IZN
Interdisziplinäres Zentrum für Neurowissenschaften der Ruprecht-Karls-Universität Heidelberg

Report 2001-2002
# Table of Contents

- Boards ........................................................................... 5
- Group Leaders - Core Sector ........................................... 6
- Research Groups - Outer Circle ...................................... 8
- Concept and Structure of the IZN .................................... 13
- IZN Budget and grant giving bodies ............................... 19
- Collaborations of IZN Members ..................................... 20
- Research Profiles - Core Sector ..................................... 25
  - Hilmar Bading ............................................................ 26
  - Roland Brandt .......................................................... 28
  - Francesca Ciccolini ..................................................... 30
  - Uwe Ernsberger ........................................................ 32
  - Hans-Hermann Gerdes ................................................ 34
  - Siegfried Mense ......................................................... 36
  - Hannah Monyer ........................................................ 38
  - Andrei Rozov ............................................................ 40
  - Horst Simon .............................................................. 42
  - Jacqueline Trotter ....................................................... 44
  - Kerry L. Tucker ........................................................ 46
  - Klaus Unsicker ........................................................ 48
  - William Wisden ........................................................ 50
- Research Profiles - Outer Circle ..................................... 53
  - Bernd W. Böttiger ....................................................... 54
  - Andreas Draguhn ....................................................... 55
  - Herta Flor ................................................................. 56
  - Rainer Friedrich ......................................................... 57
  - Harald Hutter ............................................................ 58
  - Marika Kiessling ........................................................ 59
  - Joachim Kirsch .......................................................... 60
  - Ulrich Misgeld ............................................................ 61
  - Stefan Offermanns ..................................................... 62
  - G. Elisabeth Pollerberg ............................................... 63
  - Klaus Sartor .............................................................. 64
  - Johannes Schröder ..................................................... 65
  - Markus Schwaninger .................................................. 66
  - Peter H. Seeburg ......................................................... 67
  - Jeremy C. Smith ........................................................ 68
  - Rainer Spanagel ......................................................... 69
  - Brigitte Wildemann ................................................... 70
  - Joachim Wittbrodt ...................................................... 71
- Central Facilities ............................................................... 74
- IZN Teaching Program .................................................. 76
- Publications of IZN members, 2001-2002 ........................ 76
- Symposia and Seminars .................................................. 87
- Guest Scientists 2001-2002 ............................................. 95
- Diploma and Doctoral Theses .......................................... 110
Boards

Board of Directors

Hilmar Bading, Professor Dr.
Hannah Monyer, Professor Dr.
Klaus Unsicker, Professor Dr. (acting director)

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<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Research Area</th>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hannah Monyer, Professor Dr.</td>
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<td>Neuronal synchrony and plasticity</td>
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<td>Kerry Tucker, Ph.D. (as of 07/03)</td>
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<td>Andrei Rozov, Dr.</td>
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<td>Klaus Unsicker, Professor Dr.</td>
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<tr>
<td>William Wisden, Ph.D.</td>
<td></td>
<td>Inhibitory ion channels</td>
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</tr>
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</table>
Research Groups - Outer Circle

ZMBH

Konrad Beyreuther
Alzheimer’s disease: etiology, physiological and pathophysiological functions of APP and presenilins

Tobias Hartmann
Cellular regulation mechanisms of protein degradation and protein transport in Alzheimer’s and Parkinson disease

Joachim Herz
Lipids and their receptors in neurodegenerative diseases

Renato Paro
Chromatin and epigenetics, Alzheimer’s Drosophila model

Blanche Schwappach
Targeting of ion channels

Faculty of Biology

G. Elisabeth Pollerberg
Growth and orientation of axons during development of the vertebrate nervous system

Jeremy Smith
Computer simulation of ion pumps

Faculty of Medicine Heidelberg

Dept. of Anatomy and Cell Biology

Joachim Kirsch
Ontogeny, stabilization and functional adaptation of postsynaptic membrane specializations

Department of Physiology and Pathophysiology

Andreas Draguhn
Inhibitory synapses and network oscillations

Wolfgang Kuschinsky
Proteomics and stroke

Ulrich Misgeld
Plasticity of GABA$_A$ receptor mediated inhibition

Horst Seller
Autonomic control of cardiovascular functions

Department of Pharmacology

Rohini Kuner
Molecular basis of chronic pain

Stefan Offermanns
Cellular signaling

Department of Human Genetics

Gudrun Rappold
Genetics of cognitive function and mental retardation

Department of Neuropathology

Marika Kiessling
Molecular basis of cerebral ischemia and ischemic preconditioning

Neurology

Armin Grau
Pathogenesis and genetics of stroke and Multiple Sclerosis

Werner Hacke
Molecular and cellular bases of stroke; stroke management
<table>
<thead>
<tr>
<th>Name</th>
<th>Research Areas</th>
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<tbody>
<tr>
<td>Hans-Michael Meinck</td>
<td>Movement disorders, channelopathies</td>
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<tr>
<td>Uta Meyding-Lamadé</td>
<td>Herpes simplex virus encephalitis</td>
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<tr>
<td>Markus Schwaninger</td>
<td>Molecular stroke research</td>
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<tr>
<td>Stefan Schwab/Thorsten Steiner</td>
<td>Neuromonitoring and new concepts in stroke therapy</td>
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<tr>
<td>Klaus Sartor</td>
<td>Focal cerebral ischemia, functional MR-tomography</td>
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<tr>
<td>Michael Scherg/Andre Rupp</td>
<td>Dynamic source imaging of the auditory cortex with magnetoencephalography</td>
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<td>Brigitte Wildemann</td>
<td>Peripheral immune tolerance and Multiple Sclerosis</td>
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<td>Anaesthesiology</td>
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<td>Bernd W. Böttiger</td>
<td>Experimental cerebral ischemia</td>
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<td>Pediatrics</td>
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<td>Georg Hoffmann</td>
<td>Inherited (neuro-)metabolical diseases</td>
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<td>Dietz Rating</td>
<td>Neurometabolical diseases, focal epilepsy, neurovegetative regulation in chronic pain</td>
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<td>Psychiatry</td>
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<tr>
<td>Johannes Schröder</td>
<td>Functional neuroimaging correlates of neural plasticity in age-associated neurocognitive disorders</td>
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<td>Max-Planck Institute for Medical Research</td>
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<td>Michael Brecht</td>
<td>Whisker representation</td>
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<td>Winfried Denk</td>
<td>Development and application of new optical methods for biomedical research</td>
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<td>Thomas Euler</td>
<td>Signal processing</td>
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<tr>
<td>Dirk Feldmeyer</td>
<td>Functional and morphological aspects of synaptic interactions in defined neuronal circuits of the neocortex</td>
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<td>Rainer Friedrich</td>
<td>Function and development of olfactory neural circuits</td>
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<td>Harald Hutter</td>
<td>Genetics of axon guidance in C. elegans</td>
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<td>Bert Sakmann</td>
<td>Mechanisms of fast signalling in and between nerve cells, and of long-term changes in their synaptic coupling</td>
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<tr>
<td>Peter Seeburg</td>
<td>The role of glutamate receptor subtypes in short and long-term memory</td>
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<tr>
<td>Veit Witzemann</td>
<td>Molecular structure and function of the neuromuscular synapse during development</td>
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<td>Research Groups - Outer Circle</td>
<td>Neurology Medical Faculty Mannheim</td>
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<tr>
<td><strong>German Cancer Research Center</strong></td>
<td><strong>Neurology Medical Faculty Mannheim</strong></td>
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<td>Christof Niehrs</td>
<td>Achim Gass</td>
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<td>Embryonal cell fate during early vertebrate development</td>
<td>Contrast imaging for studying stroke and Multiple Sclerosis</td>
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<td>Heike Pöpperl</td>
<td>Klaus Faßbender</td>
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<td>Hox genes in nervous system development</td>
<td>Neuroimmunology</td>
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<td>Günther Schütz</td>
<td>Michael Daffertshofer</td>
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<td>Mechanisms of gene activation by extra-cellular signals</td>
<td>Clinical and experimental brain ischemia</td>
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<td><strong>EMBL</strong></td>
<td>Michael Hennerici</td>
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<td>Mathias Treier</td>
<td>Molecular and cellular bases of stroke</td>
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<td>Mammalian organogenesis and homeostasis</td>
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<td>Jochen Wittbrodt</td>
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<td>Vertebrate retina development and differentiation</td>
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<td><strong>Central Institute for Mental Health (ZI) Mannheim</strong></td>
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<td>Dusan Bartsch</td>
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<td>Molecular biology of normal and pathological learning and memory</td>
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<td>Dieter Braus</td>
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<td>The influence of pharmacological treatment strategies on glutaminergic activity and neuroplasticity in major psychiatric disorders</td>
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<td>Herta Flor</td>
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<td>Learning and neuronal plasticity</td>
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<td>Fritz Henn</td>
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<td>Neuroplastic changes in the development of depression and actions of antidepressant medications in reversing depression</td>
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<td>Rainer Spanagel</td>
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<td>The neurobiology of drug dependence</td>
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Concept and Structure of the IZN
Concept and Structure of the IZN

Objectives

The IZN has three objectives:

• "Bundling" of fundamental neuroscience research, to create synergies and increase refinement of scientific capacity

• intensify research in the fringe areas between basic and clinical neurosciences

• promote interactive research with the fields of physics, chemistry, mathematics and scientific computing

Aims

The main goal of the IZN is to promote the quality of science performed by its members, boost collaborations, provide joint service units, and proceed towards integration of basic and clinical neurosciences. Consistent application of the performance principle, regular external evaluation, early independence for promising scientists, performance-related distribution of resources, the establishment of a common infrastructure, and the establishment of an interdisciplinary postgraduate course of study in neurobiology are therefore essential aims of the IZN.

Neurosciences in Heidelberg

Heidelberg is one of the strongholds of neuroscientific research in Europe. Groups at the University and University Hospital, the Max-Planck-Institute for Medical Research (MPIMf), the German Cancer Research Centre (DKFZ), the European Molecular Biology Laboratory (EMBL) and the Mannheim Central Institute for Mental Health (ZI) occupy top rankings internationally. Publications in leading journals, external funding, and distinctions bestowed on outstanding personalities reflect the high-calibre and scientific standards of Heidelberg’s neuroscience groups. Joint projects with the giant pharmaceutical and medium-sized biotechnology companies in the Heidelberg-Mannheim-Ludwigshafen region emphasize the links between basic and applied neurosciences.

Brief history and structure of the IZN

The IZN was founded in 2000 and officially opened on June 16 in the presence of dignitaries representing the Baden-Württemberg Ministry for Science, Research, and Art, and the University. The organizational form of the centre, approved by the Senate of the University and published as the Centre’s Administration and Usage Regulations (Verwaltungs- und Benutzungs-Ordnung, VBO), allows a group structure according to which both regular professors with tenure and scientists appointed on limited-term contracts can act as group leaders. This structure guarantees scientific continuity and allows constant innovation at the same time.

IZN core sector

The initial compound structure of the IZN was made up of three departments forming its "core sector": Neurobiology (Faculty of Biological Sciences), Clinical Neurobiology, and Neuroanatomy (Faculty of Medicine). Together with an Associate Professorship in Developmental Neuroscience, which has been advertised, and an anticipated fourth department (Faculty of Biological Sciences), the "core sector" of the IZN is the basis for the desired interdisciplinary nature of the Centre. The core sector of the IZN currently com-
Concept and Structure of the IZN

prises 12 independent research groups. Research group leaders are introduced in the research profiles (see pp 15).

IZN outer circle

Selected groups working in neurosciences at both University and non-University institutions in Heidelberg and Mannheim together make up the outer circle. Members are outstanding neuroscience groups in the Medical Faculties of Heidelberg and Mannheim, in the Faculty for Biological Sciences, in the Max-Planck-Institute for Medical Research (MPIMF), in the German Cancer Research Center (DKFZ), and at the European Molecular Biology Laboratories (EMBL). Members of the outer circle groups interact with the core groups in research, participate in graduate teaching, share central facilities of the core units, and provide methods and technologies to the entire IZN: Membership of the outer circle is subject to the approval of the Advisory Board of the IZN. For a list of candidates, see pp. 8

Structure of the IZN
Developments in the IZN since 2000

Since its foundation in June 2000 the IZN has considerably changed and gained international visibility. Scientists at the IZN have been enormously successful with major discoveries in molecular, cellular, developmental, and systems neuroscience.

- **Hilmar Bading** was appointed as Professor and Chair of Neurobiology and successor of Wieland Huttner. He moved his group from Cambridge, UK, and has finished restructuring his facilities at buildings INF 364 and 345. Soon after his arrival Hilmar received the Wolfgang Paul-Award of the Alexander von Humboldt Foundation, one of the highest and most generously endowed awards in science.

- **Michael Brand** was appointed to a C3-equivalent position at the new Max-Planck-Institute of Molecular Cell Biology and Genetics in Dresden.

- **Roland Brandt** was appointed as Professor and Chair of Neurobiology at the University of Osnabrück, after declining an offer to become a Professor of Molecular Neurology at the University of Bonn.

- **Roberto Bruzzone** moved his INSERM position from the Institut Pasteur to Heidelberg and established a guest group in Clinical Neurobiology.

- **Francesca Ciccolini** moved from Cambridge, UK, and established her own group in Neurobiology.

- **Hans-Hermann Gerdes** served as the acting head of Neurobiology until Hilmar’s arrival. He obtained second and third rankings on two lists for full professorships at the Universities of Osnabrück and Stuttgart, respectively.

- **Wieland Huttner** was appointed as a director at the new Max-Planck-Institute of Molecular Cell Biology and Genetics in Dresden.

- **Dieter Langosch** was appointed to a Professorship and Chair in Biophysics at the Technical University of Munich.

- **Hannah Monyer** was appointed to a Schilling-Stiftung Professorship in Clinical Neurobiology and as Chair of the new Department of Clinical Neurobiology. She moved her group from the Max-Planck-Institute of Medical Research to their new facilities in building INF 364. She established a new Graduate College in Neurobiology, initiated, together with Peter Seeburg, the BMBF funded Heidelberg/Mannheim Genome Network in Neurosciences, and was instrumental in the reorganization of the transgenic animal facility on campus.

- **Andrei Rozov** moved from the Max-Planck-Institute of Medical Research to the Department of Clinical Neurobiology and established his own group.

- **Elly Tanaka** became a group leader at the Max-Planck-Institute of Molecular Cell Biology and Genetics in Dresden.

- **Jacqueline Trotter** was appointed as Professor of Medical Biology at the University of Mainz and is currently moving her group.

- **Kerry Tucker**, previously a postdoctoral fellow with Yves-Alain Barde in Munich and Basle, was granted an independent research group by the German Research Foundation (DFG) within the Sonderforschungsbereich 488. He will establish his group in building INF 345 starting on 1 July, 2003.

- **Klaus Unsicker** was awarded the Aschoff-Medal of the Medical Faculty of the University of Freiburg and contin-
Concept and Structure of the IZN

ued to serve as speaker of the Sonderforschungsbereich 488 and the DFG Research Group “Aminergic Systems”.

• Bill Wisden pioneered the moves from Cambridge, UK, to Heidelberg. He became a group leader within the Department of Clinical Neurobiology.

We welcome all new group leaders and wish the leaving colleagues all the best with their new and challenging positions.

New Appointments to further consolidate the IZN core sector

• Andreas Draguhn, formerly at the Physiology department of the Charité, Humboldt University Berlin, and Joachim Kirsch, former Chair and Professor of Anatomy and Cell Biology at the University of Ulm, have been appointed as Professors and Chairs of Neurophysiology and Medical Cell Biology, respectively. Depending on the consent of the Scientific Advisory Board of the IZN, the group leaders of the IZN have unanimously agreed to incorporate the research groups of Andreas Draguhn, Joachim Kirsch, and Ulrich Misgeld, Professor of Physiology, into the core sector of the IZN.

New Appointments to the IZN outer circle

Recent appointments made to the IZN outer circle include the following:

• Dusan Bartsch, former member of the Kandel laboratory at Columbia University, New York, was appointed as Professor of Molecular Neuroscience at the Central Institute for Mental Health (ZI) Mannheim.

• Herta Flor, former Chair in Psychology at the Humboldt-University Berlin, was appointed to a Chair and Professorship in Neuropsychology at the ZI and University of Heidelberg. Professor Flor has successfully installed her research group and initiated a DFG-funded Clinical Research Group on Pain. She is also the speaker of a Sonderforschungsbereich Initiative “Learning, Memory, and Brain Plasticity. Implications for Psychopathology”.

