MS70.O02

pH- and sodium-induced changes in a sodium/proton antiporter

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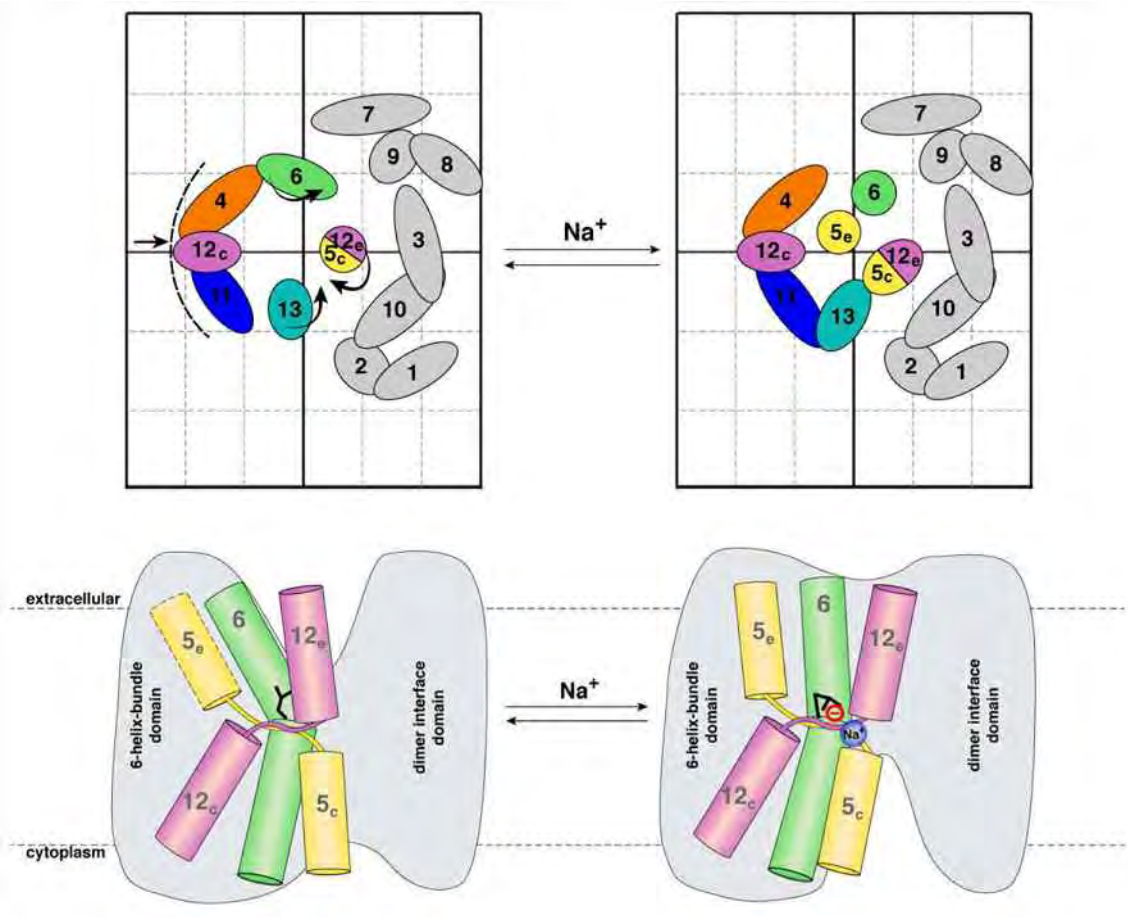
Na^+/H^+ antiporters are essential secondary-active transporters that are found across all biological kingdoms and play a crucial role in the pH, sodium and cell volume homeostasis. MjNhaP1 is an archaeal electroneutral Na^+/H^+-antiporter resembling the human NHE1 exchanger. Substrate-induced conformational changes in MjNhaP1 were examined by electron crystallography of 2D crystals in a range of physiological pH and Na^+ conditions. In the absence of sodium, changes in pH had no major effect on the structure of MjNhaP1, whereas changes in Na^+ concentration caused a marked conformational change that was largely pH-independent. Crystallographically determined, apparent dissociation constants indicated ~10-fold stronger Na^+ binding at pH 8 than at pH 4, consistent with substrate competition for a common ion-binding site. In conjunction with a new 3D EM map of MjNhaP1 a model for transport mechanism is proposed. Conformational changes occur in the 6-helix bundle region of MjNhaP1 that is thought to harbour the ion translocation site. Na^+-binding converts the antiporter from the apo- or proton-bound, outward-open state to the Na^+-bound, inward-open state. Oscillation between these two states result in rapid Na^+/H^+ antiport.

[1] *Paulino and Kühlbrandt. eLife 2014;3:e01412*



Keywords: electron crystallography, membrane protein structure, conformational changes