**Introduction**

Mitochondria are found within nearly all cells of the body and are responsible for generating energy from the food we eat (Figure 1). They contain their own genes (mitochondrial DNA) which are essential for the mitochondria to make energy. If the mitochondria are not working properly, this can lead to mitochondrial DNA disease. A common feature of these diseases is weakness and wasting of the muscles, which is known as mitochondrial myopathy.

Mitochondrial myopathies are often caused by mutations within the mitochondrial genes. These genes are only inherited from the mother and so if a woman has a mutation, there is a significant risk that the mutation will be passed to her children. One approach to prevent this transmission is pronuclear transfer between human embryos which involves replacing the bad mitochondria from the affected mother’s embryo with good mitochondria from a healthy donor embryo (Figure 2).

**Methods and Results**

The aim of this project is to determine if pronuclear transfer between human embryos has the potential to prevent transmission of mitochondrial DNA disease. To do this, we have used abnormally fertilised human embryos donated to research by consenting patients undergoing fertility treatment at Newcastle Fertility Centre at Life. We have optimised a technique to remove the pronuclei from these embryos and then transfer them to a different embryo that has also had its pronuclei removed (Figure 3).

We have also shown that very few mitochondria are transferred with the pronuclei during the procedure, suggesting that no bad mitochondria would be detected in the manipulated embryos following pronuclear transfer.

These experiments reveal that the technique of pronuclear transfer is feasible in human embryos and has the potential to prevent transmission of mitochondrial DNA disease.

**Conclusions**

The technique of pronuclear transfer between abnormally fertilised human embryos has been optimised. We can remove intact pronuclei from these embryos and transfer them to different embryos that have also had the pronuclei removed.

Following pronuclear transfer, the manipulated embryos show good survival and onward development.

We have also shown that very few mitochondria are transferred with the pronuclei during the procedure, suggesting that no bad mitochondria would be detected in the manipulated embryos following pronuclear transfer.

**Future Work**

- The main goal of this research is to provide a treatment option that would give mother’s with mitochondrial DNA disease the possibility of having a healthy child.
- Further studies are imperative to ensure the safety and efficiency of this technique. We have a unique opportunity to carry out this work on normal embryos donated to research through an egg share scheme.
- There would need to be a change in the law in the UK if this technique were to be offered as a treatment to patients. This was recently discussed by an expert scientific panel at the request of the Secretary of State for Health and several recommendations were made.

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