• Christof Niehrs, DKFZ, was appointed to a Chair and Professorship in Developmental Biology at the Faculty of Biology, after declining offers from the universities of Bochum and Karlsruhe. Christof received the prestigious Science Prize of the State of Baden-Württemberg in 2001 and the Leibniz Prize of the German Research Foundation in 2003.

• Stefan Offermanns was appointed to the Chair and Professorship in Molecular Pharmacology at the Medical Faculty. He contributed significantly to the reorganization of the transgenic animal facility.

• Renato Paro was appointed as C4-Professor in Molecular Biology at the ZMBH, University of Heidelberg, after declining offers of professorships in Mainz and Karlsruhe.
Recent developments at the University of Heidelberg with an impact on the IZN

Funding instruments

The Sonderforschungsbereich 488 "Molecular and cellular bases of neural development" was reviewed for its second funding period (2003-2005) and passed the Bewilligungsausschuss of the DFG. A new SFB initiative "Learning, Memory, and Brain Plasticity" has been submitted to the DFG. In addition to the already existing DFG Research and Clinical Research Groups ("Aminergic Systems", "Pain"), new initiatives for DFG-funded Research Groups in the areas of "White Matter", "Cerebral Ischemia", and "Pain" have been launched.

The largest funding instruments with participation of the Heidelberg neuroscience community provided by the Federal Ministry for Education and Science (BMBF) include the national Genome/NeuroNet, BioFuture, and MedNet Ischemia projects.

BIOQUANT

Members of the IZN and SFB 488 have been part of the successful initiative to establish a new research concept in quantitative, physics- and mathematics-oriented biology (BIOQUANT). A new building on the INF campus will accommodate three C4-groups and numerous infrastructure and junior groups from biophysics, computer simulation and modeling, molecular cell biology, infectiology, and neurobiology.

New transgenic animal facility

Members of the SFB 488 and IZN (H. Monyer, S. Offermanns, P. Seeburg) supported by the Deans of the faculties of Biological Sciences and Medicine have been instrumental in the re-organization of the new facility for transgenic animals. Dr. J. Weiss, former director of the ZMBH transgenic facility, has been appointed as the new director. The facility is of utmost importance to the IZN to build up and maintain the highest standards in transgenic animal research.

New laboratories for IZN junior groups in building INF 345

Two stories in building INF 345 have been completely rebuilt and will accommodate, amongst others, several junior groups of the IZN.

Anticipated future developments in the IZN

Expected new appointments

- Joachim Herz, Dallas, is currently negotiating for a Professorship in Molecular Biology at the ZMBH.
- Walter Rosenthal, Berlin, is negotiating for a Chair and Professorship in Pharmacology, Medical Faculty.
- A C3-Professorship in Developmental Neurobiology in the Faculty of Biological Sciences has been advertised.

Funds and positions for the IZN

At present, the IZN has no central funds and almost no central positions from the University other than what the three departments of the IZN core sector have contributed at the time when the IZN was founded. One position for an administrator is jointly financed by the University and the Medical Faculty for a period of two years. The subsequent status of this position is uncertain. The lack of an IZN central fund means that the establishment and equipment of new junior
Concept and Structure of the IZN

groups, service units, and even of professorships must be financed through the funds and positions of the three core departments. This is an entirely unacceptable situation, and we shall ask the Scientific Advisory Board to support the IZN’s initiative to establish central funds for the IZN.

IZN central building

At present, the departments of the IZN core sector including those that we expect to join the IZN soon, the IZN junior groups, and the service units of the IZN are housed in four different buildings dispersed over the entire INF campus. This situation is entirely unsatisfactory, does not favor scientific interactions, and is uneconomical, since it requires duplicating essential equipment in different locations. Moreover, the IZN lacks a seminar room of adequate size. Previous plans to make building INF 364 entirely available to the IZN have not been realized as yet. Therefore, an IZN central building is an important request for the near future.
IZN Budget and grant giving bodies

The three departments of the IZN core sector are financed by basic funding (Grundausstattung, GA) of the University and University Clinic, and by grants (Ergänzungsausstattung, EA) from:

- DFG
- BMBF
- Alexander von Humboldt Foundation
- Volkswagen-Stiftung
- Schilling-Stiftung
- Hertie-Stiftung
- Stiftung Verum
- Fonds der Chemischen Industrie
- Alzheimer Forschung Initiative e.V.
- Deutsches Krebsforschungszentrum, Tumorzentrum, Heidelberg
- EC
- Human Frontier Science Program Organization
- Landesforschungsschwerpunkt Baden-Württemberg
- Landesgraduiertenkolleg
- Medizinische Fakultät Heidelberg
- Kooperationsprojekt Forschungsförderung der Medizinischen Fakultät
- Studienstiftung des Deutschen Volkes
- Forskerakademiet Danmark
- Wilhelm Sander Stiftung

- Nachlass Herbert Dauss sowie Stiftung für Krebs- und Scharlachforschung
- Konrad Adenauer Stiftung
- Allergan, Bayer AG, BASF, Biopharm, Boehringer Ingelheim, Leica, Merck Sharpe and Dohme, Novartis Pharma AG, SIRS-Lab, Steigerwald, Till Photonics

The amount and distribution of these funds (in k EUR) for the years 2001-2002 are shown in the table below:

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<thead>
<tr>
<th>Department</th>
<th>GA</th>
<th>EA</th>
<th>Ratio EA/ GA</th>
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<tbody>
<tr>
<td>Neurobiology</td>
<td>1178.0</td>
<td>2616.8</td>
<td>2.22</td>
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<tr>
<td>Clin. Neurobiology</td>
<td>698.7</td>
<td>2039.8</td>
<td>2.92</td>
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<tr>
<td>Neuroanatomy</td>
<td>2159.4</td>
<td>3874.2</td>
<td>1.79</td>
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<tr>
<td>Total, core depts.</td>
<td>4036.1</td>
<td>8530.8</td>
<td>2.31</td>
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Personnel is financed as follows:

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<th>GA</th>
<th>EA</th>
<th>Ratio EA/ GA</th>
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<tbody>
<tr>
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<td>44</td>
<td>1.91</td>
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<tr>
<td>Students</td>
<td>3</td>
<td>3</td>
<td>1.00</td>
</tr>
<tr>
<td>Technicians</td>
<td>26</td>
<td>13</td>
<td>0.50</td>
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</tbody>
</table>

The tables show clearly that the majority of the funding of the three departments of the „core sector“ comes from the „Ergänzungsausstattung“.
Collaborations of IZN Members

Internal cooperations within the IZN are indicated by dark background.

<table>
<thead>
<tr>
<th>Country</th>
<th>Laboratory</th>
<th>Name</th>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany, Heidelberg</td>
<td>DKFZ</td>
<td>Günther Schütz</td>
<td>Nuclear signaling and network plasticity in neurons from CREB knock-out mice</td>
</tr>
<tr>
<td>Germany, Heidelberg</td>
<td>ZIHN, Neuroanatomy, Unsicker group</td>
<td>Lavinia Bhatt</td>
<td>Synaptotagmin expression in sympathetic ganglia</td>
</tr>
<tr>
<td>Germany, Heidelberg</td>
<td>ZIHN, Clinical Neurobiology, Monyer group</td>
<td>Jakob von Engelhardt</td>
<td>CHAT expression in mouse brain</td>
</tr>
</tbody>
</table>

Planned:

| Germany, Heidelberg | ZIHN, Neurobiology | Ciccolini Group | Nuclear calcium signaling in stem cell differentiation |
| Germany, Heidelberg | Max Planck Institute for Medical Research | Feldmeyer Group | Paired recordings of cultured hippocampal neurons |
| Germany, Heidelberg | Max Planck Institute for Medical Research | Friedrich Group | Nuclear calcium signaling in the zebrafish olfactory bulb |

Francesca Ciccolini

| Germany, Heidelberg | ZIHN, Neurobiology | Hilmar Bading | Role of nuclear calcium signalling in neural stem cell differentiation |
| Germany, Heidelberg | ZIHN, SFB 488 | Kerry Tucker | In vitro development of neurosphere from a GFP-expressing mouse |

Roland Brandt

| Germany, Frankfurt | MPI Hirnforschung | H. Rohrer | RCAS infection |
| France, Paris | ENS | C. Goridis | Phox2b mutant mice |
| UK, London | King’s College | P. J. Mason | c-ret overexpression |
| UK, London | University College | M. Koltzenburg | Neuron differentiation markers |

Hans-Hermann Gerdes

<p>| Germany, Heidelberg | ZIHN, Clinical Neurobiology | B. Wisden | CABA receptor trafficking |
| Germany, Heidelberg | ZIHN, Neuroanatomy | K. Unsicker | Sorting of TGF beta 2 |
| Germany, Heidelberg | ZIHN, MPIIMF | P. Seeburg, G. Kohr | CABA receptor trafficking |
| Germany, Hamburg-Eppendorf | Institute for Human Genetics, Universitätsklinikum | K. Kutsche | Functional Genomics |
| Germany, Rostock | Institute of Cell Biology and Biosystems Technology | S. Kuznetsov | Regulation of myosin Va activity |
| Austria, Salzburg | Institute of Molecular Biology, Austrian Academy of Sciences | G. Kreil, G. Lepperding | Trafficking of Hyaluronasy-synthase |
| USA | NIH | J. Hammer | Role of myosin Va in secretory granule transport |
| Belgium, Leuven | Dept. for Human Genetics | J. Creemers | Trafficking of furin endoprotease |
| Switzerland, Lausanne | Institut de Biologie Cellulaire et de Morphologie, University of Lausanne | R. Regazzi | Role of Rab protein trafficking of secretory granules |</p>
<table>
<thead>
<tr>
<th>Country</th>
<th>Laboratory</th>
<th>Name</th>
<th>Project Title</th>
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</thead>
<tbody>
<tr>
<td>Norway, Oslo</td>
<td>Div. Molecular Cell Biology, Dept. of Biology, Univ. Oslo</td>
<td>O. Bakke</td>
<td>Involvement of adaptor proteins in polarized secretion</td>
</tr>
<tr>
<td>Austria, Vienna</td>
<td>Brain Research Institute</td>
<td>W. Sieghart</td>
<td>GABA receptor trafficking</td>
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<tr>
<td>UK, London</td>
<td>Laboratory Secretory Pathways Laboratory</td>
<td>S. Tooze</td>
<td>Secretory granule maturation</td>
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<tr>
<td>USA, Toronto</td>
<td>Dept. Physiology, Toronto University</td>
<td>B. Sessle</td>
<td>Skeletal muscle as a source of temporomandibular pain</td>
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<tr>
<td>USA, Atlanta</td>
<td>Dept. Physical Med. &amp; Rehab, Emory University, Atlanta</td>
<td>D.G. Simons</td>
<td>Mechanisms of trigger point formation</td>
</tr>
<tr>
<td>Germany, Mannheim</td>
<td>Central Institute for Mental Health</td>
<td>H. Flor</td>
<td>Cortical imaging during experimental muscle pain</td>
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<tr>
<td>Germany, Kiel</td>
<td>Ulologische Klinik, Universität Kiel</td>
<td>K.-P. Jänemann</td>
<td>Mechanisms of sacral neuromodulation</td>
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<tr>
<td>Germany, München</td>
<td>Friedrich-Baur-Institut, Universitäts-Klinik München</td>
<td>D. Pongratz</td>
<td>Morphology of myofascial trigger points</td>
</tr>
<tr>
<td>Germany, Berlin</td>
<td>Dept. Pharmacol., Charité, University Berlin</td>
<td>T. Unger</td>
<td>Receptor molecules on muscle nociceptors</td>
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<tr>
<td>Denmark, Aalborg</td>
<td>Institute of Sensory Motor Interaction, Aalborg Univ.</td>
<td>L. Arendt-Nielsen</td>
<td>Non-noceptive sensations from skeletal muscle</td>
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<tr>
<td>Norway, Bergen</td>
<td>Dept. Physiology, Bergen University</td>
<td>K. Hole</td>
<td>Spinal mechanisms of muscle pain</td>
</tr>
<tr>
<td>Canada, Toronto</td>
<td>Dept. Physiology, Toronto University</td>
<td>B. Sessle</td>
<td>Skeletal muscle as a source of temporomandibular pain</td>
</tr>
<tr>
<td>USA, Atlanta</td>
<td>Dept. Physical Med. &amp; Rehab, Emory University, Atlanta</td>
<td>D.G. Simons</td>
<td>Mechanisms of trigger point formation</td>
</tr>
<tr>
<td>Germany, Heidelberg</td>
<td>Max Planck Institute for Medical Research</td>
<td>Peter Seeburg</td>
<td>Mice with regulated ablation of the NRT1b subunit</td>
</tr>
<tr>
<td>Germany, Heidelberg</td>
<td>Max Planck Institute for Medical Research</td>
<td>Peter Seeburg</td>
<td>Generation of transgenic mice with altered C-termini in the NR2A and 2B subunit</td>
</tr>
</tbody>
</table>

**Collaborations of IZN Members**

**Siegfried Mense**

- Germany, Mannheim | Central Institute for Mental Health | H. Flor | Cortical imaging during experimental muscle pain |
- Germany, Otto-Selz-Institut | P. Holzl | Arginine for treatment of pain |
- Germany, Ulologische Klinik, Universität Kiel | K.-P. Jänemann | Mechanisms of sacral neuromodulation |
- Germany, Friedrich-Baur-Institut, Universitäts-Klinik München | D. Pongratz | Morphology of myofascial trigger points |
- Germany, Berlin | Dept. Pharmacol., Charité, University Berlin | T. Unger | Receptor molecules on muscle nociceptors |
- Denmark, Aalborg | Institute of Sensory Motor Interaction, Aalborg Univ. | L. Arendt-Nielsen | Non-noceptive sensations from skeletal muscle |
- Norway, Bergen | Dept. Physiology, Bergen University | K. Hole | Spinal mechanisms of muscle pain |
- Canada, Toronto | Dept. Physiology, Toronto University | B. Sessle | Skeletal muscle as a source of temporomandibular pain |
- USA, Atlanta | Dept. Physical Med. & Rehab, Emory University, Atlanta | D.G. Simons | Mechanisms of trigger point formation |

**Hannah Monyer**

- Germany, Heidelberg | Max Planck Institute for Medical Research | Peter Seeburg | Mice with regulated ablation of the NRT1b subunit |
- Germany, Heidelberg | Max Planck Institute for Medical Research | Peter Seeburg | Generation of transgenic mice with altered C-termini in the NR2A and 2B subunit |

**Country** | **Laboratory** | **Name** | **Project Title** |
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<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Germany, Heidelberg</td>
<td>IZN, Clinical Neurobiology, University of Heidelberg</td>
<td>Bill Wisden</td>
<td>Mice with altered GABA receptors in parvalbumin-positive cells</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>IZN, Clinical Neurobiology, University of Heidelberg</td>
<td>Bill Wisden</td>
<td>AMPA receptor KO in cerebellar granule cells</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>IZN, Clinical Neurobiology, University of Heidelberg</td>
<td>Andre Rozov</td>
<td>Functional characterization of in vivo labeled GABA-ergic interneurons</td>
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<tr>
<td>USA, New York</td>
<td>SUNY Health Science Center, Brooklyn</td>
<td>Roger Traub</td>
<td>The role of AMPA receptors in GABAergic interneurons for network synchronicity</td>
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<tr>
<td>UK, Leeds</td>
<td>School of Biomedical Sciences, University of Leeds</td>
<td>Miles</td>
<td>The role of AMPA receptors in GABAergic interneurons for network synchronicity</td>
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<td>UK, Leeds</td>
<td>School of Biomedical Sciences, University of Leeds</td>
<td>Eberhard Buhl</td>
<td>The role of AMPA receptors in GABAergic interneurons for network synchronicity</td>
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<tr>
<td>Netherlands, Amsterdam</td>
<td>Institute of Neurobiology, University of Amsterdam</td>
<td>Hans van Hooft</td>
<td>Characterization of a subclass of hippocampal interneurons</td>
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<tr>
<td>Germany, Freiburg</td>
<td>Anatomical Institute, University of Freiburg</td>
<td>Michael Frotscher</td>
<td>Molecular and functional characterization of ChAT positive interneurons in the hippocampus</td>
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<tr>
<td>USA, New York</td>
<td>Dept. Neuroscience, Albert Einstein College of Medicine</td>
<td>Alexander Penado</td>
<td>Slow wave activity in postnatal cortex in gap junction KO mice</td>
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<tr>
<td>UK, Edinburgh</td>
<td>Dept. Neuroscience, University of Edinburgh</td>
<td>Richard Morris</td>
<td>Postdoc exchange to analyse transgenic mice generated in our lab</td>
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<tr>
<td>France, Paris</td>
<td>Pasteur Institute</td>
<td>Roberto Bruzzone</td>
<td>Visiting scientist; functional characterization of recombinant Pannexins</td>
</tr>
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</table>

