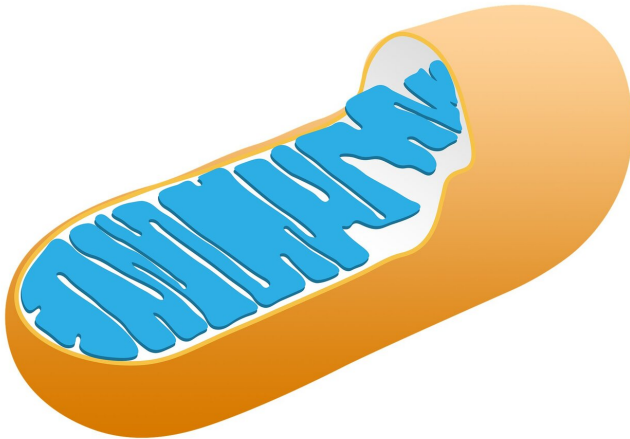


New way to tackle mitochondrial disease

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Diseases affecting mitochondria, the powerhouses of cells, are often caused by mutations in the mitochondrial DNA. Symptoms of such mitochondrial diseases in mice can be ameliorated by increasing their levels of mitochondrial DNA, according to a study by researchers at Karolinska Institutet. The study is published in *Science Advances* and could lead to a novel treatment strategy for such mitochondrial diseases.

Mitochondria are highly dynamic structures inside cells that provide cellular energy. Mitochondria contain their own DNA, called mitochondrial DNA (mtDNA), and there are thousands of copies of mtDNA in a cell.

Dysfunctional [mitochondria](#) can lead to serious diseases, which mostly affect tissues with high energy demands such as the brain, skeletal muscle and heart. To date, these diseases are still lacking effective treatments and clinical

management remains mostly symptomatic.

Mitochondrial disorders are often caused by mutations – genetic changes – in the mitochondrial DNA. But in most disease cases, there are still some copies of normal mitochondrial DNA. Therefore, mutated and normal mitochondrial DNA co-exist in the same cell. The mutated mtDNA will only cause symptoms when the number of copies exceed a critical threshold.

Toward new treatment strategies

Researchers at Karolinska Institutet now show that it is possible to improve mitochondrial disease in mice by increasing the total number of mtDNA copies. The results are published in a study in the journal *Science Advances*.

"Our study demonstrates that the increase of the absolute levels of mtDNA in mice can improve mitochondrial function and improve symptoms of mitochondrial disease, even though the absolute amount of mutated mtDNA increases," says Roberta Filograna, researcher at the Department of Medical Biochemistry and Biophysics at Karolinska Institutet and first author of the study. "This suggests that approaches to increase mtDNA copy number could provide a novel therapeutic strategy for treatment of mitochondrial diseases."

The study used a [mouse model](#) with a pathogenic mtDNA mutation. The levels of mitochondrial DNA were manipulated by either increasing or decreasing the expression of a protein (TFAM), known to control the [mitochondrial](#) copy number. The researchers then looked at both the general condition of the mice and at molecular changes in different organs and at different [disease](#) stages, to see how they depended on the mtDNA levels.

More information: R. Filograna et al. Modulation of mtDNA copy number ameliorates the pathological consequences of a heteroplasmic mtDNA mutation in the mouse, *Science Advances* (2019). [DOI: 10.1126/sciadv.aav9824](https://doi.org/10.1126/sciadv.aav9824)

Provided by Karolinska Institutet

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