

SFB 35 Colloquia in Membrane Transport

20.05.2011, 14.00: Leseraum Pharmakologie

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"Ion coupling and dynamics of amino acid transporters"

Amino acids, which are important for cellular function and metabolism, are transported across cell membranes by specific transporter proteins. If the transport is uphill, against a transmembrane concentration gradient of the amino acid, it is often coupled to the co- or counter-transport of a driving inorganic ion, which provides free energy by flowing down its own transmembrane concentration gradient. In mammalian cells, active amino acid transport is often driven by the co-transport of Na⁺ ion(s). The transporters are thought to catalyze transport by simultaneously binding extracellular amino acid and Na⁺ ion(s) in their transmembrane domain, followed by a structural rearrangement of the transporter-amino-acid-Na⁺ complex to allow dissociation of the substrates into the intracellular space. Therefore, transport is a multistep process that is composed of a number of sequential, individual reaction steps. Here, I describe ongoing efforts in our laboratory to dissect the mechanism of this multistep transport reaction, by applying rapid chemical kinetic techniques and measuring kinetic and thermodynamic parameters of amino acid interaction with the transport protein in two different model systems, the glutamate transporter EAAC1, and the neutral amino acid transporter ASCT2. Using structure-function analysis, we have also identified novel sites of interaction with the cation in these transporters.