**Andrei Rozov**

- Germany, Heidelberg | MPI for Medical Research | P. H. Seeburg | Analysis of transgenic mice with genetically modified glutamate receptors |
Collaborations of IZN Members

<table>
<thead>
<tr>
<th>Country</th>
<th>Laboratory</th>
<th>Name</th>
<th>Project Title</th>
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<tr>
<td>Germany, Heidelberg</td>
<td>MPI for Medical Research</td>
<td>B. Sakmann</td>
<td>Mechanisms of LTP-induction</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>Dept. of Clinical Neurobiology University Hospital for Neurology</td>
<td>H. Monyer</td>
<td>Functional characterization of in vivo labeled GABA-ergic interneurons</td>
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<tr>
<td>USA, New York</td>
<td>Dept. of Neurobiology and Behavior State University of New York at Stony Brook</td>
<td>L.P. Wollmuth</td>
<td>Multivesicular release in neocortical excitatory synapses</td>
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<tr>
<td>Netherlands, Amsterdam</td>
<td>Dept. of Experimental Neurophysiology Vrije University Amsterdam</td>
<td>N. Burnashev</td>
<td>Postsynaptic mechanisms of LTP</td>
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<tr>
<td>UK, Leeds</td>
<td>School of Biomedical Sciences, University of Leeds</td>
<td>M. Whittington</td>
<td>Generation of theta frequency oscillations in neocortical networks</td>
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**Horst Simon**

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<th>Country</th>
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<tr>
<td>Germany, Heidelberg</td>
<td>IZN, Neuroanatomy</td>
<td>Klaus Unsicker</td>
<td>Quantitative determinations of dopamine in the nigrostriatal system</td>
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<tr>
<td>Germany, Heidelberg</td>
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<td>Uwe Ernsberger</td>
<td>Synaptotagmin expression in sympathetic ganglia</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>Physiology and Pathophysiology</td>
<td>Ulrich Misgeld</td>
<td>KATP-channel activity in midbrain dopaminergic neurons</td>
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<td>Germany, Heidelberg</td>
<td>DKFZ</td>
<td>Günther Schütz</td>
<td>Microarray analysis of inducible dopaminergic cell lines</td>
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<td>USA</td>
<td>Department of Molecular and Cellular Biology Baylor College of Medicine</td>
<td>Joseph Bryan</td>
<td>Sur1 and the maintenance of midbrain dopaminergic neurons</td>
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<td>Sweden, Stockholm</td>
<td>Ludwig Institute for Cancer Research Karolinska Institute</td>
<td>Thomas Perlmutter</td>
<td>Nurr1 and the dopaminergic projection to the basal ganglia</td>
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<td>USA</td>
<td>Department of Genetics University of Pennsylvania Medical School</td>
<td>Klaus Kästner</td>
<td>Role of HNF3a in postnatal midbrain dopaminergic neurons</td>
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<th>Project Title</th>
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<tbody>
<tr>
<td>USA, Stanford</td>
<td>Department of Pathology Stanford University School of Medicine</td>
<td>Michael Cleary</td>
<td>Pbx1 and midbrain dopaminergic neurons</td>
</tr>
<tr>
<td>Canada, Calgary</td>
<td>Department of Psychology, Faculty of Social Science Department of Neuroscience, Faculty of Medicine</td>
<td>Richard Dyck</td>
<td>Behavioral deficits in brain specific ErbB4 mutant mice</td>
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<tr>
<td>Germany, Martinsried</td>
<td>MPI of Neurobiology Department of Molecular Neurobiology</td>
<td>Rüdiger Klein</td>
<td>ErbB4 and the midbrain dopaminergic neurons</td>
</tr>
<tr>
<td>Canada, Calgary</td>
<td>Neuroscience Research Group Dept. of Cell Biology and Anatomy University of Calgary</td>
<td>Cairine Logan</td>
<td>Engrafted dependent survival of midbrain dopaminergic neurons</td>
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**Jacqueline Trotter**

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<tr>
<td>USA</td>
<td>SUNY</td>
<td>J. Levine</td>
<td>Joint paper</td>
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<tr>
<td>Germany, Martinsried</td>
<td>MPI</td>
<td>C. Linnington</td>
<td>See above</td>
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<tr>
<td>Germany, Göttingen</td>
<td>MPI</td>
<td>K.A. Nave</td>
<td>Joint papers</td>
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<tr>
<td>Germany, Berlin</td>
<td>Max Delbrück Center Berlin</td>
<td>F. Kirchhoff, H. Kettenmann</td>
<td>Joint papers</td>
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<td>Germany, Düsseldorf</td>
<td>University Düsseldorf</td>
<td>H.W. Müller</td>
<td>Joint paper</td>
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<td>Germany, Düsseldorf</td>
<td>University Düsseldorf</td>
<td>H.P. Hartung</td>
<td>Joint paper</td>
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**Kerry L. Tucker**

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<tbody>
<tr>
<td>Germany, Heidelberg</td>
<td>IZN, Neurobiology</td>
<td>Francesca Ciccolini</td>
<td>In vitro development of neurospheres from a GFP-expressing mouse</td>
</tr>
<tr>
<td>Germany, Martinsried</td>
<td>Magdalena Gaetz, Max Planck Institute for Neurobiology</td>
<td>Paolo Malatesta</td>
<td>PACS sorting of neurons using GFP as a marker</td>
</tr>
<tr>
<td>Germany, Bonn</td>
<td>Oliver Brustle, University Bonn</td>
<td>Marius Wernig</td>
<td>Use of GFP-labelled ES cells to repair damaged brain tissue</td>
</tr>
</tbody>
</table>
### Collaborations of IZN Members

<table>
<thead>
<tr>
<th>Country</th>
<th>Laboratory</th>
<th>Name</th>
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</tr>
</thead>
<tbody>
<tr>
<td>USA, New York</td>
<td>Albany Medical College</td>
<td>Frank Rice</td>
<td>Mystacial pad innervation in tau knock-out mice</td>
</tr>
<tr>
<td>USA, New York</td>
<td>Peter Davies, Albert Einstein Medical College</td>
<td>Cathy Andorfer</td>
<td>Mouse models of Alzheimer’s disease</td>
</tr>
<tr>
<td>Germany, Frankfurt</td>
<td>Goethe University</td>
<td>Thomas Deller</td>
<td>Lesion-induced reorganization of the hippocampus</td>
</tr>
<tr>
<td>Sweden, Stockholm</td>
<td>Patrik Ernfors, Karolinska Institute</td>
<td>Christel Baudet</td>
<td>New mouse models of Alzheimer’s disease</td>
</tr>
<tr>
<td>Switzerland, Basel</td>
<td>Friedrich Miescher Institute</td>
<td>Andrea Spetz</td>
<td>Genomic imprinting and brain development</td>
</tr>
<tr>
<td>USA, Waltham</td>
<td>Univ. of Massachusetts Med. School</td>
<td>Athena Andradas</td>
<td>Functional analysis of the tau gene promoter</td>
</tr>
<tr>
<td>USA, Columbus</td>
<td>Ohio State University</td>
<td>Lyn Jakeman</td>
<td>Repair of injured spinal cord</td>
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**Klaus Unsicker**

<table>
<thead>
<tr>
<th>Country</th>
<th>Laboratory</th>
<th>Name</th>
<th>Project Title</th>
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</thead>
<tbody>
<tr>
<td>Germany, Heidelberg</td>
<td>IZN, Neuroanatomy</td>
<td>Uwe Ernsberger</td>
<td>SA cell lineage</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>IZN, Clinical Neurobiology</td>
<td>Hannah Monyer</td>
<td>Gap junction communication in FGF mutant mice</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>Institute for Physiology and Pathophysiology</td>
<td>Ulrich Misgeld</td>
<td>Growth factors regulating the developmental switch in GABA signaling</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>Institute for Pharmacology</td>
<td>Stefan Offermanns</td>
<td>Neural crest development in mice with mutations in G-protein signaling</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>Neurology</td>
<td>Markus Schwaninger</td>
<td>Roles of endogenous FGF and other growth factors in ischemia</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>DKFZ</td>
<td>Gunther Schütz</td>
<td>GR and CREB signaling in the development of the SA cell lineage</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>DKFZ</td>
<td>Christof Niehrs</td>
<td>Cloning of a receptor for GDF-15</td>
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<tr>
<td>Germany, Mannheim</td>
<td>Central Institute for Mental Health, Dept. Psychopharmacology</td>
<td>Rainer Spanagel</td>
<td>Behavioral alterations in mice with trkB/trkC haploinsufficiencies</td>
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<tr>
<td>USA, Bethesda</td>
<td>Chemoprevention, NIH, NCI</td>
<td>Anita Roberts, Kathy Flanders</td>
<td>TGF-β in the nervous system</td>
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</table>

**Bill Wisden**

<table>
<thead>
<tr>
<th>Country</th>
<th>Laboratory</th>
<th>Name</th>
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<tbody>
<tr>
<td>Germany, Heidelberg</td>
<td>IZN, Institute for Anatomy and Cell Biology</td>
<td>J. Kirsch</td>
<td>Planned work on role of gephyrin at developing synapses</td>
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<tr>
<td>Germany, Heidelberg</td>
<td>Physiology</td>
<td>A. Draguhn</td>
<td>Planned work on electrophysiology on transgenic mice overexpressing GABA-C receptors</td>
</tr>
<tr>
<td>Country</td>
<td>Laboratory</td>
<td>Name</td>
<td>Project Title</td>
</tr>
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<tr>
<td>Germany, Heidelberg</td>
<td>MPI for Medical Research</td>
<td>P. Seeburg</td>
<td>Ongoing. Cerebellar granule cell-specific knockout of the NMDA receptor NR1 subunit gene</td>
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<tr>
<td>Germany, Mannheim</td>
<td>Central Institute for Mental Health, Dept. Psychopharmacology</td>
<td>R. Spanagel</td>
<td>Planned work on behavioural characterization of mouse mutants lacking functional potassium channel and neurotransmitter receptor genes in cerebellum</td>
</tr>
<tr>
<td>Germany, Heidelberg</td>
<td>IZN. Clinical Neurobiology</td>
<td>H. Monyer</td>
<td>Two projects ongoing. Cerebellar granule cell-specific knockout of AMPA receptor GluR-D subunit. Developing transgenic techniques for reversible modulation of neurons.</td>
</tr>
<tr>
<td>UK, Oxford</td>
<td>MRC Oxford</td>
<td>Peter Somogyi</td>
<td>Reversibly modulating neural activity: electrophysiology</td>
</tr>
<tr>
<td>Finland, Helsinki</td>
<td>University of Helsinki</td>
<td>Esa Korpi</td>
<td>Reversibly modulating neural activity. Animal behaviour</td>
</tr>
<tr>
<td>Austria, Vienna</td>
<td>University of Vienna</td>
<td>Werner Sieghart</td>
<td>Reversibly modulating neural activity: pharmacology</td>
</tr>
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<td>UK, London</td>
<td>Dept. Pharmacology, University College</td>
<td>Mark Farrant/ Stuart Cull-Candy</td>
<td>Granule cell physiology: GABA-A receptors</td>
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<td>UK, London</td>
<td>Imperial College</td>
<td>Stephen Brickley</td>
<td>Granule cell physiology: Potassium channels</td>
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<td>UK, London</td>
<td>MRC LMCB, University College</td>
<td>Stephen Moss</td>
<td>GABA-C receptors in brain</td>
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Research Profiles
Nuclear calcium signaling

Hilmar Bading

MD 1984 University of Heidelberg
Postdoctoral work at the Max-Planck Institut für Molekulare Genetik, Berlin, and at Harvard Medical School, Boston, USA
Group leader at the MRC Laboratory of Molecular Biology, Cambridge, UK, 1993–2001,
Professor of Neurobiology, IZN, since 2001.

Current Research

Spatial calcium signaling

Neuronal activity-induced changes in the intracellular calcium concentration control many processes in the developing and the adult nervous system. Calcium is required for neurotransmitter release and activates mechanisms that affect synaptic connectivity, promote survival, or cause cell death. Calcium also signals to the nucleus to induce gene expression, which may be relevant for long-lasting plasticity and survival. For synapse-to-nucleus communication, neurons exploit the spatial and temporal diversity of calcium transients associated with electrical activation. Induction of transcription and the biological responses of neurons depend on how calcium enters the neurons, the amplitude of the signal, how long it lasts and what subcellular compartment it invades.

The decoding, by transcriptional regulators, of information contained in a given calcium transient provides a mechanism through which neuronal impulse patterns specify gene induction. However, it remains to be established exactly what type of calcium signal is needed for activity-dependent neuronal processes. Our central hypothesis is that increases in the nuclear calcium concentration, evoked by synaptic activity, are key regulators of long-lasting, gene expression-dependent plasticity and neuronal survival.

Opposing functions of synaptic and extrasynaptic NMDA receptors

A second aspect of spatial calcium signaling is the localization of the calcium entry channel, in particular that of the N-Methyl-D-Aspartate (NMDA) type of glutamate receptor. Calcium entry through synaptic NMDA receptors stimulates the transcription-regulating complex CREB/CBP, induces brain-derived neurotrophic factor (BDNF) gene expression, and enhances neuronal survival. In striking contrast, extrasynaptic NMDA receptors couple to CREB shut-off and cell death pathways. Thus, the decision of whether a neuron survives (and perhaps undergoes plasticity) or dies after glutamate exposure is dependent on the localization of the NMDA receptor activated. This concept of differential signaling by synaptic and extrasynaptic NMDA receptors has wide-ranging implications in particular for the understanding and treatment of neuro-pathological conditions such as stroke in which brain damage may be caused by the stimulation of extrasynaptic NMDA receptors.
Future Projects and Goals

One objective of our future research program is to analyse the relationship between synaptic stimuli, spatial calcium signaling, and activation of gene expression. Based on mechanistic insight into transcription regulation and information on the nature of calcium signals and candidate target genes, we will develop tools to selectively generate or interfere with calcium-regulated nuclear events. Their effects on neuronal plasticity will be tested using multi-electrode array (MEA) technology; MEAs allow us to record firing patterns of groups of hippocampal neurons and to monitor signal-induced changes in network behaviour. A second goal is to investigate the coupling of extrasynaptic NMDA receptors to cell death pathways and to determine the role of nuclear calcium signaling in synaptic NMDA receptor-induced survival programs.

Selected Publications


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Fig. 2: Expression of an EYFP-coupled, membrane bound blocker of calcium/calmodulin in hippocampal neurons.
Cytoskeletal mechanisms during neuronal development and degeneration

Roland Brandt

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1990-1994 Postdoctoral work at the Center for Neurologic Diseases, Harvard Medical School, Boston
1994-2002 Independent Group Leader at the Department of Neurobiology, IZN, University of Heidelberg
Since 2002 Full Professor of Neurobiology and Head of Department at the University of Osnabrück

Current Research

Neurons are one of the most extreme cell types in that they contain processes which can reach a meter or longer and contain more than 99% of the cellular volume [4]. This requires the presence of a sophisticated molecular machinery in order to establish and maintain such a morphology. The cytoskeleton is the major intraneuronal structure that determines the shape of a neuron. From that it is not surprising that cytoskeletal mechanisms have an important role during the development of neurons and that abnormalities in the cytoskeletal organization are a hallmark of many neurodegenerative diseases. The group concentrates on the function of microtubules and their associated proteins, on neurofilaments and on the membrane cortex during neuronal development and neurodegeneration. In particular, a major part of the group concentrates on studying the involvement of the neuronal microtubule-associated protein tau during neurodegenerative processes in Alzheimer’s disease and other tauopathies. In the past years, effective gene-transfer techniques based on several viral vectors (HSV, Sindbis virus) have been established in the lab as a tool to express wildtype and disease-like modified tau constructs (“pseudo-hyperphosphorylated tau” [3, 5]) in dissociated neurons and organotypic brain cultures. These techniques are used to analyze the role of tau modifications, in particular a disease-like hyperphosphorylation, during neurodegeneration. In another project, a panel of new monoclonal antibodies has been generated against a fraction enriched for innerperipherial membrane proteins [2] and characterized in order to analyze the role of selected components of the neuronal cytoskeleton during development and neurodegenerative processes.

