MDR transporters and other membrane proteins

Molecular Microscopy of Membranes

ABC (ATP-binding cassette) transporters are membrane transporters that hydrolyse ATP for the transmembrane transport of various amphiphilic molecules including lipids, peptides, homones, sterols, antigens. Several ABCs confer a multidrug resistance phenotype (MDR) to bacteria against antibiotics and to human against drugs used in anticancer treatments.

We have characterized by electron crystallography and single particle analysis at medium resolution the 3D architecture of BmrA, a bacterial MDR homolog of the human PgP, embedded in a lipidic membrane. We have found that in apo conformation, BmrA has a V shaped conformation with dis-engaged nucleotide binding sites. The surrounding lipid bilayer is curved around BmrA with nonsymmetrical distribution of lipids on membrane leaflets. In post-hydrolytic conformation, BmrA has a cylindrical shape and membranes are planar. This demonstrated at molecular resolution that a transmembrane protein can actively remodel membrane. Our project aims to understand this interplay between protein and the surrounding membrane.

We have also described the molecular architecture at medium resolution of ABCG2 (Breast Cancer Resistance Protein), of BmrC/BmrD, a bacterial heterodimer MDR transporter, and two MDRs from plants NtPdr1, NtPdr5.

Fig.3D reconstruction of BmrA, a bacterial homodimeric MDR transporter in open apo conformation and embedded in membrane. The lipidic leaflet is curved around the open V shaped protein. After addition of ATP, curved membranes are transformed into planar membranes.

ABCs Related publications:


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ABCs Related grants:


People involved in the ABC project

Daniel Lévy (PI), Su-Jin Paik (PhD Student), A. Di Cicco (IE, EM Manager); J. Manzi (IR, Biochemistry)

Collaborations:

P. Bassereau (PCC), M. Dahan (PCC, Institut Curie), E. Margeat (CBS, CNRS, Montpellier), P. Tieleman (University Calgary, Canada), S. Wilkens (University of Syracuse, USA), M. Boutry (ULB, Louvain, Belgique)

Photosynthetic core complexes, related publications (team members in bold):

During the years 2000-2007, we have combined electron crystallography, reconstitution in lipid membranes and functional studies to describe the structure of several individual photosynthetic
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complexes and the formation of supercomplexes of transmembrane proteins.


