NEUROSCIENCE

Thesis Programme of the Curriculum
"Doctor of Philosophy"

Coordination:

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Short description:

Neuroscience is currently one of the main focuses of both national and international research programmes. The aim of neuroscience research is the elucidation of the normal function of the nervous system as well as the discovery of the molecular mechanism underlying the pathological changes in neurological and psychiatric disorders.

The nervous system is an organ system that is highly complex and involves different cell types as well as neuronal networks. This complexity is reflected by the fact that 60% of all known genes are expressed in the nervous system and 30% of the genes are nervous system specific. One third of all known human disorders is primarily neurological or has marked neurological involvement. As the ability for regeneration of the nervous system is limited, many of these disorders lead to chronic functional deficits and thus to an enormous burden on individuals and the society.

Modern neuroscience is multi-disciplinary and involves such disciplines as biochemistry, molecular neurobiology, cellular neurobiology, neurophysiology, neuropharmacology, neuroanatomy, neuropathology, neuroimmunology, clinical neuroscience, psychology, psychiatry and neurology. The aim of the neuroscience programme is to educate the students in a comprehensive, multi-disciplinary way in preparation for work within the field of neuroscience. Besides the practical dissertation, this accompanying program gives not only the theoretical backbone but also guides the students through a practical course to learn the most important techniques by actually doing them. If you are interested in this exiting field of research then search the list of participating research units, get in contact with the group leaders and apply for open positions.

The entire neuroscience PhD programme is held in the English language.

Recommended literature:

For the Neuroscience Programme we recommend:

Principles of Neural Science; Kandel RE, Schwartz JH, Jessell TM (Fourth Edition 2000) McGraw-Hill (ISBN 0-8385-7701-6)

Neuroscience. Exploring the Brain; Bear, MF, Connors, BW, Paradiso MA (Third Edition 2006) Lippincott, Williams & Wilkins, Baltimore, MD, USA

Molecular Neuropharmacology. A Foundation for Clinical Neuroscience. Nestler E.J., Hyman, S.E., Malenka, R.C. McGraw-Hill Co (2001) ISBN: 0-07-112065-3

Courses:

Basic Seminars (4 semester hours):
Passing the lecture series Basics of Neuroscience (A) is required, followed by one advanced level module (B). Students who have already successfully completed this course before beginning their PhD studies have to take four advanced level lectures.

A) **Basics of Neuroscience (3 semester hours)** This series of 45 lectures is held in a block in October and covers the following topics: i) neuroanatomy, ii) biochemistry and pharmacology of the nervous system, iii) neurophysiology, and iv) Pathobiology of the nervous system. Based on the knowledge of the lecture neurobiology (VO 300322) a broad spectrum of basic neuroscience will be covered.

B) **One of the following lectures can be chosen (1 semester hour)**
- Basic immunology of inflammatory diseases of the nervous system (H. Lassmann)
- Cell type-specific features of the CNS (J. Berger, M. Bradl, J. Bauer, S. Forss-Petter)
- The role of neuronal plasticity under physiological and pathological conditions (J. Sandkühler)
- Biochemical basis of psychiatric and neurologic diseases (W. Sieghart)
- Cellular and molecular biology of the neuron (M. Kiebler, G. Vendra, A. Konecna))
- Methods and techniques in Neuroscience (J. Berger et al.)

PhD Seminars and Practical Course (8 semester hours)
Passing the PhD Seminar "Methods and Techniques in Neuroscience" is required. However, if the PhD student has already passed "Methods and Techniques in Neuroscience" (or the equivalent Lab Course "Basics of Neuroscience") before the start of the PhD program, eight semester hours of specialized, individual research PhD Seminars should be completed.

A) PhD-Seminar "Methods and Techniques in Neuroscience" (practical course; 8 semester hours) Nine research units lead small groups of students (max. 12) through the theory and practice of techniques used in neuroscience research. The topics covered are i) neuroanatomy/histology; ii) biochemistry and pharmacology of nerve conduction; iii) neurophysiology; iv) ligand-gated jon channels; v) molecular neurobiology; vi) synaptogenesis; vii) neuroimmunology; viii) neuronal cell biology; ix) magnetic resonance and optical imaging.

B) Specialized PhD-Seminar (8 semester hours) These seminars are devoted to special topics of the individual research unit in which the PhD thesis is performed. On a weekly basis, the PhD students, post-docs and supervisors discuss the ongoing research projects of the laboratory and develop novel research topics. During these seminars, the students should acquire the ability to independently develop novel strategies to solve scientificproblems using up-to-date literature as well as the know-how of the research unit members.

Journal Club and Progress Report (12 semester hours)
A) Journal Club (6 semester hours) The Journal Club takes place on a weekly basis. The doctoral students have to attend the Journal Club each week. Each semester the PhD-Journal Club has a different thematic focus.

B) Work in Progress (6 semester hours) Every semester, in January and in July, the doctoral students present their work at Work in Progress sessions held over two days, with the participation of all the other students and the scientific staff of the Center for Brain Research and associated program partners. In the summer semester, in addition, the students give an oral or poster presentation at a PhD symposium including all the PhD students and supervising members of the Medical University of Vienna . The regular, critical review of the work by the multi-disciplinary background of the attending scientists at these sessions should ensure optimized strategies and guidance for the student's research program.

VO BASICS OF NEUROSCIENCE 3 st

Lectures from 8:15 - 10:30 from first week in October and
from 8:15 - 9:45 in the following weeks
The lectures take place in the lecture room, 1st floor,
Center for Brain Research, Spitalgasse 4, 1090 Vienna
and will be held in English language

Block 1: Neuroanatomy

Lecture 1: Histology of neurons, classification of neurons, gliacells; (CNS) astrocytes, oligodendrocytes, microglia, ependymal cells; (PNS) Schwann cells

Lecture 2: Central nervous system (from spinal cord to neocortex), meninges, ventricles, blood supply, peripheral nervous system

Lecture 3: Functional systems: reflexes, the sensomotoric und autonomic nervous system, from sensory organ to basal ganglia and neocortex

Block 2: Biochemistry and Pharmacology of the Nervous System

Lecture 4
General synaptic model
Ways for a molecule to pass a membrane;
ion channels: (as examples: K_V-and Na_V-channels)

Lecture 5
general list of Neurotransmitters, including their biosynthesis and distribution

Lecture 6
excitatory vs. inhibitory neurotransmission:
ionotropic vs metabotropic receptors;
Cys-Loop-receptors; as examples: (muscular and neuronal) nACh-Receptors

Lecture 7
ionotropic receptors:
GABA receptors and their ligands (benzodiazepines, barbiturates,…)
glycine–receptors and their anchoring at the synapse (gephyrin)
ionotropic glutamate receptors

Lecture 8
Metabotropic G-protein coupled receptors

Lecture 9
neurotransmitter inactivation; neurotransmitter transporters; drugs acting on neurotransmitter transporters (cocain, ecstasy, amphetamines, SSRI,…)

Lectures 10 – 15: Cell Biology of the Neuron: an overview is given on current topics in Cell Biology of the Neuron. The four topics will be discussed in significantly more detail in the Advanced Lecture Course Advanced Neuronal Cell Biology to be given in the summer term 2009.

Lecture 10: The formation of an axon – an overview
Current models and ideas are discussed how a neuron decides to form an axon.

Lecture 11+12: Dendrite development and synapse formation – an overview
Current models and ideas are discussed how a neuron decides to form dendrites and how synaptogenesis is thought to occur.

Lecture 13: Transport processes in nerve cells, e.g. proteins, e.g. receptor trafficking, vesicles, organelles.

Lecture 14+15: Synaptic structure and function: Spinogenesis: the formation and maintenance of dendritic spines; molecular architecture of dendritic spines and the postsynaptic density; NMDA Receptor complex; the role of adhesion molecules at the synapse; mitochondria at the synapse

Block 3: Neurophysiology

Membrane physiology

Lecture 16: Short overview over cell membrane, ion concentration differences in neurons, electrical gradient, chemical gradient, driving force, equilibrium potential, Nernst equation, resting membrane potential (RMP), Goldman equation

Lecture 17: Fundamental electrical terms (current, voltage, resisatance, capacitor,…), Ohm's law; electrical model of a cell; electrical equivalent circuits (part I)

Lecture 18: Electrical equivalent circuits (part II); current voltage response of an ideal membrane, current voltage relations of channels

Lecture 19: Action potential (AP); ionic basis for AP; different phases of an AP; AP firing patterns, diversity of APs due to presence of different ion channels; APs in nerve membrane

Lecture 20: Action potential propagation, electrotonic potentials, length constant; continuous and saltatory propagation; Patch-clamp technique

Lecture 21: Synaptic transmission; gap junctions as electrical synapses; chemical synapses; postsynaptic currents and potentials at excitatory and inhibitory synapses

Biological neural networks

Lecture 22: General aspects of biological neural networks; Information flow through nervous systems; neurons and synapses as elements of biological neural networks

Lecture 23: Mechansism of information processing (feedback, feedforward; parallel processing;…) examples of simple networks; example of complex neural network

Microscopic methods for the detection of fluorescence

Lecture 24: Fluorescence microscopy, confocal microscopy, 2-photon-laser-scanning microscopy; Principles, advantages & disadvantages of each method, stainings, examples of use in neurobiology

Sensory Physiology

Lecture 25: Fundamentals of sensory systems, sensory input and perception, sensory modality, converting external signals into neuronal information, signal transduction, encoding sensory information

Lecture 26: Example: nociception, signal processing under physiological and pathophysiological conditions exemplified by acute and by neuropathic pain mechanisms

Learning, Memory and Synaptic Plasticity

Lecture 27: Types and processes of memories, physiological and structural changes at synapse level, Hebb&LTP, facilitation, depression, depotentiation, properties, phases, cellular mechanisms

Lecture 28: Link between LTP and learning/memory, role of dendritic spines in memory processing

Block 4: Pathobiology of the Nervous System

Disorders of Neurotransmitter Dysfunction

Lecture 29: Disorders of Neurotransmitter dysfunction
Epilepsy: imbalance of excitatory and inhibitory transmission; the molecular mechanisms of the Fragile X syndrome; insight into addiction; cannabinoids, endocannabinoids

Lecture 35: Depression and Schizophrenia
Monoamine and other biological hypotheses, neurocircuitry changes, animal models, mechanisms of action of antidepressant and antipsychotic drugs

De- and Regeneration

Lecture 30: Mechanisms of neuronal degeneration; outside and inside signals: excitotoxicity, energy failure, oxidative damage, non-classical cell death pathways, neuronal dysfunction due to damage of neuronal cell processes

Lecture 31: Axonal degeneration and regeneration in the peripheral nervous system; Injury signals, Wallerian Degeneration, debris removal, mechanisms of normal and abnormal regeneration

Lecture 32: Axonal regeneration in the CNS; Differences to PNS; mechanisms of inhibition; cellular sources of inhibitory molecules;

Lecture 33: Generation and regeneration of myelin in the CNS and PNS; Basics of Schwann cell and oligodendrocyte development; essential differences between both types of cells

Lecture 34: Stem cells as therapeutic tools for CNS injuries; stem cells in the healthy CNS; current approaches and problems

Lecture 36: Alzheimer's Disease; General introduction, genetic, pathology, molecular mechanisms

Lecture 37: Parkinson's disease; Neuropathology, neurochemistry, neurocircuitry changes involved in clinical signs, mechanisms of therapy, pathogenetic mechanisms of neurodegeneration, concepts for etiology

Lecture 38: The special role of lipids in the nervous system; Special functions of different lipid classes in the nervous system, metabolism of lipids in the CNS, "Brain food" ω3 polyunsaturated fatty acids

Lecture 39: Cellular Organelles and there special role in the nervous system; Energy metabolism in the brain; intracellular degradation; leukodystrophies

Lecture 40: Myelin proteins and Leukodystrophies; The major myelin proteins and their functions; Differences between the PNS and the CNS; Lessons from dys- and demyelinated animal models; Dysfunctions lead to inherited diseases

Neuroimmunology

Lecture 41: Interaction of the nervous system with the immune system; innate (microglia cells, perivascular macrophages) and adaptive arms (T cells) of the immune system in the intact CNS; blood-brain barrier; immune surveillance, development of immune responses

Lecture 42: Degeneration as trigger for CNS inflammation; Effects of degeneration on immune surveillance and inflammation; examples of human diseases and experimental models

Lecture 43: Infection and inflammation in the CNS; most common pathogens (bacteria/viruses), routes of infection, mechanisms of tissue damage, mechanisms of immune control

Lecture 44: Autoimmune diseases in the nervous system; Discussion of antibody-mediated and T cell mediated diseases of the CNS and PNS, and of diseases with complex pathogenesis

Lecture 45: CNS injury-induced immunodepression; Stroke; damage and local immune reactions in the CNS; anti-inflammatory pathways in the periphery induced by CNS injury; cholinergic anti-inflammatory pathway

Detailed information on "Techniques in Neuroscience"

(Practical course; 8 semester hours)
The course starts around mid-November and finishes before the Christmas holidays commence.
The practical work takes place from 9:00-12:00 and 13:00-16:00 at the Center for Brain Research, 1090 Vienna, Spitalgasse 4
Due to the timetables of the involved researchers, the order of the Blocks might change.

Block 1: Neuroanatomy/Histology

Tutors: R. Höftberger, J. Bauer

Practical human neuroanatomy:
The practical part of the neuroanatomy lecture will take place in the autopsy room of the Institute of Neurologie, AKH 4J, MUW. Classification and topology of the central nervous system will be repeated and demonstrated on formalin-fixed human brains, with a special focus on areas that are involved in degenerative, metabolic, vascular, and inflammatory CNS diseases. Moreover, brains with pathological changes, including vascular lesions (infarcts), brain tumours, and neurodegeneration will be shown. Finally, students learn how to cut a brain and perform neuropathological sampling of different brain regions.

Histopathology:
Lecture:
Anatomy of the central and peripheral nervous system;
Functional systems and their organization in the nervous system;
Cellular structure, function and interaction of nerve cells and glia cells

Demonstrations:
Techniques for visualization of cells and structures of the nervous system;
Visualisation techniques in light- and electron microscopy
Immunocytochemistry
In Situ Hybridization

Practical exercises:
Practice of immunohistochemistry and in situ hybridisation;
Basics of light microscopic interpretation of tissue sections of the nervous system

Block 2: Biochemistry and Pharmacology of Synaptic Transmission

Tutors: W. Sieghart, C. Pifl, K. Fuchs, M. Berger

Binding of radioligands to receptors on brain sections, autoradiography (Theory and demonstration: M. Berger)

Uptake and release of transmitters from cell cultures with subsequent HPLC analysis, demonstration of the mechanism of action of amphetamine and cocaine (Theory and demonstration: C. Pifl)

Benzodiazepine binding assays using brain membranes, Scatchard analysis and inhibition experiments (Theory, practical experiments, demonstration, calculation of results: K. Fuchs, W. Sieghart and collaborators)

Block 3: Neurophysiology

Tutors: J. Sandkühler; B. Heinke

Lectures:
- Principles of signal processing in the nervous system (Signal transduction in receptor cells, storage and weighing of information, feature extraction in neural networks)
- Principle features of sensory systems (morphology of receptors, organization of sensory systems)
- Signal processing in the nervous system under pathological conditions exemplified by pain mechanisms

Demonstrations:
- Preparation of spinal cord slices
- Whole-cell patch-clamp recordings of postsynaptic currents and potentials
- Measurement of Ca^{2+} gradients in living cells

Exercises:
- Patch-clamp recordings in whole-cell configuration (in current- and voltage-clamp mode), Measurement of action potential firing patterns
- Realistic computer simulation of electrophysiological properties of neurons

Block 4: Ligand-gated Ion Channels

Tutors: S. Huck, P. Scholze, J. Ramerstorfer

General goal:
Calcium homeostasis in cultured neurons and glial cells; dual-electrode voltage clamp in Xenopus oocytes

Basic knowledge:
Analysis of ligand-gated ion channels in nerve cells and in heterologous expression systems

Practical skills:
Preparing recording electrodes; choice of buffer solutions; RNA injection in *Xenopus laevis* oocytes; operating voltage-clamp amplifiers; software to record and analyse currents; dose-response curves of agonists and antagonists at ligand-gated ion channels; loading of cells with the Ca^{++}-sensitive dye Fura2; Ca^{++} transients in response to nicotinic ACh receptor activation and action potentials.

Block 5: Molecular Neurobiology

Tutors: J. Berger; S. Forss-Petter

Theoretical instruction:

- Molecular mechanisms of neuronal cell differentiation.
- Aspects concerning regulation of gene expression in the nervous system.
- Quantitative and qualitative methods for analysis of gene expression (based on detection of mRNA).

Lab demonstrations and practical lab exercises:

- Cell culture models in neuroscience.
- Differentiation of neuronal precursor to neuron-like cells; observation of morphological changes (by light microscopy).
- Detection and quantitative analysis of the induction of neuron-specific genes during differentiation using Real-Time RT-PCR.
- 2-Dimensional gel electrophoresis for analysis of the peroxisomal proteome (*demonstr*.)

Block 6: Synaptogenesis

Tutor: R. Herbst

Lecture:
- Introduction in the devopment and function of the motor system
- Introduction into molecular aspects involved in synaptogenesis
- The neuromuscular synapse: a model system

Demonstrations and practical exercises:
- Acetylcholine receptor clustering assay (differentiation and induction of muscle cell cultures, acetylcholine receptor staining, fluorescence microscopy)
- Acetylcholine receptor pull-down and analysis by Western blotting (Acetylcholine receptor labelling, generation of cell lysates, SDS-PAGE, Western blotting)
- NMJ staining (immunohistochemistry, muscle fiber dissection, fluorescence microscopy)

Block 7: Neuroimmunology

Tutor: M. Bradl; B. Schwerer

Lecture and demonstrations:
Neuroimmunological techniques to determine T-cell and antibody reactivities; interactions between cells of the immune system and cells of the central nervous system.

Laboratory courses:
Antibody detections with ELISA; isolation of T-cells from lymphatic tissue, specificity tests to determine antigen-recognition of auto-aggressive T cells; testing antigen recognition and cytokine secretion with ELISPOTs; analysing immune-mediated tissue damage.

Block 8: Neuronal Cell Biology

Tutor: M. Kiebler

During this practical course, the students are introduced to two independent lines of experiments: first, the uses of biochemical separations and detection methods for the study of gene expression in neural cells and tissues. Soluble lysates of mammalian neural tissue will be created and differential extractions of functionally significant proteins will be performed. These proteins are then detected by SDS-PAGE and quantitative Western blots using infrared fluorescence detection (Li-Cor system). Secondly, the students will transiently transfect primary cultures of hippocampal neurons using DNA/CaPOi precipitates and COS-7 fibroblasts using lipofection. Expression of fluorescent proteins in mammalian cells will be then monitored using multi-colour fluorescence microscopy. Finally, immunocytochemistry will be performed on both transfected neurons and COS cells. Neurons will be immunostained with different neuronal markers (e.g. MAP2 and tau for dendrites and axons, respectively) and with markers of either pre- (e.g. synapsin I) or post-synaptic (e.g. PSD95) sites, and images will be acquired using digital imaging hardware and software.

Block 9: Magnetic Resonance and Optical Imaging

Functional Magnetic Resonance Imaging
Tutor: Prof. Dr. Roland Beisteiner et al.

It intends to present an overview about the background and applicability of the fMRI technique. The contents comprises:
- Neuroanatomical Basis for Functional Imaging
- Physical Basis of fMRI and Experimental Standard Setups
- Event related fMRI
- Standard Data Analysis
- Clinical fMRI diagnostics
- Examples for motor localization
- Examples for language localization
- Examples for memory localization
- Examples for a neuroscientific applications
- Practical Examples with Hands On Session

Optical Imaging
Turtors: H.U. Dodt, K. Becker, N. Jährling

- In the first lecture advanced methods in light microscopy are introduced. It will be explained how microscopical techniques like phase-contrast, DIC, fluorescence microscopy, confocal microscopy and others work and are applied in daily practice.

- Ultramicroscopy is a new microscopical technique which allows for 3D reconstruction of specimens which are too large for conventional confocal microscopy. In this lecture the students will be introduced in this novel technique.

- 3D-image reconstruction requires the use of sophisticated image reconstruction software. Different software packages for this purpose already exist on the market. In this exercise students will learn how to reconstruct 3D-objects from ultramicroscopical data with Amira 4.1.

Detailed information on “special neuroscience lectures”

- **Basic immunology of inflammatory diseases of the nervous system**
  - Basic mechanisms of immune nervous system interactions
  - Immune surveillance of the nervous system
  - Interactions between immune system, nervous system and endocrine system in normal immunity and immune mediated diseases
  - Infectious diseases of the nervous system: interaction of pathogens with nervous tissue, invasion of pathogens into the central and peripheral nervous system; immune control of CNS infection; immune mediated CNS damage; infection induced autoimmunity of the nervous system; therapeutic consequences
  - Autoimmune diseases: principal mechanisms of autoimmunity; mechanisms of immune mediated tissue damage; control of autoimmunity and therapeutic consequences
  - Immune mediated mechanisms in the pathogenesis of neurodegeneration
  - Protective autoimmunity and regeneration in the central nervous system
  - Diseases: bacterial meningitis and encephalitis, virus induced diseases (AIDS, herpes virus encephalitis, subacute sclerosing
  panencephalitis, etc.) multiple sclerosis and other inflammatory demyelinating diseases
  - Antibody mediated diseases of the peripheral nervous system and the neuro-muscular junction (for instance myasthenia gravis)

  (H. Lassmann)

- **Cell type-specific features of the CNS**

  This lecture series will focus on cell type-specific mechanisms and features of the CNS, including aspects of Development (cell lineage, origin, interactions, migration, differentiation); Histology and Cell biology (cell-specific markers, morphology, intracellular transport, neurotransmitter localisation and release, intercellular interactions); Regulation of gene expression (transcription, translation, post-translational modification and signal transduction); Molecular mechanism of inherited neurodegenerative disorders and corresponding disease models (e.g. Huntington disease, leukodystrophies, Alexander disease) for neurons and glia."

  (J. Berger, M. Bradl, S. Forss-Petter and J.Bauer)

- **The role of neuronal plasticity under physiological and pathological conditions**

  Long-lasting changes in properties of individual neurons or the connection among them is called neuronal plasticity. Neuronal plasticity can be observed from the earliest moments of neuronal development until adulthood.

  Here, we will focus on neuronal plasticity that is required for learning and memory formation in the adult under normal conditions. In addition we will discuss neuronal plasticity that may become relevant for the aetiology and pathogenesis of diseases of the nervous system. Principles of neuronal plasticity will be presented first followed by discussions of relevant state-of-the-art publications.

  (J. Sandkühler)

- **Biochemical basis of psychiatric and neurologic diseases**

  This one-hour lecture (1-stg) will be held as a block of 7 lectures on selected Thursdays, 17h-19h, at the Center for Brain Research, 1st floor, large seminar room, during the summer semester only. The exact days when the lecture will be held will be announced at the homepage of the Center for Brain Research.

