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News

DNA swap could avoid inherited diseases

Experiments in monkeys show how mothers can avoid passing on mitochondrial DNA mutations to their offspring.

David Cyranoski

A technique to transfer genetic material from one egg cell to another could be used to prevent the inheritance of diseases caused by faults in the DNA of mitochondria, the 'power plants' of the cell.

In experiments using rhesus macaques, US researchers transferred DNA from the nucleus of one egg into another egg which had had its nucleus removed, without carrying over any mitochondrial DNA in the process — a crucial improvement on existing DNA-transfer techniques. The eggs were then fertilized with sperm and implanted into females, which produced offspring that had mitochondrial DNA from one female and nuclear DNA from another¹.

Leaving behind all the mitochondrial DNA that could carry disease-causing mutations, and the fact that it was done in primates, make the work "highly innovative and very promising", says David Thorburn, a geneticist specializing in mitochondrial disease at the Murdoch Childrens Research Institute in Melbourne, Australia. "It should be able to mimic the human situation more closely than mice. If proven safe [in humans] this could provide a huge advance."

Mitochondrial DNA is passed only from mothers to their offspring, as the mitochondria in sperm do not contribute any DNA to the embryo. Mutations in mitochondrial DNA are linked to a variety of diseases, including type 2 diabetes, mitochondrial myopathies, and Leigh syndrome, a neurodegenerative disease that usually strikes infants, robbing them of motor control (see **Mitochondrial disease: Powerhouse of disease**). At least 1 in every 200 births is thought to have a potentially pathogenic mitochondrial DNA mutation².

Embryos can be screened before they are implanted into a female when assisted reproductive techniques such as *in vitro* fertilization (IVF) are used, although published reports are scarce³. It is also unclear how highly concentrated the mitochondrial mutations must be to trigger disease.

Surprising transfer

The problem of diagnosis could be avoided by replacing the mitochondrial DNA completely. Writing in this week's *Nature*, Shoukhrat Mitalipov from and his team at the Oregon National Primate Research Center in Beaverton, transferred the chromosomes of the nuclear DNA from one unfertilized rhesus monkey egg to another unfertilized egg that had had its nuclear DNA removed.

Fifteen embryos were transplanted into 9 surrogate mothers; three became pregnant, one with twins, and four offspring were born (only three of these offspring have been reported in the *Nature* paper). That's similar to the success rate of conventional *in vitro* fertilization treatment in humans, says Mitalipov.

So far there have been no abnormalities in the offspring, two of which were named Mito and Tracker after the MitoTracker dye that is routinely used to detect and image mitochondria in cells.

Three sets of DNA tests showed that the donor mother's mitochondrial DNA was almost entirely absent. Mitalipov was surprised: "We knew the approach would be pretty efficient but did not expect that mitochondrial DNA replacement would be complete."

The research relied on a technique developed by Mitalipov when he and his team created cloned rhesus macaque embryos and used them to make embryonic stem cells in 2007⁴. They used an imaging system to isolate the chromosomes without damaging them, and the same system was crucial for transferring chromosomes from a nucleus without carrying mitochondrial DNA along for the ride, says Mitalipov.



Monkey magic: this rhesus macaque was created using the nuclear DNA of one mother, and the mitochondrial DNA of another.

Oregon National Primate Research



Mito and Tracker.

Mitalipov says that human chromosome complexes might be more sensitive, but he sees no reason that the procedure could not be made to work, perhaps even within two years, in humans.

Thorburn says there are a couple other safety concerns, such as the possibility that mitochondrial DNA and nuclear DNA from different sources might not always be compatible. Strict regulations on work with embryos, procurement of unfertilized eggs, and nuclear transfer are also likely to slow down both research and application in humans (see [The ethics of egg manipulation](#)). Mitalipov adds that he is also expecting resistance on ethical grounds because the method introduces permanent changes to the germ line

The mitochondrial-disease community, however, is ready to see the research progress. "There are costs and risks, but the benefits outweigh the drawbacks," says Carlos Moraes, a cell biologist at the University of Miami in Florida, and member of the United Mitochondrial Disease Foundation's Scientific and Medical Advisory Board in Pittsburgh, Pennsylvania.

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