

## **Protein molecules in mitochondria clearly assigned for the first time**

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Graphical abstract. Credit: DOI: 10.1016/j.cmet.2021.11.001

Mitochondria are key components of our cells. Cell respiration and control of many metabolic and signaling processes take place within them. In order for the biochemical reactions to take place flawlessly, complex interactions between specialized protein molecules are required. Yet up to now, it wasn't known how many of the proteins in cells are also actual components of the mitochondria because the technology for such precise allocation was unavailable. A team working with Prof. Dr. Bettina Warscheid, Prof. Dr. Nils Wiedemann, Prof. Dr. Nikolaus Pfanner and Prof. Dr. Claudine Kraft of the Excellence Cluster CIBSS Centre for Integrative Biological Signaling Studies at the University of Freiburg, and Dr. Sven Dennerlein of the University of Göttingen, have used new methods to examine successfully and precisely the composition human mitochondria. Their results are published in *Cell Metabolism*.

## **Combination of several experimental approaches**

Earlier, proteins were described as mitochondrial when biochemical analysis techniques found they were present in purified mitochondria. Today, this method is known to be imprecise. "The <u>detection systems</u> have meanwhile become so sensitive that most proteins—independent of their origin in the cell—show up in purified mitochondria," Wiedemann explains. To overcome this problem, the researchers combined several experimental approaches. They compared the <u>protein</u> composition of highly purified and less highly purified mitochondria with each other, and with data from other cell components as well. In further experiments, they blocked the transport of proteins from inside the cell into the mitochondria. This allowed them to see which proteins normally entered the mitochondria in this way. "By using these different



approaches, we were able to identify 1134 proteins that are present in mitochondria, and actually found this in several independent experiments and in different human cell types, which make the results very reliable, explains Warscheid, whose team identified the previously unknown components of mitochondria.

## Study connections between diseases of the cardiovascular and nervous systems

In order to determine the functions of the previously unknown proteins, the researchers examined their interactions with other proteins within the mitochondria. This enabled them, for instance, to describe a protein required for the assembly of molecular machinery for cell respiration. "Our analysis of such properties in the context of disease symptoms illustrates, for example, that defects in proteins which are vital for the formation of the energy provider ATP often affect the cardiovascular system in particular," explains Wiedemann. Overall, defects in mitochondrial proteins particularly frequently lead to disease of the cardiovascular and nervous systems The research team's new findings will allow these relationships to be studied in detail.

**More information:** Marcel Morgenstern et al, Quantitative highconfidence human mitochondrial proteome and its dynamics in cellular context, *Cell Metabolism* (2021). DOI: 10.1016/j.cmet.2021.11.001

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