  1. Lecture: Central and peripheral nervous system, neurons, axonal transport, targeting, synaptogenesis, glia cells, nervous system tumors, demyelinating diseases.
  2. Lecture: Resting potential, action potential, voltage clamp, patch clamp, structure and function of ion channels, ion channel diseases.
  3. Lecture: Transmitters, mechanism of synaptic transmission, epsp, ipsp, receptors, signal transduction, electrical synapse.
  4. Lecture: Acetylcholine system, myasthenia gravis, noradrenalin system, dopamine system, plasticity of the nervous system, Parkinson’s disease.
  5. Lecture: Serotonin system, depression, GABA system, epilepsy, anxiety.
  6. Lecture: Glutamate system, Huntington’s disease, learning, memory
  7. Lecture: Alzheimer’s disease, peptide systems, pain, addiction, schizophrenia

  (W. Sieghart)

- **Cellular and molecular biology of the neuron**

  Abstract: This lecture series is designed to introduce into cell and molecular biological topics of nerve cells. It serves a dual function: on one side, basics and general concepts will be outlined, e.g. cell lineage, cell polarity, axon guidance, dendrite development and dendritic spine morphogenesis, protein and RNA sorting, the secretory and endocytotic pathways, axoplasmic transport, and the neuronal cytoskeleton. On the other side, current topics of neuro- and cell biology will be discussed, e.g. neuronal stem cells, small RNAs (siRNAs, microRNAs and their role in the brain), as well as the hippocampus and its role for learning and memory. Therefore, the lecture series is open for students at all levels, e.g. undergraduate students and PhD students, since most lectures do not necessarily require previous knowledge of the topic. This lecture series has been given at the University of Tübingen to both biology as well as to neurosciences students holding a bachelor degree as part of the cell biology or the Graduate School for Neural Sciences programmes and have been continuously updated. These lectures are available through the internet.
  (M. Kiebler, Georgia Vendra and Anetta Konecna)

  Detailed list of lectures:
  1. General assembly + Introduction into the lecture series
  2. Architecture and development of the invertebrate nervous system (NS)
  3. Architecture and development of the vertebrate nervous system (NS):
     - Neural induction and patterning
     - Neural stem cells and cell fate determination
  4. Cell migration in the developing vertebrate NS
  5. Axon guidance
  6. Cell polarity in the nervous system
  7. The diverse functions of RNA localization - RNA localization in the nervous system
  8. Mechanisms of RNA localization – RNA imaging
  9. Regulation of gene expression and mRNA translation in the NS
  10. Trafficking in the CNS: SNARE hypothesis, motor proteins
  11. Dendrite development and synapse formation
  12. Structure and function of the mature synapse
  13. Cell biology of learning & memory (part I)
  14. Cell biology of learning & memory (part II)
  15. Final exam

List of Research groups and techniques

As it is not possible to enter the "Neuroscience programme" without a research position, it is most important to find the research position you are most interested in among the research units listed below. Go to the website of the Center for Brain Research for research units of the Center for Brain Research or to the website given beside the name of the head of the research unit (for laboratories not located in the Center for Brain Research) to get more information on the topic and methodology followed within the respective group.

The availability of research positions is rapidly changing. Some of the currently available positions e.g. those of the Center for Brain Research, Medical University of Vienna, can be found on the homepage. Even if currently no research position is available within the research unit you are mostly interested in, it might be beneficial to contact the head of the respective research unit for a better estimation of availability in the future. Only highly motivated applicants will be able to enter the programme.

Research groups at the Center for Brain Research, Medical University Vienna, Spitalgasse 4, 1090 Vienna, Austria
Open positions and information on the research topics and used methodology and publications can be found at the WWW-site: http://www.univie.ac.at/brainresearch/

Berger, Johannes	Topic: Molecular mechanisms in neurodegeneration, X-ALD e-Mail: johannes.berger@meduniwien.ac.at Tel: (+43-1-) 4277 62812
Bradl, Monika	Topic: Cellular neuroimmunology e-Mail: monika.bradl@meduniwien.ac.at Tel: (+43-1-) 4277 62813
Ernst, Margot	Topic: GABA A receptor: structure, function and pharmacology; Bioinformatics e-Mail: margot.ernst@meduniwien.ac.at Tel (+43-1-) 4277 62895
Fuchs, Karoline	Topic: Molecular genetic investigation of psychiatric and neurological diseases e-mail: karoline.fuchs@meduniwien.ac.at Tel: (+43-1-) 4277 62952
Herbst, Ruth	Topic: Development and Function of Neuromuscular Synapses e-mail: ruth.herbst@meduniwien.ac.at Tel: (+43-1-) 4277 62910
Huck, Sigismund	Topic: Biology of nicotinic receptors, mechanisms of transmitter release, Ca^{++} homeostasis e-Mail: sigismund.huck@meduniwien.ac.at Tel: (+43-1-) 4277 62872
Kiebler, Michael	Topic: RNA localization in mammalian neurons e-mail: michael.kiebler@meduniwien.ac.at Tel: (+43-1-) 4277 62920
Konecna, Anetta	Topic: Biochemistry of neuronal RNPs e-Mail: anetta.konecna@meduniwien.ac.at Tel : (+43-1-) 4277 62921
Lassmann, Hans	Topic: Inflammatory brain diseases, Multiple Sclerosis and experimental models e-mail: hans.lassmann@meduniwien.ac.at Tel: (+43-1-) 4277 62811

Pifl, Christian	Topic: Pharmacology of neurotransmitters; Molecular mechanisms underlying Parkinson´s Disease and psychostimulant drugs e-Mail: christian.pifl@meduniwien.ac.at Tel: (+43-1-) 4277 62894
Sandkühler, Jürgen	Topic: Synaptic plasticity in health and disease e-Mail: jürgen.sandkühler@meduniwien.ac.at Tel: (+43-1-) 4277 62834
Sarto-Jackson, Isabella	Topic: Constructing Inhibitory Synapses – interaction of $GABA_A$ receptors with other receptors or proteins e-Mail: isabella.sarto-jackson@meduniwien.ac.at Tel (+43-1-) 4277 62953
Scholze, Petra	Topic: nicotinic Acetylcholine receptors, Neurotransmitter Transporters e-Mail: petra.scholze@meduniwien.ac.at Tel: (+43-1-) 4277 62873
Sieghart, Werner	Topic: GABA A receptor: structure, function and pharmacology e-Mail: werner.sieghart@meduniwien.ac.at Tel: (+43-1-) 4277 62950
Vendra, Georgia	Topic: Visualization of RNA transport in living neurons e-Mail: georgia.vendra@meduniwien.ac.at Tel: (+43-1-) 4277 62921

Univ. Prof. Dr. Johannes Berger
Division of Neuroimmunology, Center for Brain Research,
Medical University of Vienna
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Description of thesis projects:
Currently the main interest of our research is related to peroxisomes. Peroxisomes are lipid-metabolising organelles that are present in nearly all eukaryotic cells and perform functions that are essential for life. Genomic and proteomic approaches are performed with the aim to gain insight into the role of peroxisomes in the nervous system. In addition to the general aspects of peroxisomes in health and disease, our research is focused on X-linked Adrenoleukodystrophy (X-ALD), the most common peroxisomal disorder. X-ALD is an inherited neurodegenerative disorder that is associated with inflammation and irreversible destruction of myelin in the brain. We are using cell culture and mouse models that lack functional ALD protein to study the basic pathomechanisms of X-ALD and to test novel molecular strategies for therapeutic intervention (pharmacological gene therapy).

Techniques and infrastructure:
Cell culture of cell lines and primary cells, variety of transfection techniques (lipofection, electroporation, DEAE-dextran transfection, Calcium phosphate transfection, viral infection), immunofluorescence, reporter gene assays (ß-gal- and luciferase-assay), PCR, RT-PCR, Real Time PCR (TaqMan and Sybergreen), DNA and RNA isolations, Northern Blot, Southern Blot, Dot Blot, cDNA cloning, use of RACE-libraries, site-directed mutagenesis, Electrophoretic mobility shift assay, microarray analysis, Transgenic and Knock-Out mouse models, preparation of membrane fractions, subcellular fractionation, a variety of different enzyme assays including acyl-CoA synthetase assay and mitochondrial and peroxisomal ß-oxidation, Western Blot analysis, immunoprecipitations, 2D-gel electrophoresis (IEF and NEFGE),

Thesis Topics:
Identification of the molecular basis leading to neurodegeneration and inflammation in X-linked adrenoleukodystrophy.

Elucidation of the role of peroxisomes in the CNS in health and disease

Curriculum Vitae

Univ. Prof. Dr. Johannes Berger

Center for Brain Research, Medical University Vienna, Spitalgasse 4, 1090 Vienna

Personal Data

Date of Birth:	26.05.1964
Place of Birth:	Vienna
Nationality	Austria

Education

1991-1992	Military service
1989-1991	Thesis at the Sandoz Research Institute (SFI), Department of Antiretroviral Therapy: Analysis of Functional Domains in the HIV-1 Rev and HTLV-I Rex *trans* -Regulatory Proteins. Degree: Dr. rer. nat. (Ph.D)
1988-1989	Diploma at Institute of Tumour Biology and Cancer Research, University of Vienna; Degree: Mag. rer. nat. (Master Sc)
1984-1989	Studies of Biology / Genetics; University of Vienna

Career History

Since 2007	Univ. Prof. for Pathobiology of the Nervous System, Medical University Vienna
Since 2003	Ao. Univ. Prof. in Biochemistry, Faculty of Science and Mathematics, University of Vienna
1999-2007	Associate professor and head of a research unit for molecular biology at the Brain Research Institute, Medicine University Vienna.
1999	Habilitation in Molecular biology, Medical Univ. Vienna
1993	Establishment of a research group for molecular neurobiology. Identification and characterization of genes, domains and mutations concerning inherited disorders of the nervous system.
1992	Organization and set-up of a molecular biology laboratory.
1992-1999	Univ. Assistant at the Institute of Neurology, Faculty of Medicine, Univ. of Vienna.

Career-related Activities

since 2005	Coordination of Integrated EU project to decipher the biological function of peroxisomes in health and disease
2004-2007	Coordinator of an EU-project concerning the development of novel therapeutic strategies for X-linked adrenoleukodystrophy
2002 and 2006	Establishment of a Neuroscience programme as well as a PhD programme at the Brain Research Institute in Vienna
Since 2001	Lecturer at the Faculty of Science and Mathematics, Univ. of Vienna: e.g. Neurobiology and Molecular Biology of the Brain;
Since 1996	Reviewing for several international journals including: Hum Mol Genet, Hum Mutat, Hum Genet, Mol Genet Metab, J Med Genet, Eur J Hum Genet, J Inherit Metab Dis, Electrophoresis, J Lipid Res, Brain Pathol, Acta Neuropathol, Neuroscience, The Lancet, FEBS Lett, J Biol Chem
since 1996	Member of the referee board of the Neurological Foundation of New Zealand
since 1994	Lecture at the Medical Univ. of Vienna: e.g. Introduction to Neurobiology; Biochemistry; Chemistry
since 1993	Officer for biological safety for the Neurological Institute, the Brain Research Institute and since 2001 for the shared animal-facility Borschkegasse, Univ. of Vienna,
since 1990	Supervision of graduate students, and laboratory courses.

Awards

2001	Kardinal-Innitzer-Förderungspreis

2003	OTTO LOEWI AWARD (financed by GlaxoSmithKline, awarded by the Austrian Neuroscience Association)
2005	Medical University of Vienna-Researcher of the Month

Memberships
Austrian Neuroscience Association
Austrian association for biochemistry and molecular biology

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*
05.07.2007-04.07.2011	COST-Action BM0604	Myelin Orphan in Health - MYELINET
01.01.2005-31.12.2008	EU-Project	Peroxisomes in health and disease
01.01.2005-31.12.2006	Myelin Project	Pharmacological gene therapy in X-ALD
01.01.2004-31.08.2008	WWTF	The inflammatory cerebral form of X-ALD: From the molecular mechanism of inflammation to the prediction of clinical outcome and treatment efficiencies
01.04.2004-31.03.2007	EU-Project	X-linked Adrenoleukodystrophy (X-ALD): pathogenesis, animal model and therapy. An european project
01.10.2003-01.01.2009	ELA-Project	X-linked Adrenoleukodystrophy (X-ALD): pathogenesis, animal models and therapy
01.04.2002-30.11.2005	FWF	Proteom-Analyse von Peroxisomen
01.06.2001-31.05.2004	ÖNB	Stimulation of ALDR gene expression in Macrophages/Microglia cells: A novel therapeutic approach for X-linked Adrenoleukodystrophy
13.04.2000-31.12.2003	FWF	X-linked Adrenoleukodystrophy and the Very Long-Chain Acyl-CoA Synthetase

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
13.04.2000-28.02. 2004	Mag. Peter Fraisl	Isolation and charakterisation of VLACS isoforms
14.12.2000-31.03 2004	Mag. Mihaela Zigman	Functional analysis of the peroxisomal membrane proteins ALDP and ALDRP
18.04.2002-08.03.2005	Mag. Heidelinde Rampler	Characterisation of the transcriptional regulation of the ABCD2 gene
18.02.2002-30.09.2005	Mag. Iris Oezen	Influence of the accumulation of very long-chain fatty acids on mitochondrial function in adrenoleukodystrophy protein deficiency
01.01.2005-30.08.2007	Dr. Martina Dumser	Mouse models for X-linked adrenoleukodystrophy
1.4.2006 -	Dipl. Ing, Mag. Christoph Wiesinger	Characterisation of the substrate specificity of peroxisomal ABC-transporters with the main focus oon PMP70 and ALDP
21.08.2006-	Mag. Zahid Muneer	Evaluation of microglia/macrophages cells as potential targets for pharmacological gene therapy in X-linked adrenoleukodystrophy
06.10.2007-	Mag. Jianqiu Kou	Characterisation of the peroxisomal HMGCR

Publications
60 original publications in scientific journals, six reviews and book chapters, and one book as editor together with Dr. Köhler and Dr. Stöckler; >30 invited lectures, one patent;
8 DNA-sequence entries including the descriptions of five new genes

Peer reviewed manuscripts 2003-2008 (original research and reviews)

First, last or corresponding author manuscripts:

Rampler H., Weinhofer I., Netik A., Forss-Petter S., Brown PJ., Oplinger JA., Bugaut M., **Berger J**. (2003) Evaluation of the therapeutic potential of PPAR alpha agonists for X-linked adrenoleukodystrophy. Mol. Genet. Metab. 80: 398-407.

Fraisl P., Forss-Petter S., Zigman M., **Berger J.** (2004) Murine bubblegum orthologue is a microsomal very long-chain acyl-CoA synthetase. Biochem J. 377: 85-93.

Oezen I., Rossmanith W., Forss-Petter S., Kemp S., Voigtländer T., Moser-Thier., Wanders R., Bittner R., **Berger J.** (2005) Accumulation of very long-chain fatty acids does not affect mitochondrial function in Adrneoleukodystrophy protein deficiency. Hum. Mol. Genet. 14: 1127-1137.

Weinhofer I., Forss-Petter S., Kunze M., Zigman M., **Berger J.** (2005) X-linked adrenoleukodystrophy mice edemonstrate abnormalities in cholesterol metabolism. FEBS Letters 579: 5512-5516.

Weinhofer I., Kunze M., Rampler H., Bookout A.L., Forss-Petter S., **Berger J.** (2005) LXRalpha interferes with SREBP1c-mediated Abcd2 expression: novel cross-talk in gene regulation. J. Biol. Chem. 280: 41243-41251.

Berger J., Forss-Petter S., Oezen I., Weinhofer I. (2005) Pharmacological treatment based on gene redundancy: a novel therapeutic approach for X-linked adrenoelukodystrophy In: **Berger J.** Stöckler-Ipsiroglu S. and Köhler W.; Understanding and Treating of X-linked adrenoleukodystrophy: Present State and Future Prospectives, 1st edn. SPS-Publications, Heilbronn

Weinhofer I., Kunze M., Stangl H., Porter F.D., **Berger J.** (2006) Peroxisomal cholesterol biosynthesis and Smith-Lemli-Opitz syndrome. Biochem. Bioph. Res. Comm. 345: 205-209.

Fraisl P., Tanaka H., Forss-Petter S, Lassmann H., Nishimune Y., **Berger J.** (2006) A novel mammalian bubblegum-related acyl-CoA synthetase restricted to testes and possibly involved in spermatogenesis. Arch. Biochem. Biophys. 451: 23-33.

Rauschka H., Colsch B., Baumann N., Wevers R., Schmidbauer M., Krammer M., Turpin J.C., Lefevre M., Olivier C., Tardieu S., Krivit W., Moser H., Moser A., Volkmar Gieselmann V., Zalc B., Cox T., Reuner U., Tylki-Szymanska A., Aboul-Enein F., LeGuern E., Bernheimer H., **Berger J.** (2006) Late onset metachromatic leukodystrophy: genotype strongly influences phenotype. Neurology 67: 859-863.

Berger J., Gärtner J. (2006) X-linked adrenoleukodystrophy: Clinical, biochemical and pathogenetic aspects. BBA-Mol. Cell. Res. 1763:1721-1732

Höftberger R., Kunze M., Weinhofer I., Aboul-Enein F., Voigtländer T., Oezen I., Amann G., Bernheimer H., Budka H., **Berger J.** (2007) Distribution and cellular localization of adrenoleukodystrophy protein in human tissues: Implications for X-linked adrenoleukodystrophy. Neurobiol. Dis. 28:165-174.

Co-author manuscripts:

Lassmann H., Reindl M., Rauschka H., **Berger J.,** Aboul-Enein F., Berger T., Zurbriggen A., Luterotti A., Brück W., Weber JR., Ullrich R., Schmidbauer M., Jellinger K., Vanddevelde M. (2003) A new paraclinical CSF marker for hypoxia-like tissue damage in multiple sclerosis lesions. Brain 126: 1347-1357.

Fourcade S., Savary S., Gondcaille C., **Berger J.,** Netik A., Cadepond F., Etr ME., Molzer B., Bugaut M. (2003) Thyroid hormone induction of the drenoleukodystrophy-related gene (ABCD2). Mol. Pharmacol. 63: 1296-1303.

Mashek D.G., Bornfeldt K.E., Coleman R.A., **Berger J.,** Bernlohr D.A., Black P., DiRusso C.C., Farber S.A., Guo W., Hashimoto N., Khodiyar V., Kuypers F.A., Maltais L. J., Nebert D.W., Renieri A., Schaffer J.E., Stahl A., Watkins P.A. , Vasiliou V., Yamamoto T.T. (2004) Revised nomenclature for the mammalian long chain acyl-CoA synthetase (ACS) gene family. J. Lipid Res. 45: 1958-1961.

Birner P., Preusser M., Gelpi E., **Berger J.,** Gatterbauer B., Ambros I.M., Ambros P.F., Acker T., Plate

K.H., Harris A.L., Hainfellner J.A. (2004) Expression of hypoxia-related tissue factors correlates with diminished survival of adjuvantly treated patients with chromosome 1p-aberrant oligodendroglial neoplasms: therapeutic implications. Clin. Cancer Res. 10: 6567-6571.

Pei Z., Fraisl P., **Berger J.,** Jia Z., Forss-Petter S., Watkins P. (2004) Mouse very long-chain acyl-CoA synthetase 3/Fatty Acid Transporter Protein 3 Catalyzes fatty acid activation but not fatty acid transport in MA-10 cells. J. Biol. Chem. 279: 54454-54462.

Neuberger G., Kunze M., Eisenhaber F., **Berger J.,** Hartig A., Brocard C. (2004) Hidden localisation motifs: Naturally occurring peroxisomal targeting signals in non-peroxisomal proteins. Genome Biol. 5: R97.

DiRusso C. C., Li H, Drwis D, Watkins P, **Berger J.,** Black P.N. (2005) Comparative biochemical studies of the murine fatty acid transport proteins (FATP) expressed in yeast. J. Biol. Chem. 280: 16829-16837.

Lugowska A., **Berger J.,** Tylki-Szymanska A., Löschl B., Molzer B., Zobel M., Czartoryska B. (2005) Molecular and phenotypic characteristics of metachromatic leukodystrophy patients from Poland. Clin. Genet. 68: 48-54.

Lugowska A., Amaral O., **Berger J.,** Berna L., Bosshard N.U., Chabas A., Fensom A., Gieselmann V., Gorovenko NG., Lissens W., Mansson J.E., Marcap A., Michelakakis H., Bernheimer H., Olkhovych N.V., Regis S., Sinke R., Tylki-Szymanska A., Czartoryska B. (2005) Mutations c.459+1G>A and p.P426L in the ARSA gene: prevalence in metachromatic leukodystrophy patients from European countries. Mol. Genet. Metab. 86: 353-359.

Golovko Y.M., Rosenberger T.A., Fargeman N.J., Feddersen S., Cole N.B, Pribill I., **Berger J.,** Nussbaum R.L., Murphy E.J. (2006) Acyl-CoA Synthetase activity links wild-type but not mutant α-synuclein to brain arachidonate metabolism. Biochemistry 45: 6956-6966.

Yang J-W., Afjehi-Sadat L., Gelpi E., Kunze M., Höger H., Fleckner J., **Berger J.,** Lubec G (2006) Proteom Profiling in the rat Harderian gland. J. Proteome Res. 5: 1751-1762.

Hochmeister S., Grundtner R., Bauer J., Engelhardt B., Lyck R., Gordon G., Korosec T., Kutzelnigg A., **Berger J.,** Bradl M., Bittner R.E., Lassmann H., (2006) Dysferlin Is a New Marker for Leaky Brain Blood Vessels in Multiple Sclerosis. J. Neuropath. Exp. Neurol. 65:855-865.

Barceló-Coblijn G., Golkovko MY., Weinhofer I., **Berger J.,** Murphy E.J. (2007) Brain neutral lipids mass is increased in α-synuclein gene ablated mice. J. Neurochem. 101:132-141.

Dumser M., Bauer J., Lassmann H., **Berger J.,** Forss-Petter S. (2007) Lack of Adrenoleukodystrophy protein enhances oligodendrocyte disturbance and microglia activation in mice with combined Abcd1/Mag deficiency. Acta. Neuropath. 114:573-586.

Wiese S., Gronemeyer T., Ofmann R., Kunze M., Grou CP:, Almeida JA., Eisenacher M., Stephan C., Hayen H., Pawlas M., Bunse C., Schollenberger L., Korosec T., Waterham HR., Schliebs W., Erdmann R., **Berger J.,** Meyer HE., Just W., Azevedo JE., Wanders RJA., Warscheid B. (2007) Proteomic characterization of mouse kidney peroxiosmes by tandem mass spectrometry and protein correlation profiling. Mol Cell Proteomics 2007 6: 2045-2057.

Invited Talks:

more than 30

Univ.Doz. Dr. Monika Bradl
Division of Neuroimmunology, Center for Brain Research,
Medical University of Vienna
monika.bradl@meduniwien.ac.at

Description of thesis project:

Abstract:

Our research centers around three major topics.
Topic 1 deals with the bidirectional communication between cells of the immune system with the intact and degenerative central nervous system (CNS). These interactions are studied at the cellular and molecular level, using different models of in vitro culture.
Topic 2 deals with the development and differentiation of microglia cells, their heterogeneity, and their contribution to tissue injury and repair.
Topic 3 is a joint venture between the group of Prof. Lassmann and my group. Here, we use gene expression studies and microarray analysis of archival tissue specimen with well defined pathological changes (for example, from patients suffering from multiple sclerosis, Alzheimer´s disease or meningitis) to learn more about specific molecular/cellular pathways leading to the tissue damage observed in these patients.
All these studies should provide informations about the factors and signals that guide cells of the immune system to certain areas of the intact, inflamed or degenerative CNS, mediate tissue damage and repair, and lead to the resolution of inflammatory lesions within the CNS.