Future Projects and Goals

We have recently shown that tau constructs that simulate a disease-like hyperphosphorylation induce neurodegenerative mechanisms in dissociated neurons that are associated with apoptotic processes [5]. A major focus of our work concentrates on (a) identifying the molecular mechanisms and the potential interference with other disease-relevant phenomena.

Schematic representation of the mechanism how modifications of tau protein may contribute to the pathology of Alzheimer’s disease (for details see Shahani & Brandt, 2002)
factors during tau-induced neurodegeneration, and (b) developing complex culture and animal models that could serve as models for tau pathologies.

In additional projects we will use our new antibodies to better understand the role of individual cytoskeletal components during neuronal development. This includes (a) use of an antibody that detects the protein gravin, a human kinase-anchoring protein that associates with the actin cortex of neurons and may be involved in localizing kinases to selected regions of developing neurites and (b) analysis of O-glycosylation of neurofilaments during neuronal development and degeneration with a novel antibody that specifically detects an O-glycosylated epitope in NF-M.

Selected Publications


Structure of the group

Group leader  Roland Brandt
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Neural stem cell development and role of calcium signalling in neural precursor differentiation

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Group Leader at the Department of Neurobiology, IZN, since 2002

Current Research

Neural stem cells capable of generating neurons and macroglia are present both in the embryonic and adult mammalian brain. Since neural stem cells can be grown and differentiated in vitro they have attracted great interest mainly as a potential source of transplantable tissue. However, neural stem cells play also a major physiological role in the context of the embryonic as well as adult brain. In recent years, the notion that the generation of neurons in the mammalian central nervous system stops shortly after birth has been challenged. Indeed, in certain regions of the brain, neurogenesis persists throughout the adult life and the newly generated neurons may be important for memory formation and repair of small cellular losses. Thus, understanding how neural stem cell proliferation and differentiation is regulated may lead not only to a major clinical breakthrough but also provide fundamental insight into brain functioning.

Neural stem cell development

Embryonic and adult neural stem cells are both defined by their ability to generate more stem cells (self-renewal) and to give rise to multiple cell types (multipotentiality). Despite these common features, neural stem cells during development modify their properties according to temporal and regional clues. For example, neural stem cells from different brain regions give rise to region-specific progeny. Similarly, early and late stem cells differ in their ability to respond to growth factors, cell phenotype, and differentiation potential. The reasons regulating these modifications are not understood. Fundamental questions are which are the molecular mechanisms underlying these changes? Which signals are regulating these modifications? Do these modifications reflect a change in the physiological role of neural stem cells? One of the major problems in answering these questions is the absence of neural stem cells markers to allow direct neural stem cell studies. Our focus is to find strategies to isolate and purify neural stem cells from different developmental stages to directly study them.

Calcium signalling during neural stem cell differentiation

The proliferation and differentiation of neural stem cells are regulated by environmental signals and by cell-cell interactions. How this variety of signals interacts to direct neural precursor behaviour is not understood. While many growth and neurotrophic factors can influence neuronal differentiation, several lines of evidence suggest that Ca$^{2+}$ signals may be key regulators of this process. Changes in the intracellular Ca$^{2+}$ concentration as a result of spontaneous or signal-regulated events are a characteristic of many developmental systems and appear to be involved in the initiation of the differentiation process. We recently found that progenitors...
derived from neural stem cells generate spontaneous calcium signals during the process of differentiation. Key questions are: What is the functional significance of these calcium events? What is the relationship between calcium signals and known modulators of neural precursor differentiation? We are using cultures enriched in neural stem cells to study the effect of calcium signalling on neural stem cell differentiation.

Future Projects and Goals

Growth factor responsiveness to find neural stem cells
The major focus of the lab is to use FACS-based techniques to isolate neural stem cells from embryonic and adult mammalian brain to allow direct neural stem cell studies. We recently found that a hallmark of the transition between early and late neural stem cells is the acquisition of EGF responsiveness. This ability to respond to EGF is mostly regulated at the level of EGFR expression and can be induced in early stem cells by a brief exposure to FGF-2. Thus EGFR, alone or in combination with other differentiation stage specific markers, can be a very powerful tool to purify small cellular subset highly enriched in stem cells from the embryonic brain.

Spontaneous calcium signals
We want to understand the role of the spontaneous calcium signals in neural stem cell proliferation and differentiation. In particular we are interested to investigate whether these calcium signals regulate the timing of neural precursor division. To this end we will set up conditions to modulate the frequency of these events and to determine the effect of these modulations on neural precursor cell cycle and the onset of differentiation.

Selected Publications


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Research Profiles

Development of nerve cells and generation of neuronal diversity

Uwe Ernsberger

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1988-1991 University of California, San Diego, USA: Research Fellow of the DFG and MDA
1992-1998 Max-Planck-Institute for Brain Research, Frankfurt, since 1999 IZN and Department of Anatomy, Ruprecht-Karls-University, Heidelberg

Current Research

In recent years, significant progress has been made to understand the generation of neuronal diversity. The peripheral sympathetic ganglia of mammals and birds constitute one of the key models used for the study of this question. They contain two neuron populations which develop from the same precursor pool but differ in their transmitter, noradrenaline and acetylcholine, respectively. In addition, endocrine cells of the adrenal medulla are also derived from these precursors. Our interest is to unravel growth factors and transcription factors which are crucially involved in the regulation of these differentiation paths. Analysis of signals regulating general neuronal genes such as neurofilaments or neurexins will shed light on the bifurcation of neuronal and endocrine lineages. Characterizing signals regulating neuron population-specific traits such as transmitter-synthesizing enzymes will show how diversification of neuronal lineages operates.

Noradrenergic induction – specifying neurons by coordinate gene expression

Noradrenergic properties are induced early during sympathetic neurogenesis by BMP growth factors and Phox2 transcription factors in birds and mammals. Comparing the expression of tyrosine hydroxylase and dopamine β-hydroxylase, we could show that these two enzymes in the noradrenaline biosynthesis cascade are expressed at the same time. The induction by the same growth and transcription factors suggests regulation of these enzymes of noradrena-line biosynthesis as a synexpression group that is conserved in evolution from birds to mammals.

Common mechanisms for inducing transmitter synthesis and release genes

Synaptotagmin I as a putative calcium sensor of transmitter release and neurexin I as a putative organizer of synaptic protein complexes are general neuronal genes expressed in many classes of neurons. They become detectable in sympathetic neurons shortly after acquisition of the noradrenergic phenotype. Overexpression studies show that both genes can be induced by BMP growth factors and Phox2 transcription factors. Thus, it appears that induction of general and population-specific neuronal characters involves common mechanisms.

Neuronal maturation and bifurcation of neuronal and endocrine lineages

Induction of noradrenergic and general neuronal properties does not lead directly to a mature sympathetic neuron. Further differentiation is accompanied by increased expression of synaptotagmin I and neurexin I. In contrast, adrenal chromaffin cells show reduced or no expression of these and other general neuronal markers such as neurofilament M and SCG10. Thus, the maturation of neuronal gene expression is an essential landmark of neuron differentiation and of bifurcation.

General neuronal markers such as SCG10 and NF-M (neurofilament M) are expressed in a large number if not all neuron classes.

Population-specific neuronal markers are expressed in restricted neuron classes such as TH (tyrosine hydroxylase) in the sympathetic ganglia on this trunk cross section.
Generation of neuronal diversity in sympathetic ganglia

Choline acetyltransferase (ChAT) and the vesicular acetylcholine transporter (VAChT) are two main features of cholinergic neurons which are coordinately transcribed from the cholinergic gene locus. The loss of ChAT and VAChT expression in sympathetic ganglia of c-ret mutant mice indicates that signaling via receptors for growth factors of the GDNF family is necessary for the development of cholinergic sympathetic neurons. Expression of c-ret in cholinergic sympathetic neurons of the chick embryo suggests that its role may be evolutionary conserved. Thus, signaling via BMP and GDNF family receptors contributes to the generation of neuronal diversity in the sympathetic system.

Future Research and Goals

BMP growth factors and Phox2 transcription factors may not suffice to generate mature sympathetic neurons. Rather, a partially differentiated cell type seems to result which may correspond to the sympathoadrenal progenitor. Studying the expression of general neuronal genes, we are searching for factors which may be essential for the maturation of neuronal properties and the bifurcation of neuronal and endocrine lineages.

In addition, we analyze the diversification of transmitter properties in sympathetic ganglia. c-ret function in chick and mouse embryos is altered to demonstrate the role of c-ret signaling in cholinergic differentiation and bifurcation of neuronal differentiation paths.

With this approach we want to show how differentiation and diversification are regulated to orchestrate the expression of general neuronal properties with the acquisition of population-specific characters during neuronal development.

Selected Publications


Structure of the Group

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Membrane traffic in neuronal cell systems

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Current Research

Signal transmission between neurons occurs mostly at chemical synapses, which represent functionally and structurally highly specialized contact points between axons and dendrites. At presynaptic axonal endings signaling molecules are liberated from two types of neurosecretory vesicles: the small synaptic vesicles (SSVs) containing classical neurotransmitters such as GABA and neurosecretory granules (SGs) storing neuropeptides. Neuropeptides play a major role in modulation of neurotransmission. At the postsynapses of dendrites, signaling molecules of other neurons are perceived by neurotransmitter and hormone receptors. Our research focusses on two aspects of membrane traffic underlying synaptic transmission: axonal transport of SGs and dendritic transport of neurotransmitter receptors.

Biogenesis and transport of secretory granules

Secretory granules (SGs) are formed as short-lived vesicular intermediates at the trans-Golgi network. These intermediates undergo a complex and poorly understood maturation process resulting in mature SGs. A major objective of our laboratory has been to study the sorting of neuropeptides into SGs. This led to the identification of a specific sorting signal. To gain insight into the transport dynamics of newly formed SGs, we express GFP fusion proteins to specifically label SGs in living cells. This facilitates the study of budding, transport and docking of SGs in real time. One of our surprising findings is that SGs from neuroendocrine PC12 cells possess a dual transport system: after microtubule-dependent delivery to the cell periphery, SGs exhibit a myosin-dependent transport leading to their restriction and even dispersal in the F-actin rich cortex. Using live cell imaging in combination with in vitro motility assays and biochemical approaches, the recruitment and regulation of the respective motor proteins is under investigation. One emphasis is to analyze whether myosins play a role in the maturation of SGs. Furthermore we are interested in analyzing the mechanism of axon-specific targeting of SGs in polarized neurons.

Dendritic membrane traffic

The dendritic tree comprises one of the most complex subdomain structures of the plasma membrane and very little is known about trafficking pathways involved in the formation and maintenance of this structure. We are focussing on the transport of neurotransmitter receptors as one of the most prominent protein classes in dendrites. These receptors are composed of several subunits and vary in subunit composition throughout the dendritic tree. One possibility is that their differences in structure result in differences in synaptic plasticity. To analyze how membrane traffic is linked to synaptic plasticity, we are studying the selective transport of GFP-tagged subunits of the GABA_A receptor to postsynapses by multi-color imaging in combination with biochemical approaches. One interesting observation is that the differential trafficking of selected subunits depends on the developmental stage of hippocampal neurons. We are currently addressing the correlative transport dynamics, the site of integration into the plasma membrane and the endocytosis rate of the respective receptor subunits during neuronal development.

Future Projects and Goals

One major goal is the characterization of the structural sorting determinants of neurotransmitter receptor subunits and the identification of proteins interacting with these domains. Furthermore, we will study dendritic traffic in a more physiological context using organotypic cultures of brain tissue. By
combining optical methods with computer-based approaches, we will pursue a time-resolved, 3-dimensional reconstruction of dendritic transport in neuronal networks.

Selected Publications


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Figure 1. Scheme illustrating the role of myosin Va in the transport of secretory granules. After microtubule-dependent delivery to the cell periphery, myosin Va facilitates the distribution of SGs in the F-actin-rich cortex. TGN, trans-Golgi network; MT, microtubule; PM, plasmam-
1. Peripheral and spinal mechanisms of muscle pain
2. Neurotransmitters involved in the neuromodulation of the reflex bladder

Siegfried Mense
Dr. med., Universität Bonn 1973; Assistant Professor, University of North Carolina at Chapel Hill, USA, 1978-1979; Habilitation, Universität Kiel, 1979; Universitätsprofessor, Universität Heidelberg 1985

Current Research
1. Muscle pain. Peripheral level
In experimental animals in vivo, the hypothesis is being tested if purinergic and vanilloid receptors - which were originally detected on nociceptive endings in the skin - are also present on muscle nociceptors. Single fibre recordings from nociceptive muscle afferents have shown that ATP, capsaicin, and acidic solutions (pH 5 and 6) are effective stimulants for muscle nociceptors. This finding is also of clinical importance, because muscle inflammation and ischemia, respectively, are associated with a lowered pH. Therefore, the pain of myositis and intermittent claudication are likely to be mediated by nociceptive endings equipped with vanilloid receptors. In contrast, the pain of muscle trauma – which is associated with necrosis of muscle fibers and release of ATP - could be mediated by endings expressing purinergic receptors.

In the literature, the hypothesis has been formulated that nociceptive endings (in the skin) possess either purinergic or vanilloid receptors. This hypothesis appears not to be true for muscle nociceptors, because many endings recorded by our group responded to both ATP and acidic solutions. To exclude an influence of the acidic nature of the ATP solution, the solution was adjusted to a pH of 7.4. Immunohistochemical evaluations of DRG cells stained retrogradely from the sural muscle likewise showed that a considerable proportion of neurones expressed both P2X3 and VR-1 receptors.

Experiments employing a block of primary afferent fibres from muscle and skin with tetrodotoxin (TTX) demonstrated that many of the nociceptive fibres from muscle possess TTX-resistant sodium channels, and that the group IV-fibre input from muscle is subject to a stronger inhibition by large afferent fibres than is the cutaneous C-fibre input.

2. Spinal level
Previous studies of our group had demonstrated that the gaseous transmitter nitric oxide (NO) has a direct inhibitory action on nociceptive dorsal horn neurones, or conversely, that a spinal lack of NO is an excitatory stimulus for these cells. From evidence in the literature it appears, however, that at the supraspinal level NO has a pronociceptive or pro-hyperalgesic action.

In follow-up experiments we investigated the role of cyclic guanosine monophosphate (cGMP) in these NO actions. The results obtained so far support the assumption that the effects of NO are mediated through the NO-cGMP pathway: a lack of cGMP induced in the spinal cord by spinal superfusion with a blocker of the NO-sensitive guanylyl cyclase (ODQ) was followed by an activation of nociceptive neurones as was lack of NO. A spinal increase of cGMP caused by superfusion with a phosphodiesterase V blocker (sildenafil) had no effect on the discharges of the dorsal horn neurones. In contrast, sildenafil administered supraspinally by injection into the third cerebral ventricle (Fig. 1) had an excitatory action on the spinal sensory neurones. These data show that the NO-cGMP pathway has an opposite action on sensory neurones at the spinal and supraspinal level. Following systemic (oral) administration of sildenafil, the excitatory supraspinal actions appear to prevail, because the effect consisted in an activation of sensory spinal neurones.
2. Neuromodulation of hyperactive urinary bladder

Neuromodulation was performed by electrical stimulation of sacral nerves through electrodes positioned in the sacral foramen S1 (sacral neuromodulation) in rats with an inflammatory reflex bladder. The first experimental data indicate that activation of thick afferent fibres (at low intensities of stimulation) has weaker effects on the hyperactivity of the bladder than activation of thin fibres (at high intensities of stimulation). Short periods of stimulation caused inhibitions or reductions of the hyperactivity of the bladder that outlasted the period of stimulation by far. In conclusion, short periods of sacral stimulation at high intensities appear to be the most effective method to reduce the hyperactivity of an inflammatory reflex bladder.

Future projects and goals

Muscle pain. Future experiments will address the potential role of growth hormones, neurotrophic factors, and cytokines (BDNF, NGF, TNF-α, GDNF) as well as of NO as activating or sensitising agents of peripheral muscle nociceptors. Since some of these agents are likely to have different actions in intact and pathologically altered tissues, the experiments will be performed in rats with intact and inflamed muscle.

A further goal is to investigate the role of glial cells in the mediation of muscle pain.

Reflex bladder. The next question to solve is the identity of the neurotransmitters/neuromodulators that are released by sacral neuromodulation from the primary afferent fibres and that influence the hyperactivity of the reflex bladder.

Selected publications from 1999 to 2002


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Neuronal synchrony and plasticity

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Group leader at the ZMBH
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Current Research

The studies of this lab are directed at the identification of genes critically involved in the generation of synchronous oscillation in neuronal networks and on the role of NMDA receptor subtypes in different forms of plasticity.

