procedures under consideration ("Pro-Nuclear Transfer" and "Embryo Cell Nuclear Transfer") involve the direct destruction of at least one embryo and the subsequent use of its parts to create a new, cloned embryo with superior biology. Given the uncontested scientific evidence that human life begins at the moment of sperm-egg fusion,⁵ Pro-Nuclear Transfer and Embryo Cell Nuclear Transfer are not only destructive human experimentation, they are also both forms of eugenic, reproductive cloning, conducted at a very early stage of the human life span.

2. Pro-Nuclear Transfer

In Pro-Nuclear Transfer (Figure 3), a single-cell embryo is created using sperm and egg from the intended



⁵ Condic, M.L. (2008). When does human life begin? A scientific perspective. Westchester Institute White Paper 1, 1-18. Westchester Institute for Ethics & the Human Person, Thornwood, NY. (available at: <http://www.bdfund.org/whitepapers>). [Reprinted in: Natl Cathol Bioeth Quart. 9, 127-208.]; Condic, M.L. (2014). When does human life begin? The scientific evidence and terminology revisited. Journal of Law and Public Policy. Vol. 8 No. 1: 44-81.; Condic, M.L. (2014). Totipotency: What it is and what it is not. Stem Cells and Development 23, 796-812.

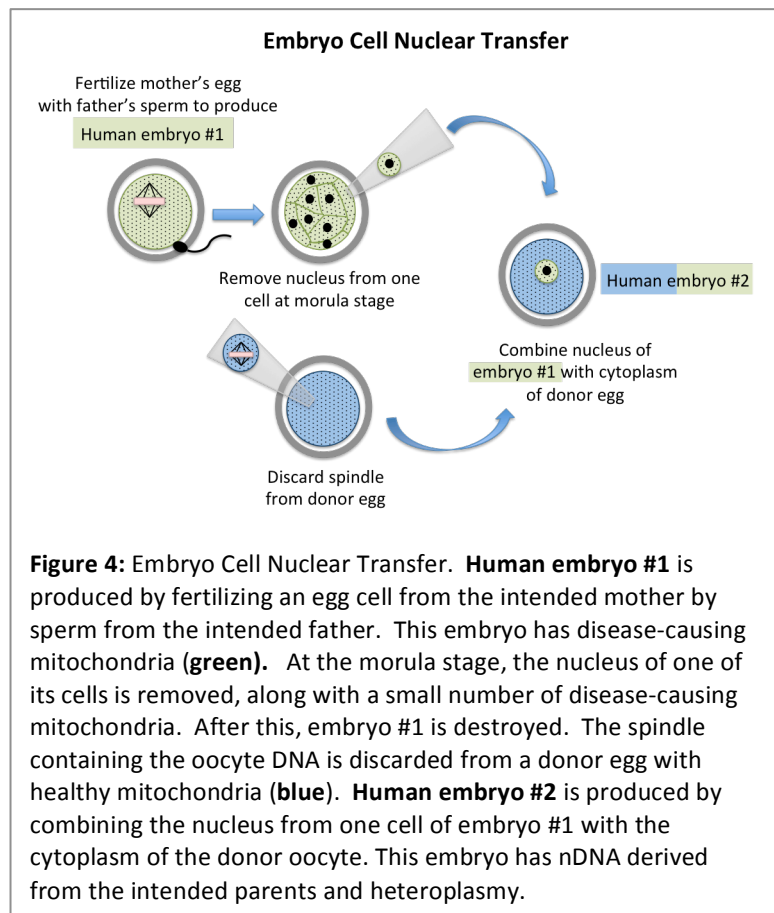
mother and father. This embryo has disease-causing mitochondria from the mother. At the same time, a second embryo is created using a donor egg with healthy mitochondria and donor sperm. Based on a large body of uncontested scientific evidence, these one-cell human embryos are clearly human beings at the earliest stage of the natural lifespan.⁶

In the next step of this procedure, the “pro-nuclei” (nuclei derived from the sperm and egg, containing the embryo’s nDNA; see Figure 1) are removed from both embryos—killing them both. Then a *new* embryo is produced by transferring the pronuclei from the intended parents to the healthy cytoplasm derived from the “host” embryo. This is a form of destructive human cloning; i.e. the nuclear DNA of one human being is used to create a genetic copy or “clone” of that individual by transfer to egg-derived cytoplasm from a host embryo, killing the original embryo and the host embryo in the process (see “Serious Ethical Concerns”).

