Researchers demonstrate how a molecular barrel structure serves various functions in the mitochondria

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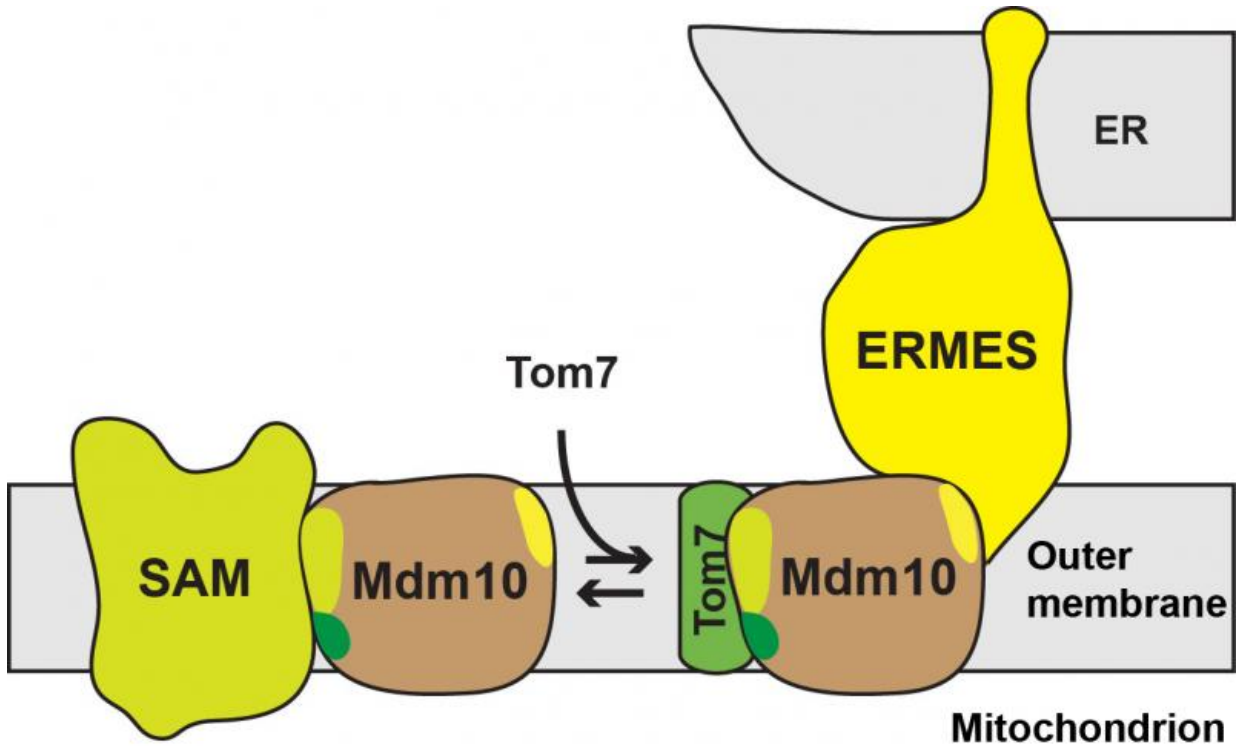

Credit: Albert-Ludwigs-Universität Freiburg

Freiburg researchers have discovered that the molecular barrel protein Mdm10 can carry out various functions for the development and maintenance of mitochondrial structure by binding to protein machines.

Mitochondria are the cell's powerhouses, for instance producing the energy for cell metabolism. The team led by Prof. Dr. Nikolaus Pfanner and Dr. Thomas Becker from the University of Freiburg's Institute of Biochemistry and Molecular Biology published the findings together with further colleagues in the journal *Nature Communications*.

On the one hand, mitochondria rely on the import of proteins from the cytosol, the aqueous component of the cell, yet on the other hand they are also dependent on the exchange of fatty lipids, the basic structural component of biological membranes, with the endoplasmic reticulum (ER), a network of membrane structures in the cytosol. Protein machines in the mitochondrial outer membrane play a key role in this exchange: The TOM complex is the entrance gate to the mitochondria for the proteins from the cytosol. A second protein machine, the SAM complex, integrates proteins into the outer membrane. Mitochondria are connected to the ER via molecular bridges, facilitating the exchange of lipids and enabling the development of the mitochondrial structure. One such bridge is the so-called ERMES complex. The protein Mdm10, which develops a beta-barrel structure, binds to the SAM complex and is also a component of the ERMES complex. The outer membrane protein Tom7 regulates the distribution of Mdm10 between the protein complexes. Until now, little was known about the functions of Mdm10 at these two protein machines.

Freiburg scientists from Collaborative Research Center 746, "Functional Specificity by Coupling and Modification of Proteins," and the Cluster of Excellence BIOSS Center for Biological Signalling Studies demonstrated in cooperation with a research group led by Prof. Dr. Enrico Schleiff from the University of Frankfurt that the binding sites for the SAM and ERMES complexes are located on different sides of the beta-barrel structure of Mdm10. The doctoral candidate Lars Ellenrieder from Becker's group also succeeded in identifying the particular functions of Mdm10 at the SAM and ERMES complexes. The

protein forms the mitochondrial membrane anchor for the ERMES complex and is thus essential for the maintenance of the lipid composition and the structure of the mitochondria. In cooperation with a research group led by Prof. Dr. Richard Wagner at Jacobs University Bremen, the researchers also demonstrated that Mdm10 forms a channel and is involved in the import of proteins to the outer membrane at the SAM complex.

More information: Lars Ellenrieder et al. Separating mitochondrial protein assembly and endoplasmic reticulum tethering by selective coupling of Mdm10, *Nature Communications* (2016). DOI: 10.1038/NCOMMS13021

Provided by Albert Ludwigs University of Freiburg