

Transport of enantiomeric substrates by archaeal homologs of mammalian glutamate transporters

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Mammalian glutamate transporters (belonging to Solute Carrier Family 1 of transporters) are crucial players in neuronal communication as they perform neurotransmitter reuptake from the synaptic cleft. Besides L-glutamate and L-aspartate, they also recognize D-aspartate, which might participate in mammalian neurotransmission and/or neuromodulation. We investigated binding and transport of enantiomeric substrates in archaeal homologue of glutamate transporters - Glt_{TK} from *Thermococcus kodakarensis*. We observed that Glt_{TK} transports D-aspartate with identical Na⁺ : substrate coupling stoichiometry as L-aspartate, and that the affinities (K_d and K_m) for the two substrates are very similar. Additionally we solved a crystal structure of Glt_{TK} with bound D-aspartate at 2.8 Å resolution and compared it with the L-aspartate bound Glt_{TK} structure. The new structure explains how the geometrically different molecules L- and D-aspartate are recognized and transported by the protein in the same way and provides a clue to explain the puzzling observation why mammalian SLC1A transporters readily transport L- but not D-glutamate.