Does the Crystal Structure of Ammonium Transporter Tell us its Function?

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Ammonium is one of the most important nitrogen sources for bacteria, fungi and plants but it is toxic to animals. The ammonium transport proteins (Mep/Amt/Rh) are present in all domains of life, but the chemical identity of their substrate was uncertain. We have solved the structure of wild type AmtB from *E. coli* in two crystal forms at 1.8 and 2.1 Å resolution, respectively. Substrate transport occurs through a narrow, mainly hydrophobic pore located at the centre of each monomer of the trimeric AmtB. At the periplasmic entry, a binding site for NH_4^+ is observed. Two phenylalanine side chains (F107 and F215) block access into the pore from the periplasmic side. Further into the pore, the side chains of two highly conserved histidine residues (H168 and H318) bridged by a H-bond, lie adjacent with their edges pointing into the cavity. These histidine residues may facilitate the deprotonation of an ammonium ion entering the pore. Adiabatic free energy calculations support that an electrostatic barrier between H168 and H318 hinders the permeation of cations but not that of the uncharged NH_3. The structural data and energetic considerations strongly indicate that the Mep/Amt/Rh proteins are ammonia gas channels [1]. Interestingly at the cytoplasmic exit of the pore, two different conformational states are observed which might be related to the inactivation mechanism by its regulatory partner.

[1] Zheng L., Kostrewa D., Berneche S., Winkler F.K., Li X.D., *Proc Natl Acad Sci U S A*., 2004, **101**,17090.

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