Molecular mechanisms underlying synchronous activity in the central nervous system

Molecular and functional characterization of native glutamate receptors in identified neurones has revealed that GABAergic interneurones are endowed with receptors that are functionally different from those present in glutamatergic principal cells. The differential expression of glutamate receptors in these subsets of neurones is not restricted to glutamate receptors but has been extended to other gene families. The repertoire of receptors expressed in GABAergic interneurones is of particular interest in view of the growing evidence that their functional role extends beyond providing the main source of inhibition in the adult CNS. A number of compelling studies and computational simulations data provide evidence that networks of inhibitory neurones play a pivotal role in the generation of certain forms of oscillations that arise as a network property. Oscillatory activity in the gamma frequency range (40 Hz) has been proposed to be critical for object representation using temporal coding.

The goal of our studies is to identify the ‘key’ molecules in GABAergic interneurones that underlie oscillatory activity and that are involved in controlling synchronous firing of ensembles. The individual projects entail single-cell PCR in the acute slice preparation, in situ hybridization and immunochemistry in brain slices and the generation of transgenic mice with altered expression of critical genes (e.g., AMPA receptors, metabotropic glutamate receptors, connexins) in GABAergic interneurones.

Given the large diversity of GABAergic interneurones (based on the presence of certain parameters, for instance chemical markers, morphological criteria, connectivities), present projects aim at the identification of GABAergic subpopulations of neurones (e.g., parvalbumin-, somatostatin-, calretinin-positive cells). To this end transgenic mice are produced in which these neuronal subpopulations are labelled using the in vivo marker green fluorescent protein. The subsequent electrophysiological studies on fluorescent neurones in these mice should aid in identifying the GABAergic cell types involved in different forms of network oscillations.

Finally, these studies include the identification of neurones that are electrically coupled via gap junctions and the elucidation of their role in the generation of oscillatory and synchronous activity.

NMDA receptors neuronal plasticity and vulnerability

The NMDA receptor, a subtype of the glutamate receptor family, is critical for the induction of different forms of plastic changes in the brain. Molecular and functional characterization of different NMDA receptor subtypes has revealed critical amino acids that confer the receptor different properties with respect to kinetics, channel block by magnesium, sensitivity to pH etc. The differential regulation of NMDA receptor subtype expression with respect to brain areas and cell types exerts an important function in the developmentally regulated change of neuronal plasticity.

Projects pertaining to this research programme aim at defining the molecular basis of the differential NMDA receptor subtypes...
efficacy and include the generation of transgenic mice in which the switch from the 'young' to the 'adult' form of NMDA receptors is prevented and studies of the cellular localization of the 'young' form of NMDA receptors. The analysis of these mice is performed using electrophysiological techniques.

In cell culture obtained from cortical neurones, excitotoxic vulnerability is tested and the possible differential involvement of specific receptor subtypes is investigated.

Future Projects and Goals

So far our studies regarding GABAergic network activity and related projects entailed molecular, functional (electrophysiological) and anatomical characterization of receptor expression in identified cell population. The link to behaviour has been missing so far. It is our aim to add this aspect to our work. Also, one project pertaining to the identification of downstream cascades after NMDA receptor overstimulation will entail chip analysis.

Selected Publications


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Fig. 1 Subpopulations of electrically coupled GABAergic interneurons form distinct networks promoting synchronous neuronal activity.

Fig. 2 In situ hybridization showing developmental regulation of the NR2A but not NR2B subunit (left panels). Cortical cultures (A) are vulnerable to glutamate receptor induced toxicity (B, in blue staining indicate dead cells after ten minutes of NMDA exposure).
Mechanisms of short lasting synaptic plasticity

Andrei Rozov

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Current Research

Short-term modifications in the efficacy of synapses are observed in synaptic connections of the central nervous system when the presynaptic neuron is repetitively active. Successive unitary postsynaptic potentials, evoked by a train of presynaptic action potentials, can increase (facilitate) or decrease (depress) in amplitude, depending on the identity of the two neurons that form a connection. An increase of the probability of transmitter release caused by successive APs in the presynaptic terminal is postulated to underlie short-term facilitation of PSPs. Short-term synaptic enhancement occurring in the time scale of tens of milliseconds to several seconds is thought to be a calcium dependent process. The intracellular concentration of calcium at the release site depends on the distance between Ca\(^{2+}\) channels and the Ca\(^{2+}\) sensor as well as on the properties of endogenous Ca\(^{2+}\) buffers. It has been generally accepted that short-lasting synaptic enhancement is entirely presynaptic and involves an additional Ca\(^{2+}\) sensor, which is different from the one responsible for the transmitter release.

However, we have shown first, that at synapses characterized by high release probability and expressing Ca\(^{2+}\) permeable, polyamine sensitive AMPA receptor channels on the postsynaptic site, rapid activity dependent relief from polyamine block increases postsynaptic responses (Figure 1). Second, we have demonstrated that at neocortical excitatory connections facilitation is due to accumulation of free Ca\(^{2+}\). We suggest that at these synapses facilitation requires not only low release rate, but also relatively long diffusional distance between Ca\(^{2+}\) channels and Ca\(^{2+}\) sensor. Additionally, in the same study we have proposed a novel mechanism for paired pulse facilitation, which can operate in terminals with an increased buffer capacity and can arise from the local partial saturation of Ca\(^{2+}\) buffers. Recently we have found evidence that this mechanism indeed underlies facilitation in calbindin-D28K containing terminals (Figure 2).

In addition we are involved in studies of 1) the contribution of AMPAR desensitization to synaptic depression 2) mechanisms of LTP induction 3) electrical coupling between cortical interneurons.

Future Projects and Goals

In the future we would like to pursue investigation of general mechanisms of synaptic plasticity mainly in two directions 1) How do postsynaptic density proteins participate in long lasting changes of synaptic strength. 2) How do mGluR and GABA\(_B\) receptors contribute to synaptic depression. However, the most interesting topic is: what is the functional meaning of short-lasting synaptic changes at the system level. Addressing this question one requires the combination of molecular biological assays, in particular transgenic approaches, with modern physiological techniques. For instance, voltage sensitive dye imaging from a single neuron and large brain regions may provide information about the role of facilitation and depression in lateral and recurrent inhibition; two photon microscopy can be used to measure from very small structures like spines and presynaptic terminals; whole cell in vivo recording allows not only recording from cells under physiological conditions but also the use of physiological stimulation instead of artificial current injection.
Selected Publications


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Figure 1. Simultaneous whole-cell recordings were made at 34°C and 1.6 mM extracellular Ca²⁺ from a triplet (schematically shown on top) in which the same pyramidal neuron (P) innervated two multipolar interneurons (M). One multipolar cell (M1) was loaded with the PA-containing, another (M2) with the PA-free intracellular solutions. EPSPs evoked by 2 action potentials elicited in the pyramidal cell at 20 Hz facilitated in M1 (left trace) and depressed in M2 (right trace). The plot shows pairwise comparison of EPSP2/EPSP1 ratios measured from triplets. The connected symbols represent amplitude ratios of EPSPs evoked simultaneously in multipolar interneurons loaded with the PA-containing (closed circles) and with the PA-free (open circles) intracellular solutions following 20 Hz stimulation of the same presynaptic pyramidal neuron.

Figure 2. EPSCs recorded from CA3 pyramidal cells during paired-pulse stimulation (10 Hz) of mossy fibers in WT (MF, upper traces) and CB-KO mice (MF CB-KO, lower traces) In MF an increase of [Ca²⁺]o increases facilitation, a decrease of [Ca²⁺]o reduces facilitation. In MF CB-KO an increase of [Ca²⁺]o reduces facilitation, a decrease of [Ca²⁺]o increases facilitation. B. The graph compares the effects of changes in [Ca²⁺]o on facilitation at MF to CA3 pyramidal cell synapses (open squares) with that at MF to CA3 pyramidal cell synapses in CB-KO mice (closed circles). In order to compare across several experiments made on different connections, PPRs were normalized to that measured in 2 mM [Ca²⁺]o.
Development and maintenance of midbrain dopaminergic neurons

Horst Simon

Diplom in Biochemistry and Molecular Biology, ETH-Zürich, Switzerland
Ph.D. with Andrew Lumsden, Guy’s Hospital, University of London, UK
Postdoc with Dennis O’Leary, The Salk Institute, La Jolla, CA, USA
Group Leader, Anatomy and Cell Biology III since 1999

Current Research

The research of our laboratory is directed to the molecules involved in the development and adult maintenance of the midbrain dopaminergic (mDA) neurons. We investigate the genes involved in their induction, determination of their cell fate, establishment and maintenance of their axonal projections and their synaptic connections as well as those that are essential for their survival. Our approaches are gain of function experiments introducing over-expression vectors in cell culture and in chicken embryos by electroporation, and loss of function studies involving homologous recombinant knockout mutant mice, conditional mutant mice based on the loxP/Cre system and RNA interference on primary cell culture.

Transcriptional Regulation of their Cell Fate

Midbrain dopaminergic neurons are the largest source of dopamine in the mammalian central nervous system, located in three distinct nuclei, substantia nigra compacta (SNC), the ventral tegmentum and the retrorubral field. They are associated to one of the most prominent human neurological disorders, Parkinson’s Disease (PD). PD is caused by the degenerative loss of the dopaminergic neurons in the SNC, which leads to a diminished release of dopamine in the basal ganglia, one of the major centers of voluntary motor control. The symptoms are tremor, muscular rigidity, akinesia and loss of postural reflex. The disease affects approximately 2% of the human population when they are over 65 years of age.

Despite the medical relevance of midbrain dopaminergic neurons, only a few regulatory elements have been identified and successfully linked to cellular properties of this neuronal population. We recently showed that two closely related transcription factors, engrailed-1 and engrailed-2, are cell autonomously required for the survival of dopaminergic neurons in the SNC. Lack of all four alleles of the two transcription factors in mutant mice or their silencing by RNA interference in primary cell culture induces caspase-3 dependent apoptotic cell death in postmitotic dopaminergic neurons. This is similar to the mechanism that has been suggested to be responsible for the degeneration of this cell group in Parkinson’s patients or in the case of neurotoxin-induced depletion of nigral dopaminergic neurons in animal models of PD. Mutant mice lacking three alleles (En1-/-;En2-/-) exhibit a specific, progressive loss of dopaminergic neurons in the lateral SNC, the population of cells most affected in human patients. Interestingly, α-Synuclein, a gene that has been recently genetically linked to the loss of midbrain dopaminergic neurons during Parkinson’s Disease, seems to be regulated by engrailed-1 and -2.

Our recently performed differential display experiment revealed amongst others two more transcription factors specifically expressed by midbrain dopaminergic neurons, these

Fig. 1: Dopamine circuit in the rat brain
are the homeobox transcription factor, Pbx1, and the winged helix transcription factor, HNFα. Analysis of the Pbx1 null mutants revealed an involvement in axonal pathway finding related to the release of a chemoattractive diffusible factor from the developing basal ganglia, the main innervation target of this neuronal population. HNF3α is likely involved in the regulation of $K_{ATP}$ channels. In midbrain dopaminergic neurons, the most prominent $K_{ATP}$ channel is a complex of two proteins, Sur1 and Kir6.2. Loss of function studies on mutant mice revealed that they are survival relevant for the midbrain dopaminergic neurons. Mice deficient of either of the two genes show a progressive loss of dopaminergic cells in the SNC after birth.

**Future Projects and Goals**

Our long term goal is the identification and characterisation of the transcriptional networks which determines the cellular properties of the mDA neurons. This includes the transcription factors as well as downstream molecules. One emphasis is the identification of genes which cause or avoid physiological stress in this neuronal population potentially linking them PD. A long term aim is the establishment of cell culture systems which mimic this physiological stress and may be useful to screen for active pharmacological components.

**Selected Publications**


**Structure of the group**

<table>
<thead>
<tr>
<th>Group leader</th>
<th>Horst Simon</th>
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<tr>
<td>Graduate students</td>
<td>Lavinia Alberi</td>
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<td>Daniel Gherbassi</td>
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**Figure 2:** Specific loss of dopaminergic neurons in lateral substantia nigra compacta (SNC) of adult mutant mice, heterozygous for the En1 null mutation and homozygous for the En2 null mutation (En-1+/-; En2-/-)

**Figure 3:** Caspase dependent apoptotic cell death in engrailed deficient mDA neurons
Molecular cell biology of neuron-glia interaction and myelination

Jacqueline Trotter

PhD 1979 University of York, England. Postdoctoral work at the Max-Planck Institut für Immunbiologie, Germany. Stanford University School of Medicine, USA and the University of Heidelberg. Group Leader at the Department of Neurobiology, IZN, since 1991. July 1999 Hermann and Lilly Schilling Stiftung Professor for Neuroscience, Dept. of Neurobiology, University of Heidelberg. April 2000: C3 Professor of Cell Biology at the University of Mainz.

Current Research

Myelination of axons in the vertebrate nervous system is essential for the fast propagation of action potentials. The multilamellar myelin sheath is a specialised, polarised, lipid-rich domain of the glial cell plasma membrane, synthesised by oligodendrocytes in the CNS and Schwann cells in the PNS. Loss of myelin, results in paralysis. Our aim is to define the molecules of glial precursor cells regulating the migration to and interaction with myelination-competent neurones and to elucidate the cell biological principles underlying the synthesis of myelin. The mechanism of sorting and compartmentation of proteins and lipids in myelinating glia, for example via lipid rafts, is also a central topic. These topics are additionally of clinical relevance in the context of de- and dysmyelinating diseases (e.g. Multiple Sclerosis), the migration of neural tumours and the missorting of glial proteins and lipids in the pathology of human disease. Recent work is also addressing the interaction of glial progenitor cells with neurones at synapses.

The AN2/NG2 Glycoprotein in Development and Disease

We have recently shown that the AN2 glycoprotein is the mouse homologue of human and rat NG2. It is expressed by migratory oligodendroglial and Schwann cell precursors and is down-regulated as these cells mature. It is also expressed by synaptic glia and may play a role in regulating synaptic activity and network properties. A subset of patients with the demyelinating disease Multiple Sclerosis, synthesise antibodies against NG2: this may contribute to the poor repair seen in these patients as the precursor cells responsible for remyelination are attacked. Additionally, the antibodies may be interfering with synaptic function. We have cloned mouse NG2 and generated fusion proteins and specific antisera for the different regions of the molecule. These provide tools to investigate the function of the molecule. We have recently shown that the C-terminus of NG2 binds to the PDZ protein GRIP and thus forms a complex with AMPA receptors in synaptic glia and immature oligodendrocytes. We have also identified a link between the cytoplasmic region of NG2 and the cytoskeleton which may play a role in cell and cell process movement and cell migration.

Oligodendroglia sort GPI-anchored adhesion molecules associated with Signalling Complexes into lipid rafts in the early phases of Glial-Axon recognition

In maturing oligodendrocytes, the glycosylphosphatidylinositol-anchored proteins F3 and NCAM 120 associate with the intracellular tyrosine kinase Fyn and the myelin lipids cholesterol and glycosphingolipids in detergent-resistant ‘rafts’. The activity of Fyn is highest during myelination.
These complexes may thus couple adhesion molecules to signal transduction cascades inside the glial cell whose activation stimulates the myelination programme. Ligation of such adhesion molecules by axonal ligands may thus induce cytoskeletal changes leading to the wrapping of axons and the laying down of the multilamellar sheath. We have shown that in oligodendrocytes Fyn associates with the microtubule associated protein Tau and also with Tubulin. Disruption of the Fyn-Tau interaction in cultured oligodendrocytes inhibits process outgrowth. Rafts may be a site of signal-transduction within the glial-axonal unit and serve to polarise vesicle traffic towards the glial axonal contact site.

The Sorting of Myelin Components in Oligodendrocytes

The generation of the myelin sheath involves the selective targeting to and exclusion of distinct proteins and lipids to the specialised subdomains of myelin: e.g. compact myelin, the adaxonal membrane and the paranodes. We are using primary cultures of oligodendroglia to analyse the cell biological principles underlying this sorting out of cellular proteins and lipids to generate myelin. We have shown that oligodendrocytes use lipid rafts to sort the main myelin protein, PLP into the forming sheath.

Future Projects and Goals

1) Elucidation of the adhesion molecules regulating the migration of glial progenitor cells and their connection to the cell cytoskeleton. In particular, the role of the AN2/NG2 proteoglycan in this process.

2) What is the role of NG2+ glia at synapses: do neurons express receptors for the glycoprotein?

