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The moral position of mitochondrial gene transfer

Diseases caused by mitochondrial DNA, also known as mtDNA, are inherited and affect approximately 1 in 5,000 to 10,000 children. The mutations' results are linked to severe clinical symptoms. The mitochondrial genome is passed down maternally, which is where the mutation that causes these diseases arises. It can also impact vital organs that depend on cellular energy production. In order to prevent the transmission of these mutations, there are multiple reproductive techniques that have been proposed, including the replacement of mutated mtDNA in oocytes and/or embryos. There are concerns surrounding the efficacy, safety, and ethicality of the scientific proposals to prevent mitochondrial disease, which shall be discussed further.

The advancements in assisted reproductive technology have led to the development of methods to replace mtDNA in oocytes or zygotes with healthy donor mitochondria. This offers women with mtDNA mutations a chance to prevent passing the condition(s) to their children. There are two microsurgical techniques proposed; spindle transfer and pronuclear transfer have both been created. Spindle transfer is the means of transferring the spindle from a mature oocyte which contains nuclear DNA into an enucleated donor oocyte. This results in a fertilizable oocyte that is free from mutated mtDNA. There are records of successful experiments in non-human primates that display the promise of viable infants produced with only donor-derived mtDNA. The animal development was observed to be standard with the other primates within the species that do not have the mtDNA replacement or the mtDNA mutations. Pronuclear transfer is conducted at the zygote stage, when pronuclei are visible. Originally produced with mice subjects, it included proof-of-concept and results that yielded to the effectiveness of preventing mtDNA mutations transmitting to the embryo. There has also been testing with human zygotes that allowed tests of feasibility.

The possibility of the procedure's failure was recorded to be undetectable, or below 2%, in comparison to the mutated DNA resulting in a 60% or higher threshold when considering the manifestation of mitochondrial diseases. This clarifies the efficacy of the treatment. However, the ethicality and safety are still to be considered, even with high-yielding results. Examination of the morality surrounding mtDNA transfer has taken place extensively, including in the United Kingdom; a council on bioethics declared a report that the benefits received from the children and families can be acceptable if the techniques are successfully proven to be safe and effective. The efficacy has already been proven through the statistics, and the safety has been explained through the results of the spindle transfer and the primates. Therefore, the ethicality of the procedure can be approved as safe and moral, due to the highly successful benefits and the minimal drawbacks from the treatment.

Besides the straightforward concern of morality, a few other questions have been raised about the donor-parent-child relationship due to the nature of DNA transplantation coming from another female and being delivered into an embryo. This can be cleared effectively because the DNA donated is so small, it only constitutes 0.1% of the embryo's overall DNA. The mitochondrial DNA translates into a very small amount of amino acid substitutions, it does not

replace large amounts of the DNA sequence in the individual. Furthermore, the donors can be matched to the haplotype of the mitochondrial DNA to prevent any possible differences.

Overall, the main concerns surrounding the mtDNA transplantation in effort to prevent mitochondrial diseases can be nullified by the statistics and testing provided. The procedure requires more clinical trials and studies to solidify its practice in the medical and genetic fields, but it already has a strong foundation.

References

Mitalipov, S et al. Clinical and ethical implications of mitochondrial gene transfer. Trends Endocrinol Metab.; https://pubmed.ncbi.nlm.nih.gov/24373414/(2014).