



Press Release

Lipids Support Protein Machinery

University of Freiburg researchers discover that integration of molecular barrels into the membrane depends on its composition

In the membranes of mitochondria – the power stations of the cell – are many different embedded proteins. These proteins perform key functions for the mitochondria. A team led by the biochemist Dr. **Thomas Becker** from the University of Freiburg discovered that lipids – the fatlike substances that form the basic building blocks of biological membranes – help a protein machinery to integrate proteins into the outer membrane of mitochondria. The researchers published their findings in the current issue of the *Journal of Biological Chemistry*.

Mitochondria perform vital functions for the cell. They produce the energy for cell metabolism, for example. Mitochondrial dysfunctions can cause severe neurological diseases. Certain proteins of the outer membrane that form a so-called beta-barrel structure are essential for the development of the mitochondria. These proteins enable the transport of proteins and metabolic intermediates, or so-called metabolites. Ribosomes within the cytosol – the cell fluid – produce these beta-barrel proteins. The protein translocases, which are two protein machineries in the outer membrane of the mitochondria, integrate the barrel structures into the membrane. The translocase of the outer membrane, in short TOM complex, transports the proteins from the cytosol into the mitochondria. The so-called SAM complex then integrates the proteins into the membrane. While TOM and SAM are well researched by scientists, the role of lipids is still only poorly understood.

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■ In mitochondria, the main building block of the membranes are the so-called phospholipids, of which phosphatidylcholine (PC) is the most abundant one. Becker's team discovered a previously unknown role of PC in the development of beta-barrel proteins. The scientists found out that the function of the SAM complex depends on the concentration of PC in the membrane. In collaboration with the research group of Professor Dr. **Günther Daum** from the Graz University of Technology in Austria, the team from the University of Freiburg analysed the mitochondria of baker's yeast mutants, which had a significantly lower concentration of PC. **Max-Hinderk Schuler** from Becker's research group at the Institute for Biochemistry and Molecular Biology of the University of Freiburg demonstrated that, in the mutated baker's yeast, the integration of the beta-barrel proteins into the outer membrane is impaired. This can be explained by the fact that the function and stability of the SAM complex in these mutants is disturbed. In contrast, the activity of the TOM complex is not inhibited. This means that beta-barrel proteins can pass the TOM complex unimpeded, while their integration into the outer membrane does not occur at full speed when the concentration of PC is reduced. This work shows that protein machinery and lipids are closely connected in protein transport and that the integration of the beta-barrel proteins in the target membrane depends on the composition of the membrane.

This project is a collaboration of the Collaborative Research Centre 746: Functional Specificity by Coupling and Modifications of Proteins, the Cluster of Excellence BIOSS Centre for Biological Signalling Studies and a project grant from the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG).

Original publication:

Schuler, M.-H., Di Bartolomeo, F., Böttinger, L., Horvath, S.E., Wenz, L.-S., Daum, G. and Becker, T. (2015) Phosphatidylcholine affects the role of the sorting and assembly machinery in the biogenesis of mitochondrial β -barrel proteins. *J. Biol. Chem.* 290, 26523-26532. DOI: 10.1074/jbc.M115.687921

Caption:

The University of Freiburg achieves top positions in all university rankings. Its research, teaching, and continuing education have received prestigious awards in nationwide competitions. Over 24,000 students from 100 nations are enrolled in 188 degree programs. Around 5,000 teachers and administrative employees put in their effort every day – and experience that family friendliness, equal opportunity, and environmental protection are more than just empty phrases here.

■ In the baker's yeast, mitochondria form a network that is coloured with a fluorescent green here. Image: Dr. Łukasz Opaliński, AG Becker

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