In this procedure, as in Maternal Spindle Transfer, there is significant risk of damaging manipulated cells, causing development of the resulting, cloned embryo to be abnormal. In addition, two embryos are created and then destroyed in the process of producing the third, cloned embryo. Finally, this procedure involves the intentional creation of a “defective” human being (“Human Embryo #1”; Figure 3) who is then destroyed so that parts of the body (the pro-nuclei) can be used to clone a new human being, who is viewed as biologically superior. Pro-Nuclear Transfer is not a medical therapy designed to cure an individual disease. It is a manipulation that *destroys* both the individual with disease and a second healthy individual who is unrelated to the parents in order to cobble together a *superior* individual from the body parts. It is *destructive, eugenic, reproductive* human cloning.

3. Embryo Cell Nuclear Transfer

Embryo Cell Nuclear Transfer (Figure 4) is similar to Pro-Nuclear Transfer, except that only one embryo is produced from the sperm and egg of the intended parents. This embryo is allowed to develop for a day or two and then a nucleus from one of its cells is used to produce a new, cloned embryo by transferring the nucleus to a donor



⁶ ibid

egg cell with healthy mitochondria that has had its own nucleus removed. The original embryo with the mitochondrial disease is then destroyed.

In this case, as in the two procedures above, there is a significant risk of damaging the egg cell or the transferred nucleus, resulting in abnormal or failed development of the resulting cloned embryo. And Embryo Cell Nuclear Transfer is also a form of eugenic, reproductive human cloning where a “defective” human being is destroyed to obtain desirable parts (in this case, unique nDNA derived from both parents) to construct a superior human being.

II. Serious Medical Risks

All three of the proposed procedures are highly likely to be unsafe for the resulting children, setting aside the requirement that embryos are deliberately destroyed by the procedures themselves. Surprisingly, the large number of serious medical risks associated with the proposed “therapeutic” techniques have not been seriously discussed. ***Importantly, any one of the concerns listed below is sufficient to justify a ban on the proposed procedures as unsafe for use in human subjects.***

1. Risks associated with damage to the nucleus or the egg: As noted above, all of the proposed techniques carry an inherent and significant risk of damage to the nucleus or to the egg cell. While four live-born monkeys have been produced using this technique, this “success” does not reflect the large number of embryos that were so damaged or defective, they were unable to progress to maturity. Indeed, in two separate papers using Maternal Spindle Transfer, only 46 out of 85 monkey embryos produced⁷ or 19 out of 60 human embryos produced⁸ were able to progress even to the blastocyst stage (approximately day 5-7 of development). In the first study, 15 monkey embryos were transferred to surrogate mothers, yet only four pregnancies resulted. Therefore the “healthy” offspring produced by this technique represent a small fraction of all the embryos that were originally generated, *indicating that this procedure was lethal for the great majority of the embryos it produced*. Moreover, although these four animals appear normal,⁹ this is hardly a sufficient number to conclude the procedure is safe, even for the small number of individuals that survive the procedure itself.

2. Risks associated with nuclear transfer (cloning): It is unambiguously established by a large number of independent studies that cloned animals are not healthy. Despite decades of experience, cloning is an inherently risky procedure, with success rates typically in the range of 0.1-1%; i.e. 99.9-99% of all cloned animals are so abnormal they do not survive to live birth.¹⁰

⁷ Mitochondrial gene replacement in primate offspring and embryonic stem cells. Tachibana M, Sparman M, Sritanaudomchai H, Ma H, Clepper L, Woodward J, Li Y, Ramsey C, Kolotushkina O, Mitalipov S. Nature. 2009 Sep 17;461(7262):367-72.

⁸ Towards germline gene therapy of inherited mitochondrial diseases. Tachibana M, Amato P, Sparman M, Woodward J, Sanchis DM, Ma H, Gutierrez NM, Tippner-Hedges R, Kang E, Lee HS, Ramsey C, Masterson K, Battaglia D, Lee D, Wu D, Jensen J, Patton P, Gokhale S, Stouffer R, Mitalipov S. Nature. 2013 Jan 31;493(7434):627-31.