Techniques and infrastructure:

We have a well-equipped cell culture laboratory and facilities for molecular biology.
The techniques currently used are

- histology
- all molecular techniques used for the isolation and characterization of RNA and DNA
- microarray analysis
- PCR analysis
- all cell culture techniques, starting from the setup of primary cultures of glia, microglia, macrophages and T cells to the production of T cell lines and clones
- all techniques needed to study the behaviour of defined cell populations (i.e specificity tests, life video microscopy)
- all techniques needed to characterize the production and/or secretion of proteins (i.e. FACS analysis, Elisa, Elispot)

Thesis and diploma topics:

The thesis will cover different aspects of the immune surveillance or inflammation of the intact and degenerating CNS, or mechanisms and consequences of the activation and differentiation of microglia cells

Curriculum Vitae

Univ. Doz. Dr. Monika Bradl

Medical University Vienna, Center for Brain Research, Division of Neuroimmunology
Spitalgasse 4, A-1090 Vienna, Austria

Personal Data

Date of Birth:	04.08.1961
Place of Birth:	Lindau
Nationality	German

Education

October 2003	Approval of equivalence of habilitation at the Medical University of Vienna
January 2003	Habilitation in "Neuroimmunology",
March 1989	obtained degree: Dr. rer. nat.
1986	obtained degree: Dipl.-Biol.
1980 –1986	studied "Biology" at the Julius Maximilians University Würzburg, Germany
1980	Matura

Career History

October 2003	Approval of equivalence of habilitation – **venia docendi** at the Medical University of Vienna
January 2003	**Habilitation** in "Neuroimmunology", Ludwig-Maximilians-University, München, Germany;
since March 2002	Medical University Vienna, Center of Brain Research, Dept. Neuroimmunology. Head of the group for "Cellular Neuroimmunology".
1992-2002	Group leader at the Max-Planck-Institute for Neurobiology in Martinsried in the department of Neuroimmunology
1989 – 1992	Postdoctoral period at the Fox Chase Cancer Center, Philadelphia, USA
1986 – 1989	Thesis work at the Max-Planck-Society, Clinical Research Group for multiple sclerosis. Degree **Dr. rer. nat.**, Julius Maximilians University, Würzburg, Germany
1986	diploma in "Biology": **Dipl.-Biol.**
1980 - 1986	studied "Biology" at the Julius Maximilians University, Würzburg, Germany

Career-related Activities

Acquisition of grants

Contribution to text books

Reviewer for scientific journals

Training of diploma students and PhD students

Lecturer at the Medical University of Vienna, and at the University of Vienna

establishments of research groups:
1. Medical University of Vienna, Center for Brain Research Dept. Neuroimmunology
2. Max-Planck-Institute for Neurobiology, Dept. Neuroimmunology, Martinsried, Germany

Habilitation for "Neuroimmunology"

Postdoctoral training at the Fox Chase Cancer Center, Philadelphia, USA

Memberships
Member of the International Society for Neuroimmunology (ISNI)
Member of the Austrian Society for Allergology and Immunology (ÖGAI)

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*
01.01.2003-31.08.2006	FWF	Differentiation and development of microglia cells
01.01.2004-31.08.2008	WWTF	The inflammatory cerebral form of X-ALD: From the molecular mechanism of inflammation to the prediction of clinical outcome and treatment efficiencies
01.01.2006-31.12.2007	ÖNB	Untersuchungen des anti-inflammatorischen cholinergen Systems bei degenerativen und entzündlichen Erkrankungen des ZNS
01.03.2007-31.12.2008	WFL	Microglia diversity and its consequences for neuroprotection and immune regulation

PhD and supervision of diploma students in the last 5 years (2003-2008)

Period	*Name of student*	*Topic*
01.02.2003-28.02.2006	Mag. Roland Grundtner	Characterization of T cells engaged in CNS immune surveillance
01.11.2005-31.10.2008	Dr. Milena Adzemovic	Differentiation of microglia cells in vivo
01.01.2007-31.12.2009	Mag. Eva-Maria Nicolussi	RNA analysis of archival MS and EAE tissues
01.01.2007-31.12.2009	Mag. Rakhi Sharma	joint project with Prof. Lassmann: Molecular analysis of inflammatory lesions in pattern III multiple sclerosis cases and their corresponding animal model
01.10.2007-31.09.2010	Mag. Marie-Therese Fischer	joint project with Prof. Lassmann: Molecular analysis of chronic progressive multiple sclerosis cases and their corresponding animal models.
01.05.2004-31.04.2005	Beate Hartinger	diploma thesis: Neuregulin expression in the spinal cord and its

		consequences for the function of microglia cells
01.09.2004- 31.08.2005	Manuel Zeitelhofer	diploma thesis: Dendritic cells in the central nervous system
01.07.2005- 31.06.2006	Lucia Schoderböck	diploma thesis: Molecular characterization of microglia cells in the central nervous system
01.02.2006- 31.08.2006	Susanna Olscher	diploma thesis: Transmigration of dendritic cells through the blood-brain barrier
01.01.2006- 31.10.2006	Claudia Crupinschi	diploma thesis: Molecular characterization of microglia cell activation
01.04.2006- 31.11.2006	Eva-Maria Nicolussi	diploma thesis: Molecular characterization of inflammatory lesions of the central nervous system
01.03.2007- 31.09.2007	Marie-Therese Fischer	diploma thesis: Plasticity of microglia cell activation
01.12.2007- 31.05.2008	Ephraem Leitner	diploma thesis: Characterizations of microglia subpopulations

Publications

Peer reviewed manuscripts 2003-2008 (original research and reviews)
First, last or corresponding author manuscripts:

Bradl, M. and Hohlfeld, R. (2003). Neuroscience for Neurologists: molecular pathogenesis of neuroinflammation. *J. Neurol. Neurosurg. Psychiatry* 74:1364-1370

Aboul-Enein, F., Bauer, J., Klein, M., Schubart, A., Flügel, A., Ritter, T., Kawakami, N., Siedler, F., Linington, C., Wekerle, H., Lassmann, H., **Bradl, M**. (2004). Selective and antigen dependent effects of myelin degeneration on central nervous system inflammation. *J. Neurop. Exp. Neurol.* 63:1284-1296

Bradl, M., Bauer, J., Flügel A., Wekerle H., and Lassmann, H. (2005). Complementary contribution of CD4 and CD8 T lymphocytes to T cell infiltration of the intact and the degenerative spinal cord. *Am. J. Path.* 166: 1441-1450

Bradl, M., and Lassmann, H. (2005) The role of autoimmunity in multiple sclerosis. In: Molecular Autoimmunity. Zouali, M. (ed), Springer Science+Business Media, New York, p. 209-225.

Bradl, M. (2006) Progenitors and precursors of neurons and glial cells. In: Janigro, D. (ed). Cell cycle in CNS development. Humana Press, Totowa, New Jersey, USA, pp 23-29.

Aboul-Enein, A., Weiser, P., Höftberger, R., Lassmann, H., and **Bradl, M.** (2006) Transient axonal injury in the absence of demyelination: a correlate of clinical disease in acute experimental autoimmune encephalomyelitis. Acta Neuropathol. 111: 539-547

Grundtner, R., Dornmair, K., Dahm, R., Flügel, A., Kawakami, N., Zeitelhofer, M., Schoderboeck, L., Nosov, M., Selzer, E., Willheim, M., Kiebler, M., Wekerle, H., Lassmann, H., and **Bradl, M.** (2007). Transition from enhanced T cell infiltration to inflammation in the myelin-degenerative central nervous system. Neurobiol. Dis. 28: 261-275

Bradl, M., Dornmair, K., and Hohlfeld, R. New tools for investigating the immuno-pathogenesis of MS:

principles and applications. In: Multiple Sclerosis: a comprehensive text, ed. Raine, C.S., McFarland, H.F., and Hohlfeld, R., p.284-299, Elsevier, Philadelphia 2008.

Co-author manuscripts:

Kawakami, N., Lassmann, S., Li, Z., Odoardi, F., Ritter, T., Ziemssen, T., Klinkert, W.E.F., Ellwart, J.W., **Bradl, M**., Krivacic, K., Lassmann, H., Ransohoff, R.M., Volk, H.-D., Wekerle, H., Linington, C., and Flügel, A. (2004). The activation status of neuroantigen-specific T cells in the target organ determines the clinical outcome of autoimmune encephalomyelitis. *J. Exp. Med.* 199:185-197

Sosnová, M., **Bradl, M.,** and Forrester, J.V. (2005) $CD34^+$ corneal stromal cells are haematopoietic stem cells. Stem Cells 23:507-515

Kawakami, N., Odoardi, F., Ziemssen, T., **Bradl, M.,** Ritter, T., Neuhaus, O., Lassmann, H., Wekerle, H., and Flügel, A. (2005) Autoimmune CD4+ T cell memory: Life long persistence of encephalitogenic T cell clones in healthy immune repertoires. J. Immunol. 175: 69-81

Hochmeister, S., Grundtner, R., Bauer, J., Engelhardt, B., Lyck, R., Gordon, G., Korosec, T., Kutzelnigg, A., Berger, J., **Bradl, M.,** Bittner, R. E., Lassmann, H. (2006) Dysferlin is a new marker for leaky brain bloodvessels in multiple sclerosis, J. Neuropath. Exp. Neurol. 65:855-865

Dal Bianco, A., **Bradl, M.,** Frischer, J., Kutzelnigg, A., Jellinger, K., and Lassmann, H. Multiple sclerosis and Alzheimer´s disease. (2008) Ann. Neurol. 63: 174-183.

Dr. Margot Ernst
Division of Biochemistry and Molecular Biology, Research Group for Molecular Neurobiology
Center for Brain Resarch, Medical University of Vienna
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Description of thesis project: $GABA_A$ receptor: structure, function and pharmacology; Bioinformatics

Abstract:
Gamma- Aminobutyric acid (GABA) is the major inhibitory transmitter in the central nervous system. Most of the actions of GABA are mediated by $GABA_A$ receptors. These are chloride ion channels that can be opened by GABA and are the site of action of a large variety of clinically and pharmacologically important drugs, such as benzodiazepines, barbiturates, neuroactive steroids, anesthetics and convulsants. Recently the 3D structures of related proteins from the superfamily of pentameric ligand gated ion channels ("cys-loop receptors)" have been reported, offering completely new insights into the molecular mechanisms governing the intriguingly complex pharmacology of these receptors. The structure of $GABA_A$ receptors can now be predicted on the basis of homology with the related proteins, and the predictions can be used to generate testable hypotheses about ligand binding sites, conformational states that govern receptor function, and many more issues of pharmacological interest.

Description of thesis projects:
We study the structure and pharmacology of $GABA_A$ receptors. One core technique in our work is structure prediction by computational modeling. As structure determines function, we try to conclude from predicted structures the functional properties such as selectivity among ligands, for example for diazepam sensitive and diazepam insensitive receptor subtypes. In order to test the predictions, we also perform, in a network of collaborations, experimental studies. Presently, in cooperation with the Sieghart and Huck labs, an electrophysiological investigation of novel binding sites on $GABA_A$ receptors is performed.
For future group members, both computational and experimental thesis projects are possible.

Techniques and infrastructure:
Computational projects: Comparative and homology modeling to predict receptor structure, various tools to analyse and assess the quality of the prediction, computational docking of ligands (in cooperation with the Gerhard F. Ecker lab at the University of Vienna), and associated computational methods.
Experimental projects: In cooperation with the Sieghart and Huck labs: Mutagenesis and recombinant expression of receptors, radio ligand binding assays, Xenopus oocyte electrophysiology, patch clamp in HEK cells.

Thesis Topics:
Molecular mechanisms that govern ligand recognition and binding, receptor subtype selectivity of ligands, transduction of ligand effects (allosteric modulation and GABA-mimetic effects, currently the focus is on allosteric modulators) are the scope of topics to choose from. Depending on the candidates's background and the available funding, topics will be chosen within this framework.

Curriculum Vitae

Dr. Margot Ernst
Center for Brain Research, Medical University Vienna, Spitalgasse 4, 1090 Vienna
margot.ernst@meduniwien.ac.at

Personal Data

Date of Birth:	17.12.1966
Place of Birth:	Vienna
Nationality	Austria

Education

1992	US-american PhD in Chemistry, nostrified at the Univ. Graz
1987 – 1992	PhD Student at the School of Chemistry, Georgia Institute of Technology as Fulbright Scholar
1984 – 1987	First Diploma in Chemistry, University Vienna
1984	AHS-Matura (High school degree)

Career History

since July 2002	Contract Assistant at the Center for Brain Research
7/2001- 7/2002	Post Doc in the group of Prof. Dr. Werner Sieghart, Univ. Vienna
1992 – 1995	Post Doc in the group of Doz. Dr. Alexander Sax, Department of Theoretical Chemistry, K.F. University Graz
1987 – 1992	Teaching Assistant at the School of Chemistry, Georgia Institute of Technology

Teaching Record

Laboraty corses in general and physical chemistry at the School of Chemistry, Georgia Institute of Technology
POL groups at the MUW
SSM1 "Science and Medicine" Seminar and Electives
Participation in the Neuroscience seminar series "Work in Progress", Divisional seminar series, Supervision of diploma theses and elective course (Wahlbeispiele).

Carrer related activities

Kinderuni lectures, Brainweek organization, University meets popper lecturer

Invited lectures

- Invited lecturer at a Continuing Education Workshop "Biomolecular Structure" for faculty at California State University, Fullerton in 2003
- Organization and supervision of participants of a crystallization workshop held at the Center for Brain Research in April 2004.
- Organization and lecturing at a Continuing Education Programme of the Austrian Pedagogic Institute for AHS Teachers in March 2005.

Awards

1992 – 1994 Gaussian International Fellow by Gaussian, Inc.

Memberships

Austrian Neuroscience Association

Sources of funding in last 5 years (2003 – 2008)

Period	*Organization*	*Short Title*	
2007-2010	FWF P19653-B11	Identification of binding sites on $GABA_A$ receptors	

PhD supervision in last 5 years (2003 – 2008)

Period	*Name of student*	*Topic*
ongoing	Dr. Daniela Meisel	Identification of $GABA_A$ receptor ligands interacting with a novel binding site
ongoing	Mag. Lars Richter	Ligand docking into the $GABA_A$ receptor.
ongoing	Mag. Joachim Ramerstorfer	Structure and pharmacology of $GABA_A$ receptors

Peer reviewed manuscripts 2003-2008 (original research and reviews)
First, last or corresponding author manuscripts:

Ernst, M., S. Bruckner, S. Boresch and W. Sieghart (2005). Comparative models of $GABA_A$ receptor extracellular and transmembrane domains: important insights in pharmacology and function. *Mol Pharmacol* 68(5): 1291-300.

Ernst, M., D. Brauchart, S. Boresch and W. Sieghart (2003). Comparative modeling of $GABA_A$ receptors: limits, insights, future developments. *Neuroscience* 119(4): 933-43.

Co-author manuscripts:

Clayton T, Chen JL, Ernst M, Richter L, Cromer BA, Morton CJ, Ng H, Kaczorowski CC, Helmstetter FJ, Furtmüller R, Ecker G, Parker MW, Sieghart W, Cook JM (2007) An Updated Unified Pharmacophore Model of the Benzodiazepine Binding Site on gamma-Aminobutyric Acid(a) Receptors: Correlation with Comparative Models. *Curr Med Chem.*;14(26):2755-75.

Tan KR, Gonthier A, Baur R, Ernst M, Goeldner M, Sigel E. (2007) Proximity-accelerated chemical coupling reaction in the benzodiazepine-binding site of gamma-aminobutyric acid type A receptors: superposition of different allosteric modulators. *J Biol Chem*. Sep 7;282(36):26316-25.

Sarto-Jackson I, Furtmueller R, Ernst M, Huck S, Sieghart W. (2007) Spontaneous cross-link of mutated alpha1 subunits during GABA(A) receptor assembly. *J Biol Chem.* Feb 16;282(7):4354-63.

Sarto-Jackson I., Ramerstorfer J., Ernst M., Sieghart W. (2006) Identification of Amino Acid Residues Important for Assembly of $GABA_A$ Receptor α_1 and γ_2 Subunits. *Journal of Neurochemistry*, 96:983-95

Sieghart, W. and Ernst, M. (2005) Heterogeneity of $GABA_A$ Receptors: Revived Interest in the Development of Subtype-selective Drugs. *Curr. Med. Chem. - Central Nervous System Agents* 5 217- 242

Ogris, W., A. Poltl, B. Hauer, M. Ernst, A. Oberto, P. Wulff, H. Hoger, W. Wisden and W. Sieghart (2004). Affinity of various benzodiazepine site ligands in mice with a point mutation in the $GABA_A$ receptor gamma2 subunit. *Biochem Pharmacol* 68(8): 1621-9.

Dr. Karoline Fuchs
Division of Biochemistry and Molecular Biology, Research Group for Molecular Neurobiology (Prof. W. Sieghart) Center for Brain Resarch, Medical University of Vienna
karoline.fuchs@meduniwien.ac.at

Description of thesis project:

Abstract:

I am supervising a small group (consisting of Dr. Lydia Urak, Dr. Alexandra Schosser, Mirjana Stojanovic and Nahid Fathi) performing molecular genetic investigations in psychiatric and neurologic diseases. We identified a linkage of chromosome 3q29 for bipolar and schizophrenic patients that now has to be further narrowed down (collaboration with Dr. Alexandra Schosser and Univ.Prof. Dr. Harald Aschauer, Univ. Clinic for Psychiatry). In addition, over the last few years we demonstrated that a mutation in the promoter region of the β3 subunit of GABA-A receptors probably is associated with childhood absence epilepsy (collaboration with Univ.Prof. Dr. Martha Feucht, Univ. Clinic for Pediatrics). A manuscript describing our results on childhood absence epilepsy has been published in 2006.

Techniques and Infrastructure

The Division of Biochemistry and Molecular Biology of the Center for Brain Research is excellently equipped for all types of biochemical and molecular biological techniques. In my group we are perfoming subcellular fractionation of brain tissue, extraction and purification of $GABA_A$ receptors by ligand affinity chromatography or immunoaffinity chromatography, density gradient centrifugation, cell culture techniques, cell transfection techniques, recombinant receptor expression, generation of mutated, chimeric or truncated subunits, immunohistochemical studies in cell culture, receptor binding studies, electrophysiological studies, generation and purification of antibodies, Western blots, immunoprecipitation, immunohistochemistry, and molecular genetic techniques.

Thesis Topic

Molecular genetic investigations of psychiatric and neurologic diseases

Techniques used: Isolation of DNA from blood of patients suffering from psychiatric and neurologic diseases as well as their family members (collected by the groups of Univ. Prof. Dr. H. Aschauer, University Clinic for Psychiatry, or of Univ. Prof. Dr. M. Feucht, University Clinic for Pediatrics), RFLP analysis, SNP analysis, sequencing, haplotype analysis, reporter gene assays, association studies, linkage studies.

Curriculum Vitae

Dr. Karoline Fuchs

Address Hardeggasse 67/42/11, 1220 Wien

Personal Data

Date of Birth:	27. 4. 1955
Place of Birth:	Grieskirchen, Upper Austria
Nationality	Austria

Education

21. November 1985	Graduation: Dr. rer. nat, University of Vienna
From 1982 – to 1985	Ph.D.study under the supervision of Univ. Prof. Dr. Hoffmann-Ostenhof and Univ. Prof.Dr. G. Högenauer
29. April 1982	Graduation: Mag. rer. nat, University of Vienna
from1976 to 1982	Study of biochemistry, University of Vienna
from 1973 to 1976	Study of chemistry, University of Vienna
25. June 1973	Matura with excellent success
from 1969 to 1973	"Musisch Pädagogisches Realgymnasium", Grieskirchen, Upper Austria
from 1965 to 1969	„Hauptschule", Haag, Upper Austria
from 1961 to 1965	Primary School, Rottenbach, Upper Austria

Career History

Since 2.Jan. 2001	"Vertragsassistent" at the Center for Brain Research, Medical University of Vienna
from 4.8.1989 to 16.7. 2000	Assistant of Univ. Prof. Dr. Werner Sieghart at the Section of Biochemical Psychiatry, University Clinic for Psychiatry, A-1090 Vienna

Career-related Activities

Teaching activities

from WS 1989/90 to SS 1996	"Praktische Diagnostik und Therapie in der Psychiatrie"
Since 2002:	Involved in : lecture and practical demonstrations "Basics of Neuroscience" Literature-Seminar; Seminar "Work in Progress"
2003	"Selbstorganisiertes Lernen (SOL) "

Awards

1996	Schizophrenia – Award of the Section Psychiatry of the Austrian Society for Neurology and Psychiatry for the paper "Schizophrenia and the dopamine-ß-hydroxylase gene: results of a linkage and association study"
1998	Schizophrenia – Award of the Section Psychiatry of the Austrian Society for Neurology and Psychiatry for the paper "Genetic polymorphisms of drug metabolism (CYP2D6) and tardive dyskinesia in schizophrenia"
2000	Research – Award of the AGNBP and the Austrian Society for Neurology and Psychiatry for the paper "Genome Scan for susceptibility loci for schizophrenia" (Neuropsychobiology 42, 175-182)
2001	Schizophrenia – Award of the Austrian Society for Neuropsychopharmacology and Biological Psychiatry for the paper "Genome Scan for Susceptibility Loci for Psychotic Disorders" (accepted in Biological Psychiatry)

Memberships
Austrian Society for Biochemistry and Molecular Biology
Austrian Neuroscience Association German Neuroscience Society
Since 2004 Treasurer of the Austrian Neuroscience Association

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*	

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
2003-2005	Lydia Urak (Dr. med. Sci)	Association of GABRB3 gene and CAE

Publications
59 peer reviewed publications in scientific journals, 4 book chapters

Peer reviewed manuscripts 2003-2008 (original research and reviews)
First, last or corresponding author manuscripts:

L. Urak, M. Feucht, N. Fathi, K. Hornik, **K. Fuchs** (2006). Hum. Mol. Genet. 15, 2533-2541.

Co-author manuscripts:

M. Willeit, N. Praschak-Rieder, A. Neumeister, P. Zill, J. Stastny, F. Leisch, E. Hilger, N. Thierry, A. Konstantinidis, D. Winkler, **K. Fuchs**, W. Sieghart, H.N. Aschauer, M. Ackenheil, B. Bondy, S. Kasper (2003) Mol. Psychiatry 8, 942-946.

X. Li, H. Cao, C. Zhang, R. Furtmüller, **K. Fuchs**, S. Huck, W. Sieghart, J. Cook (2003). J Med Chem. 46(26):5567-5570.

A. Pöltl, B. Hauer, **K. Fuchs**, V. Tretter, W. Sieghart (2003) J. Neurochem. 87, 1444-1455.

Schosser, K. **Fuchs, F.** Leisch, U. Bailer, K. Meszaros, E. Lenzinger, U. Willinger, R. Strobl, A. Heiden, C. Gebhardt, S. Kasper, W. Sieghart, K. Hornik, H.N. Aschauer (2004). J. Psychiat. Res. 38, 357-364.

U. Bailer, G. Wiesegger, F. Leisch, **K. Fuchs**, I. Leitner, M. Letmaier, A. Konstantinidis, J. Stastny, W. Sieghart, K. Hornik, B. Mitterauer, S. Kasper, H.N. Aschauer (2005). Eur. Neuropsychopharmacol. 15, 51-55.

W. Ogris, R. Lehner**, K. Fuchs,** B. Furtmüller, H. Höger, G.E. Homanics, W. Sieghart (2005) J. Neurochemistry, 96, 136-147.

A. Schosser, K. Fuchs, T. Scharl, F. Leisch, U. Bailer, S. Kasper, W. Sieghart, K. Hornik, H.N. Aschauer (2007) Eur. Neuropsychopharmacology 17, 501-505.

Dr. Ruth Herbst
Medical University of Vienna
ruth.herbst@meduniwien.ac.at

Description of thesis project:
Synapses are essential relay stations, which transduce information between different cells. The process of synapses formation requires complex cellular and molecular steps like transformation of a motile growth cone into a differentiated nerve terminal, induction of local gene expression and aggregation of proteins to the site of innervation. The neuromuscular synapse, due to its size, simplicity and accessibility has been a model system for many researchers to study synapse formation. In addition, neuromuscular synapses are absolute required for survival since they control all movements within an organism including breathing. Neuromuscular synapses develop when a motor neuron reaches a developing muscle fiber. Signals from the nerve induce differentiation of the postsynaptic muscle membrane and in turn, signals from the muscle induce differentiation of the presynaptic nerve terminal. A hallmark of postsynaptic differentiation is the concentration of acetylcholine receptors (AChRs), the receptors for the neurotransmitter acetylcholine, at synaptic sites. The high concentration of AChRs ensures a reliable and stable transmission of action potentials to the muscle necessary to govern the movements within the lifetime of a vertebrate organism. Our research interests are focused on the characterization of the molecular mechanisms that regulate neuromuscular synapse formation and maintenance. Projects are designed to study the different aspects of synapse formation, in particular postsynaptic differentiation, in cell culture and animal models.

Techniques and infrastructure:
We use molecular biology techniques like DNA manipulation, RNA and protein analysis. These include Southern, Northern and Western blotting, PCR, RT-PCR and cloning. We perform yeast-two-hybrid screens, co-immunoprecipitation, GST-pull-down and protein purifications (HIS, GST, etc). We rely in our experiments on cell culture systems like muscle cell lines and primary cells. We perform cell transfections and retroviral infections, immunocytochemistry and fluorescence microscopy. To analyze synapses in vivo we use transgenic mouse models. Mouse tissues are studied by immunohistochemistry.

