SFB 35 Colloquia in Membrane Transport

20.03.2009, 15.00: Leseraum Pharmakologie

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"Molecular aspects of coupled, uncoupled and leak currents in glutamate and dopamine transporters"

L-glutamic acid (glutamate) is a ubiquitous metabolite from the mitochondria and a neu-rotransmitter in neurons that express vesicular glutamate transporters (vGLUTs). Dopa-mine on the other hand is a neurotransmitter in those neurons that contains tyrosine hy-droxylase and vesicular monoamine transporters (vMATs). vGLUT and vMAT accumulate their substrate into synaptic vesicles, which upon fusion with the pre-synaptic membrane release the neurotransmitter into the perisynaptic space. The released neurotransmitter elicits a postsynaptic response through its pre- and post-synaptic receptors. Excitatory amino acid transporters (EAATs) and the dopamine transporter (DAT) remove the re-leased glutamate and dopamine, respectively, whereby they modulate the postsynaptic response. The plasmamembrane localized EAATs utilize the electrochemical energy from the sodium and potassium gradients created by Na+-K+-ATPase. In each stoichiometric, i.e. coupled, cycle the EAATs translocate one glutamate together with one proton and three sodium ions in exchange for one potassium ion. In the presence of glutamate EAATs also mediate a chloride flux, that does not influence the coupled cycle, and is therefore termed uncou-pled. We investigated and characterized the coupled and uncoupled fluxes as part of structure-function investigations aimed at understanding the molecular basis of the cation dependence of EAATs. In contrast to glutamate transporters, DAT utilizes only the electrochemical energy from the sodium gradient created by the Na+-K+-ATPase. DATs translocate one dopamine to-gether with two sodium and one chloride ion and results in the coupled, i.e. stoichiomet-ric, current. Human DAT is the best characterized of the DATs and mediates a leak cur-rent in absence of dopamine and a poorly characterized uncoupled chloride current in presence of dopamine. I will present some recent unpublished electrophysiological data on the functional differences, and similarities, between species homologues of DAT with special focus on the leak and uncoupled currents.