⁹ Ibid.

¹⁰ Cloning from stem cells: different lineages, different species, same story. Oback B. Reprod Fertil Dev. 2009;21(1):83-94. Climbing Mount Efficiency--small steps, not giant leaps towards higher cloning success in farm

Even the rare individuals who do survive exhibit serious dysregulation of multiple genes that result in significant medical problems.¹¹ These abnormalities do not arise as a consequence of subtle, gestational irregularities, but are seen from the very beginning. Direct examination of embryonic stem cell lines derived from cloned embryos at approximately 5-7 days of development also shows that, like the embryos they are derived from, cloned ESCs are also clearly "abnormal" when compared to ESCs derived from fertilization.¹² In light of the strong evidence that cloning produces abnormal embryos, Pro-nuclear transfer and Embryo Cell Nuclear Transfer (both forms of reproductive cloning) are not safe for use in humans.

3. Risks associated with producing babies in vitro: While most human infants born as a result of assisted reproductive technologies (ART) are healthy by most measures,¹³ a growing body of data indicates that children produced in the laboratory are at significantly greater risk for a wide range of medical issues, including neurological disorders,¹⁴ cancer¹⁵, congenital

animals. Oback B. *Reprod Domest Anim.* 2008 Jul;43 Suppl 2:407-16.; Cloning adult farm animals: a review of the possibilities and problems associated with somatic cell nuclear transfer. Edwards JL, Schrick FN, McCracken MD, van Amstel SR, Hopkins FM, Welborn MG, Davies CJ. *Am J Reprod Immunol.* 2003 Aug;50(2):113-23.; Cloning: experience from the mouse and other animals. Yanagimachi R. *Mol Cell Endocrinol.* 2002 Feb 22;187(1-2):241-8.

¹¹ Nuclear transfer-derived epiblast stem cells are transcriptionally and epigenetically distinguishable from their fertilized-derived counterparts. Maruotti J, Dai XP, Brochard V, Jouneau L, Liu J, Bonnet-Garnier A, Jammes H, Vallier L, Brons IG, Pedersen R, Renard JP, Zhou Q, Jouneau A. *Stem Cells.* 2010 Apr;28(4):743-52.; Comparative analysis of nuclear transfer embryo-derived mouse embryonic stem cells. Part II: gene regulation. Kobolak J, Horsch M, Geissler S, Mamo S, Beckers J, Dinnyes A. *Cell Reprogram.* 2012 Feb;14(1):68-78.; Comparative analysis of nuclear transfer embryo-derived mouse embryonic stem cells. Part I: cellular characterization. Kobolak J, Mamo S, Rungsiwiwut R, Ujhelly O, Csonka E, Hadlaczky G, Dinnyes A. *Cell Reprogram.* 2012 Feb;14(1):56-67.; Differential methylation status of imprinted genes in nuclear transfer derived ES (NT-ES) cells. Chang G, Liu S, Wang F, Zhang Y, Kou Z, Chen D, Gao S. *Genomics.* 2009 Feb;93(2):112-9.; Nuclear transfer alters the DNA methylation status of specific genes in fertilized and parthenogenetically activated mouse embryonic stem cells. Hikichi T, Kohda T, Wakayama S, Ishino F, Wakayama T. *Stem Cells.* 2008 Mar;26(3):783-8.

¹² Reprogramming efficiency following somatic cell nuclear transfer is influenced by the differentiation and methylation state of the donor nucleus. Blelloch R, Wang Z, Meissner A, Pollard S, Smith A, Jaenisch R. *Stem Cells.* 2006 Sep;24(9):2007-13.; Inefficient reprogramming of the hematopoietic stem cell genome following nuclear transfer. Inoue K, Ogonuki N, Miki H, Hirose M, Noda S, Kim JM, Aoki F, Miyoshi H, Ogura A. *J Cell Sci.* 2006 May 15;119 (Pt 10):1985-91.; Developmental ability of cloned embryos from neural stem cells. Mizutani E, Ohta H, Kishigami S, Van Thuan N, Hikichi T, Wakayama S, Kosaka M, Sato E, Wakayama T. *Reproduction.* 2006 Dec;132(6):849-57.

