MASS SPECTROMETRY

Membrane protein complexes exposed

A vesicle-based mass spectrometry method enables the analysis of protein complexes in native membranes.

Native mass spectrometry is a powerful tool for the characterization of subunit stoichiometries and lipid-binding properties of membrane protein complexes. However, current approaches require detergent extraction or another form of chemical intervention, such as the incorporation of complexes into nanodiscs or bicelles, before analysis. Applications are further restricted by the need for high amounts of protein.

Carol Robinson at the University of Oxford and her colleagues developed a detergent- and chemical-free approach for the analysis of protein complexes from native membranes that overcomes these limitations. First, vesicles are prepared from the isolated membranes of interest. These vesicles are then disrupted by sonication and injected via nano-electrospray into the high electric field of the mass spectrometer, which leads to ejection of the protein assemblies from the membrane. The team developed a protocol for the interpretation of the spectra that also utilizes lipidomics and proteomics data from the vesicles and enables the user to identify membrane protein complexes.

The researchers applied their method to study the outer and inner membranes of *Escherichia coli* and gained new insights into the interactions of bacterial membrane proteins with lipids, chaperones, and cofactors. They found that the chaperone protein DnaK interacts with the porin OmpA, and that up to three cardiolipin molecules associate with the β-barrel assembly machinery in the outer membrane. It was more challenging to analyze the inner *E. coli* membrane because it contains more proteins. The authors identified various subassemblies of multidrug efflux pumps, and observed that F_1F_0 ATP synthase remains associated with the SecYEG protein translocation system after membrane insertion.

They also characterized the complexes from protein-rich bovine inner mitochondrial membranes, thus demonstrating the broad applicability of this approach. The method might also enable investigations into how disease-causing mutations and drugs affect the composition and stability of membrane protein complexes.

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Research papers

Chorev, D. S. et al. Protein assemblies ejected directly from native membranes yield complexes for mass spectrometry. *Science* **362**, 829–834 (2018).

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