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A multifunctional device regulates mitochondrial genomes

A small enzyme takes on opposing tasks to keep cells in balance. Even under stress conditions.

If you are healthy and your body has everything it needs, your cells are also in balance. But what happens in stressful situations such as lack of food? How are the states of emergency regulated?

Scientists at the Max Planck Institute for Biology of Aging have now found answers to these exciting questions and the results surprised even other scientists.

In every cell of your body you can find small organelles called mitochondria, which are known as the powerhouse of the cell. Here, most of the energy for cell biological processes is converted. In contrast to all other cell organelles, mitochondria contain their own genome, the DNA, which is present in numerous copies. However, in periods of stress such as food shortages, the number of DNA copies is reduced and the DNA building blocks are recycled in the cell.

Although degradation of mitochondrial DNA has long been known, it remained unclear what the underlying mechanism is and which enzyme is responsible for the degradation. "The mitochondrial DNA polymerase itself, which is responsible for DNA synthesis and quality control, also breaks it down," explains Max Planck Research Group Leader Martin Graef, adding: "This was really unexpected, and even experts in the field advised against testing this possible mechanism because it seemed so unlikely to them".

The recently published study by the group clearly demonstrates the two opposing

functions of this enzyme, which plays a key role in maintaining mitochondrial DNA balance. If this balance is out of control it can lead to devastating diseases.

The novel insights form the basis for establishing future therapeutic approaches. Numerous diseases affecting both infants and the elderly are due to mitochondrial dysfunction. In addition, the gained understanding of the polymerase's multifunctionality offers the opportunity for a better understanding and, ultimately, manipulation of cancer cells.

The research was performed in collaboration with CECAD.



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Original publication:

Tânia Catarina Medeiros, Ryan Lee Thomas, Ruben Ghillebert, Martin Graef (2018) Autophagy balances mtDNA synthesis and degradation by DNA polymerase POLG during starvation. Journal of Cell Biology DOI: 10.1083/jcb.201801168 | Published March 8, 2018

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