¹³ Comparing indicators of health and development of singleton young adults conceived with and without assisted reproductive technology. Halliday J, Wilson C, Hammarberg K, Doyle LW, Bruinsma F, McLachlan R, McBain J, Berg T, Fisher JR, Amor D. *Fertil Steril.* 2014 Apr;101(4):1055-63.

¹⁴ Cerebral palsy, autism spectrum disorders, and developmental delay in children born after assisted conception: a systematic review and meta-analysis. Hvidtjorn D, Schieve L, Schendel D, Jacobsson B, Svaerke C, Thorsen P. *Arch Pediatr Adolesc Med.* 2009 Jan;163(1):72-83.; Is there an increased risk for drug treated attention deficit/hyperactivity disorder in children born after in vitro fertilization? Källén AJ, Finnström OO, Lindam AP, Nilsson EM, Nygren KG, Otterblad Olausson PM. *Eur J Paediatr Neurol.* 2011 May;15(3):247-53.; A cross-sectional evaluation of the first cohort of young adults conceived by in vitro fertilization in the United States. Beydoun HA, Sicignano N, Beydoun MA, Matson DO, Bocca S, Stadtmauer L, Oehninger S. *Fertil Steril.* 2010 Nov;94(6):2043-9.; Association of assisted reproductive technology (ART) treatment and parental infertility diagnosis with autism in ART-conceived children. Kissin DM, Zhang Y, Boulet SL, Fountain C, Bearman P, Schieve L, Yeargin-Allsopp M, Jamieson DJ. *Hum Reprod.* 2015 Feb;30(2):454-65.

¹⁵ In vitro fertilization and risk of childhood leukemia in Greece and Sweden. Petridou ET, Sargentanis TN, Panagopoulou P, Moschovi M, Polychronopoulou S, Baka M, Pourtsidis A, Athanassiadou F, Kalmanti M, Sidi V, Dessypris N, Frangakis C, Matsoukis IL, Stefanadis C, Skalkidou A, Stephansson O, Adami HO, Kieler H. *Pediatr*

abnormalities,¹⁶ and imprinting disorders (Beckwith-Wiedemann syndrome, Silver-Russell syndrome, Angelman syndrome and others).¹⁷ Similar results are well established in multiple species of animals produced by ART¹⁸. Moreover, ART-produced individuals are at significantly higher risk for premature birth and low birth weight, with all of the many long-term consequences associated with these events.¹⁹ While some argue that these medical problems are caused by the “subfertility” of the parents, children conceived by ART are at greater risk compared to children of similarly “subfertile” parents who conceived naturally.²⁰ In many cases,

Blood Cancer. 2012 Jun;58(6):930-6.; Incidence of retinoblastoma in children born after in-vitro fertilisation. Moll AC, Imhof SM, Cruysberg JR, Schouten-van Meeteren AY, Boers M, van Leeuwen FE. *Lancet*. 2003 Jan 25;361(9354):309-10.; Incidence of retinoblastoma in Dutch children conceived by IVF: an expanded study. Marees T, Dommering CJ, Imhof SM, Kors WA, Ringens PJ, van Leeuwen FE, Moll AC. *Hum Reprod*. 2009 Dec;24(12):3220-4.

¹⁶ Birth defects in children conceived by in vitro fertilization and intracytoplasmic sperm injection: a meta-analysis. Wen J, Jiang J, Ding C, Dai J, Liu Y, Xia Y, Liu J, Hu Z. *Fertil Steril*. 2012 Jun;97(6):1331-7.e1-4.; In vitro fertilization is associated with an increase in major birth defects. Olson CK, Keppler-Noreuil KM, Romitti PA, Budelier WT, Ryan G, Sparks AE, Van Voorhis BJ. *Fertil Steril*. 2005 Nov;84(5):1308-15.; Obstetric outcomes and congenital abnormalities after in vitro maturation, in vitro fertilization, and intracytoplasmic sperm injection. Buckett WM, Chian RC, Holzer H, Dean N, Usher R, Tan SL. *Obstet Gynecol*. 2007 Oct;110(4):885-91.