Thesis Topic:
Resarch topics center around the molecular mechanisms involved in neuromuscular synapse formation. The main focus lies on a receptor tyrosine kinase called MuSK, which is essential for synapse formation. Projects concentrate on studying MuSK function by examining MuSK signalling and MuSK trafficking.

Curriculum Vitae

Dr. Ruth HERBST

Center for Brain Research, Spitalgasse 4, A-1090 Wien

Personal Data

Date of Birth:	17.2.1968
Place of Birth:	Weiz, Stmk
Nationality	Austria

Education

from – to		
	1991-1996	PhD studies (Molecular Biology), IMP, Vienna and University of Sheffield, UK.
	1986-1991	Studies in Genetics/Microbiology, University of Vienna, with distinction
	1986	University entrance qualification (Matura), Realgymnasium Birkfeld, with distinction

Career History

from – to		
	2002-present	Group leader, Center for Brain Research, Medical University Vienna
	1996-2001	Postdoctoral Fellow at the Skirball Institute, Molecular Neurobiology Program, New York University Medical Center, New York, NY, USA
	1993-1996	PhD studies at the Institute of Molecular Medicine, University of Sheffield, UK
	1991-1993	PhD studies at the Institute of Molecular Pathology (IMP) in Vienna
	1990-1991	Diploma studies at the Institute of Microbiology and Genetics, University of Vienna

Career-related Activities

from – to	
	Acquisition of grants Reviewer of scientific journals Training of Diploma and PhD students Lecturer at the Medical University Vienna and University of Vienna

Awards

Year		
	2005-2008	APART Habilitation Fellowship, Austrian Academy of Sciences
	2002-2004	Erwin-Schrödinger Return Fellowship, FWF
	2000	Poster prize award at the 11th IMP spring conference in Vienna, Austria
	1996-1998	Erwin-Schrödinger Postdoctoral Fellowship, FWF
	1993	Short-term studentship from the University of Vienna for studies abroad

Memberships

Austrian Neuroscience Association
Society of Neuroscience

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*	
2002-2005	FWF	Signaling by MuSK and Agrin: Characterization of downstream components.	
2003-2004	OENB	Dissecting the role of MuSK in AChR clustering	
2005-2008	OENB	Myasthenia gravis and MuSK autoantibodies	
2006-2010	FWF	Characterization of a novel MuSK Interaction Partner	

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
7/2002-3/2006	Viktoria Nizhynska	Agrin/MuSK Signaling at the Neuromuscular Synapse
1/2007-	Barbara Woller	Characterization of a novel MuSK binding protein and its role during MuSK trafficking
2/2007-	Susan Luiskandl	Characterization of MuSK trafficking and its role during NMJ formation and maintenance
3/2007-	Sania Mazhar	MuSK functions during agrin-dependent and agrin-independent AChR clustering

Publications
10 peer reviewed publications in scientific journals, - book chapters, 6 invited lectures

Peer reviewed manuscripts 2003-2008 (original research and reviews)
First, last or corresponding author manuscripts:

Nishynska, V., Neumüller, R. and **Herbst, R.** (2007), Phosphpinositide 3-kinase acts through the small GTPases Rac and Cdc42 during agrin-induced acetylcholine receptor clustering. *Dev. Neurobiology 67 (8), 1047-1058.*

Herbst, R., Iskratsch, T. and Bittner, R.E., Disrupted architecture of neuromuscular junctions in glycosylation-defective large^{myd} mice. *(submitted)*

Co-author manuscripts:

Chevessier, F., Faraut, B., Ravel-Chapuis, A., Richard, P., Gaudon, K., Bauche, S., Prioleau, C., **Herbst, R.,** Goillot, E., Ioos, C., Azulay, J.P., Attarain, S., Leroy, J.P., Fournier, E., Legay, C., Schaeffer, L., Koenig, J., Fardeau, M., Eymard, B., Pouget, J., Hantai, D. (2004), MuSK, a new target for mutations causing congenital myasthenic syndrome. *Hum Mol Genet.* 13, 3229-40.

Chevessier F., Faraut B., Ravel-Chapuis A., Richard P., Gaudon K., Bauche S., Prioleau C., **Herbst R.**, Goillot E., Ioos C., Azulay J.P., Attarian S., Leroy J.P., Fournier E., Legay C., Schaeffer L., Koenig J., Fardeau M., Eymard B., Pouget J., Hantai D. (2005), Towards the molecular elucidation of congenital myasthenic syndromes: identification of mutations in MuSK. *Acta Myol.* 24(2):55-9.

Galabova-Kovacs, G., Catalanotti, F., Matzen, D., Reyes, G.X., Zezula, J., **Herbst, R**., Silva A., Walter, I. and Baccarini, M. (2008), Essential role of B-Raf in oligodendrocyte maturation and myelination during postnatal CNS development. *J. Cell. Biol. 180 (5): 947-55.*

Ruggio, M., **Herbst, R.**, Kim, N., Jevskec, M., Fak, J., Burden, S.J. and Darnell, RB, The splicing factor Nova regulates motor neuron outgrowth and formation of the neuromuscular junction *(submitted).*

Invited Talks 2003-2008

Society of Psychiatry and Neurology, AKH Wien, 2003
Institute de Myologie, Hospital de Salpetriere, Paris, 2004
Chesa Laret Meeting, Sils, CH, 2008

ao.Univ.Prof. Dr. Sigismund Huck
Division of Biochemistry and Molecular Biology, Center for Brain Research,
Medical University of Vienna
sigismund.huck@meduniwien.ac.at

Description of thesis project:

Abstract:

My key interests are the neueonal nicotinic acetylcholine receptor (nAChR) and mechanisms of transmitter release and reuptake.
Using the cell culture model of the superior cervical ganglion (SCG) as part of the sympathetic nervous system we have previously described differential targeting of two types of nicotinic receptors to somatic and presynaptic sites, respectively (Kristufek et al., 1999). Neither the targeting mechanisms nor the subunit composition of these receptors is known.
In order to understand these fundamental mechanisms of nicotinic receptor properties and function we then investigated SCG neurons from mice with targeted deletions of distinct nAChR subunit genes. Our detailed study on mice lacking the nAChR α5 subunit revealed diverse effects of the knockout on either somatic or presynaptic receptors (Fischer et al., 2005). Mice without the α5 nAChR subunit were particularly striking by showing a substantial increase of nicotine-induced [3H]-noradrenaline release. In contrast, mice lacking the β2-subunit show minor changes of somatic nAChRs only, whereas no effects were seen when the α7 nAChR subunit gene was deleted (unpublished observation). In an accompanying series of experiments we have investigated presynaptic nAChRs in slice preparations of cortex, hippocampus, and striatum of control mice, and in the striatal slice of α5 and β2 knockout animals (Scholze et al., 2007). These experiments are important since to date presynaptic nicotinic receptors in mice have only been studied in synaptosomal preparations. We know, however, that properties of these receptors in the rat differ depending on the technique used for their investigation (slice *vs*. synaptosomes). Our own experiments furthermore reveal major species differences of nicotinic receptors in rat and mice.
We currently maintain 7 different colonies of mice lacking distinct nAChR subunits. These mice offer unique insights into assembling mechanisms, and into the biophysical and pharmacological properties of receptors that result from various combinations of nAChR subunits. More importantly, the modulation of these receptors by second messenger systems such as calcium, PKC, and PKA can be studied in the very same cells where receptors are normally expressed.
In a project led by Petra Scholze we presently analyze the subunit composition of nAChRs with immunological techniques (radioactive ligand binding; immunoprecipitation; immunoabsorbtion; Western blot; solid phase RIA; immunohistochemistry). Petra has already been successful in raising subunit-specific antibodies against distinct nAChR subunits and has begun to apply these techniques to the analysis of nAChRs obtained from the various mice strains.
With the intention of finding out whether deletion of distinct subunits induces compensatory changes at the level of mRNA of nAChR subunits we have employed Real Time PCR analysis. Our results indicate that no such changes occur (Putz et al., 2008). With these sensitive techniques we also found a developmental regulation of the nAChR subunit α4 in newborn mice. The α4 subunit (together with β2) is of major importance in the central nervous system, though its role in the peripheral (sympathetic) nervous system has been in doubt. This question is currently been followed up with the immunological techniques mentioned above.

Techniques and infrastructure:

Personal expertise: Primary cell and tissue (explants) cultures from various parts of the nervous system, cell culture and transfection of HEK293 cells, expression of recombinant receptors, Patch clamp recordings; fura2 calcium imaging; transmitter release from brain slices; immunofluorescence, standard techniques in molecular biology (cloning, genotyping, RT-PCR, PCR, 5'-RACE, ...), standard techniques in protein chemistry (antibody generation, Western Blot, immunoprecipitation,...), radioligand binding assays

Infrastructure: Cell and tissue culture facilities; 3 patch clamp setups, one calcium imaging setup, superfusion chambers for studying transmitter release from cell cultures and slice preparations, basic equipment for molecular biology and cell transfection (PCR, Biorad Gel-Doc 2000 gel documentation). 3 fluorescence microscopes.

Thesis Topic:

Pharmacology of $GABA_A$ receptor subtypes

Techniques used: Effects of novel drugs synthesized by Robert Dodd (Gif-sur-Yvette, France) or Jim Cook (Univ. Milwaukee, Wis. USA) on various recombinant $GABA_A$ receptor subtypes using electrophysiological investigations in Xenopus oocytes or receptor binding studies in HEK cells (electrophysiology supervised by Joachim Ramerstorfer and Sigismund Huck).

Functional properties of distinct nAChRs in their natural environment

Techniques used: Neuronal cell cultures; Patch Clamp recordings (whole cell; perforated patch; cell-attached patches); Fura2 calcium imaging; receptor characterization with pharmacological tools.

Curriculum Vitae

Ao.Univ.Prof. Dr. Sigismund Huck

Center for Brain Research, Division of Biochemistry and Molecular Biology, Spitalgasse 4, A-1090 Vienna, Austria

Personal Data

Date of Birth:	21. 09. 1946
Place of Birth:	Göttingen, Germany
Nationality	Austria

Education

1966 - 1972	Medical School at the University of Vienna
1957 - 1965	Humanistisches Gymnasium Kalksburg, Vienna

Career History

1999 - 2003	Deputy director, Brain Research Institute
1995 - 1999	Temporary head of Department of Neuropharmacology
1995	tit. a.o. Professor
1989 and 1995	Visiting Associate Professor, Center for Neurobiology and Behavior, CPS Columbia University, New York
1985	Visiting Fellow, Department of Neurophysiology, Max Planck Institute of Psychiatry Munich, Germany
1985	Venia Docendi for Pharmacology and Toxicology
1979 - 1980	Visiting Research Assistant Professor, Department of Pharmacology, New York University Medical School
1972	Assistant Professor, Department of Neuropharmacology University of Vienna

Career-related Activities

2005 - 2007	Chairman, Program of European Neuroscience Schools (PENS)
2003	Organizer of the international Symposium “Synaptogenesis” in Vienna
2003 -	Coordinator “Gehirn, Nervensystem, Schmerz”, MCW Block 19
2001 –	Secretary, Board of IBRO (International Brain Research Organization) Schools
1998 - 2002	Chairman of the Schools Committee, and Member of the Executive Board, Federation of European Neuroscience Societies (FENS)
1995 - 1997	President of the Austrian Neuroscience Association
1994	Organizer of the 17th Annual Meeting of the European Neuroscience Association

Awards

1985	Humboldt Fellowship
1984	Hoechst Award
1979	Max-Kade Fellowship

Memberships

Society for Neuroscience
Austrian Neuroscience Association (thus Federation of European Neuroscience Societies)
Austrian Pharmacological Association

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*	*K€/year*
10/2001 – 10/2004	FWF	OCT3 in the rat sympathetic nervous system	

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
2/2001 - 7/2003	Harald FISCHER	Morphological and functional characterization of somatic and prejunctional nicotinic ACh channels in the rodent sympathetic nervous system
2/2002 – 11/2007	Gernot PUTZ	mRNA levels of nAChR subunits in control mice and in mice with targeted deletions of the α5, α7, and the β2 subunit
Ongoing	Reinhard DAVID	Generation and Characterization of Polyclonal Antibodies Directed Against the Nicotinic Acetylcholine Receptor (nAChR) Subunits α3, α4, α5, β2 and β4 for the Investigation of nAChRs Composition and Compensation in Knock-Out Mice

Publications
49 peer reviewed publications in scientific journals

Peer reviewed manuscripts 2003-2008 (original research and reviews)
First, last or corresponding author manuscripts:

Fischer, H., Orr-Urtreger, A., Role, L.W., **Huck, S.** 2005. Selective deletion of the α5 subunit differentially affects somatic-dendritic versus axonally targeted nicotinic ACh receptors in mouse. *J. Physiol*. 563:119 – 137

Scholze, P., Orr-Urtreger, A., Changeux, J.-P., McIntosh, J. M., and **Huck**, S. 2007. Catecholamine outflow from mouse and rat brain slice preparations evoked by nicotinic acetylcholine receptor activation and electrical field stimulation. *Br. J. Pharmacol.,* 151: 414-422

Co-author manuscripts:

Li, X., Cao, H., Zhang, Z., Furtmueller, R., Fuchs, K., **Huck, S.,** Sieghart, W., Deschamps, J., Cook, J.M. 2003. Synthesis, in vitro affinity and efficacy of the first bivalent a5 subtype-selective BzR/GABAA antagonist.*J. Med. Chem*. 46:5567-5570

Sarto-Jackson I, Furtmueller R, Ernst M, **Huck S**, Sieghart W. 2007. Spontaneous Cross-link of Mutated α1 Subunits during GABAA Receptor Assembly. *J. Biol Chem*.282:4354-63.

Savic MM, Huang S, Furtmuller R, Clayton T, **Huck S**, Obradovic DI, Ugresic ND, Sieghart W, Bokonjic DR, Cook JM. Are GABA(A) 2008. Receptors Containing alpha5 Subunits Contributing to the Sedative Properties of Benzodiazepine Site Agonists? *Neuropsychopharmacology* 33: 332-339

Putz, G., Kristufek, D., Orr-Urtreger, A., Changeux, J.-P., **Huck, S**., and Scholze, P. (2008). Nicotinic ACh receptor-subunit mRNAs in the mouse superior cervical ganglion are regulated by development but not by deletion of distinct subunit genes. *J. Neurosci. Res*. 86, 972-981

Univ.Prof.Dr. Michael Kiebler
Division of Neuronal Cell Biology, Center for Brain Research, Medical Universit of Vienna
michael.kiebler@meduniwien.ac.at

Description of thesis project:

Dendritic RNA transport and local protein synthesis in polarized neurons

Abstract:
Synapses – the contact sites between nerve cells – are the elementary units of many if not all brain functions. It is thought that the modification of individual synapses represents the molecular correlate to learning and memory. The molecular players in this cascade, however, are largely unknown. My laboratory has recently taken several independent approaches to tackle this important neurobiological question. First, we identified candidate proteins, e.g. Staufen1, Staufen2 and Barentsz, that are thought to be involved in dendritic mRNA transport in mature, polarized neurons. We are currently studying the role of these molecules in this process by dual-color time-lapse videomicroscopy, as well as using biochemical and molecular approaches. Secondly, we are in the process of generating convential knock-out and transgenic mice that lack Staufen proteins to analyze their role in vivo. Thirdly, we are studying local protein synthesis at (activated) synapses. In this project, we want to elucidate how local translation affects the rearrangement of existing dendritic spines and the formation of new synapses. Gaining insight into the underlying molecular mechanism will help to understand how we acquire, store and retrieve memories.

Techniques and infrastructure:
Primary cultures of hippocampal neurons; cultured neuroblastoma and fibroblasts. Transfection methods to transiently transfect these cells. SDS-PAGE and Western blots (Odyssey infrared imaging system, Li-Cor), generation of polyclonal antibodies, co-immunoprecipitation experiments. Fluorescent timelapse videomicroscopy using state-of-the-art CCD cameras and imaging software. Semi-automatic microinjection system for neurons. Molecular biology including standard cloning procedures, generation of mutant or truncated proteins, *in situ* hybridization, immunostaining, expression of tagged proteins (GFP, HA, TAP, his_6, etc) in neurons and fibroblasts, RNA interference in mammalian cells.

Thesis Topic:
Molecular approaches to study dendritic RNA transport and local protein synthesis in mammalian neurons

Curriculum Vitae

Michael A. Kiebler, PhD
Division of Neuronal Cell Biology, Center for Brain Research, Medical University of Vienna,
Spitalgasse 4, 1090 Wien; phone: 0043-1-4277-62920, fax: 0043-1-4277-62928,
email: michael.kiebler@meduniwien.ac.at

Personal Data

Date of Birth:	2.2.1964
Place of Birth:	Munich, Germany
Nationality	German

Education

1989 – 1993	PhD in biochemistry: University of Munich (LMU), Germany, Supervisor: Prof. Walter Neupert
1983 to 1989	Diploma in chemistry, University of Munich (LMU), Germany, Supervisor: Prof. Walter Neupert
1983 to 1989	Studies in chemistry
1974 to 1983	German Highschool, Munich

Career History

2005 - present	Full professor and head of the Department of Neuronal Cell Biology, Medical University of Vienna, Vienna, Austria
1999 to 2005	Junior Group Leader, Max-Planck-Institute for Developmental Biology, Tübingen, Germany
1997 to 1999	Postdoctoral Fellow with Dr. Carlos Dotti, EMBL Heidelberg, Germany
1993 to 1996	Postdoctoral Fellow with Prof. Eric R. Kandel, Center for Learning & Memory, College of Physicians & Surgeons, Columbia University, New York, New York, USA

Career-related Activities

2000 - 2005	Faculty member of the Graduate School for Neural Sciences & Behavioural Sciences, University of Tübingen
2002	Co-organizer of the SFB meeting on “RNA transport, protein trafficking and Cell polarity and migration”, May 3rd to May 4th, 2002, Tübingen
2001-2004	Official representative of the MPI for Developmental Biology in the Biology-Medicine-Section (BMS) of the Max-Planck-Society (executive body of the Max-Planck-Society to recruit new scientific members / directors)

Awards

2004 to 2005	Fellowship at the associate professor level (Exzellenzprogramm Neurowissenschaften, C2/C3) from the Hertie-Stiftung, Frankfurt.
1997 to 1998	Postdoctoral Fellow of the Deutsche Forschungs-gemeinschaft (DFG)
1995 to 1996	Postdoctoral Fellow of the Human Frontier Science Programm Organization (HFSPO)
1994 to 1995	Postdoctoral Fellow of the Deutsche Forschungs-gemeinschaft (DFG)

Memberships

2004	ASBMB
2003 to 2005	Society of Neuroscience
1993-1999	American Society of Cell Biology

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*
2004-2006	Schram-Stiftung im Stifterverband der dt.	Isolation of Staufen2-containing transport particles from rat brain

	Wissenschaft.	
2001-2006	Sonderforschungs-Bereich SFB446, Tübingen, Deutschland	In vivo analyis of the Staufen-dependent mRNA transport in mammalian cells
2001-2005	Human Frontier Science Programme Organization, network grant	Molecular basis of mRNA transport along microtubules

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
2002	Martin Köhrmann	Staufen1-dependent particle transport in living neurons
2003	Anke Deitinghoff-Voß	Isolation of Staufen1-containing particles from rat brain
2004	Sven Kröning	The role of Barentsz in dendritic RNA transport
2005	Bernhard Götze	Staufen2 and its role in dendritic spine formation and maintenance in polarized neurons
2006	Fabian Tübing	Timelapse videomicroscopy of fluorescently labeled RNAs in living neurons
2008	John Vessey	Characterization of the Translational Repressor Pumilio 2 in Cultured Hippocampal Neurons
2008	Yunli Xie	Functional Characterization of Staufen2 and Septin7 in Hippocampal Neurons
2008	Daniela Karra	Isolierung und Charakterisierung von Staufen- und Barentsz- enthaltenden Komplexen aus Rattenhirn

Publications
34 peer reviewed publications in scientific journals, 1 book chapter
Peer reviewed manuscripts 2003-2008 (original research and reviews)
First, last or corresponding author manuscripts:

Xie Y, Vessey JP, Konecna A, Dahm R, Macchi P, and **Kiebler MA** (2007). The dendritic spine-associated GTPase Septin 7 is crucial for dendrite branching and dendritic spine morphology (Report). *Curr. Biol*. 17, 1746-51.

Vessey J, Vaccani A, Xie Y, Dahm R., Karra D, **Kiebler MA** and Macchi P (2006). Dendritic localization of the translational repressor Pumilio 2 and its contribution to dendritic stress granules. *J. Neurosci*. 26, 6496-6508.

Goetze B, Tuebing F, Xie Y, Dorostkar MM, Thomas S, Pehl U, Boehm S, Macchi P, and **Kiebler MA** (2006). The brain specific double-stranded RNA binding protein Staufen2 is required for dendritic spine morphogenesis. *J. Cell Biol*. 172, 221-231.

Kiebler MA and Bassell GJ (2006). Neuronal RNA granules: movers and makers (Mini-Review). Neuron 51, 685-690.

Jansen R.-P. & **Kiebler MA** 2005. Intracellular RNA sorting, transport and localization (meeting report). *Nature Structural and Molecular Biology* 12, 826-829.

Kiebler MA, Jansen R.-P., Dahm R, and Macchi P, (2005). A putative nuclear function for mammalian Staufen (Research focus). *Trends in Biochemistry* 30:228-231.

Dahm R, and **Kiebler M.** (2005). Cell biology: silenced RNA on the move. *Nature* 438, 432-5 (News & Views to Hüttelmaier et al. (Singer lab), *Nature* 438, 512-5.

Macchi P, Brownawell AM, Grunewald B, DesGroseillers L, Macara IG, and **Kiebler MA**. 2004. The brain specific double-stranded RNA-binding protein Staufen2: nucleolar accumulation and isoform

specific Exportin-5 dependent export. *J. Biol. Chem.* 279:31440-31444.

Goetze B, Grunewald B, Baldassa S and **Kiebler MA**. 2004. Chemically controlled formation of a DNA/calcium phosphate coprecipitate: application for transfection of mature hippocampal neurons. *J. Neurobiol.* 60:517-25.

Goetze B, Grunewald B, **Kiebler MA** and Macchi P. 2003. Coupling the iron responsive element (IRE) to GFP- an inducible system to study translation in a single living cell. *Science STKE protocol,* Oct. 14th, Issue 204, pp. PL12.

Macchi P, Kröning S, Palacios I, Baldassa S, Grunewald B, Ambrosino C, Goetze B, Lupas A, St Johnston D and **Kiebler MA**. 2003. Barentsz, a new component of the Staufen-containing ribonucleoprotein particles in mammalian cells, interacts with Staufen in a RNA-dependent manner. *J. Neurosci.* 23:5778-5788.

Mallardo M, Deitinghoff A, Müller J, Goetze B, Macchi P, Peters C and **Kiebler MA**. 2003. Isolation and characterization of Staufen-containing ribonucleoprotein particles from rat brain. *Proc. Natl. Acad. Sci. USA* 100:2100-2105.

Macchi P, Hemraj I, Grunewald B, Mallardo M, Goetze B and **Kiebler MA**. 2003. A GFP-based system to uncouple mRNA transport from translation in a single living neuron. Mol. Biol. Cell 14:1570 – 1582.

Co-author manuscripts:

Grundtner R, Dornmair K, Dahm R, Flügel A, Kawakami N, Zeitelhofer M, Schoderböck L, Nosov M, Selzer E, Willheim M, **Kiebler MA**, Wekerle H, Lassmann H, and Bradl M (2007). CNS inflammation in the myelin degenerative central nervous system is triggered by the presence of polyclonal T lymphocyte infiltrates and T cell interactions with local target structures. *Neurobiology of Disease* 28, 261-275.

Schratt G, Tuebing F, Nigh EA, Kane C, Sabatini MW, **Kiebler MA** and Greenberg ME (2006). A brain-specific microRNA regulates dendritic spine development. *Nature* 439, 283-289.

Martel C, Macchi P, Furic L, **Kiebler MA** and DesGroseillers L. 2005. Staufen1 is imported into the nucleolus via a bipartite nuclear localization signal and several modulatory determinants. Biochem. J. 393, 245-254.

