REPRODUCTIVE CLONING LOOPHOLE

To Prevent Transmission of Mitochondrial Disease of Mitochondrial Origin

3ZA(5) and 3(6): LOOPHOLE

Human Fertilisation and

Embryology Bill

June 2008

DIAGRAM 1(a)

3ZA(5): REPRODUCTIVE CLONING LOOPHOLE

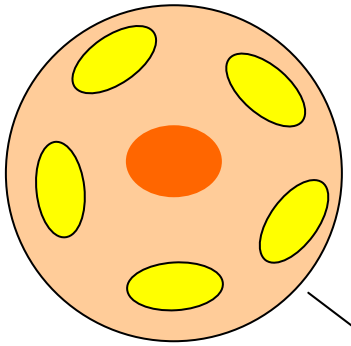
(Compare with Diagram 1b)

MITOCHONDRIAL DISEASE OF MITOCHONDRIAL ORIGIN

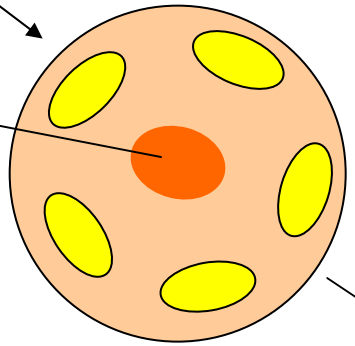
One possible type of 'permitted' egg and embryo to prevent transmission of mitochondrial disease of *mitochondrial* origin:

EGG NUCLEAR TRANSFER + IVF

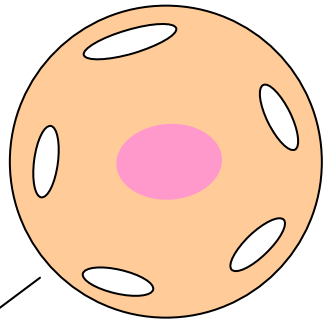
(1) Donor egg with healthy mitochondria

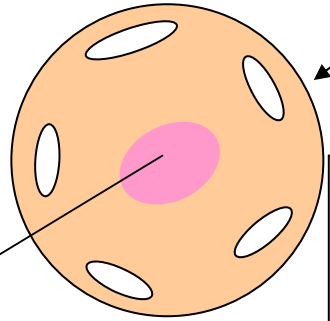


(2) Nucleus is removed from the donor egg

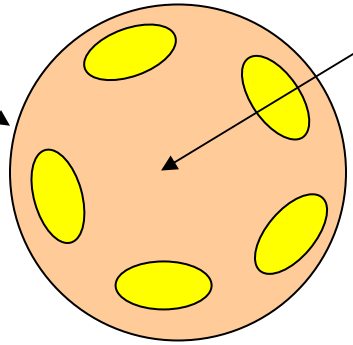


(3) Egg from a woman With mitochondrial disease

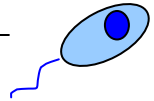




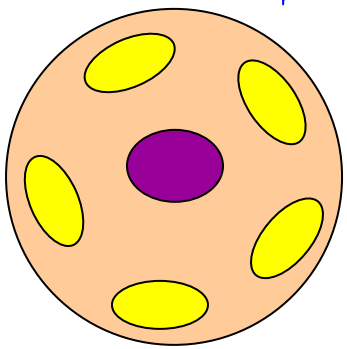
(4) The nucleus of the egg with unhealthy mitochondria is removed and placed into the donor egg with healthy mitochondria.



(5) PERMITTED EGG according to 3ZA(5): Reconstructed egg with nucleus of the woman with mitochondrial disease, and mitochondria from the egg donor with healthy mitochondria



(6) IVF



(7) PERMITTED EMBRYO according to 3ZA(5) since nuclear and mitochondrial DNA can be altered under 3ZA(5)

Embryo created by nuclear transfer between eggs, followed by IVF. Nuclear DNA is from the woman with mitochondrial disease, and mitochondrial DNA is from the egg donor.

OOCYTE NUCLEAR TRANSFER INTO AN ENUCLEATED EGG FOLLOWED BY IVF

A similar procedure **(PRONUCLEAR TRANSFER)** could be carried out using one-celled embryos: IVF would be carried out first, followed by nuclear transfer at the one-celled embryo stage into either an enucleated egg or one-celled embryo. All procedures would therefore involve a combination of cell nuclear transfer and IVF, and the embryos would have genes from one man and two women (nuclear genes from one woman and mitochondrial genes from the second woman). None of these eggs or embryos, including those in this diagram, would be 'permitted' eggs or embryos under 3ZA(2)-(4), which ban alterations in nuclear and mitochondrial DNA. However, 3ZA(5) can over-ride all these restrictions, subject to affirmative resolution.

