HELLENIC NATIONAL BIOETHICS COMMISSION

R E C O M M E N D A T I O N

MITOCHONDRIAL REPLACEMENT

FOR THE PREVENTION OF MITOCHONDRIAL DISEASES

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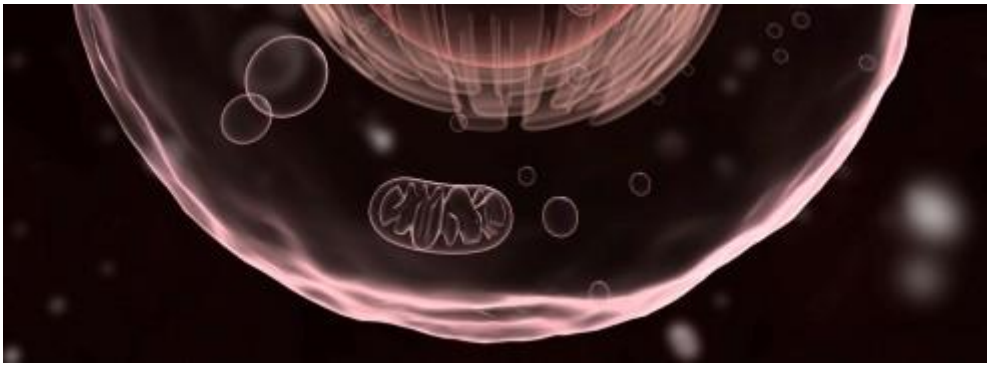

HELLENIC NATIONAL BIOETHICS COMMISSION

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I. Introduction

The Hellenic National Bioethics Commission examined the issue of Mitochondrial Replacement Therapy (MRT) and the potential future clinical applications of such technologies, after a relevant enquiry submitted by the Ministry of Health concerning "Mitochondrial and Maternal Spindle Transfer Techniques", whether or under which conditions should such techniques be approved. MRT aims to prevent the transmission of mitochondrial diseases to children and involves the use of gametes from three donors within the context of *in vitro* fertilization. This is the reason why babies born with this method are often called "three-parent babies."

The utility of MRT for the prevention of mitochondrial diseases and the available laboratory techniques *(maternal spindle transfer or maternal chromosomes transfer - MST and pronuclear transfer - PNT)* have been presented in a previous Recommendation published by the Commission on July 7th, 2014 (Contemporary Issues Of "Choice" In Reproduction). In the 2014 Recommendation, the Commission highlighted the need for more clinical studies in order to establish the efficacy and safety of MRT techniques.

II. The Facts

MRT for the prevention of mitochondrial diseases remains timely and continues to challenge the scientific community, especially after it was approved by the Human Fertilisation and Embryology Authority (HFEA) in the United Kingdom in 2015.[1] Despite the approval of the method in principle, the HFEA was expecting the conclusion of a number of experimental tests that would determine the safety and the efficacy of MRT.[2] Among others, results were being expected from MRT experiments on ovaries carrying mutations in their mitochondrial DNA (mtDNA), or ova (eggs) from women with mitochondrial diseases, in order to study the effect of

[1] The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015. (http://www.legislation.gov.uk/uksi/2015/572/contents/made).

[2] The Human Fertilisation and Embryology Authority. Mitochondrial donation regulations. http://www.hfea.gov.uk/9942.html.

these mutations, as well as from experiments investigating the possibility of heteroplasmy in tissues of human embryos.[3]

Recently, on March 16th 2017, the HFEA announced the approval of the first application of MRT by a fertility clinic in Newcastle.[4] Following an inspection conducted by the HFEA, it was found that the clinic was adequately equipped in terms of both infrastructure and personnel expertise, and thus a license for performing the PNT technique was granted.[5] The HFEA will now judge each patient application individually and if approved, patients can undergo MRT in the Newcastle clinic.

III. The ethical issues

MRT raises two kinds of ethical issues, as it is the case with every new technological application in the field of medically assisted reproduction.[6]

1. The issue of safety for this method, both for the expected child as well as for the woman that will carry the embryo with the altered mtDNA, must be considered as a priority. Prior to any clinical applications, there must be satisfactory results from pro-clinical experiments that will guarantee the safety of the method. The Commission deems that pro-clinical *in vitro* research in laboratory animal models or conducting studies on human embryos, should be encouraged at an international level since the method offers exciting future prospects; however, it is necessary to intensify controls for inadmissible clinical applications.[6]
2. If there are sufficient guarantees for the safety of the method in the future, the Commission deems that -at least in comparison with genome editing in

[3] HFEA. Third scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception: 2014 update. London, UK: HFEA.
[4] HFEA statement on mitochondrial donation. 16 March 2017 http://www.hfea.gov.uk/10635.html.
[5] Licence Committee - minutes. Centre 0017 (Newcastle Fertility at Life) Variation of Licensed Activities to include Mitochondria Pronuclear Transfer (PNT). http://ifqtesting.blob.core.windows.net/umbraco-website/1331/2017-03-09-licence-committee-minutes-variation-of-licensed-activities-to-include-mitochondria-pronuclear-transfer-pnt-centre-0017.pdf.
[6] See National Academy of Sciences (U.S.) - Committee on The Ethical and Social Policy Considerations of Novel Techniques for Prevention of Maternal Transmission of Mitochondrial DNA Diseases, της Εθνικής Ακαδημίας Επιστημών, Έκθεση με θέμα "Mitochondrial Replacement Techniques: Ethical, Social, and Policy Considerations", The National Academies Press, Washington, DC, 2016. https://www.nap.edu/download/21871

embryos[7]- there are no concerns that the clinical applications of mtDNA replacement does not raise issues of aberration towards positive eugenics. After all, any issues raised by the involvement of a third person (woman donor) in the reproduction process can be addressed in a similar way as in heterologous artificial insemination (e.g. securing donor anonymity), and thus avoid possible future issues in terms of family relationships.

IV. Recommendations

Judging by the lack of sufficient evidence at an international level, and in order to substantiate the efficacy and the safety of MRT, the Commission is —for the time being— against all clinical applications of this method. Any future clinical studies should limit to cases of women facing the risk of transmitting severe mitochondrial diseases, while the pathogenicity of the mutation they carry is indisputable and a serious manifestation of the disease is expected. Given the complexity of the aforementioned techniques, such clinical trials should only be conducted at specifically certified clinics.[6] This applies especially to Greece due to the emergent procedure, ran by the competent Greek National Authority of Assisted Reproduction, to control and certify the quality of provided services in the field of medically assisted reproduction. For the Commission it is necessary to tackle current issues in this particular field, in order to test new methods, such as MRT. In any case, the law governing the Greek National Authority of Assisted Reproduction needs to be amended so that the Authority may have the jurisdiction to license fertility centers, provided that there are more scientific data regarding the efficacy and the safety of MRT.

Nevertheless, the Commission is willing to further examine the issue when there are sufficient new data about the safety and the efficacy of MRT techniques.

Athens, April 4th 2017

[7] Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations; National Academy of Sciences; National Academy of Medicine; National Academies of Sciences, Engineering, and Medicine, The National Academies Press, Washington, DC, 2016. http://www.nap.edu/24623