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Major breakthrough offers hope of preventing mitochondrial diseases

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(PhysOrg.com) -- Scientists at Newcastle University have developed a pioneering technique which enables them for the first time to successfully transfer DNA between two human eggs. The technique has the potential to help prevent the transmission of serious inherited disorders known as mitochondrial diseases.

The study, led by Dr Mary Herbert and Professor Doug Turnbull, and funded primarily by the Muscular Dystrophy Campaign, the Medical Research Council and the Wellcome Trust, is published today in the journal *Nature*.

Every cell in our body needs energy to function. This energy is provided by mitochondria, often referred to as the cells' 'batteries'. Mitochondria are found in every cell, along with the cell nucleus, which contains the genes that determine our individual characteristics. The information required to create these 'batteries' - the mitochondrial DNA - is passed down the maternal line, from mother to child.

A mother's egg contains a copy of her own DNA - twenty-three chromosomes - as well as DNA for her mitochondria. The amount of genetic material contained in mitochondrial DNA is very small - 13 protein-producing genes, compared to an estimated 23,000 genes that we inherit from our parents - and this information is used solely to generate the energy produced by the 'batteries'.

Like all DNA, the DNA in mitochondria can mutate and mothers can

pass these mutations onto their children. Around one in 200 children are born each year with mutations which in most cases cause only mild or asymptomatic forms of mitochondrial disease. However, around one in 6,500 children are born with severe mitochondrial diseases, which include muscular weakness, blindness, fatal heart failure, liver failure, learning disability and diabetes and can lead to death in early infancy.

There are no treatments available to cure these conditions and mothers face the agonising choice of whether to risk having a child who may be affected by such a disease or not to have children at all.

Now, researchers at Newcastle University have developed a technique which allows them to replace these 'batteries'. This is the first time such a technique has been used in fertilised human eggs.

A fertilised egg usually contains two pronuclei - genetic material from the egg and sperm - as well as mitochondria. The technique developed by the Newcastle team involves extracting the pronuclei but leaving behind the mitochondria. The researchers then take a fertilised egg from a donor, remove its pronuclei and replace them with the extracted pronuclei. This new fertilised egg contains the DNA of the father and mother, and the mitochondria from the donor.

"What we've done is like changing the battery on a laptop. The energy supply now works properly, but none of the information on the hard drive has been changed," explains Professor Turnbull. "A child born using this method would have correctly functioning mitochondria, but in every other respect would get all their genetic information from their father and mother."

The Newcastle team used their technique to create a total of eighty zygotes (fertilised eggs). These were cultured for six to eight days in the laboratory to monitor development as far as the blastocyst stage (the

stage at which it has divided into a group of around one hundred cells) in line with the terms of the licence granted by the Human Fertility and Embryology Authority (HFEA) in 2005.

In some cases, a very small amount of the mother's mitochondrial DNA was carried over to the new egg. Since severe diseases only occurs with large amounts of mutations, this would be very unlikely to affect a child's health.

The research is a proof of principle that researchers should be able to prevent transmission of mitochondrial diseases, thereby allowing the mother to give birth to a healthy child.

"This is a very exciting development with immense potential to help families at risk from mitochondrial diseases," says Professor Turnbull. "We have no way of curing these diseases at the moment, but this technique could allow us to prevent the diseases occurring in the first place. It is important that we do all we can to help these families and give them the chance to have healthy children, something most of us take for granted."

The Newcastle team used eggs which were unsuitable for IVF; for example, eggs with one or three pronuclei, rather than the normal two. This is common in the IVF process and affects around one in ten fertilised eggs. The eggs were donated by couples attending the Newcastle Fertility Centre at Life. The egg donation programme and the ethical and regulatory aspects of the project are led by Professor Alison Murdoch.

The team is now planning further studies that will provide further evidence of the safety of this procedure. The Human Fertility and Embryology (HFE) Act as amended in 2009, currently prevents fertility treatment using these techniques. However, the HFE Act includes the

provision for the Secretary of State to make provisions for this to be permitted in the future.

Provided by Newcastle University