Extracting cellular 'engines' may aid in understanding mitochondrial diseases

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Medical researchers who crave a means of exploring the genetic culprits behind a host of neuromuscular disorders may have just had their wish granted by a team working at the National Institute of Standards and Technology, where scientists have performed surgery on single cells to extract and examine their mitochondria.

The scientists reached into these cells and extracted their "engines"—the mitochondria that are in large part responsible for our metabolism. Many human cells contain hundreds of mitochondria, which were thought to be free-swimming organisms millions of years ago and which still possess their own DNA. Mutations in this mitochondrial DNA (mtDNA) are directly related to a large class of mitochondrial-based diseases, which have a range of symptoms that include early onset blindness, seizures, hearing loss, dementia, etc. In the general population, one out of every 200 people possesses a mtDNA mutation that may develop into a mitochondrial disease.

Investigating more deeply has been problematic, though, because the way mitochondria mix and spread their DNA within and among cells is poorly understood. "The trouble is that it's very difficult to extract single mitochondria from an individual cell," says NIST physicist Joseph Reiner. "For years, the best technique has been to break open a group of cells and collect the mitochondria from all of them in a kind of soup. As you might guess, it's hard to determine which mitochondria came from what cells—yet that's what we need to know."

The research team, which also includes scientists from Gettysburg College, has potentially solved this problem by realizing that several devices and techniques can be used together to extract a single mitochondrion from a cell that possesses a genetic mutation. They employed a method** previously used to extract single chromosomes from isolated rice cells where a laser pulse makes an incision in a cell's outer membrane. Another laser is used as a "tweezer" to isolate a mitochondrion, which then can be extracted by a tiny pipette whose tip is less than a micrometer wide.

This approach allowed the team to place a single mitochondrion into a small test tube, where they could explore the mitochondrion's genetic makeup by conventional means. The team found the mutation present throughout the entire cell was also found within individual mitochondria, a find suggesting that broad genetic research on mitochondrial disease may be possible at last.

"Getting an object as tiny as this from tweezer to test tube is not easy," says Koren Deckman, a biochemist from Gettysburg College. "But by building on more than a decade of work that has gone on at NIST and elsewhere, we now have a way to see the mitochondria we extract all the way through the transfer process, meaning we can be sure the sample came from a very specific cell. This could give medical scientists the inroad they need for understanding these diseases."

More information: * J.E. Reiner, R.B. Kishore, B.C. Levin, T. Albanetti, N. Boire, A. Knipe, K. Helmerson and K.H. Deckman. Detection of heteroplasmic mitochondrial DNA in single mitochondria. *PLoS ONE* 5(12): e14359. doi:10.1371/journal.pone.0014359

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