3) What is the role of the antibody against AN2 in the pathology of MS? Are specific regions of the molecule immunogenic in patients?

4) Analysis of the axon-glial interaction and signaltransduction: Definition of the signals required to initiate and maintain myelination. The role of the src kinase members Fyn and Lyn expressed by glia in this process. What are the axonal and glial partner adhesion molecules? What is the role of raft-associated cytoskeleton?

5) Definition of the cellular sorting and transport processes utilised by oligodendrocytes to build up the domain structure of myelin. How and where in the cell are the different microdomains generated, leading ultimately to the subdomains of myelin? What is the role of neuronal contact in this process?

Selected Publications


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Control of peripheral nerve outgrowth in embryonic mouse development

Kerry L. Tucker

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Current Research

In the developing nervous system, newborn neurons elaborate axonal processes that navigate complicated pathways and often travel long distances before they reach their target. Ultimately one would like to study this developmental process as it occurs in the organism. Ideal would be a means to directly and non-invasively observe the behavior of outgrowing nerves in their native environment. To do this, we have engineered a mouse to express the enhanced green fluorescent protein (EGFP), which produces an intense fluorescence signal upon light excitation. The gene encoding EGFP was inserted into the mouse genome in such a way that expression is specific to neurons, and the levels of EGFP produced are high enough to clearly label the entire length of outgrowing axons (see Figure 1). The tEGFP mouse line was used to establish an embryonic slice-culture method in which we can perform time-lapse imaging of the peripheral outgrowth of nerves of the spinal and cranial ganglia.

We have worked with the four members of the neurotrophin family, which includes nerve growth factor (NGF), brain-derived growth factor (BDNF), neurotrophin-3 (NT-3), and neurotrophin-4. Using recombinant neurotrophins and function-blocking antibodies to them, we were able to demonstrate that NGF, NT-3 and BDNF play a crucial role in promoting the growth of nerves in the forelimb. As neurotrophins are not expected to be the only molecules involved in this process, we are extending these studies using three complementary experimental approaches.

Time-lapse imaging

We are performing high-resolution imaging of nerve outgrowth into the embryonic limb, which is innervated by spinal nerves derived from motor neurons of the ventral spinal cord and sensory neurons of the dorsal root ganglia. We will employ a microscope set-up allowing for cultivation of embryo slices upon the microscope stage itself, with the use of a contained tissue-culture environment. We have begun our studies using the tEGFP mice, and with new lines derived from crosses between the tEGFP mice and mutants in two gene families known to be important for early outgrowth of spinal nerves, the neurotrophins and the semaphorins.

Reverse genetic analysis of nerve outgrowth

We have developed a simple system for reliable expression of genes of interest specifically in neurons, such that heterologous cDNAs are switched on shortly after the birth of the transgenic neurons. This allows for overexpression of normal and mutant forms of genes of relevance to axonal extension, to test for their effects upon axonal growth in vitro and in the developing mouse embryo. This system is also being engineered to allow for the inducible activation of genes of interest within neurons, allowing for temporal as well as special specificity.
ENU mutagenesis

The tEGFP mouse allows the direct visualization of all nerves derived from the cranial and spinal ganglia, in a developmental time-frame extending from early neurogenesis to late stages of gestation. This feature opens the possibility of an examination of general defects in this complicated process, through the induction of random mutations via chemical mutagens such as ethyl-nitroso-urea (ENU). To uncover recessive mutations, mutagenized males are mated with their daughters, and litters of embryos examined at specific time points during embryogenesis. The entire peripheral nervous system is screened for defects in gangliogenesis and axonal outgrowth through visual inspection of embryos, using fluorescent microscopy. We have identified three initial mutations that bear defects in outgrowth of various cranial ganglia and in the development of the tenecephalon (see Figure 2).

The uncovered mutants will be further analyzed through histochemical analysis, in vitro culturing of slices from mutant embryos, and, ultimately, positional cloning of the mutated gene in question. Where relevant, both engineered and ENU-induced mutants will be imaged in our slice culture system, to better ascertain the nature of the defects. These approaches are expected to give us new insights into the wiring of the nervous system, as it develops in the animal itself.

![WT](image1.jpg) ![ES](image2.jpg)

Fig. 2: Mutant E5 showing ectopic cells (arrow, right) in tenecephalon of a mid-gestation embryo. Note lack of such cells in wild type (WT) tenecephalon. (arrowhead = ocular branch of trigeminal nerve; e = eye)

Selected Publications


Structure of the group

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TGF-βs, FGFs and neurotrophins in neural development and functions

Klaus Unsicker

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Current Research

Development of distinct cell phenotypes, neuron survival, network formation, and responses to lesions in the nervous system depend on the concerted actions of numerous, largely multifunctional growth factors. Ongoing projects in the group include the following: (1) specification of neural crest (NC) derived neuronal and neuroendocrine cells and their integration into neural circuitries, (2) functional characterization and signaling of a novel member of the TGF-βs, GDF-15, (3) significance of neurotrophin signaling for the development and maintenance of CNS aminergic systems, and (4) roles of FGFs and TGF-βs in neuronal and astroglial functions.

The NC as a paradigm for studying generation of cell diversity

The NC gives rise to diverse neuronal, endocrine, and mesenchymal cell types and, hence, is an excellent model for exploring mechanisms involved in the generation of cell diversity. We focus on the sympathoadrenal (SA) cell lineage, which gives rise to sympathetic neurons and neuroendocrine chromaffin cells. We have found that glucocorticoid signaling, contrary to a previous hypothesis, is not essential or sufficient for generating chromaffin cells. We are currently studying the roles of BMP-4 and transcription factors in the specification of chromaffin as opposed to neuronal cells using loss- and gain-of-function paradigms. The bhlh transcription factor MASH-1 is important for the development of a major subpopulation of chromaffin cells. BMP-4 is highly and persistently expressed in all locations, where chromaffin cells develop, suggesting that it may play a role, by itself or in synergy with other factors, in suppressing neuronal and promoting endocrine features in SA progenitors.

Development and maintenance of the neural circuitry that links CNS and peripheral portions of the sympathetic nervous system

Sympathetic neurons and chromaffin cells are innervated by preganglionic sympathetic neurons (PSN; Fig. 1) that are located in the spinal cord and develop from the same precursor pool as motoneurons. In contrast to the abundant information available for factors that affect motoneuron development, very little is known on PSN promoting factors. Using knockout mice we have established that the LIFRβ and neurotrophin-4, but not FGF-2, are important for embryonic and postnatal, respectively, development of PSN neurons.

Functional characterization and signaling of a novel member of the TGF-βs, GDF-15

GDF-15 is a novel, distant member of the TGF-βs with wide distribution in the CNS. As a trophic factor for midbrain dopaminergic neurons in vitro and in vivo it is at least as
potent as GDNF. GDF-15 is prominently upregulated in lesioned neurons suggesting functions related to executing survival or death programs. On cerebellar granule neurons GDF-15 exerts its survival promoting effect through activation of the PI3K/Akt/GSK-3 pathway. A GDF-15 knockout mouse has been generated and is currently analyzed.

Significance of neurotrophin signaling for the development and maintenance of CNS aminergic systems
BDNF, NT-3, and NT-4 have been shown to be important regulators of the development and plasticity of the dopaminergic and serotonergic systems. We use aged trkB and trkC heterozygous knockout mice to analyze functional deficits related to these aminergic systems.

Roles of FGFs and TGF-ßs in neuronal and astroglial functions
We are studying the roles of FGF-2, -5, -9, and TGF-ß2 and -ß3 in the regulation of neuronal and astroglial development and functions in the adult. Using in vitro approaches and knockout mice we have found that FGFs regulate astroglial differentiation, gap junction communication, and blood-brain-barrier permeability in a region-specific fashion (Fig. 2). Concerning TGF-ßs we focus on the molecular bases of their synergistic roles with neurotrophins, GDNF, and FGF-2 in the regulation of neuron survival.

Future Projects and Goals
Our long-term goal is to understand the hierarchies and interdependencies of molecules involved in the generation of cellular heterogeneity and cell-cell communication in the nervous system. Current work in the NC project suggests that SA progenitors destined to become neurons or chromaffin cells, respectively, may phenotypically segregate prior to reaching their final target sites. We are working on the identification of the GDF-15 receptor and hope to obtain additional cues as to its functions from the current analysis of the GDF-15 knockout. We will expand on the use of transgenic animal models to understand the roles of FGFs and TGF-ßs not only in development, but also in the context of lesions with clinical relevance.

Selected Publications

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Research Profiles

Inhibitory ion channels

William Wisden

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Group leader at the MRC Laboratory of Molecular Biology, Cambridge, UK (1993-2000)
Group leader at the Dept. of Clinical Neurobiology, University Hospital of Neurology, Heidelberg since 2001

Current Research

Brain function depends on balancing synaptic excitation and inhibition. γ-Aminobutyric acid (GABA), the most important inhibitory neurotransmitter used for this, works at GABA_A receptors. These are heteromeric transmitter-gated chloride channels. The GABA_A receptor subunit genes (α1-6, β1-3, γ1-3, δ, ε, θ, ρ and π) are differentially transcribed, and the subunits assemble combinatorially into heteromeric pentamers. Defects in GABA_A receptors cause diseases such as epilepsy. GABA_A receptors are also targets for important drugs: benzodiazepines, barbiturates and steroids.

Key questions: "How many receptor subtypes are there?", "What are these different receptor subtypes for?" and "How are the diverse expression patterns generated?" We study these problems in the cerebellum, a brain region that controls motor movements and memories. Our studies will help us understand more complicated situations in other brain regions.

Cerebellar granule cells form part of a circuit that learns and executes motor memories. For example, riding a bicycle or playing the piano both require the cerebellum. In mice this circuit is well-suited to genetic dissection; mutations can be readout as changes in motor skill. Why do different synapses in this circuit use different GABA_A receptor subtypes? This is what we want to find out.

Past work: α6 subunit gene knockout
Granule cells express six subunit genes (α1, α6, β2, β3, γ2 and δ), and make at least three subtypes of GABA_A receptor. We made a mouse line with an α6 gene disruption. Unlike the other subunit genes, α6 gene expression is restricted to cerebellar granule cells - this knock-out affected only the cerebellum. Actually, the mice have a double subunit knockout in the cerebellum: in addition to the α6 loss, δ protein also completely disappears from the granule cell surface. Thus α6 and δ make a specific type of GABA_A receptor. Surprisingly, in spite of large losses of GABA_A receptors from α6-/- granule cells, the mice are normal on cerebellar-related motor tasks.

The εδ-containing receptor is specifically extrasynaptic. Granule cells are bathed in GABA. This GABA bath is generated by transmitter diffusing from the GABAergic interneuron-granule cell synapse. As shown by Cull-Candy's group at UCL in London, GABA continuously activates extrasynaptic GABA_A receptors as a tonic background conductance. The tonic current likely modulates the dynamic range over which granule cells fire action potentials. The εδ-containing

Expression of the α1 and α6 subunit genes in the cerebellum, as seen by in situ hybridization.
GABA_A receptors are directly involved in this process: in α6−/− granule cells, the background inhibition is completely gone. This should have severe consequences, but there has been a compensation: a K^+ leak conductance has been up-regulated. This conductance may do the same job as the extrasynaptic α6δ-containing GABA_A receptors, making it harder for excitatory inputs to initiate action potentials.

**Future work: K^+ channel expression**

The α6 knockout mice have compensated for the α6 and δ protein loss by upregulating the expression of a potassium channel gene. The conventional knockout did not tell us directly the function of the α6 gene; on the other hand, it illustrated the remarkable abilities of biological systems to make do with alternative strategies. We are currently identifying the potassium channel responsible and studying how the change in its expression has occurred.

**Future work: further dissecting GABA_A receptor diversity in cerebellar granule cells.**

In addition to α6’s extrasynaptic location, this subunit colocalizes with the α1, β2/3 and γ2 subunits in the synapse. Why are both the α1 and α6 subunits needed at the synapse? We will ablate α1 and γ2 subunit gene expression specifically in cerebellar granule cells, and without affecting the rest of the brain. To do this we are using Cre recombinase (see next section).

**Future work: cerebellar granule cell-specific ablation of genes using Cre recombinase.**

We have mice lines with Cre recombinase expressed from the α6 gene (Aller, Jones, Merlo, Wisden, unpublished). This gives Cre expression in adult cerebellar granule cells. These lines will allow specific lesions of other genes in cerebellar granule cells, including K^+ channel subunit genes (see above), without affecting the rest of the brain. The Cre mice are crossed with other mouse lines with "floxed" genes - genes with lox P sites (the recognition sites for Cre recombinase) flanking key exons. This causes disruption of the target gene just in cerebellar granule cells.

**Summary**

My group researches the transmitter receptors (GABA_A) used to inhibit neuronal firing in the brain. These receptors have tremendous diversity; we want to understand why. As a simple system, we use cerebellar granule cells. These cells provide a mini-world of GABA_A receptor complexity. Mouse mutants with specifically engineered and/or deleted GABA_A receptor genes in granule cells make it possible to understand the rich diversity of GABA_A receptor in complex brain regions such as the hippocampus or neocortex.

**Selected Publications**


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Selected Research Profiles of Outer Circle Members
Experimental cerebral ischaemia

Bernd W. Böttiger

MD 1986, University of Heidelberg
1994 - 1996, Max-Planck-Institute for Neurological Research, Cologne, Germany
1997, Associate Professor of Anaesthesiology, Group Leader Molecular Biology Laboratory
1998 - 2001, Visiting Professor at the Universities of Stanford, Duke, Chicago and Pittsburgh, USA
Current position: Co-Chair of the Department of Anaesthesiology, University of Heidelberg

Current Experimental Research

A.) Improvement in neurological outcome after cardiac arrest
Cerebral damage following cardiocirculatory arrest is a major public health care issue. To date no specific treatment options (with the exception of mild hypothermia and thrombolysis in selected patients) are available to improve neurological outcome following cardiocirculatory arrest. Therefore, innovative basic and clinical research is absolutely essential. Our investigations are based on the hypothesis that apoptosis (programmed cell death) might play an important role in mechanisms involved in delayed neuronal death. Using a unique murine and rat model of global cerebral ischaemia after cardiac arrest, we are studying the effects of anti-apoptotic interventions, for example the investigation of transgenic animals overexpressing anti-apoptotic proteins such as p35, CrmA, Bcl-2, Bcl-XL or the intracerebroventricular administration of synthetic caspase inhibitors (z-DEVD-FMK).

B.) Transient focal cerebral ischaemia in a transgenic murine model
Delayed neuronal death is also a major cause of the high morbidity and mortality associated with stroke (focal cerebral ischaemia). In collaboration with the Departments of Physiology and Neurology we are investigating the efficacy of these anti-apoptotic proteins in preventing delayed neuronal death after focal cerebral ischaemia in transgenic mice (see above).

Future Projects and Goals
The goal of these investigations is to precisely characterize the mechanisms involved in delayed neuronal death so as to directly transfer these results to the clinical setting and improve neurological outcome after cardiac arrest in humans. Subsequently, different novel therapeutic strategies that inhibit the apoptotic cascade upstream and/or downstream will be tested. All these therapeutic strategies (neurotrophins, inhibition of apoptosis-inducing death receptors and caspase inhibitors) can be tested in our well-established cardiac arrest models in rats and mice.

Selected Publications

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Inhibitory synapses and network oscillations

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Since 2002 Professor of Physiology, Medical Faculty, Heidelberg University.

Current Research

We examine electrical functions of the mammalian brain at the level of single inhibitory synapses and of neuronal networks with coordinated multicellular activity. Both subjects are strongly interrelated through the dominant role of inhibitory interneurons in the synchronization of network oscillations as well as in pathological network activity (epilepsy).

Inhibitory synapses of higher mammalian brain nuclei act by the storage and release of GABA (γ-aminobutyric acid). While much is known about structure and function of GABA receptors, we focus on two additional elements: GABA-uptake and GABA-metabolism. We have analysed the functional maturation, ontogenetic expression and local specificity of the GABA transporter GAT-1 in the rodent hippocampus. At present, we analyse the regulation of inhibitory synaptic efficacy through GABA-metabolism. Our results indicate that alterations in GABA-production are an autonomous mechanism of synaptic plasticity. All projects dealing with GABAergic transmission are also applied to models of epilepsy.