Dr. Anetta Konecna
Division of Neuronal Cell Biology, Center for Brain Research,
Medical Universit of Vienna
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Description of thesis project:

Abstract:
Messenger RNA (mRNA) localization and the local protein synthesis at the synapse (or at synapses) of mature hippocampal neurons has been implicated in the process of inducing long-term synaptic potentiation, a molecular mechanism of learning and memory. The underlying molecular mechanisms of mRNA transport and regulated protein synthesis at the synapse are still largely unknown. In the Kiebler laboratory, we have recently developed an immunoprecipitation protocol to isolate native, endogenous mRNA-containing ribonucleoprotein (mRNPs) complexes from rat brain using Staufen2 and Barentsz proteins, the two best characterized markers for transport mRNPs. We have identified various classes of RNA-binding proteins (RBPs), which might work in mRNA translational repression and stability. Currently, we are extending the study at the RNA level, identifying the set of mRNA transported and/or regulated by Staufen2. We are in the process of establishing a modified immunoprecipitation method combined with UV-crosslinking in order to clone direct target mRNA of Staufen proteins. At present, there is an emerging evidence for an important role of small RNA, such as microRNAs, in regulation of gene expression. In mammalian neurons, microRNA-mediated translational repression is only beginning to be addressed. We set out to investigate the role of small RNAs, such as microRNAs, in these neuronal mRNPs. By a comprehensive proteomic analysis and characterization of RNA within neuronal RNPs, we expect to get a better insight into the molecular mechanism of dendritic mRNA localization as well as local translation at the synapse.

Techniques and infrastructure:
Antibody production and affinity purification, immnuprecipitation, density gradient separation methods, RNA isolation, radioactive labeling and cloning, crosslinking and immunoprecipitation - CLIP method (Ule et al., 2005), microRNA-based reporter assay (luciferase assay) and locked-nucleic acid in situ hybridization for microRNA detection in cultured hippocampal neurons.

Ule, J., K. Jensen, A. Mele, and R.B. Darnell. 2005. CLIP: a method for identifying protein-RNA interaction sites in living cells. *Methods*. 37:376-86.

Thesis Topic:
Biochemical characterization of neuronal transport mRNPs at the protein and RNA level; microRNA-mediated translational control of neuronal mRNAs.

Curriculum Vitae

Dr. Anetta Konecna
Center for Brain Research, Medical University Vienna, Spitalgasse 4, 1090 Vienna

Personal Data

Date of Birth:	13.05.1976
Place of Birth:	Bratislava, Slovakia
Nationality	Slovak

Education

2000 - 2006	PhD in Biochemistry: University of Zurich, Switzerland
1995 - 2000	Undergraduate studies in Molecular Biology at the Comenius University, Bratislava, Slovakia, *magna cum laude*
1995 - 1990	Bilingual french-slovak lyceum, Bratislava, Slovakia

Career history

2007 - present	Assistant Senior Postdoc, Department of Neuronal Cell Biology, Center for Brain Research, Medical University of Vienna
2006 - 2007	Postdoctoral fellowship from Swiss National Foundation in the group of Prof. Kiebler, Department of Neuronal Cell Biology, Center for Brain Research, Medical University of Vienna
2000 - 2006	PhD studies at the Biochemistry Institute, University of Zurich, Switzerland

Career-related Activities

Awards

2006 – 2007	Postdoctoral fellowship from Swiss National Foundation

Memberships

Publications

2 peer-reviewed publications in scientific journals, 0 book chapters, 0 invited lectures

Peer-reviewed manuscripts 2003-2008 (original research and reviews)

First, last and corresponding author manuscripts:

Konecna A[*], Frischknecht R[*], Kinter J[*], Ludwig A[*], Steuble M[*], Meskenaite V, Mateos J.M., Engel M, Indermühle M, Cen C, Streit P and Sonderegger P, (2006), Calsyntenin-1 docks distinct vesicular cargo to Kinesin-1, *Mol Biol Cell,* 17(8):3651-63.

Co-author manuscripts:

Xie Y, Vessey J.P., **Konecna A**, Dahm R, Macchi P and Kiebler M.A., (2007), The dendritic spine-associated GTPase Septin 7 is a regulator of dendritic branching and sendritic spine morphology, *Current Biology,* 17(20):1746-51.

o.Univ.Prof.Dr. Hans Lassmann
Division of Neuroimmunology, Center for Brain Research,
Medical University of Vienna
hans.lassmann@meduniwien.ac.at

Description of thesis project:

Abstract:

Our main focus is the immunopathology of multiple sclerosis lesions and their reflection in well defined experimental models of inflammatory demyelinating diseases. Recent studies on multiple sclerosis pathology revealed heterogenous mechanisms of tissue injury, dependent in part upon the genetic background of the patients and in part on the stage and severity of the disease process. To define the molecular mechanisms, which drive the chronic inflammatory process in the brain of MS patients and the destruction of myelin and axons are the main focus our research efforts. In particular we analyse

- The immunopathology of initial multiple sclerosis lesions, including the type and activation stage of inflammatory cells, the differential role of different T-cell subsets and autoantibodies, the patterns of microglia activation and the contribution of different microglia and macrophage toxins in the formation of the lesions.
- The mechanisms leading to a compartmentalized or trapped inflammatory reaction within the central nervous system, which gives rise to slowly progressive global brain damage in the progressive stage of multiple sclerosis
- The comparative analysis of well defined experimental models of inflammatory brain diseases mediated by different components of the immune system (T-helper cells, cytotoxic T-cells, B-cells and antibodies)

Aim of these studies is to define the dominant pathogenetic pathways of tissue injury at different stages of the disease and to identify new targets for subtype-specific therapeutic intervention.

Techniques and infrastructure:

The laboratory is well equipped for immunopathological studies and contains one of the world's largest archival collection of inflammatory brain disease in humans and experimental models. Techniques include:

- General Neuropathology
- Immunocytochemistry
- Confocal Laser Microscopy
- Electron microscopy
- In situ Hybridization
- Laser capture microdissection of tissues
- PCR analysis
- Microarray analysis

Thesis Topic:

Doctoral thesis will focus on molecular aspects of inflammatory brain damage, identifying the role of dominant pathogenetic pathways of tissue destruction at different stages and in different forms of the disease.

Curriculum Vitae

o.Univ.Prof. Dr. Hans LASSMANN

Division of Neuroimmunology, Center for Brain Research, Medical
University of Vienna, Spitalgasse 4, A-1090 Vienna, Austria

Personal Data

Date of Birth:	7.7.1949
Place of Birth:	Vienna
Nationality	Austrian

Education

from – to		
	1975-1983	training in neuropathology
	1968-1975	studies of human medicine (MD), University Vienna
	1959-1967	secondary school: BRG 18, Vienna

Career History

from – to		
	Since 2005	Corresponding Member of the Austrian Academy of Sciences
	Since 1999	o. Univ. Prof. for Neuroimmunology,
	Since 1999	Head of Division of Neuroimmunology, Center for Brain Research
	1999-2007	Acting Director – Center for Brain Research, Medical University of Vienna, Austria (the former Brain Research Institute, University of Vienna)
	1993	a.o.Univ. Prof (§31 UOG)
	1990-1996	Vice director of the Clinical Institute of Neurology (University Vienna)
	1990-1995	Head of the Research Unit for Experimental Neuropathology (Austrian Academy of Sciences)
	1983-1991	Head of Research Groups for Experimental Neuropathology at the Institute of Neurology (University of Vienna) and the Institute of Brain Research (Austrian Academy of Sciences)
	1983	Habilitation (Neuropathology)
	1975-1983	University Assistant, Institute of Neurology, Vienna; training in clinical neuropathology; research in clinical and experimental neuropathology;
	1977-1978	Visiting associate at the New York State Institute for Basic Research in Developmental Disabilities, Staten Island, New York;

Awards

1983	Kardinal Innitzer Förderungspreis
1985, 1987, 1999	Preis der Stiftung Hoechst AG
1992	The Royal College of Physicians and Surgeons of Canada: Royal College Speaker
1994	Billroth-Prize - Österreichische Ärztekammer
1994	Research Prize - Erste Österreichische Spar-Casse
1999	Winner in the Advanced Authored Category: The Medical Writers Group of the Society of Authors; Medical Book Awards 1999 sponsored by The Royal Society of Medicine (UK) für: A.Compston, G. Ebers, H. Lassmann, I. McDonald, B. Matthews & H. Wekerle: McAlpine's Multiple Sclerosis; Third Edition.
2000	Forschungspreis 2000 der Sobek Stiftung für hervorragende Forschungsleistung auf dem Gebiet der Multiplen Sklerose
2001	Steinberg-Krupp Alzheimer Forschungspreis der Deutschen Hirnliga Section Head „Demyelinating Diseases" der Faculty of 1000 Medicine; Current Science Group
2003	Highly Cited Researcher in ISI Highly Cited Researchers Project

2005	Charcot Award of the Multiple Sclerosis International Federation 2005 for Life Long Achievements in Multiple Sclerosis Research
2005	Kardinal Innitzer Würdigungspreis (Naturwissenschaften) 2005
2006	First Prize in Neurology – BMA Medical Book Competition
2007	Großes silbernes Ehrenzeichen für Verdienste um die Republik Österreich

Memberships

Chairman	Multiple Sclerosis Research Society of Vienna
Member	Medical Advisory Board of the International MS-Society
Member	Medical Advisory Board of the German MS-Society
Member of the Medical Advisory Board	Austian Multiple Sclerosis Society
Member of the Scientific Advisory Board	European School of Neuroimmunology
Member	American Association for the Advancement of Science
Member of the Scientific Advisory Panel on Neurological Diseases	European College of Neuropsychopharmacology
Member of the Executive Board	Multiple Sclerosis
Member of the Project Review Boards	Multiple Sclerosis Society of UK and Ireland
Member of the Task Force on Clinico-Pathological correlation in MS	US Multiple Sclerosis Society
Member of the Scientific Panel on Neuroimmunology	European Federation of Neurological Societies
Member	
Corresponding Member	Austrian Academy of Sciences
Section Editor	Brain Pathology
Member of the International Editorial Board of	Glia Acta Neuropathologica Apoptosis Multiple Sclerosis European Journal of Neurology Developmental Neuroscience International Archives of Allergy and Immunology The International MS Journal Neurobiology of Disease European Neurology Neuropathology

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*
1999 to 2003	BM:BWK: GZ 70.056/3	Pathogenetic heterogeneity of multiple sclerosis
Since 2000	NMSS (National multiple sclerosis society-USA) – RG-3185-07	The clinico-pathological correlates of MS-lesions
2002 to 2005	EU: QLG3-CT-2002-00612	Mechanisms of Brain Inflammation (Coordinator)
2002 to 2006	Boehringer Ingelheim – cooperative research project	Identification of new hypoxia related brain protein, involved in the pathogenesis of ischemic and inflammatory brain diseases

2003 to 2005	FWF-P16848-B02	Cortical Lesions in multiple sclerosis
2003 to 2007	FWF-P16063-B02	T-cell cytotoxicity in inflammatory brain diseases
2003 to 2007	Berlex Biosciences	New targets for MS therapy
2004 to 2007	Verlassenschaft nach Helga Prosser	Die Rolle der Mikrogliaaktivierung in der Pathogenese der Nervengewebsschädigung bei Alzheimer'scher Erkrankung
2005 to 2006	GenPat77 Pharmacogenetics AG – Feasibility Study I+II	Expression of TIRC7 in multiple sclerosis lesions
Since 2005	EU: LSHM-CT2005-018637	Neuroprotective strategies for multiple sclerosis
Since 2006	National Institutes of Health (NIH) – R01-NS049577-01A2	Genetic determinants of pathologic heterogeneity in MS
Since 2007	FWF-P19854	Innate Immunity in the Pathogenesis of initial MS lesions
Since 2007	NMSS (National multiple sclerosis society-USA) – pilot project PP1443	Feasibility of microarray studies in archival paraffin embedded MS tissue
Sinice 2007	EU: Cost Action BM0603	Inflammation in Brain Disease – NEURINFNET
Since 2007	FWF: Doktoratskolleg W1205-B09	Cell Communication in Health and Disease: Immunopathogenic mechanisms of lesion formation in multiple sclerosis

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
2002-2005	Sonja Hochmeister	Dysferlin: a new marker for blood brain barrier dysfunction
2004-2006	Peter Patrikios	Remyelination in multiple sclerosis
Since 2006	Josa Frischer	Patterns of inflammation and tissue injury in acute/relapsing vs. progressive multiple sclerosis
Since 2007	Rakhi Sharma	joint project with Dr. Bradl: Molecular analysis of inflammatory lesions in pattern III multiple sclerosis cases and their corresponding animal model
Since 2007	Marie-Therese Fischer	joint project with Dr. Bradl: Molecular analysis of chronic progressive multiple sclerosis cases and their corresponding animal models.

Publications

330 peer reviewed publications in scientific journals, 54 book chapters and reviews, in average more than 10 invited lectures/year during the last 15 years

Peer reviewed manuscripts 2003-2008 (original research and reviews)

First, last or corresponding author manuscripts:

Lassmann H (2003) Brain damage when multiple sclerosis is diagnosed clinically. Lancet 361:1317-1318; IF: 15.387;

Lassmann H (2003) Axonal injury in multiple sclerosis. J Neurol Neurosurg Psychiatry 74:695-697; IF: 2.939

Lassmann H (2003) Hypoxia-like tissue injury as a component of multiple sclerosis lesions. J Neurol Sci. 206:187-191; IF: 2.080

Kornek B, **Lassmann H** (2003) Neuropathology of multiple sclerosis-new concepts. Brain Res Bull 61:321-326; IF: 2.283

Lassmann H, Reindl M, Rauschka H, Berger J, Aboul-Enein F, Berger T, Zurbriggen A, Lutterotti A, Bruck W, Weber JR, Ullrich R, Schmidbauer M, Jellinger K, Vandevelde M (2003) A new paraclinical CSF marker for hypoxia-like tissue damage in multiple sclerosis lesions. Brain 126:1347-1357; IF: 7.122;

Aboul-Enein F, Rauschka H, Kornek B, Stadelmann C, Stefferl A, Bruck W, Lucchinetti C, Schmidbauer M, Jellinger K, **Lassmann H** (2003) Preferential loss of myelin-associated glycoprotein reflects hypoxia-like white matter damage in stroke and inflammatory brain diseases. J Neuropathol Exp Neurol 62:25-33; IF: 4.955;

Cabarrocas J, Bauer J, Piaggio E, Liblau R, **Lassmann H** (2003) Effective and selective immune surveillance of the brain by MHC class I-restricted cytotoxic T lymphocytes. Eur J Immunol 33:1174-1182; IF: 4.832;

Hoftberger R, Aboul-Enein F, Brueck W, Lucchinetti C, Rodriguez M, Schmidbauer M, Jellinger K, **Lassmann H** (2004) Expression of major histocompatibility complex class I molecules on the different cell types in multiple sclerosis lesions. Brain Pathol 14:43-50; IF: 3.838;

Aboul-Enein,-F, Bauer,-J, Klein,-M, Schubart,-A, Flugel,-A, Ritter,-T, Kawakami,-N, Siedler,-F, Linington,-C, Wekerle,-H, **Lassmann,-H**, Bradl,-M (2004) Selective and antigen-dependent effects of myelin degeneration on central nervous system inflammation. J-Neuropathol-Exp-Neurol 63:1284-96; IF: 5.005;

Lassmann H (2004) Recent neuropathological findings in MS-implications for diagnosis and therapy. J-Neurol. 251 Suppl 4: IV2-5. IF: 2.778

Lassmann H, Ransohoff RM (2004) The CD4-Th1 model for multiple sclerosis: a crucial re-appraisal. Trends Immunol 25:132-137; IF: 18.153

Grois,-N; Prayer,-D; Prosch,-H; **Lassmann,-H** (2005) Neuropathology of CNS disease in Langerhans cell histiocytosis. Brain. 128: 829-38

Aboul-Enein,-F; **Lassmann,-H** (2005) Mitochondrial damage and histotoxic hypoxia: a pathway of tissue injury in inflammatory brain disease? Acta-Neuropathol-(Berl). 109(1): 49-55

Stadelmann,-C; Ludwin,-S; Tabira,-T; Guseo,-A; Lucchinetti,-C-F; Leel-Ossy,-L; Ordinario,-A-T; Bruck,-W; **Lassmann,-H** (2005) Tissue preconditioning may explain concentric lesions in Balo's type of multiple sclerosis. Brain. 128(Pt 5): 979-87

Bradl, M., Bauer, J., Flügel A., Wekerle H., and **Lassmann, H**. (2005) Complementary contribution of CD4 and CD8 T lymphocytes to T cell infiltration of the intact and the degenerative spinal cord. Am. J. Path. 166: 1441-1450

Perron H, Lazarini F, Ruprecht K, Pechoux-Longin C, Seilhean D, Sazdovitch V, Creange A, Battail-Poirot N, Sibai G, Santoro L, Jolivet M, Darlix JL, Rieckmann P, Arzberger T, Hauw JJ, **Lassmann H** (2005) Human endogenous retrovirus (HERV)-W ENV and GAG proteins: physiological expression in human brain and pathophysiological modulation in multiple sclerosis lesions. J Neurovirol. 11(1):23-33

Kutzelnigg A, **Lassmann H** (2005) Cortical lesions and brain atrophy in MS. J Neurol Sci. 2005 Jun 15;233(1-2):55-9. Review.

Lassmann H (2005) Multiple sclerosis pathology: evolution of pathogenetic concepts. Brain Pathol 15(3):217-22.

Kutzelnigg A, Lucchinetti CF, Stadelmann C, Bruck W, Rauschka H, Bergmann M, Schmidbauer M, Parisi JE, **Lassmann H** (2005) Cortical demyelination and diffuse white matter injury in multiple sclerosis. Brain. 128(Pt 11):2705-2712

Hochmeister S, Grundtner R, Bauer J, Engelhardt B, Lyck R, Gordon G, Korosec T, Kutzelnigg A, Berger JJ, Bradl M, Bittner RE, **Lassmann H** (2006) Dysferlin is a new marker for leaky brain blood vessels in multiple sclerosis. J Neuropathol Exp Neurol. 65(9):855-865

Patrikios P, Stadelmann C, Kutzelnigg A, Rauschka H, Schmidbauer M, Laursen H, Sorensen PS, Bruck W, Lucchinetti C, **Lassmann H** (2006) Remyelination is extensive in a subset of multiple sclerosis patients. Brain 129 (Pt. 12):3165-72

Storch MK, Bauer J, Linington C, Olsson T, Weissert R, **Lassmann H (**2006) Cortical demyelination can be modeled in specific rat models of autoimmune encephalomyelitis and is major histocompatability complex (MHC) haplotype-related. J Neuropathol Exp Neurol 65(12):1137-42

Gold R, Linington C, **Lassmann H** (2006) Understanding pathogenesis and therapy of multiple sclerosis via animal

models: 70 years of merits and culprits in experimental autoimmune encephalomyelitis research. Brain 129(Pt 8):1953-1971.

Lassmann H (2006) Genetic predisposition for autoimmunity in multiple sclerosis? Lancet Neurol. 5(11):897-8

Kutzelnigg A, **Lassmann H** (2006) Cortical demyelination in multiple sclerosis: a substrate for cognitive deficits? J Neurol Sci. 15;245(1-2):123-126.

Lassmann H. (2007) Experimental models of multiple sclerosis. Rev Neurol (Paris). 2007 Jun;163(6-7):651-5. Review.

Lassmann H. (2007) New concepts on progressive multiple sclerosis. Curr Neurol Neurosci Rep. 2007 May;7(3):239-44. Review.

Lassmann H, Brück W, Lucchinetti CF. (2007) The immunopathology of multiple sclerosis: an overview. Brain Pathol. 2007 Apr;17(2):210-8.

Lassmann H. (2007) Multiple sclerosis: is there neurodegeneration independent from inflammation? J Neurol Sci. 2007 Aug 15;259(1-2):3-6.

Kutzelnigg A, Faber-Rod JC, Bauer J, Lucchinetti CF, Sorensen PS, Laursen H, Stadelmann C, Brück W, Rauschka H, Schmidbauer M, **Lassmann H.** (2007) Widespread demyelination in the cerebellar cortex in multiple sclerosis. Brain Pathol.17(1):38-44.

Lassmann H, Lucchinetti CF (2008) Cortical demyelination in CNS inflammation demyelinating disease (Editorial). Neurology 70(5):332-333

Dal-Bianco A, Bradl M, Frischer J, Kutzelnigg A, Jellinger K, **Lassmann H** (2008) Multiple sclerosis and Alzheimer's disease. Ann Neurol 63(2):174-183

Co-author manuscripts:

Lobell A, Weissert R, Eltayeb S, de Graaf KL, Wefer J, Storch MK, **Lassmann H,** Wigzell H, Olsson T (2003) Suppressive DNA vaccination in myelin oligodendrocyte glycoprotein peptide-induced experimental autoimmune encephalomyelitis involves a T1-biased immune response. J Immunol 170:1806-1813; IF: 7.014;

Trebst C, Staugaitis SM, Kivisakk P, Mahad D, Cathcart MK, Tucky B, Wei T, Rani MR, Horuk R, Aldape KD, Pardo CA, Lucchinetti CF, **Lassmann H,** Ransohoff RM (2003) CC chemokine receptor 8 in the central nervous system is associated with phagocytic macrophages. Am J Pathol 162:427-38; IF: 6.750;

Akassoglou K, Douni E, Bauer J, **Lassmann H,** Kollias G, Probert L (2003) Exclusive tumor necrosis factor (TNF) signaling by the p75TNF receptor triggers inflammatory ischemia in the CNS of transgenic mice. Proc Natl Acad Sci U S A 100:709-714;

Schroeter M, Stoll G, Weissert R, Hartung HP, **Lassmann H,** Jander S (2003) CD8+ phagocyte recruitment in rat experimental autoimmune encephalomyelitis: association with inflammatory tissue destruction. Am J Pathol 163 :1517-1524; IF: 6.750;

Sunnemark D, Eltayeb S, Wallstrom E, Appelsved L, Malmberg A, **Lassmann H,** Ericsson-Dahlstrand A, Piehl F, Olsson T (2003) Differential expression of the chemokine receptors CX3CR1 and CCR1 by microglia and macrophages in myelin-oligodendrocyte-glycoprotein-induced experimental autoimmune encephalomyelitis. Brain Pathol 13:617-629; IF: 5.652;

Becanovic K, Wallstrom E, Kornek B, Glaser A, Broman KW, Dahlman I, Olofsson P, Holmdahl R, Luthman H, **Lassmann H,** Olsson T (2003) New loci regulating rat myelin oligodendrocyte glycoprotein-induced experimental autoimmune encephalomyelitis. J Immunol 170:1062-1069; IF: 7.014;

Rauschka H, Jellinger K, **Lassmann H,** Braier F, Schmidbauer M (2003) Guillain-Barre syndrome with marked pleocytosis or a significant proportion of polymorphonuclear granulocytes in the cerebrospinal fluid: neuropathological investigation of five cases and review of differential diagnoses. Eur J Neurol 10:479-486; IF: 1.565

Wanschitz J, Maier H, Lassmann H, Budka H, Berger T (2003) Distinct time pattern of complement activation and cytotoxic T cell response in Guillain-Barre syndrome. Brain 126:2034-2042; IF: 7.122;

Kivisakk P, Mahad DJ, Callahan MK, Trebst C, Tucky B, Wei T, Wu L, Baekkevold ES, **Lassmann H,** Staugaitis SM, Campbell JJ, Ransohoff RM (2003) Human cerebrospinal fluid central memory CD4+ T cells: evidence for trafficking through choroid plexus and meninges via P-selectin. Proc Natl Acad Sci U S A 100:8389-8394; IF: 10.700;

Becanovic K, Backdahl L, Wallstrom E, Aboul-Enein F, **Lassmann H,** Olsson T, Lorentzen JC (2003) Paradoxical effects of arthritis-regulating chromosome 4 regions on myelin oligodendrocyte glycoprotein-induced encephalomyelitis in congenic rats. Eur J Immunol 33:1907-1916; IF: 4.832;

Eltayeb S, Sunnemark D, Berg AL, Nordvall G, Malmberg A, **Lassmann H,** Wallstrom E, Olsson T, Ericsson-Dahlstrand A (2003) Effector stage CC chemokine receptor-1 selective antagonism reduces multiple sclerosis-like rat disease. J Neuroimmunol 142:75-85; IF: 3.577;

Carboni S, Aboul-Enein F, Waltzinger C, Killeen N, **Lassmann H,** Pena-Rossi C (2003) CD134 plays a crucial role in the pathogenesis of EAE and is upregulated in the CNS of patients with multiple sclerosis. J Neuroimmunol 145:1-11; IF: 3.577;

Abdul-Majid KB, Wefer J, Stadelmann C, Stefferl A, **Lassmann H,** Olsson T, Harris RA (2003) Comparing the pathogenesis of experimental autoimmune encephalomyelitis in CD4-/- and CD8-/- DBA/1 mice defines qualitative roles of different T cell subsets. J Neuroimmunol 141:10-19; IF: 3.577;

Aszmann OC, Korak KJ, Rab M, Grunbeck M, **Lassmann H,** Frey M (2003) Neuroma prevention by end-to-side neurorraphy: an experimental study in rats. J Hand Surg [Am] 28:1022-1028; IF: 0.845;

Trebst C, Staugaitis SM, Tucky B, Wei T, Suzuki K, Aldape KD, Pardo CA, Troncoso J, **Lassmann H,** Ransohoff RM (2003) Chemokine receptors on infiltrating leucocytes in inflammatory pathologies of the central nervous system (CNS). Neuropathol Appl Neurobiol 29:584-595; IF: 2.950;

Cabarrocas J, Piaggio E, Zappulla JP, Desbois S, Mars LT, **Lassmann H,** Liblau RS (2004) A transgenic mouse model for T-cell ignorance of a glial autoantigen. J Autoimmun 22:179-189; IF: 2.353;

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Kuhlmann T, **Lassmann H,** Brück W (2008) Diagnosis of inflammatory demyelination in biopsy specimens: a practical approach. Acta Neuropathologica 115(3):275-287

Invited Talks 2003-2008

in average more than 10 invited lectures/year during the last 15 years

Ao.Univ.Prof. Dr. Christian Pifl
Division of Biochemistry and Molecular Biology, Center for Brain Research,
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Description of thesis project:

Two major research topics are in the focus of interest in this research group: Monoamine neurotransmitter transporters, and neurodegenerative mechanisms in Parkinson's disease.

