

**Mechanism of a bacterial multidrug ABC (ATP-binding cassette) transporter, BmrA, probed by H/D exchange and solid-state NMR - Jault Jean-Miche - Universite de Lyon, CNRS, France**

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**Abstract**

ATP-binding cassette (ABC) transporters can translocate a huge variety of molecules across a membrane by coupling transport with ATP hydrolysis. They are found in all living organisms and some members of this superfamily are involved in resistance to many unrelated compounds (e.g. antibiotics, anticancerous and antifungal) and thus confer a multidrug resistance phenotype. Our studies focus on BmrA (αBacillus multidrug resistance ATPase), a prototypical bacterial multidrug ABC transporter from *Bacillus subtilis* which is homologous to the human P-glycoprotein involved in resistance of cancerous cells to therapeutic drugs.

Using both H/D exchange and solid-state NMR, we were able to probe major conformational differences between the resting state (inward-facing conformation) and the ATP-bound state (outward-facing conformation) of BmrA, either in a solubilized detergent form or reconstituted in lipids. Our results highlight the important changes in flexibility and conformation between these two states of the catalytic cycle of BmrA, and the flexibility observed in the resting state could possibly widen the specificity for drug recognition.