DYNAMICS OF A BACTERIAL MULTIDRUG ABC TRANSPORTER USING HYDROGEN/DEUTERIUM EXCHANGE

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The study of membrane proteins remains a challenging task and approaches to unravel their dynamics are scarce. Here, we applied H/D exchange coupled to mass spectrometry to probe the motions of a bacterial multidrug ATP-Binding Cassette transporter, BmrA, in the inward (resting state) and outward (ATP-bound) facing conformations. Trypsin digestion and global or local H/D exchange support the transition between inward and outward facing conformations during the catalytic cycle of BmrA. However, in the resting state, peptides from the two intracellular domains, especially ICD2, show a much faster H/D exchange than in the closed state. This shows that these two sub-domains are very flexible in this conformation. Also, molecular dynamics simulations suggest a large fluctuation of the Ca positions from ICD2 residues in the inward facing conformation of a related transporter, MsbA. These results highlight the unexpected flexibility of ABC exporters in the resting state and underline the power of H/D exchange coupled to mass spectrometry to explore conformational changes and dynamics of large membrane proteins.

[1] *Mehmood et al.Proc. Natl. Acad. Sci. USA, in press.*