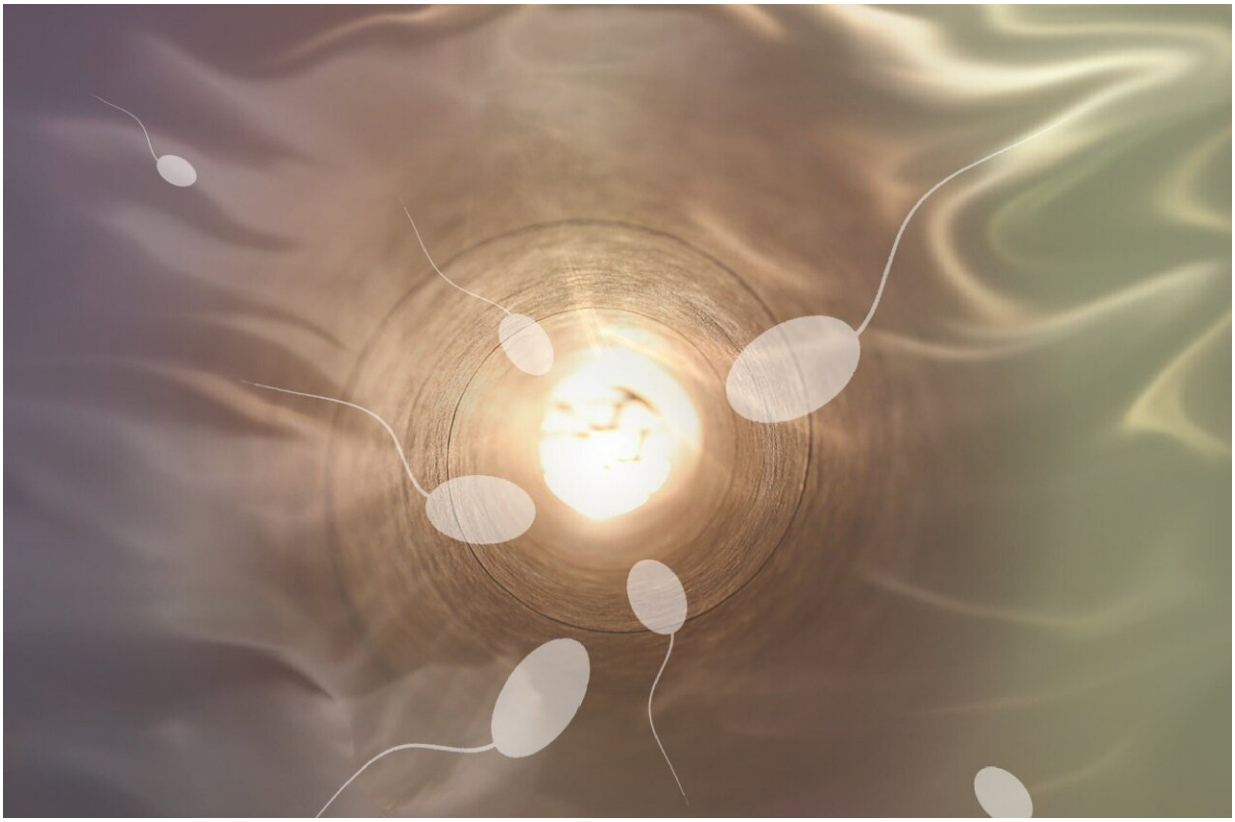
Mature sperm lack intact mitochondrial DNA, study finds

September 18 2023



Credit: Pixabay/CC0 Public Domain

New research provides insight about the bedrock scientific principle that mitochondrial DNA—the distinct genetic code embedded in the organelle that serves as the powerplant of every cell in the body—is

exclusively passed down by the mother.

The study, a collaboration among Oregon Health & Science University and other institutions, has been published in the journal *Nature Genetics*.

Scientists have long recognized the fact that mitochondrial DNA, or mtDNA, comes exclusively from egg cells in humans, meaning only the mother contributes the genetic code carried by thousands of mitochondria necessary for energy production in every cell in the body.

Previously, it was believed that paternal mtDNA was eliminated soon after a sperm fuses with an oocyte, or developing egg, during fertilization, possibly through an immune-like search-and-destroy response.

However, the study found that while mature sperm do carry a small number of mitochondria, they lack intact mtDNA.

"We found that each sperm cell does bring 100 or so mitochondria as organelles when it fertilizes an egg, but there is no mtDNA in them," said co-author Shoukhrat Mitalipov, Ph.D., director of the Center for Embryonic Cell and Gene Therapy at OHSU.

Researchers found that sperm cells are not only devoid of intact mtDNA, but they also lacked a protein essential for mtDNA maintenance, known as mitochondrial transcription factor A, or TFAM.

Scientists aren't sure why sperm are not allowed to contribute mtDNA, but Mitalipov theorizes that it may relate to the fact that a sperm uses a lot of mitochondrial energy in its biological impetus to fertilize an egg. It would thus accumulate mutations in mtDNA. The developing eggs known as oocytes, by contrast, draw energy primarily from surrounding cells, not from their own mitochondria, so maintain relatively pristine

mtDNA.

"Eggs pass on really good mtDNA at least partly because they don't use mitochondria as a source of energy," Mitalipov said.

The 100 or so organelles in sperm are swamped by hundreds of thousands of mitochondria embedded in each egg cell—each carrying the 37 genes in mitochondrial DNA. The contribution of only maternal mtDNA is believed to confer an evolutionary advantage by limiting the risk of accumulations of mtDNA mutations that cause disease in offspring.

Mitochondria control respiration and energy production within every cell of the body, so mutations in mtDNA can cause a range of potentially fatal disorders affecting organs with high-energy demands, such as the heart, muscle and brain.

To help mothers prevent passing on known mtDNA disorders to their children, Mitalipov pioneered a method called mitochondrial replacement therapy to replace mutant mtDNA through in vitro fertilization using healthy mtDNA from donor eggs.

Congress has prevented the Food and Drug Administration from overseeing clinical trials using the procedure in the U.S., so clinical trials are instead being conducted overseas, including clinical trials in the United Kingdom to prevent disease and in Greece to treat infertility.

Researchers write that the new discovery has important implications for human fertility and germ cell therapy.

"Understanding the role of TFAM during sperm maturation and its function during fertilization may hold keys to our ability to treat certain infertility disorders, and increase the efficiency of assisted reproductive

technologies," said corresponding author Dmitry Temiakov, Ph.D., a molecular biologist with Thomas Jefferson University in Philadelphia.

More information: 'Molecular basis for maternal inheritance of human mitochondrial DNA, *Nature Genetics* (2023). DOI: 10.1038/s41588-023-01505-9. www.nature.com/articles/s41588-023-01505-9

Provided by Oregon Health & Science University