¹⁷ A systematic review and meta-analysis of DNA methylation levels and imprinting disorders in children conceived by IVF/ICSI compared with children conceived spontaneously. Lazaraviciute G, Kauser M, Bhattacharya S, Haggarty P, Bhattacharya S. *Hum Reprod Update*. 2014 Nov-Dec;20(6):840-52.; Epigenetics, genomic imprinting and assisted reproductive technology. Le Bouc Y, Rossignol S, Azzi S, Steunou V, Netchine I, Gicquel C. *Ann Endocrinol (Paris)*. 2010 May;71(3):237-8.

¹⁸ Incidence of abnormal offspring from cloning and other assisted reproductive technologies. Hill JR. *Annu Rev Anim Biosci*. 2014 Feb;2:307-21.; Large offspring syndrome: a bovine model for the human loss-of-imprinting overgrowth syndrome Beckwith-Wiedemann. Chen Z, Robbins KM, Wells KD, Rivera RM. *Epigenetics*. 2013 Jun;8(6):591-601.; Cloning and assisted reproductive techniques: influence on early development and adult phenotype. Sakai RR, Tamashiro KL, Yamazaki Y, Yanagimachi R. *Birth Defects Res C Embryo Today*. 2005 Jun;75(2):151-62.; Epigenetics, genomic imprinting and assisted reproductive technology. Le Bouc Y, Rossignol S, Azzi S, Steunou V, Netchine I, Gicquel C. *Ann Endocrinol (Paris)*. 2010 May;71(3):237-8.; Imprinting disorders and assisted reproductive technology. Manipalviratn S, DeCherney A, Segars J. *Fertil Steril*. 2009 Feb;91(2):305-15.; Epigenetic change in IGF2R is associated with fetal overgrowth after sheep embryo culture. Young LE, Fernandes K, McEvoy TG, Butterwith SC, Gutierrez CG, Carolan C, Broadbent PJ, Robinson JJ, Wilmut I, Sinclair KD. *Nat Genet*. 2001 Feb;27(2):153-4.; Culture of preimplantation mouse embryos affects fetal development and the expression of imprinted genes. Khosla S, Dean W, Brown D, Reik W, Feil R. *Biol Reprod*. 2001 Mar;64(3):918-26.; Differential effects of culture on imprinted H19 expression in the preimplantation mouse embryo. Doherty AS, Mann MR, Tremblay KD, Bartolomei MS, Schultz RM. *Biol Reprod*. 2000 Jun;62(6):1526-35.; Selective loss of imprinting in the placenta following preimplantation development in culture. Mann MR, Lee SS, Doherty AS, Verona RI, Nolen LD, Schultz RM, Bartolomei MS. *Development*. 2004 Aug;131(15):3727-35.; IVF results in de novo DNA methylation and histone methylation at an Igf2-H19 imprinting epigenetic switch. Li T, Vu TH, Ulaner GA, Littman E, Ling JQ, Chen HL, Hu JF, Behr B, Giudice L, Hoffman AR. *Mol Hum Reprod*. 2005 Sep;11(9):631-40.; Errors in development of fetuses and placentas from in vitro-produced bovine embryos. Farin PW, Piedrahita JA, Farin CE. *Theriogenology*. 2006 Jan 7;65(1):178-91.; Aberrant DNA methylation of imprinted loci in superovulated oocytes. Sato A, Otsu E, Negishi H, Utsunomiya T, Arima T. *Hum Reprod*. 2007 Jan;22(1):26-35.; Superovulation alters the expression of imprinted genes in the midgestation mouse placenta. Fortier AL, Lopes FL, Darricarrère N, Martel J, Trasler JM. *Hum Mol Genet*. 2008 Jun 1;17(11):1653-65.

¹⁹ Low and very low birth weight in infants conceived with use of assisted reproductive technology. Schieve LA, Meikle SF, Ferre C, Peterson HB, Jeng G, Wilcox LS. *N Engl J Med*. 2002 Mar 7;346(10):731-7.; Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. Jackson RA, Gibson KA, Wu YW, Croughan MS. *Obstet Gynecol*. 2004 Mar;103(3):551-63.

²⁰ Why do singletons conceived after assisted reproduction technology have adverse perinatal outcome? Systematic review and meta-analysis. Pinborg A, Wennerholm UB, Romundstad LB, Loft A, Aittomäki K, Söderström-Anttila

we are only now appreciating the complications of ART, as individuals produced in the laboratory are reaching adulthood.²¹ Permitting even greater risk to ART produced children by allowing grossly invasive procedures such as cloning or Maternal Spindle transfer to also be performed is medically irresponsible.

