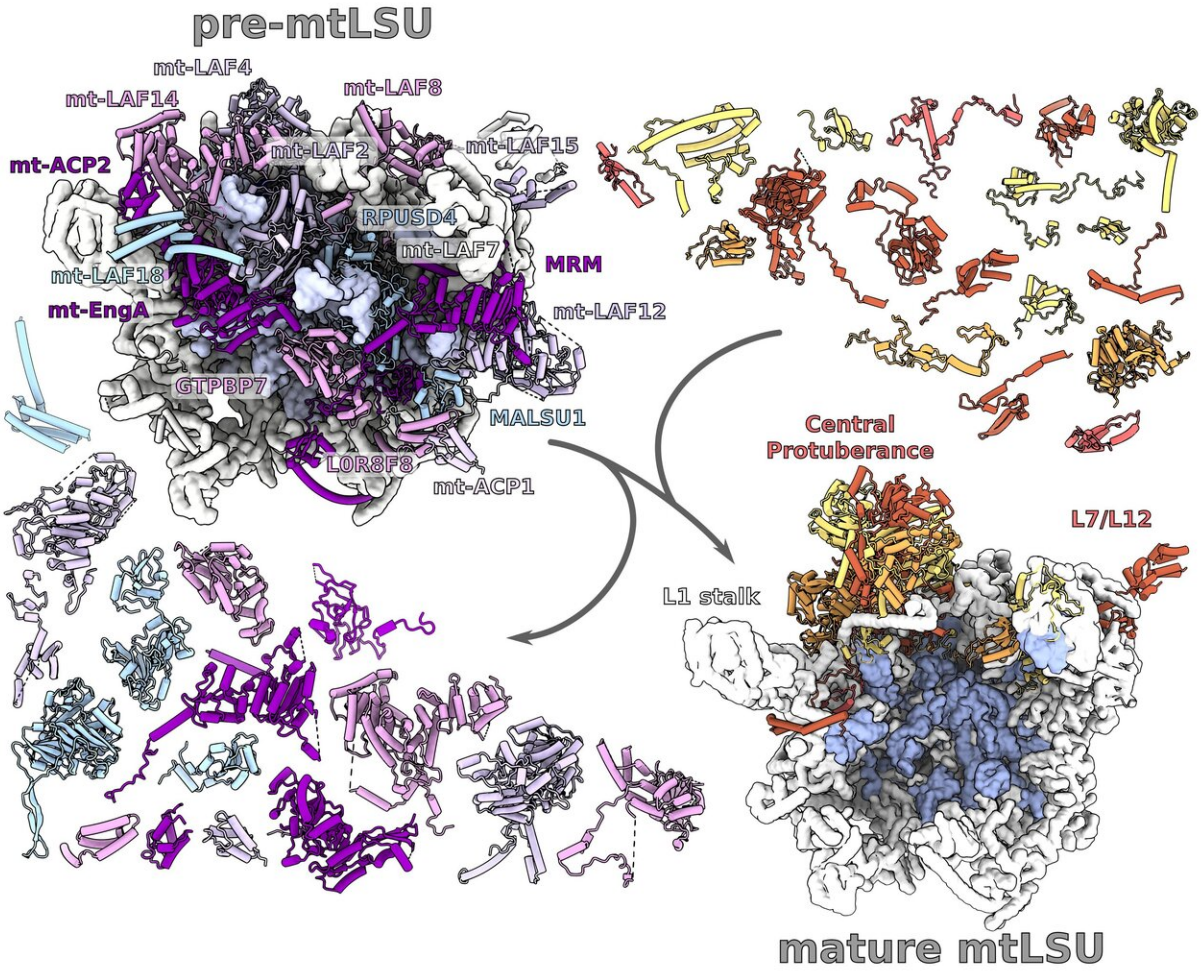
A glimpse into the formation of the mitoribosome

February 16 2021



Structure of pre-mitoribosomal large subunit with assembly factors. Credit: Victor Tobiasson

SciLifeLab Fellow Alexey Amunts and his team together with researchers from the Czech Academy of Sciences report an assembly intermediate of the ribosome in mitochondria. It reveals 22 associated factors that cooperatively organize the biogenesis process.

The mitochondrial ribosome is an intricate machine that translates the organellar genome into functional proteins. The formation of the mitochondrial ribosome is a hierarchical process involving dozens of different components. The newly published cryo-EM study by Tobiasson et al in the *EMBO Journal* characterized a key step in this process.

A complex of 2.2 MegaDalton representing a rare state of assembly of the large subunit was isolated from a model organism Trypanosoma brucei. Since the state was identified in only 3.5 % of the complexes, five cryo-EM datasets had to be collected at the SciLifeLab facility and ESRF in Grenoble and combined together.

The resulting structure revealed that the assembly factors form a network that spans a distance of 18 nanometres shielding the sensitive ribosomal core that is made of less-stable nucleic acids. The network is designed to connect all the functional regions on the mitoribosomal large subunit for their correlated maturation.

A phylogenetic analysis further showed that most of the newly identified assembly factors also exist in human, and therefore the derived characteristics represent general principles. However, an unexpected finding is that some of those factors appeared to loose their activity. Despite being deactivated, they still contribute as structural mediators for a stabilization of the functionally active partners on the mitoribosomal core. The preservation of the deactivated factors implies a mechanism of the evolutionary conservation of the sequential assembly.

The work showcases how the structural approach of studying stabilized intermediates is instrumental for understanding dynamic macromolecular processes that can be extrapolated to human counterpart metabolic pathways and provide an evolutionary insight.

More information: Victor Tobiasson et al, Interconnected assembly factors regulate the biogenesis of mitoribosomal large subunit, *The EMBO Journal* (2021). DOI: 10.15252/embj.2020106292

Provided by Science For Life Laboratory