idw - Informationsdienst Wissenschaft
Nachrichten, Termine, Experten

Pressemitteilung

Heinrich-Heine-Universität Düsseldorf
Dr.rer.nat. Arne Claussen

04.04.2025
http://idw-online.de/de/news850268

Forschungsergebnisse, Wissenschaftliche Publikationen
Biologie, Medizin
überregional

How cells repair their power plants

Medicine: Publication in Science Advances Damage to the mitochondria, the "power plants" of the cells, contributes to many diseases. Researchers from Heinrich Heine University Düsseldorf (HHU) and the University of Cologne led by HHU professor of medicine Dr David Pla-Martín, now describe in the scientific journal Science Advances how cells with defective mitochondria activate a special recycling system to eliminate damaged genetic material.

Damage to the genetic material of mitochondria – the mitochondrial DNA or mtDNA for short – can lead to diseases such as Parkinson's, Alzheimer's, amyotrophic lateral sclerosis (ALS), cardiovascular diseases and type 2 diabetes. Such damage also speeds up the ageing process. However, the cells are normally capable of identifying such damage and reacting.

Scientists from University Hospital Düsseldorf and HHU have – in collaboration with the University of Cologne and the Center for Molecular Medicine Cologne (CMMC) – discovered a mechanism, which protects and repairs the mitochondria. The research team, headed by Professor Pla-Martín from the Institute of Biochemistry and Molecular Biology I at HHU, has identified a specialised recycling system, which cells activate when they identify damage to the mtDNA.

According to the authors in Science Advances, this mechanism relies on a protein complex known as retromer and the lysosomes – cell organelles containing digestive enzymes. These special cellular compartments act like recycling centres, eliminating the damaged genetic material. This process is one of the mechanisms, which prevent the accumulation of faulty mtDNA, thus maintaining cellular health and potentially preventing diseases.

"We have identified a previously unknown cellular pathway, which is important for mitochondrial health and thus for the natural defences of our cells," explains Professor Pla-Martín, continuing: "By understanding this mechanism, we can explain how mitochondrial damage can trigger diseases like Parkinson's and Alzheimer's. This could in turn form the basis for developing preventive therapies."

In collaboration with the cell biologist Dr Parisa Kakanj from the University of Cologne, who is also a member of the CEPLAS Cluster of Excellence, Professor Pla-Martín was able to verify and extend the findings using fruit flies (Drosophila) as a model organism. Dr Kakanj showed that damaged mitochondrial DNA are eliminated much more quickly and that mitochondrial function improves significantly when the activity of the retromer complex – in particular the protein VPS35 – is increased.

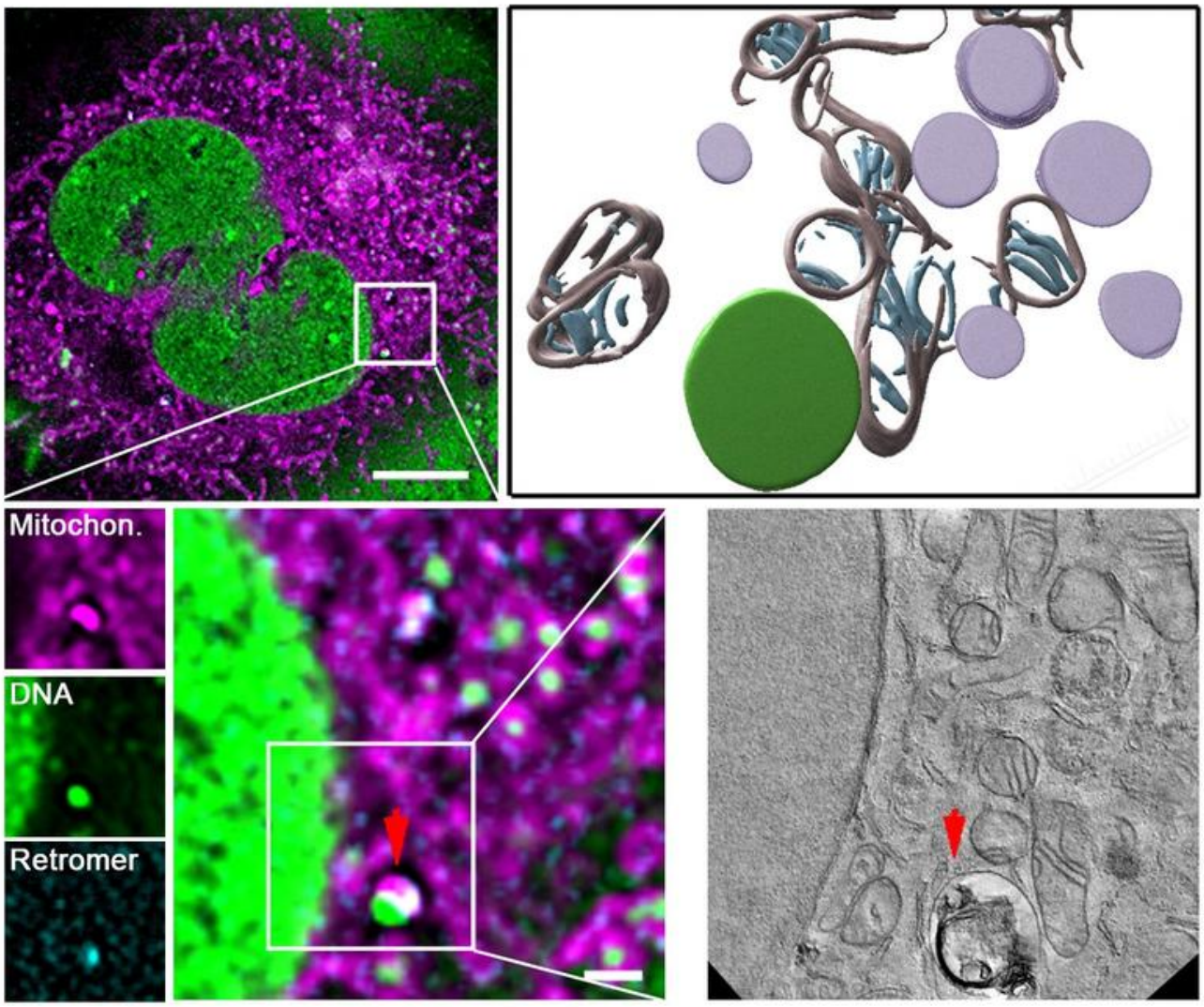
Dr Kakanj: "Using Drosophila allowed us to confirm our initial findings in human cells and demonstrate clear improvements in mitochondrial health. This opens up exciting possibilities for therapeutic strategies for treating mitochondrial diseases and age-related conditions."

Full caption:
The graphic shows images of a cell under mtDNA replication stress made using so-called Correlative Light and Electron Microscopy (for short: CLEM). The mitochondrial DNA (mtDNA, green) is ejected from the mitochondria (magenta) and taken up by a lysosome, which contains the retromer (cyan). The highlighted section was also analysed using 3D-CLEM to obtain volumetric information. (Fig.: HHU/David Pla-Martín)

Originalpublikation:

Parisa Kakanj, Mari Bonse, Arya Kshirsagar, Aylin Gökmen, Felix Gaedke, Ayesha Sen, Belén Mollá, Elisabeth Vogelsang, Astrid Schauss, Andreas Wodarz, David Pla-Martín. Retromer promotes the lysosomal turnover of mtDNA. Science Advances (2025).

DOI: 10.1126/sciadv.adr6415



CLEM images of a cell under mtDNA replication stress. (The full caption can be found below the message text.)
HHU/David Pla-Martín