BIOETHICS ADVISORY COMMITTEE SINGAPORE

PRESS RELEASE
19 APRIL 2018

PUBLIC CONSULTATION ON ETHICAL, LEGAL AND SOCIAL ISSUES ARISING FROM MITOCHONDRIAL GENOME REPLACEMENT TECHNOLOGY

The Bioethics Advisory Committee (BAC) has issued a public consultation paper on the ethical, legal and social issues arising from Mitochondrial Genome Replacement Technology (MGRT), and invites public feedback on the potential issues related to the clinical application of this emerging technology in humans. The views of the public and interested organisations will assist the BAC in formulating its recommendation on whether the clinical application of MGRT should, or should not, be permitted in Singapore. The public consultation will take place for eight weeks from 20 April 2018 to 15 June 2018.

MGRT – Previous Recommendations and Recent Developments

2. MGRT aims to prevent the transmission of mitochondrial disorders[1] from a mother to her child, by replacing abnormal mitochondria with normal mitochondria from a healthy donor, at either the egg or early embryo (zygote) stage. As mitochondria contain genetic material[2] and are passed on by a mother to her child, MGRT may result in germline modification as an inheritable genetic change would be introduced if the resulting child is also female.

3. In 2005, the BAC had recommended in its report on *Genetic Testing and Genetic Research* that the clinical practice of germline genetic modification should not be allowed for the time being, pending further evidence on the feasibility and safety of its clinical application in humans.

4. There have been significant scientific and policy developments in the field of MGRT internationally in recent years. Notably, the United Kingdom became the first country to legalise the clinical application of MGRT in 2015 and allow clinical trials for two MGRT techniques. With these developments, the BAC considers it timely and important to study the current research involving MGRT, and to review its recommendations on germline genetic modification, particularly in the context of preventing the transmission of serious mitochondrial disorders.

5. The BAC's public consultation paper examines three MGRT techniques : (i) Maternal Spindle Transfer (MST), (ii) Pronuclear Transfer (PNT), and (iii) Polar Body Transfer (PBT). All three techniques involve replacing the abnormal mitochondria in the egg / early embryo with healthy mitochondria from the egg / early embryo of a healthy donor.[3]

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1 Mitochondria are tiny organelles that are responsible for energy production in the cell. Faulty mitochondria can have serious debilitating effects. Please see the Annex for more information on mitochondrial disorders.

2 Most of the cell's DNA is located in its nucleus. However, a small amount of DNA is found in the mitochondria. The former is known as nuclear DNA, and the latter mitochondrial DNA.

3 The three MGRT techniques are described in greater detail in the Annex.

Issues and Questions for Consideration

6. The BAC would like to invite the public to contribute their views and feedback on a range of ethical, social and legal issues that could arise from clinical application of MGRT, including :

- What are the possible benefits of MGRT?
- What are the psychological or social impact on children born using such techniques?
- Why is the option to have genetically-related children important?
- Is it unfair to prevent women affected by mitochondrial disorders from access to new technology that offer them the potential to have healthy genetically-related children?
- Should the welfare of future generations take precedence over the welfare of existing individuals (i.e. the prospective parents), or *vice versa*?
- Assuming all techniques are equally safe and effective, are there any ethical distinctions to be made between the various mitochondrial replacement techniques?

7. Senior (Chief) District Judge (ret.) Richard Magnus, BAC Chair, said, "MGRT may help enable women who suffer from mitochondrial disorders to have healthy genetically-related children of their own. However, there is a need to closely evaluate the safety of MGRT and the resulting ethical, legal and social implications, and consider if Singapore is ready to permit such technology."

8. Professor Kon Oi Lian, Chair of the MGRT Review Group and BAC Deputy Chair, added, "While introducing inheritable genetic changes carries unforeseeable risks, current pre-clinical scientific evidence suggests that MGRT is not unsafe. Due to the unique characteristics of mitochondria, there are possible safeguards that could be put in place to mitigate some of the long-term risks. However, the question remains whether the potential benefits justify allowing first-in-human clinical trials."

How to Participate

9. The public consultation paper can be found on the BAC's website at www.bioethics-singapore.org and REACH at www.reach.gov.sg.

10. To facilitate discussions, BAC will be organising the following dialogue sessions :

(i) Public dialogue session on 28 April 2018 (Saturday), 2:00pm to 4:00pm, at The Pod, National Library, Level 16 (100 Victoria Street, Singapore 188064).

(ii) Dialogue session with researchers, clinicians and members of institutional ethics review boards, on 10 May 2018 (Thursday), 12:00pm to 2:00pm, at HarbourFront Centre, #09-66 (1 Maritime Square, Singapore 099253).

Those interested to attend can contact the BAC Secretariat at bioethics_singapore@moh.gov.sg.

11. The BAC welcomes feedback on the issues discussed in the consultation paper, or any other aspects of MGRT. All comments should be sent by 15 June 2018 :

- by email to : bioethics_singapore@moh.gov.sg
- by post to : Bioethics Advisory Committee Secretariat
  1 Maritime Square
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ANNEX

About the Bioethics Advisory Committee (BAC)

The BAC is an independent advisory committee that was established by the Government in December 2000 to address the ethical, legal and social issues arising from human biomedical research and its applications. BAC studies emerging areas in human biomedical research, and develops and recommends policies to the government as appropriate, with the aim of protecting the rights and welfare of individuals, while allowing the biomedical sciences to develop and realise its full potential for the benefit of mankind.

What are Mitochondrial Disorders?

Mitochondria (singular : mitochondrion) are tiny organelles found within the cytoplasm of the cell, and are mainly responsible for energy production through a process known as aerobic respiration. Mitochondrial disorders can arise from DNA abnormalities in the mitochondrial genome. Owing to its central role in cellular energy production, mitochondrial disorders often cause debilitating effects on highly energy-dependent organs and tissues including the brain (encephalopathy), the heart (cardiomyopathy), and other muscles (myopathy). Symptoms and severity vary widely amongst patients, depending on the ratio of dysfunctional to normal mitochondria in the cell, and the energy demands of the affected organ(s). There is currently no cure for mitochondrial disorders, though many of the symptoms are treatable.

What are the three MGRT techniques that the BAC is examining?

(1) Maternal Spindle Transfer (MST)
In MST, the chromosomal spindle-complex containing the nuclear DNA is removed from the prospective mother's egg, and transplanted into a donor's healthy egg from which the donor's chromosomal spindle-complex had been removed. The reconstructed egg is then fertilised and implanted into the prospective mother's womb.

(2) Pronuclear Transfer (PNT)
In PNT, the prospective mother's egg is first fertilised with the father's sperm. After fertilisation, the pronuclei are isolated and inserted into a donor's fertilised egg from which the pronuclei had been removed. The resulting zygote is then implanted into the prospective mother's womb.

(3) Polar Body Transfer (PBT)
PBT involves the manipulation of polar bodies – small cells that are produced during the formation of egg cells, and which each contains the same number of chromosomes as the nucleus of the egg cell. In PBT, which can be performed before or after fertilisation, the nuclear DNA of the donor's healthy egg or zygote is replaced by a polar body transplanted from the prospective mother's egg or zygote. The reconstructed zygote or egg (subsequently fertilised) is then implanted into the prospective mother's womb.