DIAGRAM 1(b)

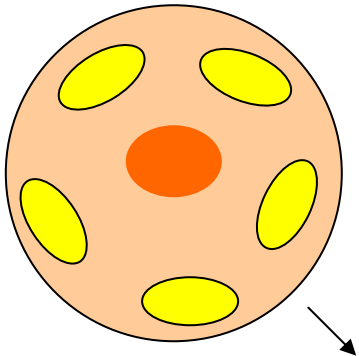
3ZA(5): REPRODUCTIVE CLONING LOOPHOLE

(Compare with Diagram 1(a))

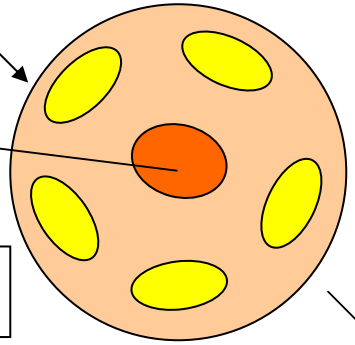
MITOCHONDRIAL DISEASE OF MITOCHONDRIAL ORIGIN
REPRODUCTIVE CLONING

One possible type of 'permitted' egg and embryo, to prevent transmission of mitochondrial disease of *mitochondrial* origin

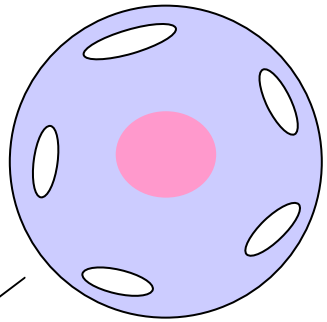
(1) Donor egg with healthy mitochondria

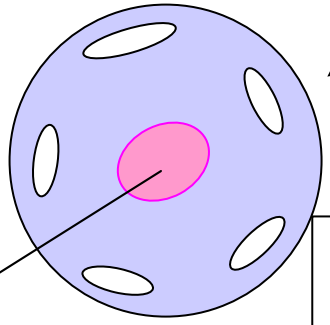


(2) Nucleus is removed From the donor egg

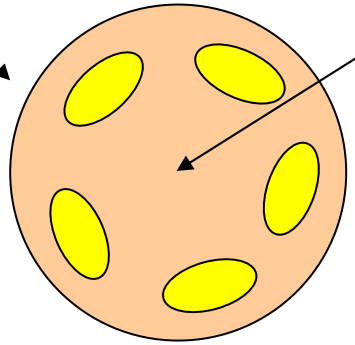


(3) ADULT SOMATIC CELL from a woman with mitochondrial disease



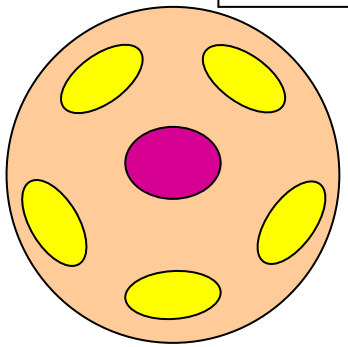


(4) SOMATIC CELL NUCLEAR TRANSFER: The nucleus of the **cell** with unhealthy mitochondria is removed and placed into the donor egg with healthy mitochondria.



(5) PERMITTED EGG according to 3ZA(5): Reconstructed egg with nucleus of woman with mitochondrial disease, and mitochondria from egg donor with healthy mitochondria

(6) ACTIVATION



(7) PERMITTED EMBRYO according to 3ZA(5) / 3(6) since nuclear/mitochondrial DNA can be altered, and an embryo does not need to be created by fertilisation, under 3ZA(5); and since the Reproductive Cloning Act would be repealed by Clause 3(6)

Embryo created by nuclear transfer from somatic cell into an enucleated egg. Nuclear DNA from woman with mitochondrial disease. Mitochondrial DNA from the egg donor. REPRODUCTIVE CLONING

SOMATIC CELL NUCLEAR TRANSFER INTO AN ENUCLEATED EGG: REPRODUCTIVE CLONING

It may be possible for a similar procedure to be carried out using somatic cell nuclear transfer into an enucleated one-celled embryo (using a donor embryo with healthy mitochondria).
None of these procedures including the procedure in this diagram could produce "permitted" eggs or embryos according to 3ZA(2)-(4), which ban embryos that are not produced by fertilisation and eggs and embryos that have alterations in nuclear or mitochondrial DNA. However, 3ZA(5) can over-ride all these restrictions, subject to affirmative resolution.