Unexpected finding in the cell's power plant

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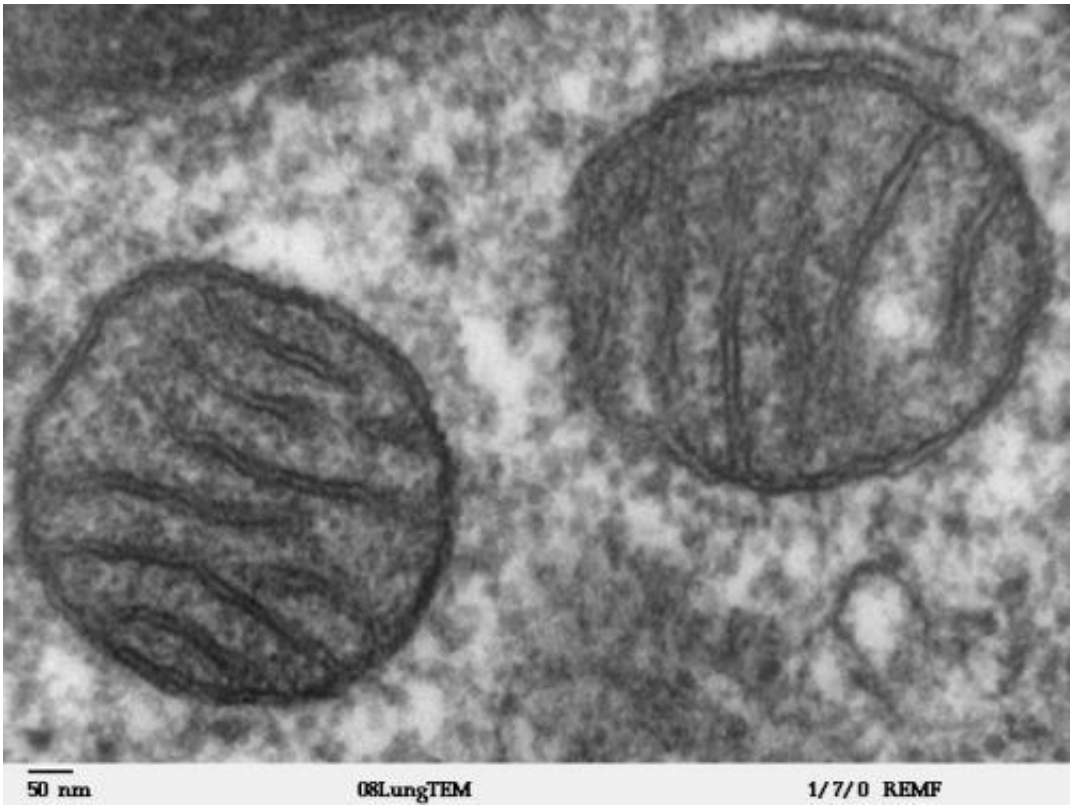

Mitochondria. Credit: Wikipedia commons

Researchers at Karolinska Institutet have discovered that the protein complex RNase P in the cell's mitochondria behaves differently than previously thought. The findings, published in *Nucleic Acids Research*, give important new clues on how certain mutations cause mitochondrial disease.

Almost all of the cell's energy is produced in the cell's own power plant, the mitochondria. The inability of mitochondria to function properly leads to mitochondrial disease, affecting about one in 4000 individuals. Genetically related mitochondrial diseases generally arise from errors in the expression of encoded proteins in the mitochondrion's genome.

When the mitochondrial genome is transcribed, long RNA strands are formed. These need to be cut down and processed to release the mature mitochondrial RNAs which are essential for the mitochondrion's internal protein synthesis. The processing of RNA begins in regions that encode mitochondrial transfer RNAs (tRNAs). Studies of this processing at a molecular level can give important clues about mitochondrial diseases because they are often caused by mutations in tRNA components.

Previous research has shown that cutting at the front end (referred to as the 5'-end) and at the rear end (the 3'-end) of the mitochondrial tRNA strand is catalysed by different components. The mitochondrial protein complex RNase P comprise three components (MRPP1, MRPP2, and MRPP3) that cut the 5´-end of the tRNA, whereas a single protein (ELAC2) cuts the 3´-end of the tRNA.

Several unexpected findings

Researchers at Karolinska Institutet have now found that two of the proteins from the RNase P complex, MRPP1 and MRPP2, surprisingly remain bound to the tRNA even after the initial 5´-processing. Even more surprisingly, these two proteins were also necessary for ELAC2 to cut in the 3´-end of the tRNA. The results explain why mutations in tRNA components that were previously believed to only be important in the initial 5´-processing can also strongly affect 3´-processing and other downstream steps in tRNA maturation.

"This novel functionality of MRPP1 and MRPP2 is important when

evaluating both the molecular and physiological effects of the mutations found in patients suffering from mitochondrial disease", says Martin Hällberg, senior researcher at Karolinska Institutet's Department of Cell and Molecular Biology and the Centre for Structural Systems Biology (CSSB) in Hamburg who led the study.

More information: Linda Reinhard et al. The MRPP1/MRPP2 complex is a tRNA-maturation platform in human mitochondria, *Nucleic Acids Research* (2017). DOI: 10.1093/nar/gkx902

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