High-frequency network oscillations at ~200 Hz ("ripples") are a characteristic pattern of hippocampal activity during slow-wave sleep and have been implicated in long-term memory formation. We analyse the mechanisms of such network oscillations in brain slices in vitro. We have found that electrical synapses (gap junctions) are needed for neuronal synchronization at this high frequency. In addition, most hippocampal projection cells receive strong GABAergic inhibition during ripples. We assume that inhibitory interneurons contribute to the coordination of fast rhythmic activity and may be the key to the selection of cells which do participate in ripples from those which stay silent.

Future Projects and Goals

We want to examine

- examine GABA-metabolism as a general mechanism of synaptic plasticity;
- compare the role of reverse GABA-uptake versus vesicular GABA-release in immature brain tissue;
- characterise alterations of GABAergic synapses and circuits in chronic epilepsy;
- analyse the modulation of GABA release by presynaptic ionotropic GABA-receptors;
- study the role of GABAergic interneurons in high-frequency network oscillations;
- establish the nature and subcellular localization of hippocampal gap junctions which are involved in ripples;
- investigate the potential role of ripples in memory formation at a mechanistic level in vitro.

Selected Publications


Structure of the group

Group leader Andreas Draguhn
Postdoctoral fellows Volker Nimmrich, N.N.
Graduate students Nikolai Axmacher, Kristin Hartmann, Nikolaus Maier, Frank Stief
Technician Petra Rook

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55
Learning and neuronal plasticity

Herta Flor

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1983-1987 Post-Doctoral and assistant professor positions at Yale University, and at the University of Pittsburgh, USA
1987-1993 DFG-Scholarship & Heisenberg fellow (DFG), University of Tübingen
1993-2000 Professor (C4) for Clinical Psychology & Somatopsychology Humboldt University, Berlin, since 2000 Professor (C4) of Neuropsychology, Central Institute of Mental Health, Mannheim

Current Research

At the core of our research lies the interaction between brain and behavior. In particular, we are interested in elucidating the neuronal correlates of learning and memory. Our research involves measures of cortical activity such as EEG and MEG, functional imaging techniques, measures of peripheral physiological activity (EMG, skin conductance, heart rate) as well as markers of endocrinological activity (e.g., cortisol).

A first line of research is focusing on neuronal plasticity in the somatosensory system and its contribution to pain memory. Using a cross-sectional approach, the relationship between neuronal reorganization within the somatosensory system and painful and non-painful phantom phenomena is assessed in both upper and lower limb amputees using EEG and fMRI measurements. Using a prospective approach, the role of the glutamatergic and GABAergic transmitter systems in modulating neuronal plasticity is investigated in amputees by using different pharmacologic blocking agents.

A second line of research concerns the contribution of neuronal plasticity in the auditory system to the development and maintenance of tinnitus symptoms. After having demonstrated that tinnitus is associated with a reorganization of the tonotopic map in the primary auditory cortex, we currently determine the effectiveness of an auditory discrimination training in improving Tinnitus severity and impairment. A third line of research targets the development and maintenance of fear memories and their neuronal correlates. Recently, we found first evidence that a hypoactive fronto-limbic fear circuitry may account for the dissociative behavior in sociopaths. By contrast, the excessive social fears in social phobics seem to reflect a hyperactive fronto-limbic circuit that can easily be activated even by neutral and per se non-threatening social cues.

Future Projects and Goals

In close cooperation with other research groups, we are launching a collaborative research grant initiative on learning and plasticity underlying psychopathology. This research lies at the intersection of neurobiology, experimental and clinical psychology and biological psychiatry and is unique in bringing together similar research designs on different levels of analysis (molecular, behavioral, clinical) of learning and plasticity. Rather than taking a nosological approach which leads to the problem of overlapping psychopathological characteristics and examining the neurobehavioral and molecular mechanisms of individual disorders, this planned initiative seeks to determine similarities and differences of the underlying mechanisms of learning and neural plasticity across a variety of disorders. We will pursue basic associative and non-associative learning mechanisms and their neuronal correlates which are fundamental for the understanding of disorders as e.g., post-traumatic stress disorder, social phobia, depression.

Selected Publications


Structure of the group

Group leader
Herta Flor

Postdoctoral fellows
Eugen Diesch, Carsten Diener, Christiane Hermann, Christoph Schneider

Graduate students
Christoph Christmann, Martin Diers, Johanna Hohmeister, Caroline Koppe, Jaana Markela-Lerenc, Claudia Rolk, Maren Struve, Michele Wessa, Katrin Zohsel

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56
Function and development of olfactory neural circuits

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Current Research

We study how complex odor information is processed by dynamic neural circuits in the brain, and how these circuits emerge during development. In the first olfactory processing center, the olfactory bulb (OB), each odor activates a particular combination of input channels (the olfactory glomeruli). The circuitry within the OB then dynamically transforms these activity patterns. We are currently investigating the function and the cellular bases of these dynamic computations, using the zebrafish and mouse as model systems. Moreover, in zebrafish we are studying the function of the embryonic olfactory system and the transition from the embryonic to the adult brain function.

In particular, we use optical imaging methods (fast CCD-cameras, 2-photon microscopy) to record the activity of single neurons and neuronal ensembles in the intact brain. For such optical approaches, the transparent zebrafish embryo is ideal. With modern optical methods such as 2-photon microscopy it is also possible to image living neurons in the mouse. Optical techniques are combined with electrophysiology, embryology and molecular biology (transgenics) to analyze the development and function of a complex neural network in the intact animal.

Future Projects and Goals

A research focus in the future will be the functional development of the neuronal circuitry in the OB. Using 2-photon microscopy, we will follow the development of individual neurons through development and record their odor response properties. In addition, we are starting to use transgenic approaches for optical recording of neuronal activity, and to exploit the large collection of zebrafish mutants. In the adult olfactory system of zebrafish and mouse, we investigate the relationship between spatial and temporal structure in odor-evoked activity patterns using high-speed voltage-sensitive dye imaging, 2-photon microscopy, and electrophysiology.

Selected Publications


Structure of the group

Group leader: Rainer Friedrich
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Graduate students: Julia Mack, Rico Tabor, Emre Yaksi
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Genetics of axon guidance in C. elegans

Harald Hutter

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Postdoctoral work at the Johns Hopkins University, Baltimore, USA
Junior group leader at the Max-Planck-Institute for Medical Research, Heidelberg, since April 1999

Current Research
The wiring of the nervous system is established during embryogenesis when all the neurons send out processes which eventually connect to their target cells to form neuronal circuits. The large number of neurons involved and the complex pattern of neurite outgrowth makes this a formidable navigational problem. We use genetic and reverse genetic approaches in the nematode Caenorhabditis elegans to identify key molecules important for axon navigation. In genetic screens for mutants with axonal outgrowth defects we have identified a number of novel genes involved in various aspects of axonal pathfinding. Two of the genes identified so far turned out to be transcription factors affecting late aspects of neuronal differentiation. These as well as several other genes are studied in more detail at the moment.

In a complementary approach we use the sequence information generated by the C. elegans genome sequencing consortium to search for candidate axon guidance genes, which are then studied using gene knock-out strategies.

Future Projects and Goals
The transcription factors identified in the genetic screens provide entry points for further analysis. Some of the target genes might directly control axon navigation and we will use different methods to identify at least some of them. Enhancer or suppressor screens will be used to identify novel genes interacting genetically with the genes identified so far. Further genetic screens are in progress and are likely to identify more of the genes essential for correct axon outgrowth.

Cell adhesion molecules are known to play an important role in axon outgrowth. The largest families are IgCAMs and cadherins and the C. elegans sequencing project has identified all the members of these families. We have established a library of mutagenized C. elegans animals, which can be screened to identify deletions in candidate genes. We have started to use this library to isolate mutations in all neurally expressed members of the IgCAM and Cadherin families moving away from the single gene analysis to study entire gene families and their interactions. In addition we will use RNAi screens for axon guidance genes with special mutants isolated in our lab, which are hypersensitive to RNAi in the nervous system. Deletion alleles in candidate genes coming from these screens will be generated and studied further.

Selected Publications

Structure of the group
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Molecular basis of cerebral ischemia and ischemic preconditioning

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Research Fellow Cornell University Medical College, Department of Neurology, New York, USA, 1983/84
Professor, University of the Saarland, Germany, 1988/89
Medical Director of the Department of Neuropathology, IZN, University of Heidelberg, since 1990

Current Research

According to current concepts, excitotoxic activation of glutamate receptors is thought to play a pivotal role in the molecular pathogenesis of postischemic delayed neuronal death (DND). This concept has recently been extended to competing genetic programs that promote neuronal survival or death, respectively. Moreover, there is compelling evidence for an impact on the brain’s response to ischemia by endogenous or exogenous induction of an ischemia-tolerant state. In particular, postischemic DND of vulnerable subsets of neurons can be prevented by ischemic preconditioning (IPC) with a sublethal noxious stimulus prior to an otherwise lethal period of brain ischemia.

Current research focuses on molecular mechanisms that are critically involved in the acquisition of a neuroprotective state. Using rodent models of temporary global and focal brain ischemia, we analyzed the regulation of neurotransmitter receptors with and without ischemia tolerance induction. We found (1) a differential expression of ionotropic and metabotropic glutamate receptor subtypes and (2) a postischemic upregulation of GABA	extsubscript{A} receptor activity, indicating that a relative shift between inhibitory and excitatory neurotransmission may promote survival of vulnerable neuronal subpopulations in the hippocampus (after global ischemia) and in the cortical penumbra (after experimental stroke, respectively).

Future Projects and Goals

The understanding of molecular mechanisms that confer neuroprotection may increasingly determine clinical outcome after stroke and help to define new therapeutic strategies. There is intriguing evidence that IPC also occurs in humans. This has raised considerable enthusiasm but calls for intense further basic research. Future projects of this research program aim at the identification of differentially expressed proteins involved in the induction of an ischemia-tolerant state, since ischemic translational inhibition has a profound effect on the expression pattern of proteins encoded by inducible genes. Therefore, analyses will focus on the protein level using proteomics and subsequent expression studies of identified target proteins by molecular biological and in situ techniques.

Selected Publications


Structure of the group

Group leader Marika Kiessling
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Ontogeny, stabilization and functional adaptation of postsynaptic membrane specializations

Joachim Kirsch

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1995 Habilitation in Anatomy, University of Frankfurt
1998-2002 Head of the Dept. of Anatomy & Cellular Neurobiology, Schilling endowed Professorship, Dept. Neurochemistry, MPI for Brain Research, Frankfurt and Center of Morphology, University of Frankfurt
1995 Habilitation in Anatomy, University of Frankfurt
1998-2002 Head of the Dept. of Anatomy & Cellular Neurobiology, Schilling endowed Professorship, Dept. Neurochemistry, MPI for Brain Research, Frankfurt and Center of Morphology, University of Frankfurt
2002- Head of the Dept. of Medical Cell Biology, Institute for Anatomy and Cell Biology, University of Heidelberg

Current Research

Information processing in the CNS depends on fast neurotransmission, which is mediated by receptor proteins that are concentrated at distinct postsynaptic membrane specializations. The molecular mechanisms, which establish these specialized membrane domains during synaptogenesis and determine the positions, size and packing densities of neurotransmitter receptor clusters, are poorly understood. Moreover, it is unclear, how specific neurotransmitter receptors are targeted to appropriate postsynaptic sites. Receptor-associated proteins are assumed to play an important role in these processes. Thus, our recent work has focused on the identification and functional characterization of molecules and mechanisms, such as synaptic activity, regulating the surface distribution neurotransmitter receptors. Furthermore, the postsynaptic membrane and the subsynaptic cell compartments are not only specialized for intercellular but also for intracellular signaling. Activation of this subsynaptic machinery, whose building elements include structural components and signaling molecules such as neuronal nitric oxide synthase, calcium/calmodulin-dependent kinase II, receptor tyrosine kinases and modulators of the activity of monomeric GTPases, is thought to mediate nuclear signaling and/or long-term changes in synaptic efficacy. Therefore, processes changing the molecular composition of the subsynaptic signaling machinery may contribute to the long-term regulation of synaptic efficacy. Based on these considerations we have investigated the molecular compositions of distinct types of receptor-associated subsynaptic protein complexes and could identify several components of secondary signaling pathways.

Future Projects and Goals

We shall continue to identify the molecular components of postsynaptic membrane specializations of both excitatory and inhibitory synapses. These projects will be performed using molecular biological approaches and proteomics. Based on our studies on polypeptides providing the structural scaffold for the organization of postsynaptic signaling complexes, we shall expand our research efforts on selected components of individual signaling pathways. These may be involved in processes controlling receptor targeting, the regulation of gene transcription and the spatial regulation of translation in the somatodendritic cell compartment. The goal of our investigations is the identification of molecular mechanisms controlling the dynamics and long-term plastic changes of synapses.

Selected Publications


Structure of the group

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Technicians: Ingeborg Vogel, NN

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60
Plasticity of GABA<sub>A</sub> receptor mediated inhibition

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Training in Neurology/Psychiatry
Postdoctoral work at MPI for Brain Research, Frankfurt/M., Departments of Neurology and Pharmacology, UC Los Angeles, California, MPI for Psychiatry, Dept. Neurophysiology, Munich Professor of Physiology, University of Heidelberg, since 1990

Current Research
GABA inhibits brain neurons by activation of postsynaptic Cl<sup>−</sup> channels, the GABA<sub>A</sub> receptors. Membrane potential changes resulting from Cl<sup>−</sup> channel activation are variable, and there is a developmental change in the GABA response from depolarizing to hyperpolarizing. Activation of inwardly rectifying K<sup>+</sup> channels through the metabotropic GABA<sub>B</sub> receptor induces also postsynaptic hyperpolarization. Our work focuses (1) on inhibition in weaver mice in which, due to the mutation of Kir 3.2, GABA<sub>B</sub> receptors do not activate K<sup>+</sup> channels, (2) the role of the neuronal cation-anion cotransporter KCC2 in setting the Cl<sup>−</sup> gradient for hyperpolarizing inhibition and (3) on presynaptic modulation of GABA release by retrograde signaling.

GABA receptor mediated postsynaptic inhibition and Cl transport

A functional assay for KCC2 revealed that KCC2 maintains a constant intracellular Cl<sup>−</sup> concentration which is set by the extracellular K<sup>+</sup> concentration. Development of transport activity in cultured hippocampal neurons involves a tyrosine kinase dependent post-translational modification which is promoted by the stimulation of IGF-1 receptors. Blockade of KCC2 by the loop diuretic furosemide requires an allosteric modulation by monovalent cations. During hepatic encephalopathy, KCC2 is the pathway across which NH<sub>4</sub><sup>+</sup> enters neurons thereby disrupting their function.

Retrograde dopaminergic modulation of postsynaptic inhibition in substantia nigra

Dopaminergic cells release dopamine from their somata and dendrites. Dopamine D1 receptors on striatonigral GABAergic termi-
Stefan Offermanns

Cellular signaling

Stefan Offermanns

MD 1991 Free University of Berlin, Germany
Postdoctoral work at California Institute of Technology and Free University of Berlin
Heisenberg fellow 1999-2000
Professor of Pharmacology and Toxicology, Heidelberg, since 2000

Current Research, Future Projects and Goals

The central theme of our research are the functions of various GTPases in cellular signaling pathways. We are especially dealing with heterotrimeric G-proteins which are regulated by G-protein-coupled receptors (GPCRs) as well as with monomeric GTPases of the Rho-family (Rho, Rac, Cdc42). In addition to projects dealing with orphan GPCRs and the function of Gq/G11-, G12/G13- and Rho-family members in platelets, immune cells and the in the cardiovascular system we have a particular interest in the role these signaling processes play in the modulation of neuronal functions as well as in neural morphogenesis.

The role of Gq11- and G12/13-mediated signaling pathways in the function and development of the CNS

There is increasing evidence that in particular GPCRs coupling to the ubiquitously expressed G-proteins of the Gq/G11- and G12/ G13-families are involved in various aspects of nervous system function. While Gq/G11 mediate the activation of β-isoforms of phospholipase C, G12/G13 lead to the activation of the small GTPase RhoA. Both pathways are involved in cell migration, axonal pathfinding as well as neuronal cell differentiation in vitro. To study the role of Gq11- and G12/13-mediated signaling processes during the development of the intact nervous system, we plan to generate and analyze mouse lines which lack Gq/G 11 and G 12/G 13 in defined compartments of the developing nervous system using Cre/loxP-mediated recombination.

