

COLLOQUIA IN MEMBRANE TRANSPORT

Venue: Medical University Vienna, Center for Physiology and Pharmacology,
Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "**Leseraum**".

(Harald Sitte, Tel.: (01) 40160 31323, harald.sitte@meduniwien.ac.at)

Monday 22.10.2012 11:00 c.t. **Haley Melikian** (host: H. Sitte)

Associate Professor of Psychiatry
Brudnick Neuropsychiatric Research Institute
UMASS Medical School
303 Belmont Street
Worcester, MA 01604

"Dopamine Transporter Cell Surface Dynamics: Mechanistic insights from novel imaging tools"

[Haley Melikian \(Haley.Melikian@umassmed.edu\)](mailto:Haley.Melikian@umassmed.edu)

Abstract:

Dopamine (DA) neurotransmission is critical for a variety of neurological functions, including movement, mood and cognition. Aberrant dopaminergic transmission is implicated in several neuropsychiatric disorders such as Parkinson's disease, addiction, schizophrenia and attention-deficit hyperactivity disorder. Following evoked release, extracellular DA is rapidly cleared from the synapse by presynaptic reuptake mediated by the plasma membrane dopamine transporter (DAT). The addictive and therapeutic psychostimulants amphetamine, cocaine and methylphenidate (Ritalin) competitively inhibit DAT function and, thus, increase extracellular DA levels. DAT is not static at the plasma membrane, but is subject to rapid endocytic trafficking to and from the cell surface, which is acutely modulated by protein kinase C (PKC) activation and amphetamine exposure. Investigations examining the molecular underpinnings of DAT trafficking have yielded conflicting results, with both clathrin-dependent and -independent mechanisms implicated in DAT internalization. Work from our laboratory investigates the cellular and molecular mechanisms that govern basal and modulated DAT membrane trafficking. In our current work, we are using a novel approach that directly couples fluorophore to DAT in order to visualize DAT surface dynamics in real time. This approach is enabling us, for the first time, to directly examine DAT internalization and to determine critical features of DAT internalization mechanisms.