Monoamine neurotransmitter transporters:

Monoamine neurotransmitter transporters are molecular targets of neurotoxins and amphetamine related drugs. Hence, they are involved in neurodegenerative processes. On the one hand side, we intend to understand the mechanism of the interaction with the transporters. Based on our biochemical and electrophysiological studies, we have suggested a new mechanism of the releasing action of amphetamines, namely sodium influx via the channel mode of plasmalemmal monoamine transporters. On the other hand, we use monoamine transporters as tools to investigate the intracellular action of transporter substrates. By these means, we have discovered a novel action of intracellular dopamine, specifically a potent inhibition of ribonucleotide reductase activity which produces a strong antiproliferative action. We use uptake assays, superfusion methods, patch-clamp techniques and subcellular preparations of post-mortem tissue to study the action of the transporters.

Neurodegenerative mechanisms in Parkinson's disease.

Parkinson's disease (PD) is the second-most common neurodegenerative disease amongst the elderly population, and is caused by the loss of dopaminergic neurons particularly in the nigrostriatal system. We are interested in the aspect of etiology which is still not understood and in the aspect of neurotransmitter changes which can give an insight into the basis of the disturbed motor function.

α-Synuclein and other proteins are not only mutated in rare forms of familial parkinsonism but also relevant for the protein and oxidative stress hypothesis of the disease. We have found an interesting interaction of α-synuclein and manganese, which in epidemiological studies turned out as risk factor for PD. We now study the effect of manganese in transgenic mice expressing the human wild type or mutated α-synuclein (collaboration with Dr. Eric K. Richfield, Environmental and Occupational Health Science Institute, Piscataway, New Jersey). In the future, we intend to investigate the interaction of various endogenous and exogenous facts implicated in PD by crossing transgenic and knock-out lines and exposing these lines to exogenous factors such as manganese and/or iron.

In brain tissue of MPTP-monkeys (collaboration with Dr. José A. Obeso, Neuroscience Division, CIMA, University of Navarra, Pamplona, Spain) and post-mortem brain tissue of patients with PD (collaboration with Dr. Stephen J. Kish, Human Neurochemical Pathology Laboratory, Centre for Addiction and Mental Health, Toronto, Ontario) we look for specifc neurochemical changes in the basal ganglia which might explain how losses of up to 70 % of dopaminergic neurons can be compensated in presymptomatic stages of the parkinsonian disease process, and for specific subregional patterns of changes which might provide the basis for Parkinson motor subtypes.

We use behavioural, neurochemical, radioligand binding and unbiased stereological cell counting methods to study the neurodegenerative mechanisms.

Curriculum Vitae

Ao.Univ.Prof. Christian Pifl

Medical Univ. of Vienna, Center for Brain Research, A-1090 Vienna, Spitalgasse 4

Personal Data

Date of Birth:	6.11. 1955
Place of Birth:	Vienna
Nationality	Austria

Education

from – to	
1976-1989	Studies of chemistry at the University of Vienna, master thesis under supervision of Prof. Dr. A. Neckel, Department for Physical Chemistry, Division of Electrochemistry 1989 graduation: Master of Natural Sciences (MSc)
1974-1981	Medical studies at the Universitiy of Vienna 1981 graduation: Doctor of Medicine (MD)
1966-1974	High school of modern languages, Theresianische Akademie in Vienna 1974 school certificate examination (Matura) with the mark outstanding
1962-1966	Elementary school in Vienna

Career History

from – to	
2000 - present	Associate professor and group leader (Molecular Pharmacology) at the Division of Biochemistry and Molecular Biology of the Center for Brain Research, Medical University of Vienna
1999	Acting chairman of the Institute of Biochemical Pharmacology and the Division of Biochemistry and Molecular Biology of the Brain Research Institute of Vienna, respectively
1998	Qualified medical specialist in pharmacology
1997	short-listed for the appointment of a Professor of Neurochemistry at the Leopold-Franzens University of Innsbruck
1994	Teaching qualification (Venia docendi) in Pharmacology and Toxicology Associate professor at the Institute of Biochemical Pharmacology of the University of Vienna
1991-1993	Research Fellow at the Duke University, Howard Hughes Medical Institute Laboratories (Dr. Marc G. Caron), North Carolina, USA on leave of absence from the University of Vienna
1983-1995	University assistant at the Institute of Biochemical Pharmacology of the University of Vienna (Chairman: Prof. Dr. O. Hornykiewicz)
1982-1983	Research assistant at the Pharmacological Institute of the University of Vienna (Chairman: Prof. DDr. O. Kraupp) in the research unit of Prof. Dr. J. Suko

Career-related Activities

from – to	
1995	Member of the Editorial Board for the Evaluation of Neuroscience Research in Austria

Awards

Year	
1984	Hoechst Award
1991, 1992	ERWIN SCHRÖDINGER fellowship for 2 consecutive years

Memberships

Since 1994	New York Academy of Sciences
Since 1996	Austrian Pharmacological Society (APHAR)
Since 1998	German Society for Experimental and Clinical Pharmacology and Toxicology (DGPT)
Since 2003	Society for Neuroscience

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*
2002 -May 2005	AUSTRIAN NATIONAL BANK ANNIVERSARY FUND # 9306	α-Synuclein and intracellular dopamine
March 2002 -Febr 2005	AUSTRIAN SCIENCE FOUNDATION #P15369	Intracellular effects of catecholamines
March 2007- Febr 2009	MEDICAL-SCIENTIFIC FONDS OF THE MAJOR OF VIENNA #2578	Effect of manganese on the brain of α-synuclein transgenic mice

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
Dec 9, 2006-	Dipl.Ing. Tamara Peneder	Effect of manganese on the brain of human α-synuclein expressing mice

Publications

45 peer reviewed publications in scientific journals, 7 book chapters, 11 invited lectures

Peer reviewed manuscripts 2003-2008 (original research and reviews)

First, last or corresponding author manuscripts:

Nanoff, C., **Pifl, C.** (2008) Neurotransmitter transporters. In Encyclopedia of Molecular Pharmacology Offermanns, Stefan; Rosenthal, Walter (Eds.), Springer

Pifl, C., and Hornykiewicz, O. (2006) Dopamine turnover is upregulated in the caudate/putamen of asymptomatic MPTP-treated rhesus monkeys. Neurochem. Internat. 49:519-524

Pifl, C., and Sperk, G. (2006) Current topics in brain dopamine research: a tribute to Professor Oleh Hornykiewicz. Wien.Klin.Wochenschr. 118, 563-565

Pifl, C., Nagy, G., Berenyi, S., Kattinger, A., Reither, H., and Antus, S. (2005) Pharmacological characterization of ecstasy synthesis byproducts with recombinant human monoamine transporters. *J Pharmacol Exp Ther* 314, 346-354

Woldman, I., Reither, H., Kattinger, A., Hornykiewicz, O., and **Pifl, C.** (2005) Dopamine inhibits cell growth and cell cycle by blocking ribonucleotide reductase. *Neuropharmacology* 48, 525-537

Pifl, C., Rebernik, P., Kattinger, A., and Reither, H. (2004) Zn^{2+} modulates currents generated by the dopamine transporter: parallel effects on amphetamine-induced charge transfer and release. *Neuropharmacology* 46, 223-231

Pifl, C., Khorchide, M., Kattinger, A., Reither, H., Hardy, J., and Hornykiewicz, O. (2004) α-Synuclein selectively increases manganese-induced viability loss in SK-N-MC neuroblastoma cells expressing the human dopamine transporter. *Neurosci.Lett.* 354, 34-37

Co-author manuscripts:

Rajput, A.H., Sitte, H.H., Rajput, A., Fenton, M.E., **Pifl, C.**, and Hornykiewicz, O. (2008) Globus pallidus dopamine and Parkinson motor subtypes: clinical and brain biochemical correlation. *Neurology* 70 16, 1403-1410

Xu, J., Zhong, N., Wang, H., Elias, J. E., Kim, C. Y., Woldman, I., **Pifl, C.,** Gygi, S. P., Geula, C., and Yankner, B. A. (2005) The Parkinson's disease-associated DJ-1 protein is a transcriptional co-activator that protects against neuronal apoptosis. *Hum.Mol.Genet.* 14, 1231-1241

Rajput, A. H., Fenton, M. E., Di Paolo, T., Sitte, H., **Pifl, C.,** and Hornykiewicz, O. (2004) Human brain dopamine metabolism in levodopa-induced dyskinesia and wearing-off. *Parkinsonism.Relat Disord.* 10, 221-226

Invited Talks 2003-2008

4

Univ.Prof. Dr. Jürgen Sandkühler
Department of Neurophysiology, Center for Brain Research,
Medical University of Vienna
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Description of thesis project:

Abstract:
The spinal cord is an outstanding model system for studying information processing in the central nervous system in general and clinically relevant pain mechanisms in particular. The spinal cord possesses well defined inputs from the periphery (sensory nerve fibres) and from the brain (descending fibre tracts) and outputs to the periphery (motoneurons and sympathetic and parasympathetic efferents) and to the brain (ascending fibre tracts). The spinal neuronal network may perform tasks as simple as monosynaptic reflexes and as complex as learning and memory formation. The spinal cord is easily accessible at all organisational levels ranging from molecular to systemic and including all presently available *in vitro* technologies as well as studies in human volunteers and patients.

In the department we study spinal mechanisms of pain. Normal sensitivity to pain is required to identify potential harmful stimuli or tissue damage and to trigger the appropriate behavioural responses. Parts of the peripheral and the central nervous systems are dedicated to serve this function (9). The pain sensors are specialized nerve fibres which are present in almost all tissues and which can normally only be activated by strong, i.e. painful (noxious) stimuli. These pain sensing nerve fibres are called nociceptive C-fibres. Pain-related information is transmitted from nociceptive C-fibres to nerve cells in spinal cord, which relay information to various brain areas. The final result of this chain of excitation is a multidimensional pain experience that includes aversive, vegetative and sensory-discriminative aspects of pain.

Pain perception may be amplified during trauma, inflammation or nerve injury so that normally non painful stimuli, e.g. movement of a joint, muscle contraction, gentle touch of the skin or even normal body temperature cause pain. Moderate pain stimuli may then trigger excruciating pain sensations. It has long been recognized that sensitization of nociceptive C-fibres in the area of trauma or inflammation causes pain amplification. This “peripheral sensitization” typically ceases when the underlying inflammation has healed. In some unfortunate pain patients the abnormal pain sensitivity may, however, persist months and even years after the primary cause for pain has disappeared. Then pain is no longer a symptom of a disease but has become a disease in its own right –the “pain disease”–. A number of studies suggest that beside peripheral sensitization other pain amplifier must exist in the central nervous system, most likely in the spinal cord and that these central pain amplifiers may cause the pain disease (5). The neuronal mechanism(s) of central pain amplification are, however, not well understood.

Nerve cells, including nociceptive nerve fibres and spinal cord nerve cells communicate with each other at specialized junctions, the so called synapses, by using one or more chemical neurotransmitter(s) (4). We have reported recently that information transfer from C-fibres to a distinct group of nerve cells in superficial spinal dorsal horn is augmented in an activity-dependent manner (2; 3). This synaptic long-term potentiation (LTP) is now considered a major cellular mechanism of pain amplification (7).

Another major factor which determines pain sensation is the level of inhibition in spinal cord. With transgenic mice which express the green fluorescent protein (GFP) it has now become possible to directly study the properties of inhibitory interneurons in slice preparations of spinal cord (1; 8). This is another major step towards sorting out the functions of spinal neuronal network properties in health and disease.

We use state-of-the-art neurophysiological and imaging technologies both, *in vitro* and *in vivo* including 2-photon laser scanning-microscopy which enables us to monitor fluorescent signals in unprecedented spatial and temporal resolution deeply within living tissues (6). We combine these imaging technologies with patch-clamp recordings, behavioural studies and immunohistochemistry.

Reference List

1. Heinke B, Ruscheweyh R, Forsthuber L, Wunderbaldinger G, Sandkühler J. Physiological, neurochemical and morphological properties of a subgroup of GABAergic spinal lamina II neurones identified by expression of green fluorescent protein in mice. J Physiol 560: 249-266, 2004.

2. Ikeda H, Heinke B, Ruscheweyh R, Sandkühler J. Synaptic plasticity in spinal lamina I projection neurons that mediate hyperalgesia. Science 299: 1237-1240, 2003.

3. Ikeda H, Stark J, Fischer H, Wagner M, Drdla R, Jäger T, Sandkühler J. Synaptic amplifier of inflammatory pain in the spinal dorsal horn. Science 312: 1659-1662, 2006.

4. Jonas P, Bischofberger J, Sandkühler J. Corelease of two fast neurotransmitters at a central synapse. Science 281: 419-424, 1998.

5. Nichols ML, Allen BJ, Rogers SD, Ghilardi JR, Honoré P, Luger NM, Finke MP, Li J, Lappi DA, Simone DA, Mantyh PW. Transmission of chronic nociception by spinal neurons expressing the substance P receptor. Science 286: 1558-1561, 1999.

6. Niggli E, Egger M. Applications of multi-photon microscopy in cell physiology. Front Biosci 9: 1598-1610, 2004.

7. Sandkühler J. Understanding LTP in pain pathways. Mol Pain 3: 9, 2007.

8. Schoffnegger D, Heinke B, Sommer C, Sandkühler J. Physiological properties of spinal lamina II GABAergic neurons in mice following peripheral nerve injury. J Physiol 577: 869-878, 2006.

9. Willis WD, Jr., Coggeshall RE. Sensory mechanisms of the spinal cord. Ascending sensory tracts and their descending control. New York: Kluwer Academic/Plenum Publishers, 2004.

Curriculum Vitae

Univ.Prof. Dr. Jürgen Sandkühler

Center for Brain Research, Medical University of Vienna, Spitalgasse 4, A-1090 Vienna

Personal Data

Date of Birth:	12.7.1957
Place of Birth:	Recklinghausen, Germany
Nationality	German

Education

1988	Diploma: State Doctorate M.D. (Dr.med.habil. Physiology, no grades
1984	Diploma: Graduation M.D. (Dr.med., with excellence)
1983 – 1984	Medical School, Freiburg University, Germany Residency, University Hospital Konstanz, Germany Diploma: State Examination, Licensure to Practice Medicine
1981 – 1984	Institute of Physiology, Heidelberg University, Germany Doctoral thesis, supervisor Prof. Manfred Zimmermann 1981 – 1982 Electrophysiological studies, Heidelberg University 1982 – 1983 Behavioural studies, Institute of Pharmacology, University of Iowa, Iowa-City, IA, U.S.A. with Prof. Gerald F. Gebhart
1977 – 1983	Medical School, Heidelberg University
1968 – 1977	Theodor-Heuss High School, Recklinghausen, Germany Diploma: University Entrance Diploma (with excellence)
1964 – 1968	Elementary School in Recklinghausen, Germany

Career History

Since 2007	Member of the editorial board of "*Science*"
Since 2007	Director, Centre for Brain Research, Medical University Vienna
2004-2007	Deputy Director, Centre for Brain Research, Medical University Vienna
Since 2001	Full Professor of Neurophysiology, Centre for Brain Research, Medical University Vienna, Department of Neurophysiology
1999 – 2001	Speaker, Multidisciplinary Research Programme *„Pain"* Medical Faculty, Heidelberg University
1996 – 1997	Institute of Physiology, Freiburg University, Germany Visiting Professor with Prof. Peter Jonas
1996 – 2001	Institute of Physiology, Heidelberg University, Germany Assistant Professor
1995	Institute of Physiology and Pharmacology, Iowa State University U.S.A., Visiting Professor with Prof. Mirjana Randic

Awards

2006	Science Award of the German Chapter of the IASP
2005	Honory Scientific Pain Award of the German Pain Society
2004	Science Award of the Austrian Chapter of the IASP
1995-2000	Heisenberg Professorship of the German Science Foundation (DFG), Bonn

Memberships

IASP
German and Austrian chapters of the IASP
Society for Neuroscience
German Neuroscience Association

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*
2008-2011	WWTF	A novel role of opioids

2005 - 2008	FWF	Synaptic mechanisms of inflammatory pain
2004 - 2005	Jubiläumsfonds der Österreichischen Nationalbank	Rolle der GABAergen Hemmung im Rückenmark beim Schmerz
2003 - 2004	Jubiläumsfonds der Stadt Wien für die Österreichische Akademie der Wissenschaften	Reversal of synaptic long-term potentiation in the nociceptive system
2003 - 2005	Medizinisch-Wissenschaftlicher Fonds des Bürgermeisters der Bundeshauptstadt Wien	Neuronale Ursachen von chronischen Schmerzen: Rolle von Lamina I Neuronen des Rückenmarks
2002 - 2005	FWF	Cellular mechanisms of hyperalgesia

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
2002 - 2003	Anne Dahlhaus	Synaptic input of rat spinal lamina I projection and unidentified neurones in vitro
2002 - 2003	Florian Müller	Reduction of glycine receptor-mediared miniature inhibitory postsynaptic currents in rat spinal lamina I neurons after peripheral inflammation
2003 - 2004	Johanna Stark	Synaptic mechanisms of hyperalgesia in vivo
2003 - 2004	Armin Goralczyk	Rolle von NO-Synthasen bei der spinalen Schmerzverarbeitung
2004 - 2007	Doris Schoffnegger	Neuropathic pain in mice
2004 -2008	Ruth Drdla	Synaptic mechanisms of hyperalgesia and allodynia *in-vivo*
Since 2004	Matthias Wagner	Einsatz der Herzlungenmaschine bei kleinen Nagern zur Anwendung der 2-Photonen Laserscanning-Mikroskopie am Rückenmark *in-vivo*
Since 2007	Jörg Leitner	Modulation of the spinal GABAergic system in neuropathy
Since 2007	Matthias Gassner	Effects of monoamines on spinal GABAergic neurons
Since 2008	Celine Heinl	Novel roles of opioids
From 2008	Henning Fenselau	To be determined

Publications
34 peer reviewed publications in scientific journals, -- book chapters, 97 invited lectures, -- patents"

Peer reviewed manuscripts 2003-2008 (original research and reviews)
First, last or corresponding author manuscripts:
Original articles:

Schoffnegger D., Ruscheweyh R., **Sandkühler J.,** (2008) Spread of excitation across modality borders in spinal dorsal horn of neuropathic rats. *Pain*, **135**: 300-310

Ruscheweyh R., Forsthuber L., Schoffnegger D., **Sandkühler J.,** (2007) Modification of classical neurochemical markers in identified primary afferent neurons with Aβ-, Aδ-, and C-fibers after chronic constriction Injury in mice. *J. Comp. Neurol.*, **502**: 325-326

Heinke B., **Sandkühler J.,** (2007) Group I metabotropic glutamate receptor-induced Ca^{2+}-gradients in

rat superficial spinal dorsal horn neurons. *Neuropharmacology*., **52**: 1015-1023

Benrath J., Kempf C., Georgieff M., **Sandkühler J.,** (2007) Xenon blocks the induction of synaptic long-term potentiation in pain pathways in the rat spinal cord in vivo. *Anesth. Analg.*, **104**: 106-111

Schoffnegger D., Heinke B., Sommer C., **Sandkühler J.** (2006) Physiological properties of spinal lamina II GABAergic neurons in mice following peripheral nerve injury. *J. Physiol*., **577**: 869-878

Ruscheweyh R., Goralzcyk A., Wunderbaldinger G., Schober A., **Sandkühler J.** (2006) Possible sources and sites of action of the nitric oxide involved in synaptic plasticity at spinal lamina I projection neurons. *Neuroscience*, **141**:977-988.

Ikeda H., Stark J., Fischer H., Wagner M., Drdla R., Jäger T., **Sandkühler J**. (2006) Synaptic amplifier of inflammatory pain in the spinal dorsal horn. *Science*, **312**: 1659-1662.

Ruscheweyh R. & **Sandkühler J.** (2005) Long-range oscillatory Ca^{2+} waves in rat spinal dorsal horn. *Europ. J. Neurosci.*, **22**: 1967-1976.

Heinke B., **Sandkühler J.** (2005) Signal transduction pathways of group I metabotropic glutamate receptor-induced long-term depression at sensory spinal synapses. *Pain*, 117:1-10

Benrath J., Brechtel C., Stark J., **Sandkühler J.** (2005) Low dose of S(+)-ketamine prevents long-term potentiation in pain pathways under strong opioid analgesia in the rat spinal cord in vivo. *Br J Anaesth.*, 95:518-23

Dahlhaus A., Ruscheweyh R., **Sandkühler J**. (2005) Synaptic input of rat spinal lamina I projection and unidentified neurons in vitro. *J. Physiol*., 566:355-368

Heinke B., Ruscheweyh R., Forsthuber L., Wunderbaldinger G., **Sandkühler J.** (2004) Physiological, neurochemical and morphological properties of a subgroup of GABAergic spinal lamina II neurons identified by expression of green fluorescent protein in mice. *J. Physiol*., 560:249-266

Benrath J., Brechtel C., Martin E., **Sandkühler J**. (2004) Low Doses of Fentanyl Block Central Sensitization in the Rat Spinal Cord In Vivo. *Anesthesiology .*, 100:1545–1551

Heinke B., Balzer E., **Sandkühler J.** (2004) Pre- and postsynaptic contributions of voltage-dependent Ca2+ channels to nociceptive transmission in rat spinal lamina I neurons*. Europ. J. Neurosci.*, 19: 103-111

Ruscheweyh R., Ikeda H., Heinke B., **Sandkühler J.** (2004) Distinctive membrane and discharge properties of rat spinal lamina I projection neurons in vitro. *J. Physiol*, 555: 527-543

Azkue J.J., Liu X.-G., Zimmermann M., **Sandkühler J.** (2003) Induction of long-term potentiation of C fibre-evoked spinal field potentials requires recruitment of group I, but not group II/III metabotropic glutamate receptors *Pain*, 106: 373-379

Müller F., Heinke B., **Sandkühler J.** (2003) Reduction of glycine receptor-mediared miniature inhibitory postsynaptic currents in rat spinal lamina I neurons after peripheral inflammtion. *Neuroscience*, 122: 799-805

Eichler M., Dahlhaus R., **Sandkühler J**. (2003) Partial correlation analysis for the identifcation of synaptic connections. *Biol. Cybern.*, 89: 289–302

Ruscheweyh R. & **Sandkühler J.** (2003) Epileptiform activity in rat spinal dorsal horn in vitro has common features with neuropathic pain. *Pain*, 105: 327-338

Ikeda H., Heinke B., Ruscheweyh R., **Sandkühler J**. (2003) Synaptic Plasticity in Spinal Lamina I Projection Neurons That Mediate Hyperalgesia. *Science*, 299: 1237-1240.

