MS101.O05

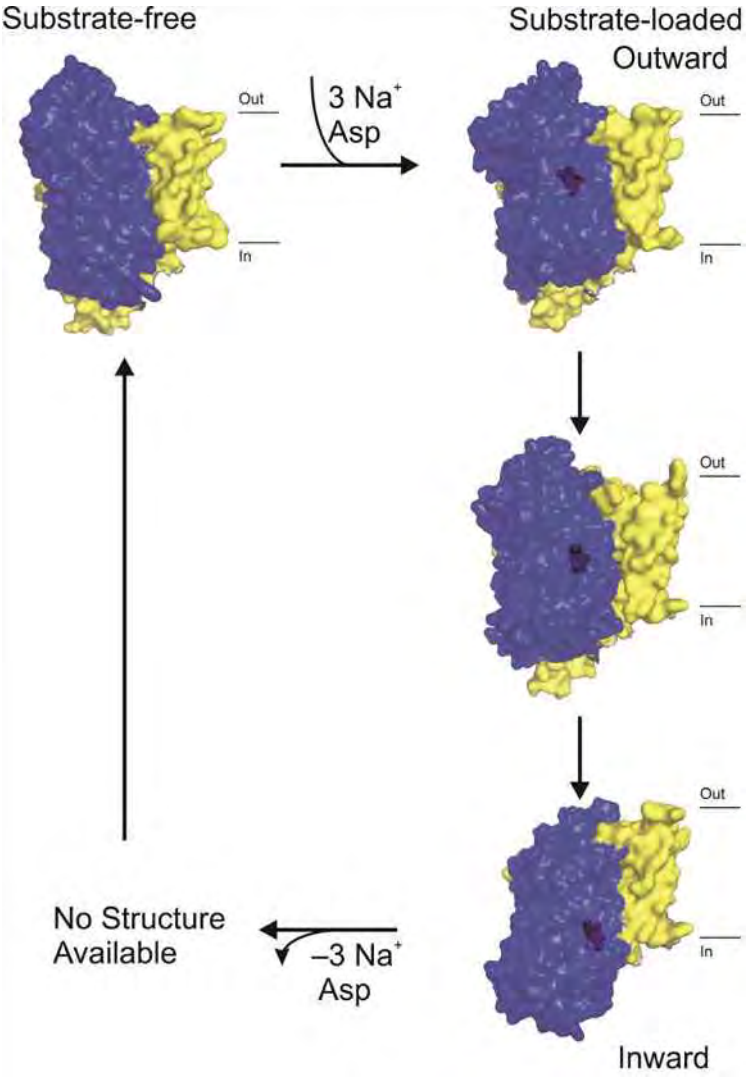
Elevator mechanism of aspartate (glutamate) transport across the membrane

A. Guskov[1], S. Jensen[1], S. Rempel[1], I. Hänelt[1], D. Slotboom[1,2]

[1]Groningen Biomolecular Sciences and Biotechnology Institute, University of Groningen, Groningen, The Netherlands, [2]Zernike Institute for Advanced Materials, University of Groningen, Groningen, The Netherlands

Archaeal homologues of human neuronal glutamate transporter catalyze the coupled uptake of aspartate and three sodium ions. After the delivery of the substrate and sodium ions in the cytoplasm the empty binding site must reorient to the outward-facing conformation to reset the transporter. Here we present a crystal structure of the substrate-free transporter GltTk from Thermococcus kodakarensis, resolved at 3 Å resolution [1]. Despite the global similarity to the previously resolved structures of aspartate transporter GltPh, there are tremendous rearrangements in the substrate-binding site. The key binding residue Arg401 moves in and partially occupies the substrate's position, while the rotation of another conserved residue Met314 completely destroys the geometry of the sodium-binding sites. This structure provides direct structural insight in the mechanism of the essential reorientation step in the translocation cycle for this type of transporters.

[1] *S. Jensen, A. Guskov, S. Rempel, et al, Nat Struct Mol Biol, 2013, 10, 1224-1226*



Keywords: Glutamate Transporter, Membrane Protein, Aspartate Transporter