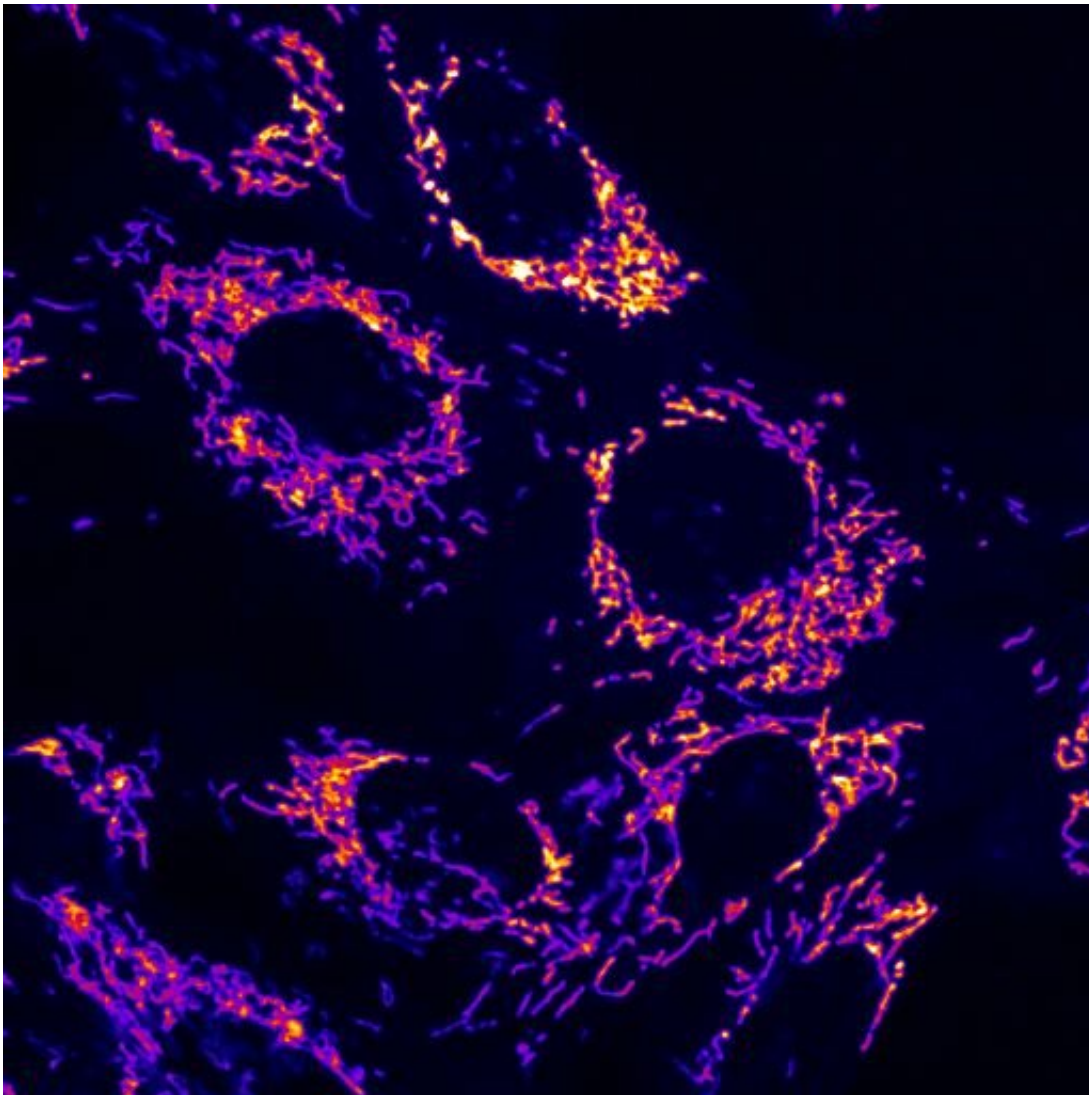


Parkinson's disease: When molecular guardians need to be protected

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Fluorescence microscopy image of tinted mitochondria. Credit: Nicola Roverato, University of Konstanz

Parkinson's disease is the second most common, age-related, neurodegenerative disease: In Germany alone, about 300,000 people are affected and experience sometimes major limitations to their quality of life. Although Parkinson's is so widespread, there is still no treatment that targets the cause of the disease and can stop it in its tracks.

However, current research provides new hope: A research team at the University of Konstanz led by Professor Marcus Groettrup describes a new approach for developing future treatments for Parkinson's. The biologists demonstrated that the ubiquitin-like protein FAT10 inhibits the molecular defense mechanisms protecting the brain from Parkinson's disease. The biological mechanism is tricky: FAT10 causes processes in our own body that degrade the body's molecular "guardians" against Parkinson's disease (the enzyme Parkin). Instead of getting rid of damaged mitochondria in brain cells, Parkin is itself disposed of by the body. The research results were published in the scientific journal *Cell Reports* on 16 March 2021.

Damaged power plants of the cells

Parkinson's [disease](#) develops as a result of nerve cells dying off in the mesencephalon (midbrain). This is caused by faulty disposal of damaged mitochondria, the cells' "power plants." When damaged mitochondria are not disposed of by the body, oxygen radicals develop in the brain. These, in turn, damage the nerve cells, causing them to die.

So that the body can dispose of mitochondria, they have to be marked by a signaling substance. This can be compared with labeling them as "broken—please throw away." The enzyme Parkin is responsible for labeling damaged mitochondria. The molecular label it gives them contains the protein ubiquitin.

Wrongly labeled

This is where the protein FAT10 comes into play. FAT10 has a very similar structure and function to ubiquitin. It is also a signaling substance that labels other molecules for disposal. Unfortunately, FAT10 is the wrong label for mitochondria. FAT10 not only labels the damaged mitochondria, but also the enzyme Parkin for the body to dispose of.

To use a picture: It would be like labeling the cell's own guardians for disposal—the very ones that otherwise label damaged mitochondria for disposal. The body then does what the labels tell it to do. The more guardians are disposed of, the fewer damaged mitochondria can be correctly labeled for disposal. What happens as a result? The [body's](#) defense processes do not dispose of the damaged mitochondria—and the [brain cells](#) themselves are damaged over time.

"We hope this discovery provides a new approach to developing an effective treatment for Parkinson's. An inhibitor for FAT10 could possibly be used to limit the disposal of Parkin and ensure that damaged [mitochondria](#) are disposed of correctly," says Marcus Groettrup.

More information: Nicola D. Roverato et al. Parkin is an E3 ligase for the ubiquitin-like modifier FAT10, which inhibits Parkin activation and mitophagy, *Cell Reports* (2021). [DOI: 10.1016/j.celrep.2021.108857](https://doi.org/10.1016/j.celrep.2021.108857)

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