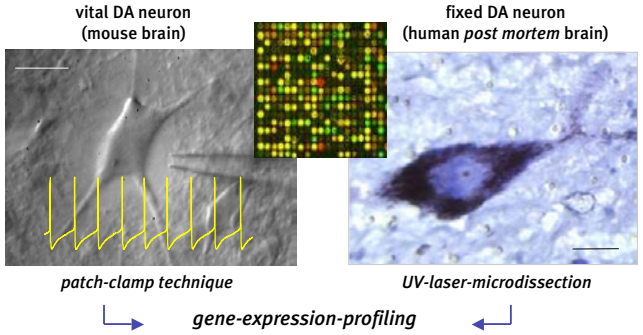
Institute of Applied Physiology

Work Group: Molecular Neurophysiology

Head: Birgit Liss

Our research is focused on the dopamine midbrain system. This system – and the activity of dopamine releasing (DA) midbrain neurons – is not only involved in motor control and movement disorders like Parkinson's disease, but also plays a crucial role in emotional and cognitive brain functions, and in related disorders such as schizophrenia, drug addiction, or attention-deficit-hyperactivity-disorders (ADHD).

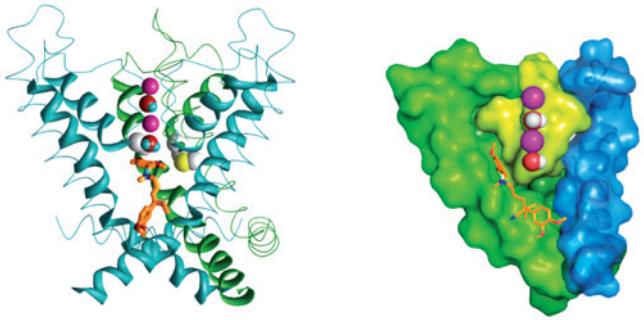
Our main research goal is to define functional and molecular mechanisms of different types of DA midbrain neurons with defined projections, which define their distinct physiological roles and their selective transitions to disease states. By combining brain-slice in vitro electrophysiology and UV laser microdissection with molecular quantitative gene expression profiling at the single cell level, we aim to define the pathophysiological signaling pathways that control DA neuron activity as well as selective activation of disease pathways, in particular in Parkinson's disease.



Schematic overview for analyzing electrophysiological function and gene expression of individual dopamine (DA) neurons from vital mouse brains (left) and post mortem human brains (right), combining brain slice patch-clamp technique (yellow trace: typical spontaneous activity of a DA neuron) or UV-laser microdissection (LMD) with gene-expression profiling (quantitative PCR after reverse transcription of mRNA, or microarray-based analysis). Scale bars: 15 µm

To address these issues, we analyze cellular function as well as gene expression of individual DA neurons from controls and from respective disease mouse models as well as from postmortem human brains. We focus on the role of ion channels and receptors, since their cell-specific activity directly defines neuronal activity in health and disease states.

The Team:
Head of Institute: B. Liss
Professor: S. Grissmer
Group Leaders/Postdocs: Z. Andronache, E. Dragicevic, M. Fauler, W. Melzer
PhD Students: J. Duda, M. Janbein, M. Orynbayev, C. Poetschke



Docking of verapamil in the inner pore of the voltage-gated potassium channels hKv1.3.

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Work Group: Ion Channel Structure/Function

Head: Stephan Grissmer

We are interested in the properties, modification and modulation of ion channels in cell membranes. We would like to clarify the physiological role of ion channels in cellular responses and in diseases. Lately, we have used molecular biological techniques in combination with electrophysiology to study structure-function relationships of potassium channels with the goal of rationally designing drugs for the modification/modulation of ion channel function. To aid this endeavor we used different blockers of potassium channels, such as tetraethylammonium, verapamil or peptide toxins, to identify the binding site of those blockers and, with the known three-dimensional structure of the blockers, to obtain a negative imprint on the channel's surface. This newly uncovered structure of each different potassium channel will guide rational drug design to be specific for each potassium channel type. Furthermore, we are also searching for endogenous proteins that can interact with ion channels and thereby possibly modulate their function.

Selected Publications:

- *Schiemann J, Schlaudraff F, Klose V, Bingmer M, Seino S, Magill PJ, Zaghloul KA, Schneider G, Liss B, Roeper J (2012): K-ATP channels in dopamine substantia nigra neurons control bursting and novelty-induced exploration. Nat Neurosci. 2012 Sep;15(9):1272-80.*
- *Gruendemann J, Schlaudraff F, Liss B (2011): UV-laser microdissection and gene expression analysis of individual neurons from post mortem Parkinson's disease brains. Methods Mol Biol. 755:363-74.*
- *Kuras Z, Grissmer S. (2009): Effect of K+ and Rb+ on the action of verapamil on a voltage-gated K channel, hKv1.3: implications for a second open state? British Journal of Pharmacology 157(5):757-768.*
- *Andronache Z, Hamilton SL, Dirksen RT, Melzer W. (2009): A retrograde signal from RyR1 alters DHP receptor inactivation and limits window Ca2+ release in muscle fibers of Y522S RyR1 knock-in mice. Proc Natl Acad Sci USA. 106(11):4531-6.*
- *Gründemann J, Schlaudraff F, Haeckel O, Liss B (2008): Elevated alpha-synuclein mRNA levels in individual UV-laser-microdissected dopaminergic substantia nigra neurons in idiopathic Parkinson's disease. Nucleic Acids Research, 6(7):e38.*
- *Lammel L, Hetzel A, Haeckel O, Jones I, Liss B, Roeper J (2008): Unique properties of mesoprefrontal neurons within a dual mesocorticolimbic dopamine system. Neuron, 57(5):760-73.*