Ruscheweyh R. & **Sandkühler J.** (2002) Lamina-specific membrane and discharge properties of rat spinal dorsal horn neurons *in vitro*. *J. Physiol.*, 541: 231-244.

Ruscheweyh R. & **Sandkühler J.** (2001) Bidirectional actions of nociceptin/orphanin FQ on δ-fibre-evoked responses in rat superficial spinal dorsal horn *in vitro*. *Neuroscience*, 107: 275-281.

Ruscheweyh R. & **Sandkühler J.** (2000) Differential action of spinal analgesics on mono- versus polysynaptic δ-fibre-evoked field potentials in superficial spinal dorsal horn in vitro. *Pain*, 88: 97-108.

Chen J., Heinke B. & **Sandkühler J.** (2000) Activation of group I metabotropic glutamate receptors induces long-term depression at sensory synapses in superficial spinal dorsal horn. *Neuropharmacology*, 39: 2231-2243

Chen J. & **Sandkühler J.** (2000) Induction of homosynaptic long-term depression at spinal synapses of sensory δ-fibers requires activation of metabotropic glutamate receptors. *Neuroscience*, 98: 139-146.

Gillardon F., Kiprianova I., **Sandkühler J.,** Hossmann K.-A. & Spranger M. (1999) Inhibition of caspases prevents cell death of hippocampal CA1 neurons, but not impairment of hippocampal long-term potentiation following global ischemia, *Neuroscience*, 93: 1219-1222.

Review articles:

Sandkühler, J. (2007) Understanding LTP in pain pathways. *Molecular Pain*, 3:9

Sandkühler, J. (2006) Long-Term Potentiation and Long-Term Depression in the Spinal Cord, In: Encyclopedia of Pain, Vol. 1, 2006, Springer Verlag, Heidelberg, New York, 2007 Robert F. Schmidt and Williams D. Willis (Eds.), pp.1058-1061.

Sandkühler, J., Kress, H.G. (2005) Opioids for chronic nonmalignant and neuropathic pain. *Eur. J. Pain*, 9: 99-100.

Sandkühler, J., Ruscheweyh, R. (2005) Opioids and central sensitisation: I. Pre-emptive analgesia. *Eur. J. Pain*, 9: 145-148.

Ruscheweyh, R., **Sandkühler, J.** (2005) Opioids and central sensitisation: II. Induction and reversal of hyperalgesia. *Eur. J. Pain*, 9: 149-152.

Sandkühler, J. (2005) Neurobiologische Grundlagen des Schmerzgedächnisses *Psychoneuro*, 31: 77-80.

Sandkühler, J. (2002) Fear the pain. *Lancet*, 360: 426.

Sandkühler, J. (2002) Physiologie und Pathophysiologie chronischer Schmerzen-Neue Erkenntnisse zur Chronifizierung. In: Schmerz Manual, BDA, Emstetten: 23-28.

Ruscheweyh, R., & **Sandkühler, J.** (2002) Role of kainate receptors in nociception. *Brain Res. Rev.*,

40: 215-222.

Sandkühler, J. (2001) Schmerzgedächtnis. Entstehung, Vermeidung und Löschung. *Deutsches Ärzteblatt*, 98/42: 2725-2730.

Sandkühler, J. (2001) Schmerzchronifizierung: Neurobiologische Ursachen und Prävention. *CF-Journal*, 2/2001, 38-40.

Sandkühler, J. (2000) Learning and memory in pain pathways, *Pain*, 88: 113-118.

Sandkühler, J., Benrath J., Brechtel C., Ruscheweyh R., Heinke B. (2000) Synaptic mechanisms of hyperalgesia, In J. Sandkühler, B. Bromm & G.F. Gebhart (Hrsg.), Nervous System Plasticity and Chronic Pain, Progress in *Brain Research*, 129, Amsterdam: Elsevier, pp 81-100. Preprint

Sandkühler, J., Benrath, J. (2000) Das nozizeptive System von Früh- und Neugeborenen, In: B. Zernikow (Hrsg.) Schmerztherapie bei Kindern, Berlin, Heidelberg, New York, Springer Verlag, pp. 1-17.

Sandkühler, J. (2000) Neurobiologie der Nozizeption. In: Anästhesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie (AINS) Band 4 Schmerztherapie, In: J. Schulte am Esch E. Martin, H. Beck & J. Motsch (Hrsg.), Stuttgart, New York: Georg Thieme Verlag, im Druck.

Benrath, J. & **Sandkühler, J.** (2000) Nozizeption bei Früh- und Neugeborenen, Der Schmerz, 14: 297-301.

Sandkühler, J. (2000) Long-lasting analgesia following TENS and acupuncture: Spinal mechanisms beyond gate control. In: M. Devor, M. Rowbotham & Z. Wiesenfeld-Hallin (Hrsg.) Proceedings of the 9th World Congress on Pain, Progress in Pain Research and Management, Vol.16, Seattle: IASP Press, 359-370.

Co-author manuscripts:

Klein T., Magerl W., Nickel U., Hopf J.-H., **Sandkühler J.,** Treede R.-D., (2007) Effects of the NMDA-receptor antagonist ketamine on perceptual correlates of long-term potentiation within the nociceptive system. *Neuropharmacology*., **52:** 655-661

Klein T., Magerl W. , Hopf H.-C., **Sandkühler J.,** Treede R.-D. (2004) Perceptual Correlates of Nociceptive Long-Term Potentiation and Long-Term Depression in Humans*. J. Neurosci.*, 24: 964-971.

Invited Talks 2003-2008

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Dr. Isabella Sarto-Jackson
Division of Biochemistry and Molecular Biology, Center for Brain Research,
Medical University of Vienna
isabella.sarto-jackson@meduniwien.ac.at

Description of thesis project:

The tight regulation and control of neuronal excitability is crucial for normal brain function. $GABA_A$ receptors, being the main inhibitory neurotransmitter receptors in the central nervous system, regulate fast interneuronal synaptic transmission. Synaptic strength is regulated by $GABA_A$ receptors according to their subcellular distribution, their subunit composition and their subtype specific electrophysiological and pharmacological profile. In addition, increasing evidence accumulates for physical association between $GABA_A$ receptors and structurally and functionally divergent families of neurotransmitter receptors. These interactions regulate synaptic strength independently of classically defined second-messenger systems.
Moreover, to mediate fast inhibition effectively, $GABA_A$ receptors require intracellular anchoring molecules as well as mechanisms that ensure the efficient turnover, the transport of mature, functional receptor proteins and the facilitated assembly of receptor intermediates. Proteins involved in the dynamic regulation of $GABA_A$ receptor biogenesis and trafficking, thus, fulfil a significant role in the orchestrated interplay of regulated neuronal excitability.

I am currently investigating the interaction of $GABA_A$ receptors with another membrane protein that might influence receptor maturation and/or transport. I have previously demonstrated the association of these proteins biochemically, by FRET analysis and by immunocytochemical methods. To reveal the function of this associated protein, I am currently performing RNAi methods as well as overexpression and co-localization studies in primary hippocampal neurons.

Techniques and Infrastructure:

I use standard molecular biological techniques, such as generation of mutated, truncated or (fluorescence-)tagged DNA constructs and RNAi techniques. These constructs are characterized by standard biochemistry methods, such as co-immunoprecipitation, Western blot analysis and density gradient centrifugation as well as by pharmacological methods, such as receptor binding studies. In addition, cell culture techniques are exploited to perform recombinant receptor expression, immunocytochemistry, FRET or RNAi studies.
Generation and purification of antibodies against the proteins investigated facilitate the experimental procedure and avoid technical shortcoming of commercially available antibodies.
Due to the excellent collaboration with other group leaders of the Center for Brain Research and other groups within the MUW, electrophysiological investigations and primary cell culture methods for immunocytochemistry and subsequent studies by confocal microscopy are regularly performed.

Thesis topic:

Constructing inhibitory synapses - Interaction of $GABA_A$ receptors with other receptors or proteins

Techniques used: Standard molecular biological and biochemical techniques. Cell culture techniques and subsequent fluorescence and confocal microscopy are applied in order to investigate the dynamic spatial and temporal regulation of $GABA_A$ receptors. A putative functional cross-talk will be investigated by pharmacological methods or electrophysiological techniques (performed in collaboration with Prof. S. Huck).

Curriculum Vitae

Dr. Isabella Sarto-Jackson
Center for Brain Research, Medical University Vienna, Spitalgasse 4, 1090 Vienna

Personal Data

Date of Birth:	4.3. 1968
Place of Birth:	Vienna, Austria
Nationality	Austrian/Italian

Education

01/1999 – 02/2002	PhD studies in Neurobiochemistry at the Medical University of Vienna
02/2002	Graduation (with distinction)
02/1997 – 12/1998	Diploma studies in Genetics at the University of Vienna
12/1998	2nd diploma examination (with distinction)
10/1995 – 06/1997	Study of Biology, field of studies: Genetics at the University of Vienna, Vienna Biocenter
06/1995	1st diploma examination
10/1988 – 06/1995	Study of Biology at the University of Vienna, Biocenter Althanstrasse (including gap years for professional carrier)
09/1978 – 06/1987	Grammar school, Vienna, Amerlingstraße
06/1987	Matura
09/1974 – 06/1978	Elementary school, Vienna, Vorgartenstraße

Career History

09/2006 - dato	Maternity leave
11/2002 – 09/2006	University Assistant at the Medical University of Vienna, Center for Brain Research, Division of Biochemistry and Molecular Biology
02/2002 – 10/2002	Post-doc (Neurobiochemisty) at the University of Vienna, Brain Research Institute, Division of Biochemistry and Molecular Biology
01/1999 – 02/2002	PhD thesis in Neurobiochemistry at the University Clinic for Psychiatry, Section of Biochemical Psychiatry, and Center for Brain Research, Division of Biochemistry and Molecular Biology
02/1997 – 12/1998	Diploma thesis in Genetics at the University of Vienna, Vienna Biocenter, Department for Microbiology and Genetics
07/1995 – 10/1995	Scientific Assistant in Molecular Biology, SANDOZ Vienna, IMD
02/1993 – 12/1994	Assistant Congress Coordinator, Austrian Institute for Healthy and Ecological Building, Vienna
04/1992 – 03/1993	Marketing Assistant, Salzburg Airlines GmbH, Vienna
01/1991 – 03/1992	Press Assistant, Austrian Institute for Healthy and Ecological Building, Vienna
07/1987 – 07/1990	Clerk, H. Skolaude GesmbH, Vienna

Career-related Activities

03/2006 – 08/2006	Journalclub Neuroscience, University of Vienna
03/2006 – 06/2006	Tutor: POL/PBL (Problem based learning)
10/2005 – 01/2006	Tutor: POL/PBL (Problem based learning)
10/2005	Lecture: SSM1, Database research for medical students
02/2005	Training to be a POL/PBL-tutor (Problem based learning)
05/2004	Co-organisation, tutorial + lecturing at the Crystallization Workshop at the Medical University of Vienna, Center for Brain Research (in collaboration with Dr. B. Rupp of the Lawrence Livermore Institute, California, USA)
11/2002	Workshop on Expression and Structural Studies of Membrane Proteins, Göteborg, Sweden
06/1999 + 09/1999	Tutorial: Experimental Genetics I, Vienna Biocenter
06/1998 + 09/1998	Tutorial: Experimental Genetics I, Vienna Biocenter
06/1997 + 09/1997	Tutorial: Experimental Genetics I, Vienna Biocenter

Awards
04/06 Theodor-Körner Prize, Austrian Federal Chamber of Labour

Memberships
Austrian Society for Biochemistry and Molecular Biology
Austrian Neuroscience Association
Austrian Association for Genetics and Genetic Engineering

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*	

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
2006 – dato	Amulya Shrivastava	$GABA_A$ receptor composition and crosstalk with other receptors mediated by protein-protein coupling (CCHD program)

Publications
10 peer reviewed publications in scientific journals, 0 book chapters, 1 invited lecture

Peer reviewed manuscripts 2003-2008 (original research and reviews)
First, last or corresponding author manuscripts:
Sarto-Jackson I., Sieghart W. (2008) $GABA_A$ receptor assembly. *Molecular Membrane Biology*, in press

Sarto-Jackson I., Furtmüller R., Ernst M., Huck S., Sieghart W. (2007) Spontaneous cross-link of mutated $\alpha 1$ subunits during $GABA_A$ receptor assembly. *Journal of Biological Chemistry*, 282: 4354-63

Sarto-Jackson I., Ramerstorfer J., Ernst M., Sieghart W. (2006) Identification of Amino Acid Residues Important for Assembly of $GABA_A$ Receptor α_1 and γ_2 Subunits. *Journal of Neurochemistry*, 96: 983-95

Ehya N.,* **Sarto I.**,* Wabnegger L., Klausberger T., Sieghart W. (2003) Identification of an Amino Acid Sequence within $GABA_A$ Receptor β_3 Subunits that is Important for Receptor Assembly. *Journal of Neurochemistry*, 84: 127-135
(*contributed equally)

Co-author manuscripts:
Pytel M., Wojtowicz T., Mercik K., **Sarto-Jackson I.**, Sieghart W., Ikonomidou C., Mozrzymas J.W. (2007) 17 beta-estradiol modulates GABAergic synaptic transmitssion and tonic currents during development in vitro. *Neuropahrmacology*, 52:1342-53

Dr. Petra Scholze
Division of Biochemistry and Molecular Biology, Center for Brain Research,
Medical University of Vienna
petra.scholze@meduniwien.ac.at

Description of thesis project:

Upon the release of the neurotransmitter acetylcholine, nicotinic acetylcholine receptors (nAChRs) mediate signal transduction between nerve and muscle cells on one hand (muscle-type receptors), and at nerve cells of the brain and the autonomic nervous system (neuronal-type receptors) on the other hand. Each receptor consists of 5 either identical (homo-pentamers) or differing (hetero-pentamers) subunits. It is important to note that the functional properties of these receptors are primarily determined by their subunit composition.

Accordingly, knowledge of the subunit composition is essential. We are addressing this question in the mouse superior cervical ganglion (SCG), a popular model for neuronal type receptors. nAChR subunits consistently found in the ganglion are α_3, α_5, α_7, β_2, and β_4. We have recently discovered that mRNA of the α_4 subunit, a principal constituent of nicotinic receptors in the brain, is also transiently expressed in the SCG of mice after birth. We know that except for α_7, these subunits assemble into hetero-pentameric receptors. The exact composition of these receptors is, however, not known. This question will be addressed by a combined use of antibodies and radioligand binding techniques. Our focus will be on mice rather than rats or chicken because we are studying mouse models with targeted deletions of distinct nAChR subunit genes in parallel.

Two of these models are of particular interest: Mice that lack the two subunits α_5 and β_2, and mice without the subunits α_5 and β_4. These two models leave SCG neurons that express definite $\alpha_3\beta_2$ or $\alpha_3\beta_4$ hetero-pentameric receptors, respectively. Interestingly, both genotypes are viable and show no gross behavioral changes. To date, such definite receptors could only be studied by heterologous expression in frog (*Xenopus*) oocytes or in cell lines, but not in a physiological environment. We will now, for the first time characterize these receptors.

Techniques and infrastructure:

Personal expertise: Primary cell and tissue (explants) cultures from various parts of the nervous system, cell culture and transfection of HEK293 cells, expression of recombinant receptors, Patch clamp recordings; fura2 calcium imaging; transmitter release from brain slices; immunofluorescence, standard techniques in molecular biology (cloning, genotyping, RT-PCR, PCR, 5'-RACE, ...), standard techniques in protein chemistry (antibody generation, Western Blot, immunoprecipitation,...), radioligand binding assays

Infrastructure: Cell and tissue culture facilities; 3 patch clamp setups, one calcium imaging setup, superfusion chambers for studying transmitter release from cell cultures and slice preparations, basic equipment for molecular biology and cell transfection (PCR, Biorad Gel-Doc 2000 gel documentation). 3 fluorescence microscopes.

Thesis topic:

Characterization of the subunit composition of nicotinic Acetylcholine receptors in mouse superior cervical ganglion (SCG) from wild-type mice and mice with targeted deletions of several nicotinic acetylcholine receptor genes.

Curriculum Vitae

Dr. Petra Scholze
Center for Brain Research, Medical University Vienna, Spitalgasse 4, 1090 Vienna

Personal Data

Date of Birth:	23.09.1971
Place of Birth:	Wien, Austria
Nationality	Austria

Education

01.02.1999	graduation as: Dr. rer. nat. (PhD)
1995-1998	PhD-Thesis at the Department of Biochemical Psychiatry, University Clinic for Psychiatry, Vienna General Hospital
28.06.1995	graduation as: Mag. rer. nat.
1994-1995	Diploma-Thesis at the Department of Biochemical Psychiatry, University Clinic for Psychiatry, Vienna General Hospital
1989-1995	Studies in Biochemistry, University of Vienna
1989	Matura with excellent success

Career History

since 06/2005	"Vertragsassistent" at the Center for Brain Research, Medical University of Vienna
2004-2005	Research fellow at the Center for Brain Research, Medical University of Vienna
2002-2004	Research Fellow of the Alexander von Humboldt Foundation to work at the Department of Neurochemistry, Max Planck Institute for Brain Research, Frankfurt / Main
1998-2002	"Vertragsassistent" at the Institute of Pharmacology, University of Vienna

Career Related Activities
Teaching activities

WS 1999/00 to SS 2002	"Pharmakologisches Seminar mit Rezeptierübungen und praktischen Demonstrationen"
Since WS 2005/06:	„Methods and Techniques in Neuroscience"
Since WS 2006/07:	"Literaturseminar Neurowissenschaften"
Since SS 2007:	„Block 19 – Gehirn Nervensystem Schmerz (Pharma)"
WS 2007/08:	„Journal Club VIII – Formation and Function of Synapses"
Since 2008:	"Problem-Orientiertes Lernen (POL) "

Awards

2002	Humboldt Fellowhip

Memberships
Austrian Neuroscience Association
Austrian Pharmacological Society
Austrian Society for Biochemistry and Molecular Biology
German Society of Experimental and Clinical Pharmacology and Toxicology (DGPT),
Society forNeuroscience

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*
01.01.2007 – 31.12.2007	Hochschuljubiläums-stiftung der Stadt Wien	Cloning of a new splice variant of the organic cation transporter OCT3
01.01.2007 – 31.12.2009	FWF	Neuronal nictonic acetylcholine recptors (nAChR) dissected

PhD supervision (bench supervision) in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
Until 11/2007	Gernot PUTZ	mRNA levels of nAChR subunits in control mice and in mice with targeted deletions of the α5, α7, and the β2 subunit
Ongoing	Reinhard DAVID	Generation and Characterization of Polyclonal Antibodies Directed Against the Nicotinic Acetylcholine Receptor (nAChR) Subunits α3, α4, α5, β2 and β4 for the Investigation of nAChRs Composition and Compensation in Knock-Out Mice

Publications
17 peer reviewed publications in scientific journals, 0 book chapters

Peer reviewed manuscripts 2003-2008 (original research and reviews)

First, last or corresponding author manuscripts
Putz G., Kristufek D., Orr-Urtreger A., Changeux J. P., Huck S. and Scholze P. (2008) Nicotinic acetylcholine receptor-subunit mRNAs in the mouse superior cervical ganglion are regulated by development but not by deletion of distinct subunit genes. J. Neurosci. Res. 86, 972-981.

Scholze P., Orr-Urtreger A., Changeux J. P., McIntosh J. M. and Huck S. (2007) Catecholamine outflow from mouse and rat brain slice preparations evoked by nicotinic acetylcholine receptor activation and electrical field stimulation. Br. J. Pharmacol. 151, 414-422.

Co-author manuscripts
Betz H., Gomeza J., Armsen W., Scholze P. and Eulenburg V. (2006) Glycine transporters: essential regulators of synaptic transmission. Biochem. Soc. Trans. 34, 55-58.

Hilber B., Scholze P., Dorostkar M. M., Sandtner W., Holy M., Boehm S., Singer E. A. and Sitte H. H. (2005) Serotonin-transporter mediated efflux: a pharmacological analysis of amphetamines and non-amphetamines. Neuropharmacology 49, 811-819.

Seidel S., Singer E. A., Just H. et al. (2005) Amphetamines Take Two to Tango: an Oligomer-Based Counter-Transport Model of Neurotransmitter Transport Explores the Amphetamine Action. Mol Pharmacol 67, 140-151.

Ohno K., Koroll M., El Far O., Scholze P., Gomeza J. and Betz H. (2004) The neuronal glycine transporter 2 interacts with the PDZ domain protein syntenin-1. Mol. Cell Neurosci. 26, 518-529.

Farhan H., Korkhov V. M., Paulitschke V., Dorostkar M. M., Scholze P., Kudalcek O., Freissmuth M. and Sitte H. H. (2004) Two discontinuous segments in the carboxy terminus are required for membrane targeting of the rat GABA transporter-1 (GAT1). J. Biol. Chem. 279, 28553-28563

Univ. Prof. Dr. Werner Sieghart
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Medical University of Vienna
werner.sieghart@meduniwien.ac.at

Description of thesis project:

gamma-Aminobutyric acid (GABA) is the major inhibitory transmitter in the central nervous system. Most of the actions of GABA are mediated by $GABA_A$ receptors. These are chloride ion channels that can be opened by GABA and are the site of action of a large variety of clinically and pharmacologically important drugs, such as benzodiazepines, barbiturates, neuroactive steroids, anesthetics and convulsants. Based on the actions of these drugs $GABA_A$ receptors modulate anxiety, excitability of the brain, motor activity, circadian rhythms, sleep, vigilance, learning and memory. $GABA_A$ receptors are composed of five subunits that can belong to different subunit classes. There are 19 different $GABA_A$ receptor subunits in the mammalian brain possibly forming an extremely large number of distinct $GABA_A$ receptor subtypes.

In our research we aim to identify those $GABA_A$ receptor subtypes that actually are present in various parts of the nervous system and to investigate their subunit composition. In addition, we are interested to identify changes in the expression of $GABA_A$ receptor subtypes under pathological conditions, such as epilepsy, fragile X-syndrome, stargazer mutation, or under various hormonal states.To better understand the formation of different $GABA_A$ receptor subtypes we study the molecular determinants of subunit assembly (collaboration with Dr. Sarto-Jackson). In addition, we are studying the pharmacology of various $GABA_A$ receptor subtypes and in collaboration with international research groups are developing new compounds with $GABA_A$ receptor subtype selectivity (collaboration with Prof. Sigismund Huck). In the course of an EU project we are aiming to clarify the structure of $GABA_A$ receptor subtypes by crystallization and X-ray crystallography. And finally, within a National Research Network we are investigating the function of $GABA_A$ receptor subtypes and specific neurons in the amygdala of mice in fear and anxiety (collaboration with Prof. Günther Sperk, Innsbruck). Furthermore, we are actively studying the location and structure of allosteric drug binding sites on $GABA_A$ receptors using homology modeling, mutagenesis and electrophysiological studies (collaboration with Dr. Margot Ernst and Prof. Sigismund Huck). Finally, we are investigating possible causes of psychiatric and neurologic diseases using molecular genetic analyses (collaboration with Dr. Karoline Fuchs, Prof. Harald Aschauer (Department of Psychiatry, MUW) and Prof. Martha Feucht (Department of Pediatrics, MUW).