4. Risks associated with heteroplasmy: In all three of the procedures outlined above, there is a significant risk of transferring some of the disease-carrying mitochondria from the mother's egg to the baby, resulting in a mix of healthy, and disease-carrying mitochondria; a condition known as a "heteroplasmy" (See Figures 2-4). In this case, heteroplasmy could cause reappearance of the disease in the offspring of any woman produced by the "three-parent" approach, due to mitochondrial "founder effects" in oogenesis.²² Even a few "bad" mitochondria can become the dominant type in any one egg, causing the mitochondrial disease to recur in any child produced from that egg.

5. Risks associated with mtDNA-nDNA incompatibility: All of the proposed procedures are forms of "germ-line engineering" that alter the genetic makeup of future generations in a permanent way. We know that in nature, mtDNA and nDNA "co-evolve" to work with each other in an efficient manner.²³ In some species,²⁴ incompatibility between the mitochondrial and nuclear genome significantly compromises the health of the individual. And there is growing evidence that such "incompatibility" also contributes to human pathology.²⁵ All of the proposed methods of "treating" mitochondrial disease introduce a permanent and unnatural mismatch

V, Nygren KG, Hazekamp J, Bergh C. Hum Reprod Update. 2013 Mar-Apr;19(2):87-104.; Perinatal outcomes in 6,338 singletons born after intrauterine insemination in Denmark, 2007 to 2012: the influence of ovarian stimulation. Malchau SS, Loft A, Henningsen AK, Nyboe Andersen A, Pinborg A. Fertil Steril. 2014 Oct;102(4):1110-1116.e2.

²¹ Assisted reproductive technology and somatic morbidity in childhood: a systematic review. Kettner LO, Henriksen TB, Bay B, Ramlau-Hansen CH, Kesmodel US. Fertil Steril. 2015 Jan 23. pii: S0015-0282(14)02520-5.; Comparing indicators of health and development of singleton young adults conceived with and without assisted reproductive technology. Halliday J, Wilson C, Hammarberg K, Doyle LW, Bruinsma F, McLachlan R, McBain J, Berg T, Fisher JR, Amor D. Fertil Steril. 2014 Apr;101(4):1055-63.; 57. A cross-sectional evaluation of the first cohort of young adults conceived by in vitro fertilization in the United States. Beydoun HA, Sicignano N, Beydoun MA, Matson DO, Bocca S, Stadtmauer L, Oehninger S. Fertil Steril. 2010 Nov;94(6):2043-9.

²² Prevention of mitochondrial disease inheritance by assisted reproductive technologies: prospects and challenges. Yabuuchi A, Beyhan Z, Kagawa N, Mori C, Ezoe K, Kato K, Aono F, Takehara Y, Kato O. Biochim Biophys Acta. 2012 May;1820(5):637-42.

²³ Mechanisms and convergence of compensatory evolution in mammalian mitochondrial tRNAs. Kern AD, Kondrashov FA. Nat Genet. 2004 Nov;36(11):1207-12.; 12. Mitochondrial-nuclear interactions: compensatory evolution or variable functional constraint among vertebrate oxidative phosphorylation genes? Zhang F, Broughton RE. Genome Biol Evol. 2013;5(10):1781-91.

²⁴ An Incompatibility between a mitochondrial tRNA and its nuclear-encoded tRNA synthetase compromises development and fitness in *Drosophila*. Meiklejohn CD, Holmbeck MA, Siddiq MA, Abt DN, Rand DM, Montooth KL. PLoS Genet. 2013;9(1):e1003238.; Mitochondrial-nuclear epistasis contributes to phenotypic variation and coadaptation in natural isolates of *Saccharomyces cerevisiae*. Paliwal S, Fiumera AC, Fiumera HL. Genetics. 2014 Nov;198(3):1251-65.; Disruption of mitochondrial function in interpopulation hybrids of *Tigriopus californicus*. Ellison CK, Burton RS. Evolution. 2006 Jul;60(7):1382-91.; Genetic architecture of metabolic rate: environment specific epistasis between mitochondrial and nuclear genes in an insect. Arnqvist G, Dowling DK, Eady P, Gay L, Tregenza T, Tuda M, Hosken DJ. Evolution. 2010 Dec;64(12):3354-63.

