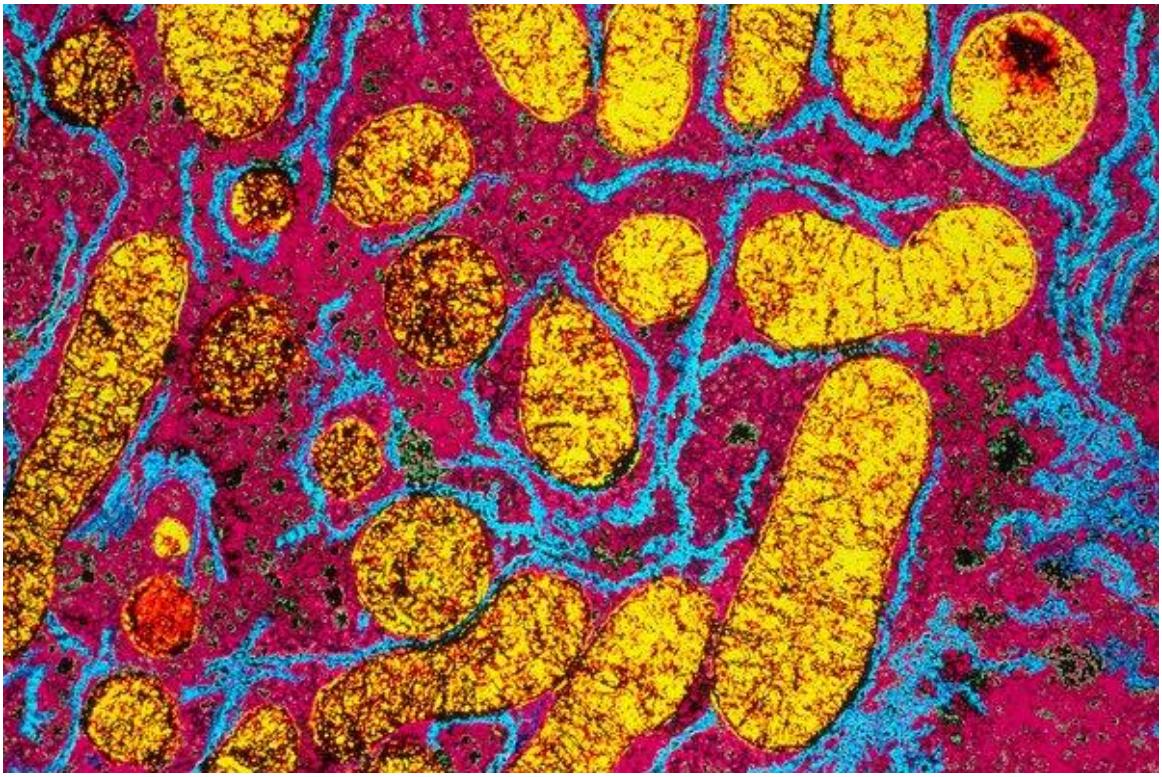
Why Do We Inherit Mitochondrial DNA Only From Our Mothers?



Mitochondria in hepatocyte cells of the liver, shown in yellow.
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By STEPH YIN **June 23, 2016** **New York Times**

For a long time, biologists thought our DNA resided only in the control center of our cells, the nucleus.

Then, in 1963, a couple at Stockholm University discovered DNA outside the nucleus. Looking through an electron microscope, Margit and Sylvan Nass noticed DNA fibers in structures called mitochondria, the energy centers of our cells.

Our mitochondrial DNA accounts for a small portion of our total DNA. It contains just 37 of the 20,000 to 25,000 protein-coding genes in our body. But it is notably distinct from DNA in the nucleus. Unlike nuclear DNA, which comes from both parents, mitochondrial DNA comes only from the mother.

Nobody fully understands why or how fathers' mitochondrial DNA gets wiped from cells. An international team of scientists recently studied mitochondria in the sperm of a roundworm called C. elegans to find answers.

Their results, published this week in the journal Science, show that paternal mitochondria in this type of roundworm have an internal self-destruct mechanism that gets activated when a sperm fuses with an egg. Delaying this mechanism, the scientists found, led to lower rates of embryo survival. Down the road, this information could help scientists better understand certain diseases and possibly improve in vitro fertilization techniques.

This work "comes closest to elucidating a key development process that has perplexed us for a long time," said Justin St. John, a professor at the Hudson Institute of Medical Research in Australia, who was not involved in the research.

It's well known that the transfer of mitochondrial DNA from mother to offspring, often called maternal inheritance, occurs in humans and most multicellular organisms. Maternal inheritance is what allows genetic testing services like 23andMe to trace our maternal ancestries. You inherited your mitochondrial DNA from your mother, who inherited hers from her mother and so forth.

Maternal inheritance also gave rise to the idea that there exists a "Mitochondrial Eve," a woman from whom all living humans inherited their mitochondrial DNA.

Before this research, it had been thought that maternal inheritance was orchestrated by processes in the mother's egg cells, said Ding Xue, a professor at the University of Colorado Boulder and one of the authors of the paper. Large structures called autophagosomes, for instance, are known to engulf paternal mitochondria shortly after a sperm penetrates an egg.

Dr. Xue and his colleagues found, however, that the paternal mitochondria in the roundworms actually started to break down before any autophagosomes reached them. "It's like a suicide mechanism," said Byung-Ho Kang, a professor at the Chinese University of Hong Kong and another author of the paper.

The researchers identified a gene, called cps-6, that seemed to initiate the breakdown process within paternal mitochondria. They found that deleting cps-6 caused paternal mitochondria to linger longer in the embryo. It also led to higher rates of embryonic death.

"This paper provides the first experimental data suggesting that it's not good to keep sperm mitochondrial DNA," said Vincent Galy, a researcher at Pierre and Marie Curie University in Paris, who was not involved in the study.

It's unclear whether having some paternal mitochondrial DNA in our cells leads to health problems. To date, there's been one reported possible case, detailed in 2002 by researchers in Denmark. In a man with mitochondrial myopathy, a neuromuscular disease, the scientists discovered a mutation on mitochondrial DNA that came from his father. It's possible, however, that the mutation occurred spontaneously after conception, rather than being inherited directly from his father.

Further research could shed light on diseases caused by mitochondrial DNA, which can lead to blindness, nerve damage and dementia, Dr. Xue said. Because it's a somewhat lengthy screening

process, doctors don't generally check patients for the inheritance of paternal mitochondria. But "as we do more studies, we might actually find that it's closely related to some human diseases," Dr. Xue said.

More studies could also expand understanding of an in vitro fertilization technique that involves injecting a single sperm directly into an egg. Some researchers have studied whether this technique leads to the presence of sperm mitochondrial DNA in the embryo, but "there are contradictory results," Dr. Galy said.

The big mystery that remains is why maternal inheritance occurs so consistently across organisms, Dr. Xue said. One theory has to do with the fact that sperm must generate a lot of energy when competing to fertilize an egg. During this time, sperm mitochondria are overworked, which could possibly damage their DNA and lead to mutations.

But this theory, and all others, are still speculative, Dr. Xue said. "This is a longstanding biological question," he said. "There must be a fundamental, important reason why most species actually adopt the same style of mitochondrial inheritance."