Techniques and Infrastructure:

The Division of Biochemistry and Molecular Biology of the Center for Brain Research is excellently equipped for all types of biochemical and molecular biological techniques. In my group we are perfoming subcellular fractionation of brain tissue, extraction and purification of $GABA_A$ receptors by ligand affinity chromatography or immunoaffinity chromatography, density gradient centrifugation, cell culture techniques, cell transfection techniques, recombinant receptor expression, generation of mutated, chimeric or truncated subunits, immunohistochemical studies in cell culture, receptor binding studies, electrophysiological studies, generation and purification of antibodies, Western blots, immuno-precipitation, immunohistochemistry, and molecular genetic techniques.

Thesis topic:

Changes in $GABA_A$ receptor subunit composition under various pathological conditions (epilepsy, fragile-X syndrome, $GABA_A$ receptor subunit knockout, transgenic mice containing point mutated $GABA_A$ receptors or overexpressed $GABA_A$ receptor subunits, etc).
Techniques used: generation, purification and characterization of antibodies, preparation of brain membrane fractions, Western blots, extraction of receptors, immunoprecipitation, immunoaffinity chromatography, receptor binding studies.

Pharmacology of $GABA_A$ receptor subtypes
Techniques used: recombinantly expressed receptors in Xenopus oocytes or HEK cells and electro-physiological and receptor binding studies).

Overexpression and purification of $GABA_A$ receptor subtypes or fragments thereof for crystallization and high throughput pharmacological investigations
Techniques used: cell culture of Sf9 cells, cloning of subunits or fractions thereof into baculoviruses, expression, purification, and characterization of receptor subtypes, pharmacological experiments using electrophysiology and receptor binding studies

Changes in $GABA_A$ receptor expression in the course of fear and anxiety
Techniques used: Immunohistochemistry, receptor extraction and determination of their subunit composition using immunoprecipitation, Western blots and receptor binding assays.

Curriculum Vitae

Univ. Prof. Dr. Werner Sieghart

Division of Biochemistry and Molecular Biology, Center for Brain Research,
Medical University of Vienna, Spitalgasse 4, 1090 Vienna, Austria

Personal Data

Date of Birth:	26. 11. 1945
Place of Birth:	Pilsen, CSSR
Nationality	Austria

Education

1973	Ph.D. in Biochemistry
1969 – 1973	Graduate study in Biochemistry with Prof. Dr. H. Tuppy, Institute for Biochemistry, University of Vienna
1963 –1969	Study of Chemistry at the University of Vienna

Career History

2002	Professor for Biochemical and Molecular Pharmacology of the Nervous System and Head, Division of Biochemistry and Molecular Biology of the Nervous System, Center for Brain Research, Medical University Vienna, Austria
since 2001	Chief of the Research Laboratory of the Section of Biochemical Psychiatry, University Clinic for Psychiatry, Medical University of Vienna, Austria
1999 - 2002	Group leader at the Brain Research Institute, Division of Biochemistry and Molecular Biology of the Nervous System, University of Vienna
1988	Professor for Neurobiochemistry
1982	Associate professor at the Section of Biochemical Psychiatry, Vienna
1980 - 2001	Chief of the Section of Biochemical Psychiatry, Vienna, and Chief of a Clinical Chemistry Laboratory performing determinations of drugs of abuse, lithium, hormones and anticonvulsants for the University Clinic for Psychiatry in Vienna and for organizations involved in therapeutic treatment of drug addicts
1979	Assistant professor at the Section of Biochemical Psychiatry, Vienna
1978	Research associate at the Section of Biochemical Psychiatry, University Clinic for Psychiatry, Vienna, Austria
1977-1978	Research associate at the Department of Pharmacology, Yale University, New Haven, CT, with Dr. Paul Greengard
1976-1977	Post doctoral fellow at the Department of Pharmacology, Yale University, New Haven, CT, with Dr. Paul Greengard
1973-1976	Post doctoral fellow at the Section of Biochemical Psychiatry, University Clinic for Psychiatry, Vienna, with Dr. Manfred Karobath

Career-related Activities

1996-1999	Project coordinator of the EC-Biotechnology project ERBIO4CT960585

Awards

1981	Hoechst – Award
1984	Sandoz – Award for Biology
1996	Schizophrenia – Award of the Section Psychiatry of the Austrian Society for Neurology and Psychiatry for the paper “Schizophrenia and the dopamine-ß-hydroxylase gene: results of a linkage and association study”
1998	Schizophrenia – Award of the Section Psychiatry of the Austrian Society for Neurology and Psychiatry for the paper “Genetic

	polymorphisms of drug metabolism (CYP2D6) and tardive dyskinesia in schizophrenia"
2000	Research – Award of the AGNBP and the Austrian Society for Neurology and Psychiatry for the paper "Genome Scan for susceptibility loci for schizophrenia" (Neuropsychobiology 42, 175-182)
2000	ZNS-Research- Award of the Austrian Society for Neurology and Psychiatry for the paper "The citalopram challenge test in patients with major depression and in healthy controls" (Psychiatry Research 88, 75-88)
2001	Schizophrenia – Award of the Austrian Society for Neuropsychopharmacology and Biological Psychiatry for the paper "Genome Scan for Susceptibility Loci for Psychotic Disorders" (accepted in Biological Psychiatry)

Memberships

Membership in national and international scientific organizations:

Austrian Biochemical Society	European Neuroscience Association
Austrian Neuroscience Association	Society for Neuroscience, USA
Austrian Society for Clinical Chemistry	International Society for Neurochemistry
European College of Neuropsychopharmacol.	International Brain Research Organization

Member of national and international scientific boards and committtees:

Since 1982	Member of the advisory board on "Brain Research" of the Austrian Ministery For science and research
1984 – 1986	Councillor of the Austrian Biochemical Society
1990 – 1992	Councillor of the Austrian Biochemical Society
Since 1990	IUPHAR Committee on nomenclature of GABA-A Receptors
Since 1993	Auditor of the Austrian Biochemical Society
1996 - 2003	Treasurer of the Austrian Neuroscience Association
Since 2000	Section Editor for "Molecular Neuroscience" of the journal "Neuroscience"
2004 - 2005	President of the Austrian Neuroscience Association

Sources of funding in last 5 years (2003-2008)

Period	*Organization*	*Short Title*
2000 - 2003	Austrian Science Fund	"Identification and subunit composition of GABA-A receptor subtypes"
2001 - 2005	Austrian Science Fund	"Identification and structure of intersubunit contact sites of GABA-A receptors"
2003 - 2005	Jubiläumsfonds OeNB	"Molecular genetic investigations on childhood absence epilepsy"
2003 - 2007	Austrian Science Fund	"Structure and pharmacology of GABA-A receptors"
2004 - 2008	Austrian Science Fund	"Changes in the subunit composition of GABA-A receptors in the course of temporal lobe epilepsy"
2007-2010	Austrian Science Fund CCHD, Grad. College	$GABA_A$ receptor crosstalk with other receptors
2007-2010	Austrian Science Fund National Res. Network	$GABA_A$ receptors and their role in fear and anxiety
2008-2012	EU project Neurocypres	Mass expression, purification, crystallization and pharmacology of $GABA_A$ receptor subtypes

PhD supervision in last 5 years (2003-2008)

Period	*Name of student*	*Topic*
2000 - 2003	Birgit Hauer	Changes in GABA-A receptor subunit composition in the brain of knockout or transgenic mice
2002 - 2005	Waltraud Ogris	GABA-A receptor composition in alpha 1-knockout

		mice
2002 - 2005	Leila Wabnegger	Expression of GABA-A receptors using the baculovirus systems
2003 - 2007	Reinhard Lehner	Changes in the composition of GABA-A receptors in mice with stargazer mutation
2004 - 2008	Sabine Hinterreiter	Changes in the composition of GABA-A receptors in an animal model of temporal lobe epilepsy
2005 -	Joachim Ramerstorfer	Structure and pharmacology of $GABA_A$ receptor subtypes
2007 -	Amulya Nidhi Shrivastava	Interaction of $GABA_A$ receptors with other receptors
2007 -	Milos Vasiljevic	Interaction of $GABA_A$ receptors with associated proteins
2008 -	Katharina Gräf	$GABA_A$ receptor subunit composition and changes thereof under various pathological conditions

Publications
216 peer reviewed publications in scientific journals, 9 invited book chapters, 122 invited lectures, 2 patents

Peer reviewed manuscripts 2003-2008 (original research and reviews)
First, last or corresponding author manuscripts: 10

N. Ehya, I. Sarto, L. Wabnegger, T. Klausberger, and **W. Sieghart** (2003) Identification of an amino acid sequence within $GABA_A$ receptor beta3 subunits that is important for receptor assembly. J. Neurochem. 84, 127-135.

M. Ernst, D. Brauchart, S. Boresch, and **W. Sieghart** (2003) Comparative modeling of $GABA_A$ receptors: limits, insights, future developments. Neurosci. 119, 933-943

A. Pöltl, B. Hauer, K. Fuchs, V. Tretter, **W. Sieghart** (2003) Subunit composition and quantitative importance of $GABA_A$ receptor subtypes in the cerebellum of mouse and rat. J. Neurochem. 87, 1444-1455.

W. Ogris, A. Pöltl, B. Hauer, M. Ernst, A. Oberto, P. Wulff, H. Höger, B. Wisden, **W. Sieghart** (2004) Affinity of various benzodiazepine site ligands in mice with a point mutation in the $GABA_A$ receptor gamma2 subunit. Biochem. Pharmacol. 68, 1621-1629

M. Ernst, S. Bruckner, S. Boresch, and **W. Sieghart** (2005) Comparative models of $GABA_A$ receptor extracellular and transmembrane domains: important insights in pharmacology and function. Mol. Pharmacol. August 15, 2005; DOI: 10.1124/mol.105.015982, [Epub ahead of print].http://molpharm.aspetjournals.org. Mol. Pharmacol. 68:1291-1300

W. Sieghart and M. Ernst (2005) Heterogeneity of $GABA_A$ receptors: revived interest in the development of subtype-selective drugs. Curr. Med. Chem. - Central Nervous System Agents 5, 217-242.

I. Sarto-Jackson, J. Ramerstorfer, M. Ernst, and **W. Sieghart** (2006) Identification of amino acid residues important for assembly of $GABA_A$ receptor alpha1 and gamma2 subunits. J. Neurochem. 96:983-995

W. Ogris, R. Lehner, K. Fuchs, B. Furtmüller, H. Höger, G.E. Homanics, and **W. Sieghart** (2006) Investigation of the abundance and subunit composition of $GABA_A$ receptor subtypes in the cerebellum of alpha1-subunit-deficient mice. J. Neurochem. 96:136-147

W. Sieghart (2006) Structure, pharmacology and function of $GABA_A$ receptor subtypes. Adv Pharmacol. 2006;54:231-63.

I. Sarto-Jackson, R. Furtmüller, M. Ernst, S. Huck, and **W. Sieghart** (2007) Spontaneous cross-link of

mutated alpha1 subunits during $GABA_A$ receptor assembly. J. Biol. Chem. 282, 4354-4363.

Co-author manuscripts: 26

M. Mitterhauser, W. Wadsak, L. Wabnegger, **W. Sieghart**, H. Viernstein, K. Kletter, R. Dudczak (2003) In vivo and in vitro evaluation of [^{18}F]FETO with respect to the adrenocortical and GABAergic system in rats. Eur J Nucl Med Mol Imaging, 30, 1398-1401.

S. Pirker, C. Schwarzer, T. Czech, C. Baumgartner, H. Pockberger, H. Maier, B. Hauer, **W. Sieghart**, S. Furtinger, and G. Sperk (2003) Increased expression of $GABA_A$ receptor beta-subunits in the hippocampus of patients with temporal lobe epilepsy. J. Neuropath. Exp. Neurol. 62, 820-834.

M. Willeit, N. Praschak-Rieder, A. Neumeister, P. Zill, F. Leisch, J. Stastny, E. Hilger, N. Thierry, A. Konstantinidis, D. Winkler, K. Fuchs, **W. Sieghart**, H. Aschauer, M. Ackenheil, B. Bondy, S. Kasper (2003) A poymorphism (5-HTTLPR) in the serotonin transporter promoter gene is associated with DSM-IV depression subtypes in seasonal affective disorder. Mol Psychiatry 8, 942-946.

X. Li, H. Cao, C. Zhang, R. Furtmüller, K. Fuchs, S. Huck, **W. Sieghart**, J. Deschamps, J.M. Cook (2003) Synthesis, in vitro affinity, and efficacy of a Bis 8-Ethynyl-4H-imidazo[1,5a]-[1,4]benzodiazepine analogue, the first bivalent alpha5 subtype selective $BzR/GABA_A$ antagonist. J. Med. Chem. 46, 5567-5570.

M. Mitterhauser, W. Wadsak, L. Wabnegger, L-K. Mien, S. Tögel, O. Laynger, **W. Sieghart**, H. Viernstein, K. Kletter, R. Dudczak (2004) Biological evaluation of 2´-[^{18}F]fluoroflumazenil ([^{18}F]FFMZ), a potential GABA receptor ligand for PET. Nuclear Medicine and Biology 31, 291-295.

A. Schosser, K. Fuchs, F. Leisch, U. Bailer, K. Meszaros, E. Lenzinger, U. Willinger, R. Strobl, A. Heiden, C. Gebhardt, S. Kasper, **W. Sieghart**, K. Hornik, H.N. Aschauer (2004) Possible linkage of schizophrenia and bipolar affective disorders to chromosome 3q29; a follow-up. J. Psychiatr. Res. 38, 357-364.

D.W. Cope, P. Wulff, A. Oberto, M.I. Aller, M. Capogna, F. Ferraguti, C. Halbsguth, H. Höger, H.E. Jolin, A. Jones, A.N.J. Mckenzie, W. Ogris, A. Pöltl, S.T. Sinkkonen, O.Y. Vekovischeva, E. R. Korpi, **W. Sieghart**, E. Sigel, P. Somogyi, W. Wisden (2004) Abolition of zolpidem sensitivity in mice with a point mutation in the $GABA_A$ receptor gamma2 subunit. Neuropharmacol. 47, 17-34.

E.M. Petrini, I. Marchionni, P. Zacchi, **W. Sieghart**, E. Cherubini (2004) Clustering of extrasynaptic $GABA_A$ receptors modulates tonic inhibition in cultured hippocampal neurons. J. Biol. Chem. Aug. 17 [Epub ahead of print], J. Biol. Chem. 279, 45833-45843.

S.T. Sinkkonen, O.Y. Vekovischeva, T. Möykkynen, W. Ogris, **W. Sieghart**, W. Wisden, and E. Korpi (2004) Behavioral correlates of an altered balance between synaptic and extrasynaptic $GABA_A$ergic inhibition in a mouse model. Eur. J. Neurosci. 20, 2168-2178.

C. Sun, **W. Sieghart**, and J. Kapur (2004) Distribution of alpha1, alpha4, gamma2 and delta subunits of $GABA_A$ receptors in hippocampal granule cells. Brain Res. 1029, 207-216.

P.S. Mangan, C. Sun, M. Carpenter, H.P. Goodkin, **W. Sieghart**, and J. Kapur (2005) Cultured hippocampal pyramidal neurons express two kinds of $GABA_A$ receptors. Mol Pharmacol. Dec. 21. [Epub ahead of print]. Mol. Pharmacol. 67, 775-788.

U. Bailer, G. Wiesegger, F. Leisch, K. Fuchs, I. Leitner, M. Letmaier, A. Konstantinidis, J.Stastny, **W.Sieghart**, K. Hornik, B. Mitterauer, S. Kasper, H.N. Aschauer (2005) No association of clock gene T3111C polymorphism and affective disorders. Eur. Neuropsychopharmacol. 15, 51-55.

D.W. Cope, C. Halbsguth, T. Karayannis, P. Wulff, F. Ferraguti, H. Hoeger, E. Leppä, A.-M. Linden, A. Oberto, W. Ogris, E.R. Korpi, **W. Sieghart**, P. Somogyi, W. Wisden, and M.

Capogna (2005) Loss of zolpidem efficacy in the hippocampus of mice with the $GABA_A$ receptor gamma2F77I point mutation. Eur. J. Neurosci. 21, 3002-3016.

S. Khom, I. Baburin, E.N. Timin, A. Hohaus, **W. Sieghart**, S. Hering (2006) Pharmacological properties of $GABA_A$ receptors containing gamma1 subunits. Mol Pharmacol. 2005, Nov. 4 [Epub ahead of print] 69, 640-649.

Catherine Croft Swanwick, Namita R. Murthy, Zakaria Mtchedlishvili, **Werner Sieghart**, Jaideep Kapur (2006) Development of GABAergic Synapses in Cultured Hippocampal Neurons. J. Comp. Neurology 495, 497-510.

H.J. Hanchar, P. Chutsrinopkun, P. Meera, P. Supavilai, **W. Sieghart**, M. Wallner, and R. Olsen (2006) Ethanol potently and competitively inhibits binding of the alcohol antagonist Ro15-4513 to alpha4/6beta3delta $GABA_A$ receptors. Proc. Natl. Acad. Sci. USA, 103, 8546-8551.

H.L. Payne, P.S. Donoghue, W.M.K. Connelly, S. Hinterreiter, P. Tiwari, J.H. Ives, V. Hann, **W. Sieghart**, G. Lees, and C.L. Thompson (2006) Aberrant $GABA_A$ receptor expression in the dentate gyrus of the epileptic mutant mouse, stargazer. J. Neurosci. 26, 8600-8608.

A. Schosser, K. Fuchs, T. Scharl, F. Leisch, U. Bailer, S. Kasper, **W. Sieghart**, K. Hornik, H.N. Aschauer (2007) Additional support for linkage of schizophrenia and bipolar disorder to chromosome 3q29. Eur. Neuropsychopharmacol. 17(6-7):501-505. Epub 2007 Mar 6.

M.M.Savic, S. Huang, R. Furtmüller, T. Clayton, S. Huck, D.I. Obradovic, N.D. Ugresic, **W. Sieghart**, D.R. Bokonjic, J.M. Cook (2008) Are GABA(A) Receptors Containing alpha5 Subunits Contributing to the Sedative Properties of Benzodiazepine Site Agonists? Neuropsychopharmacology. 33, 332-339. Epub 2007 Mar 28;

M. Pytel, T. Wojtowicz, K. Mercik, I. Sarto-Jackson, **W. Sieghart**, C. Ikonomidou, J.W. Mozrzymas (2007) 17 beta-estradiol modulates GABAergic synaptic transmission and tonic currents during development in vitro. Neuropharmacol. 52, 1342-1353.

P. Wulff, T. Goetz, E. Leppä, A.-M. Linden, M. Renzi, J.D. Swinny, O. Y. Vekovischeva, **W. Sieghart**, P. Somogyi, E. R. Korpi, M. Farrant, and W. Wisden (2007) From synapse to behaviour: rapid modulation of defined neuronal populations through engineered $GABA_A$ receptors. Nature Neurosci. 10, 923-929.

H.L. Payne, W.M. Connelly, J.H. Ives, R. Lehner, B. Furtmüller, **W. Sieghart**, P. Tiwari, J.M. Lucocq, G. Lees, C.L. Thompson (2007) $GABA_A$ alpha6-containing receptors are selectively compromised in cerebellar granule cells of the ataxic mouse, stargazer. J. Biol. Chem. 282, 29130-29143. Epub ahead of print 2007 July 23.

T. Clayton, J.L. Chen, M. Ernst, L. Richter, B.A. Cromer, C.J. Morton, H. Ng, C.C. Kaczorowski, F.J. Helmstetter, R. Furtmüller, G. Ecker, M.W. Parker, **W. Sieghart**, J.M. Cook (2007) An Updated Unified Pharmacophore Model of the Benzodiazepine Binding Site on gamma-Aminobutyric Acid(a) Receptors: Correlation with Comparative Models. Curr. Med. Chem. 14, 2755-2775.

H.L. Payne, J.H. Ives, **W. Sieghart**, and C.L. Thompson (2008) AMPA and kainate receptors mediate mutually exclusive effects on $GABA_A$ receptor expression in cultured mouse cerebellar granule neurons. J. Neurochem. 104, 173-186. Epub 2007 Nov 6.

Terunuma M, Xu J, Vithlani M, **Sieghart W**, Kittler J, Pangalos M, Haydon PG, Coulter DA, Moss SJ (2008) Deficits in phosphorylation of $GABA_A$ receptors by intimately associated protein kinase C activity underlie compromised synaptic inhibition during status epilepticus. J. Neurosci. 28, 376-384.

Savic MM, Clayton T, Furtmüller R, Gavrilovic I, Samardzic J, Savic S, Huck S, **Sieghart W**, Cook JM (2008) PWZ-029, a compound with moderate inverse agonist functional selectivity at $GABA_A$ receptors containing alpha5 subunits, improves passive, but not active avoidance learning in rats. Brain Res. 2008 Feb 19, Epub ahead of print.

Invited Talks 2003-2008 22

Dr. Georgia Vendra
Division of Neuronal Cell Biology, Center for Brain Research, Medical University of Vienna
georgia.vendra@meduniwien.ac.at

Description of thesis project:

Abstract: RNA localization is well documented in diverse cell types, as a means to target proteins to their site of function and to establish or maintain polarity. It has recently emerged that RNA localization is fundamental for the development and maintenance of a functioning nervous system. Sorting of mRNAs in developing axons or mature dendrites may allow local translation at sites and times of demand and enable growth cones and synapses to alter instantly and individually their protein repertoire in response to local stimuli.
We are currently establishing RNA localization and local translation assays in living neurons, in order to understand how dendritic RNA transport and local protein synthesis are regulated by synaptic input.

Techniques and infrastructure: Primary cultures of hippocampal neurons, RNA *in situ* hybridization, immunostainings, transfections, siRNA, injections of fluorescently labelled RNA, molecular beacons, GFP-MS2 tagging system, real-time imaging of RNA and proteins, photoactivatable or photoconvertible protein tags.

Thesis Topic: RNA transport and local translation upon synaptic activity

Curriculum Vitae

Dr. Georgia Vendra
Center for Brain Research, Medical University Vienna, Spitalgasse 4, 1090 Vienna

Personal Data

Date of Birth:	17. 06. 1976
Place of Birth:	Athens
Nationality	Greek

Education

2002 - 2006	PhD studies, Wellcome Trust Center for Cell Biology, the University of Edinburgh, UK
2000-2002	MSc in Biotechnology, Department of Biology, University of Patras, Greece (with distinction)
1995-1999	Undergraduate degree in Biology, Department of Biology, University of Patras, Greece
1995	University entrance exam with distinction, High School in Athens

Career history

2007 - present	Senior Postdoc, Department of Neuronal Cell Biology, Center for Brain Research, Medical University of Vienna
2006 - 2007	Postdoctoral research assistant, Wellcome Trust Center for Cell Biology, the University of Edinburgh, UK
2006	Research assistant, Wellcome Trust Center for Cell Biology, the University of Edinburgh, UK
1999-2001	Research Assistant, Department of Biology, University of Patras, Greece

Career-related Activities

2003-2005	Assistant tutor and demonstrator (Molecular Cell Biology tutorials and practicals), The University of Edinburgh, UK

Awards

2002 – 2006	PhD studentship from the State Scholarship Foundation of Greece for studies in UK
2000-2002	Postgraduate studentship from the General Secretariat of Research and Technology, Greece and postgraduate awards from the State Scholarship Foundation of Greece

Publications

1 peer reviewed publication in scientific journals, - book chapters, - invited lectures

Peer reviewed manuscripts (original research and reviews)

First, last or corresponding author manuscripts:

Vendra, G., Hamilton, R.S, and Davis, I. (2007). Dynactin suppresses the retrograde movement of apically localized mRNA in *Drosophila* blastoderm embryos. *RNA*, 13:1860-1867

Co-author manuscripts:

Hamilton, R.S, **Vendra, G.,** and Davis, I. ParticleStats: configurable open source programming modules for the analysis of particle motility. *(in preparation)*

Hamilton, R.S., Hartswood, E., **Vendra, G.,** Jones, C., Van De Bor, V., Finnegan, D., & Davis, I. Genome-wide secondary structure searches identify gurken-like mRNA localization signals in a family of *Drosophila* retrotransposons. *(in preparation)*