²⁵ Mitochondrial-nuclear epistasis: implications for human aging and longevity. Tranah GJ. Ageing Res Rev. 2011 Apr;10(2):238-52.

between the nuclear and the mitochondrial genome that will be inherited by all subsequent generations. Producing such genetically modified (GM) humans constitutes unethical, destructive experimentation on humans, with no guarantee of a safe outcome for either the “patient” (the cloned embryo produced) or any of the offspring of that patient. This is an unwarranted approach that puts future generations at grave risk of unforeseen consequences, in addition to the clearly foreseen destruction of a class of “defective” humans in the hope of manufacturing “superior” offspring.

III. Ethical Concerns

A. Genetic engineering, not “therapy”

Surprisingly, many people do not see an obvious ethical problem with these proposals. A medical colleague of mine recently opined, “If you take the newly formed pronucleus and put it in a different ‘body’ (i.e., another woman’s egg), are you really destroying that embryo? The individual would still develop with almost all the same genetic traits, and would potentially survive longer if the therapy worked.”

Yet the view that transfer of an embryo’s nucleus is merely a “therapeutic” approach for treatment of disease is false. The embryo produced by this procedure is not just the original child of the parents, moved to a new cytoplasmic “environment.” This would only be true if a human being were nothing more than his or her nDNA, which is clearly not the case. While our unique DNA clearly determines many aspects of our individual characteristics, we are also critically affected by the specific, non-genetic composition of the egg that produced us. As explained in detail in elsewhere,²⁶ many aspects of embryonic development, and therefore many aspects of the unique individual we end up being, depend on non-genetic components derived from the cytoplasm of the egg.

The importance of non-genetic factors in determining the unique character of a human individual is very clearly illustrated by “maternal effect mutations.”²⁷ These mutations have no effect on the development or function of the mother, but specifically disrupt development of embryos derived from her eggs. The embryo may not even have the “bad” gene (only half of the mother’s genome is passed on to any one child), but embryonic development can still be profoundly affected by the molecules present in the egg itself. Many key developmental factors work like this—in both positive and negative ways. Therefore, all three of the procedures described above would indeed generate “three-parent embryos,” whose unique traits and human identity would reflect the genetic contributions of both the genetic mother and father as well as the critical, non-genetic contributions made by the egg donor.

B. Other Serious Ethical Concerns

²⁶ Totipotency: what it is and what it is not. Condit ML. Stem Cells Dev. 2014 Apr 15;23(8):796-812.

²⁷ Genetics of mammalian reproduction: modeling the end of the germline. Matzuk MM, Burns KH. Annu Rev Physiol. 2012;74:503-28.

In addition to the concerns raised by genetic engineering and the unnatural production of genetically modified human beings with three biological parents, a number of other serious ethical concerns raised by the proposed techniques are noted briefly below.

1. Ethical issues raised by intentional production and subsequent destruction of large numbers of human beings in order to use their body parts for the production of a third, biologically superior human being; i.e. *destructive eugenic cloning*.
2. Ethical issues raised by *human reproductive cloning*.
3. Ethical issues raised by generation of a *large number of damaged embryos as "casualties"* in an attempt to produce one individual who is free from disease.
4. Ethical issues raised by the *greatly increased medical risks* for the children who survive this procedure.
5. Ethical issues raised by permanent, germ-line engineering of human beings (*GM-humans*), with no way of predicting the long-term outcomes for the individuals produced in this manner.

C. Conclusions

Producing three-parent embryos is a form of eugenic, human experimentation. In the most extreme forms (Pro-nuclear Transfer and Embryo Cell Nuclear Transfer), this approach constitutes destructive human cloning, not for research or advancement of knowledge, but rather with the express intention of producing cloned human babies. The risk to the babies produced cannot be predicted and is likely to be significant. This approach will, for the first time, produce genetically modified human beings (GM-humans). It is unsafe, unethical and irresponsible to allow such experimentation on innocent human subjects who will be forced to live with whatever unforeseen consequences may result.