Surprising features of mitochondrial protein synthesis uncovered

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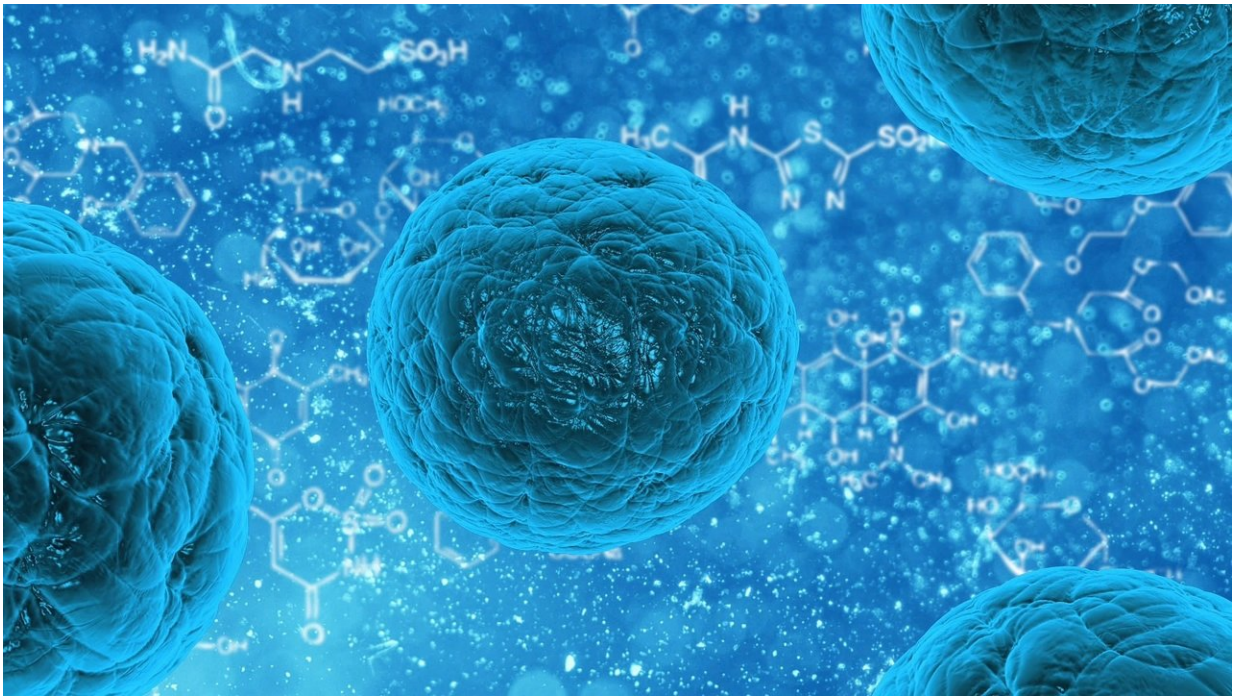

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Researchers at Karolinska Institutet have uncovered surprising features of mitochondrial protein synthesis. The study, published in *Nature Communications*, sheds light on the fundamental mechanisms used by the cell's power plant.

Mitochondria are essential organelles containing their own genome and

the machinery for its expression. Defects in mitochondrial protein synthesis result in complex pathologies, including cancer, diabetes, neurodegenerative diseases and a large, clinically diverse group of disorders called mitochondrial diseases.

Protein synthesis factories in mitochondria

Protein production within mitochondria is orchestrated by specialized ribosomes, mitoribosomes. Despite the shared ancestry of mitochondria and bacteria, the composition and structure of human mitoribosomes, and their translational factors, are significantly different to those of their bacterial counterparts.

"Whilst the mechanisms of bacterial and cytosolic translation have been studied for decades, we are only now starting to uncover how mitochondria produce proteins" notes Joanna Rorbach, Assistant Professor at the Department of Medical Biochemistry and Biophysics at Karolinska Institutet, one of the senior authors of the study.

The researchers took a multidisciplinary approach, including cryo-EM and single-molecule fluorescence methods, to reveal the early stages of mitochondrial translation.

"We show for the first time, the action of mitochondrial initiator factors and the elements of the mitoribosome that evolved mitochondria-specific mechanisms" says Anas Khawaja, postdoctoral researcher in Joanna Rorbach' group and first author of the article.

As mitochondrial protein synthesis and its dysfunction are implicit in cellular homeostasis and a growing spectrum of clinical disorders, the results represent an important step towards understanding the fundamental biochemistry of these systems, which may help yield novel therapeutic opportunities.

More information: Anas Khawaja et al. Distinct pre-initiation steps in human mitochondrial translation, *Nature Communications* (2020). DOI: 10.1038/s41467-020-16503-2