COLLOQUIA IN MEMBRANE TRANSPORT

Venue: Medical University Vienna, Center for Physiology and Pharmacology, Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "**Leseraum**".
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Friday 16.01.2015 14:00 s.t. **Christoph Fahlke** (host: W. Sandtner)

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"Glutamate transporter-associated anion channels: molecular mechanisms, physiology and pathophysiology"

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Abstract: Excitatory amino acid transporters (EAATs) form a class of glial and neuronal glutamate transporters which remove glutamate from the synaptic cleft to terminate glutamatergic synaptic transmission and to prevent neuronal damage by excessive glutamate receptor activation. EAATs are not only secondary-active glutamate transporters, but also anion-selective channels. EAAT anion channels are perfectly anion-selective, prefer large and polyatomic over small anions, and exhibit unitary current amplitudes that are small but in the range of conventional anion channels. Whereas key processes underlying glutamate transport have been identified in recent years, molecular determinants of the EAAT anion conductance still need to be clarified. We have used a combination of atomistic Molecular Dynamics simulation, fluorescence spectroscopy and cellular electrophysiology to identify a novel anion-conducting conformation that accounts for all experimental findings on EAAT anion currents.

To understand the physiological role of EAAT anion channels we are studying human diseases that are associated with mutations in genes encoding such transporters. We recently demonstrated that a point mutation identified in the *SLC1A3* gene in patients with episodic ataxia type 6 results in gain-of-function EAAT1 anion channels and postulated that EAAT anion channels might regulate intracellular [Cl^-] concentrations (Winter et al. (2012) *Brain* **135** 3416-3425). To test this hypothesis, we are currently determining intracellular chloride concentrations in glial cells from WT and *Slc1a3-/-* mice as well as from animal models for episodic ataxia.