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MECHANISM OF A BACTERIAL MULTIDRUG ABC (“ATP-BINDING CASSETTE”) TRANSPORTER, Bmra, PROBED BY H/D EXCHANGE AND SOLID-STATE NMR

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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 (“Bacillus multidrug resistance ATP”), 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.

Biography

Jault Jean-Michel is the Research Director of the CNRS and the Director of the “Molecular Microbiology and Structural Biochemistry” research unit (UMR5086) in Lyon (since January 2016). He is also a Team Leader in the same unit. He has a strong expertise in the biochemical characterization of various families of ATPases, GTPases and protein kinases. He has been working on ABC transporters for 20 years and has contributed to the identification, overexpression, purification and biochemical/biophysical characterization of several bacterial multidrug transporters leading to a better understanding of the functioning mechanism of these transporters. He published 78 peer-reviewed articles (2524 citations and h-factor of 28, Web of Science) and has one patent. He has been elected twice as a member of the ‘National Committee of Scientific Research’ (CoNRS) in the discipline of ‘Molecular and Structural Biology, Biochemistry’ (2012-2016 and 2016-2020).

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