Motion of a Membrane Enzyme as Seen by SANS

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Small Angle Neutron Scattering is a low-resolution technique enabling to probe the solution structure of individual biomacromolecules possibly in complex with its partners. In particular, concerning membrane proteins, the membrane-like environment can be made invisible in order to see only the protein. Here, we combined SANS with X-ray crystallography, cryoEM, H/D exchange coupled with mass spectrometry and limited proteolysis to reveal the flexibility and ligand-induced conformational changes of the multidrug ABC transporter BmrA.

Limited proteolysis revealed an important flexibility of BmrA WT in most steps of its catalytic cycle. Cryo-EM provided high-resolution of the closed conformation by analysis of an artificially monodisperse sample, and X-ray crystallography data enabled to build homology models of other conformations, which constituted the starting point of SANS analysis. H/D X-MS pinpointed the flexible part along the transporter sequence and SANS revealed the extent of this flexibility.

Together, these techniques enable us to describe the ABC transporter cycle in term of successive conformational equilibria, a much more realistic and accurate vision of this biological process [1].

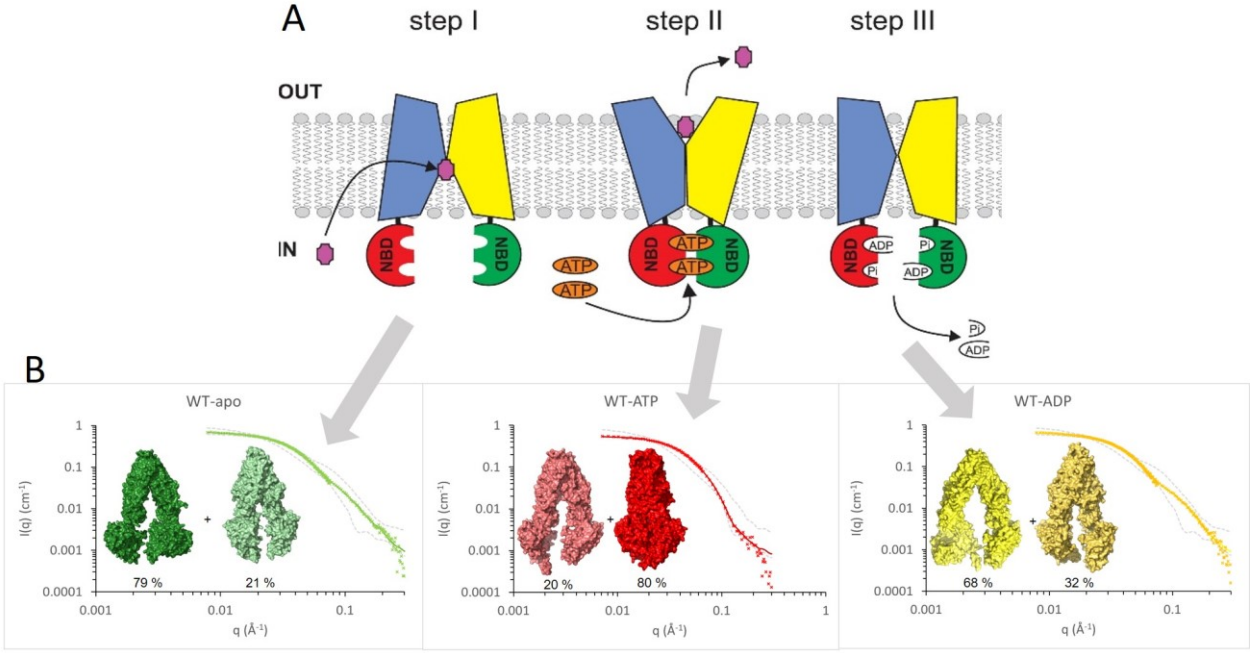

Figure 1. A: Main steps of the enzymatic cycle of ABC transporters (from [2]); B: Structural definition of these steps in solution by sequential conformational equilibria [1].

[1] Javed *et al*. in preparation (or submitted)

[2] Wannes Dermauw, Thomas Van Leeuwen, The ABC gene family in arthropods: Comparative genomics and role in insecticide transport and resistance, Insect Biochemistry and Molecular Biology, Volume 45, 2014

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