Séminaire

INSTITUT Charles SADRON
UPR 22 - CNRS - STRASBOURG

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Amphithéâtre Henri Benoît

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Interplay between conformational dynamics of a transmembrane protein and membrane mechanical properties

Transmembrane proteins mediate many essential cellular functions, e.g. communication, signaling or detoxification. There is a tight interaction between lipids and transmembrane proteins. Membrane can apply mechanical stress and impact transmembrane protein shape and function. Reciprocally, the inclusion of a transmembrane protein can induce a bending or stretching of the membrane. In particular, this interplay might play a crucial role for proteins that change conformation to mediate cargo transport.

We discuss the protein BmrA, a bacterial ABC exporter from *B.subtillis*. ABC (ATP Binding Cassette) transporters represent one of the largest families of membrane proteins. They undergo large conformational changes between an "open" state and a "closed" state to transport various substrates in or out of the cells upon ATP hydrolysis. Some lead to a phenotype of multi-drug resistance, such as the human P-glycoprotein (P-gp) that transports anti-cancer agents out the cell. BmrA shares high homology with P-gp and is expected to undergo a large conformational change.

We have studied the interplay between the conformational cycle of BmrA and membrane curvature, at the single molecule level. Single proteins are reconstituted into SUVs (small unilamellar vesicles) of various diameters (40, 60 and 140 nm) and their conformations are probed by single-molecule FRET in TIRF microscopy as a function of their hydrolytic state. We have shown that at high curvature (40 nm liposomes), BmrA conformation distribution is strongly affected, both in the presence and in the absence of ATP, as compared to larger liposomes. This shows for the first time that membrane curvature can directly affect transmembrane proteins' conformations, and consequently their function.

Les personnes souhaitant rencontrer A. Damm sont priées de prendre contact avec Thierry Charitat (thierry.charitat@ics-cnrs.unistra.fr)