Functions and signaling mechanisms of plexin-B family members

Mammalian plexins are widely-expressed transmembrane proteins which mediate the effects of transmembrane and secreted members of the semaphorin family in various tissues. In neuronal cells, they are mainly involved in the repulsive activities of semaphorins. Recently, plexins have been linked to the regulation of small GTPases of the Rho family. Activation of plexin-B1 by semaphorin 4D (Sema4D) enhances binding of GTP-bound Rac1 to plexin B1 and has been suggested to induce RhoA activation. We could demonstrate that plexin-B family members associate through their C-termini with Rho guanine-nucleotide-exchange-factors PDZ-RhoGEF and LARG. PDZ-RhoGEF/LARG mediate Sema4D/ plexin-B1-induced RhoA activation, and a dominant-negative form of PDZ-RhoGEF blocks Sema4D-induced growth cone collapse in neurons. This indicates that the interaction of mammalian plexin-B family members with the multi-domain-proteins PDZ-RhoGEF and LARG represents an essential molecular link between plexin-B and localized, RhoA-mediated downstream signaling events, which underly various plexin-mediated cellular phenomena including axonal growth cone collapse.

Selected Publications


Structure of the group

Group leader Stefan Offermanns
Postdoctoral fellows Robert Grosse, Jukka Kero, Barbara Leutgeb, Stephan Vogt, Nina Wettschureck, Alexandra Zywertz
Graduate students Dagmar Dettlaff, Arul Sakkaravarthi, Jakub Swiercz, Sorin Tunaru
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Growth and orientation of axons during development of the vertebrate nervous system

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PhD (Dr. rer. nat.) 1986, Department of Neurobiology, University of Heidelberg
Postdoctoral work (1986-87), European Molecular Biology Laboratories (EMBL), Heidelberg
Group leader (1988-1996, Max-Planck-Institute for Developmental Biology, Tübingen
Professor (1996-98), Department of Developmental Biology, Institute of Zoology, Giessen
Professor (since 1999), Department of Developmental Neurobiology, Institute of Zoology, Heidelberg

Current Research

We are interested in the cellular and molecular processes underlying the “wiring” of the vertebrate central nervous system. In particular, we study interactions of elongating axons (and the growth cones at their tips) with their environment and the transformation of such interactions into directed growth.

Using the chick embryo visual system as a model, we investigate the functions of cell adhesion molecules (CAMs) for growth and orientation of retinal ganglion cell axons. We are also investigating the role of cytoskeletal components and intracellular signalling molecules in the growth cone. We study these proteins for example in growth cones challenged with substrate borders in vitro or in axons growing in the retina, manipulated in their expression of the proteins of interest.

Future Projects and Goals

CAMs, cytoskeletal components, and intracellular signalling molecules will be investigated for their role in axonal orientation, aiming at the detection of the entire signalling process from the growth cone membrane to cytoskeleton. For this, we will employ cell biological, biochemical and molecular biological approaches. Studies will be also performed in the intact embryo (in ovo transfections, GFP life imaging) to gain insight in the complex interplay on systemic level.

Selected Publications


Structure of the group

Group leader G. Elisabeth Pollerberg
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Graduate students Michael Köster, Hasan Avci, Christian Hahn, Pavol Zelina, Bettina Mayer
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**Klaus Sartor**

**Focal cerebral ischemia, functional MR-tomography**

**Klaus Sartor**

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Postdoctoral work at Mercy Hospital & Medical Center, Chicago (USA),
AK Altona, Hamburg, and UCSF (USA)
1983 - 1989 Associate Professor at Mallinckrodt Institute of Radiology,
Washington University School of Medicine, St. Louis (USA)
Head, Division of Neuroradiology, University of Heidelberg Medical Center since 1989

**Current Research**

**Imaging of Early Stroke**
The Division of Neuroradiology is involved in a multitude of research areas, most of which are interdisciplinary in nature. A major research focus is ischemia. From 1993 to 1999, as part of a DFG research group pathophysiological studies and studies of new therapeutic strategies for stroke were conducted. Neuroradiology contributed by establishing new MRI techniques with which focal cerebral ischemia can be detected only minutes after the onset of symptoms and with which the success of therapy can be monitored. Stroke research is continued as part of a large multicenter project (http://www.kompetenznetz-schlaganfall.de/). The newly developed acute stroke protocol includes T2-weighted MRI, diffusion MRI, perfusion MRI, and MR angiography.

**Functional Magnetic Resonance Imaging**
Another area of research is functional MR imaging. Now that the initial methodology-oriented studies have been concluded, this technique is employed for the planning of brain tumor surgery as well as in pain research.

**Functional and Quantitative Techniques in MR Imaging**
In the group of Sabine Heiland, several MR techniques have been developed to study microanatomy, microvasculature and metabolism of brain in vivo. One of these new techniques is an MR method to simultaneously measure cerebrovascular parameters and the permeability of blood-brain-barrier. Another method based on diffusion-weighted MRI allows to measure the cell size as well as the permeability of the cell membranes. We also attempt to quantify the concentration of different metabolites by proton MR spectroscopy and the concentration of macromolecules (e.g. myelin) by a quantitative, volumetric method of magnetization transfer imaging.

Further projects:
- Advanced MR imaging of white matter and intracerebral hemorrhage
- MR spectroscopy and diffusion MR imaging in brain disorders of early childhood
- MR diffusion tensor imaging in brain tumors
- Intraoperative MR imaging, CT angiography and perfusion CT

**Future Projects and Goals**
Our major goal is to use quantitative and functional imaging techniques to better diagnose and understand diseases at a very early stage and to test and monitor treatment strategies. With a combination of diffusion tensor imaging, magnetic resonance spectroscopy and quantitative perfusion imaging we aim to characterize tissue types in vivo as to their microanatomy, blood supply and metabolism.

**Selected Publications**


**Structure of the group**

- **Group leader**: Klaus Sartor
- **Scientific staff**: Jochen Fiebach, Stefan Hähnel, Inga Harting, Marius Hartmann, Sabine Heiland, Klaus Kirchhof, Bodo Kress, Peter Schramm, Christoph Stippich, Thomas Wilhelm
- **Graduate students**: Jens Georgi, Gregor Jost, Holger Schmitt
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Functional neuroimaging correlates of neural plasticity in age-associated neurocognitive disorders

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Postdoctoral work at the Universities of Bochum and Heidelberg; Research Fellow UC Irvine 1992
Professor of clinical Psychiatry. Section of Geriatric Psychiatry, Heidelberg, since 2000

Current Research
The cerebral changes underlying psychiatric disorders can be reliably identified using structural and functional neuroimaging techniques, in particular magnetic resonance imaging. Previous research has investigated cerebral changes in schizophrenia and Alzheimer’s disease with respect to psychopathological symptoms, cognitive deficits, and potential molecular markers. Recent studies focus on the functional mechanisms of basic processes involved in these disorders. This approach may be illustrated by a recent study of cortical activation under a working memory task during training which revealed a reduced activation — suggesting greater efficacy — of cerebral activation in the controls but a reallocation of former hypofrontal activation patterns in patients with schizophrenia.

Future Projects and Goals
Further studies are designed to address the following questions:

- Are consistent activation changes observed during training of declarative and procedural memory functioning?
- Do these mechanisms adapt to physiological aging and age-related conditions such as mild cognitive impairment or Alzheimer’s disease?
- Which neurobiological factors, such as the Catechol-O-Methyltransferase polymorphism, APP metabolism, have modulatory effects?

Selected Publications
Hempel A. et al., (in press) Schiz Res

Structure of the group

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Molecular stroke research

Markus Schwaninger

1987 doctoral thesis in pharmacology, University of Freiburg
Training in Neurology (FU Berlin, Heidelberg)
Postdoctoral work in Molecular Pharmacology (Göttingen)
Now group leader “molecular stroke research”

Current Research

Stroke is the leading cause of disability in adults, but therapy is still limited. Important mechanisms in the molecular pathophysiology of stroke are an inflammatory response in the ischemic brain and apoptosis of neurons. In the investigation of these two key players we focus on the role of gene expression. Starting point is the characterization of gene expression in cerebral ischemia by microarray techniques. We then analyse the role of a selected number of individual genes, that are induced by cerebral ischemia and are alleged players in the inflammatory response. For this purpose we use transgenic techniques and a mouse model of cerebral ischemia. One focus of the group is the transcription factor NF-κB. In order to block activation in a cell type specific manner in the CNS we have generated mice that express the dominant NF-κB-inhibitor nrlxB in astroglial cells and neurons. In addition, we are studying transgenic mice, in collaborations with other groups, that lack components of the NF-κB signaling cascade. These studies will help to elucidate the significance of NF-κB as a central regulator of inflammation and apoptosis in the CNS.

Future Projects and Goals

To unravel the regulatory networks underlying gene induction in cerebral ischemia we will use in silico-analysis of promoters of induced genes and in vivo-experiments with mice deficient of selective transcription factors. The identified functional pathways will be tested for their clinical significance by polymorphism studies in stroke patients.

Selected Publications


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http://www.krz.uni-heidelberg.de/neuro/n/welcome_j.html
The role of glutamate receptor subtypes in short- and long-term memory

Peter H. Seeburg

PhD in Genetics 1975 University of Tuebingen
1975-1977 Postdoctoral work at UCSF
Adjunct Assist. Professor in Medicine at UCSF, Senior and Staff Scientist at Genentech, Inc., South San Francisco, 1977-1987
Full Professor, University of Heidelberg, 1987-1995,
Director at the Max-Planck-Institute for Medical Research Heidelberg, since 1996

Current Research

Generation of mouse mutants via gene manipulation in embryonic stem cells for the regulated expression of sequence-altered subunits for ionotropic glutamate receptors of the AMPA, NMDA and kainate subtypes. Sequence changes comprise functional ablation, green fluorescent protein (GFP)-fusions, mutations in the inner channel lining, mutations affecting gating kinetics and desensitization, C-terminal alterations affecting trafficking to synapses and interaction with components of intracellular signaling cascades. Expression regulation is attempted by the use of newly engineered versions of the ‘Cre-lox’ system and of tetracycline-mediated transcriptional activation/repression. Aims are to study molecular mechanisms at the postsynaptic side underlying fast excitatory synaptic transmission and activity-modulated synaptic strength.

Studies of the physiological relevance of RNA editing by adenosine deamination. These studies include the conditional ablation in mice of the three known mammalian RNA dependent adenosine deaminases, ADAR1-3, which are currently the only candidate enzymes for RNA editing by adenosine deamination. ADAR2 edits in vitro the Q/R site of GluR-B pre-mRNA and thus ensures the low permeability to calcium of hetero-oligomeric AMPA receptor channels configured with this edited subunit. Interference with Q/R site editing of GluR-B, either by an appropriate sequence change in the GluR-B gene or by ADAR2 ablation leads in the mouse to a prematurely lethal, seizure-prone phenotype. No obvious phenotypical consequences arise from ADAR2 ablation if within the GluR-B gene the ‘edited’ codon is exchanged for the unedited one. This demonstrates that of all the possible sites edited by ADAR2 (the enzyme is found in many tissues), the Q/R site in the GluR-B transcript is physiologically the most important one.

Future Projects and Goals

Investigate link between synaptic plasticity and different forms of memory

Selected Publications


Structure of the group

Group leader Peter Seeburg
Staff Miyoko Higuchi, Georg Köhr, Pavel Osten, Rolf Sprengel
Postdoctoral fellows Rachel Aronoff, Thilo Borchardt, Jochen Hartner, Hesz Krestel, Martin Schwarz, Frank Single, Daniel Spergel
Graduate students Thorsten Bus, Tanjew Dittgen, Simone Freese, Boris Hambsch, Alexander Kolleker, Liliane Layer, Pawel Licznerski, Verena Pawlak, Pradeep Punnakal, Bettina Schupp, Quan-Xiang Wei, Francesca Zammaretti,
Technicians Carmen Großkurth, Horst Großkurth, Sabine Grünewald, Annette Herold, Juliana Kern, Judith Müller

Contact

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Jeremy C. Smith

Computer simulation of ion pumps

Jeremy C. Smith
PhD London University 1985
Postdoc Harvard University Chemistry Department 1985-1989
Group Leader Biology Dept., CEA Saclay 1989-1998
Professor (C4) Biology and Physics Departments Heidelberg University 1998-

Current Research
Molecular dynamics simulations are performed of proteins and peptides. Of particular relevance to neuroscience are the investigations on ion pumps which we are now undertaking in the context of a DFG ‘Forschergruppe’ consortium aimed at obtaining a theoretical understanding of retinal proteins, together with research aimed at understanding membrane fluidity and control and modelling of the serotonin binding site of 5HT2B receptors.

Future Projects and Goals
Understanding of the functioning of membranes and membrane proteins at atomic detail.

Selected Publications

Structure of the group
Group leader Jeremy C. Smith
Emmy-Noether fellow G. Matthias Ullmann and his group
Andrei Borodich, Raghu Nath Behera, Nicolas Calimet, Edda Kloppmann


Technician Bogdan Costescu

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The neurobiology of drug dependence

Rainer Spanagel

PhD 1991 MPI of Neurobiology, Martinsried
Postdoctoral work at MPI of Psychiatry, Munich 1991-1995
Group leader at MPI of Psychiatry, Munich 1996-1999
Professor of Psychopharmacology at the Central Institute of Mental Health (CIMH) 2000
Head of the center for basic research at the CIMH 2001

Current Research

We are using a newly established model to generate alcohol-dependent rats or mice. Behavioral, pharmacological and neurochemical examinations on alcohol-dependent rodents will help us to understand the neurobiological mechanisms of addictive behavior. Studies with mutant mice will help us to identify genes involved in the initiation of drug-seeking behavior. In addition, an organ bank with different alcohol-prefering rat lines (AA, P, HAD) has been established. The aim of the organ bank is the characterization of molecular biological cascades (with DNA chip technology) involved in alcohol-derived diseases. In a comparative approach the effects of opioids and psychostimulants are studied. Our close collaboration with the Clinic of Addictive Behavior at the CIMH (Prof. K. Mann) enables us to rapidly validate our preclinical findings in human addicts. Here the primary goal is the development of new anti-relapse compounds and especially the development of individually adapted pharmacotherapy. Therefore, alcohol-dependent animals will be separated into different behavioral and neurobiological phenotypes which will then be treated with a corresponding anti-relapse compound. Reinstatement of alcohol-seeking behavior induced by different stimuli will be measured subsequently.

Future Projects and Goals

• Identification of depression relevant gene transcripts in a rat model of learned helplessness

Selected Publications


Structure of the group

Group leader Rainer Spanagel
Postdoctoral fellows Peter Gebicke-Haerter, Daniel Bachteler, Michael Cowen, Sören Siegmund, Karl Schroff, Armani Yousef, Carles Sanchis
Graduate students Carolina Abarca, Valentina Vengeliene, Tarek Zoghul, Fernando Essman
Technicians Sabrina Koch, Claudia Schäfer, Brandon Cline

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Brigitte Wildemann

Peripheral immune tolerance and Multiple Sclerosis

Brigitte Wildemann

1983 Dr. med.
1984 - 1990 Resident in Neurology and Psychiatry, Univ. of Heidelberg
1986 Research Fellow, Dept. Immunology, Hammersmith Hospital, London
1990 Licence as neurologist
1993 Habilitation
1994/1995 Research Fellow, Dept. Neurology and Neuroscience, Johns Hopkins University, Baltimore
2000 Professor of Neurology
2001 Head of section „Molecular Neuroimmunology”, Department of Neurology, University of Heidelberg

Current Research

Our present research intends to advance our understanding on the role of immunoregulatory T cells (Treg) in mediating the breakdown of immune-tolerance in multiple sclerosis (MS). Rationale Multiple sclerosis (MS) is an autoimmune and predominantly T cell mediated demyelinating disease of the central nervous system (CNS). A prerequisite for the induction of autoimmunity within the CNS is the activation and extravasation of circulating self-reactive T lymphocytes with specificity for myelin components. Since myelin-specific autoreactive T lymphocytes are uniformly present in the peripheral T cell repertoire in both patients with MS and healthy persons a dysfunction or failure of peripheral immune-tolerance mechanisms may be critically involved in the emergence of autoimmunity within the CNS. In concordance with this assumption we have recently demonstrated that peripheral T cell homeostasis is significantly impaired in patients with relapsing remitting MS as a result of an age-inappropriately declined thymic export of T lymphocytes. In experimental animal models the maintenance of immune-tolerance towards self-antigens correlates with the thymic dependent generation of a specific T cell subset that harbor an autoimmune preventive capacity and „actively” downregulate the activation and proliferation of self-reactive T lymphocytes. These professional immunoregulatory Treg lymphocytes reside in the CD4+ subset of thymocytes and peripheral T cells, constitutively coexpress CD25 and comprise 2-5% of the CD4+ T cell compartment. Although CD4+CD25+ Treg cells are also present in humans their relevance for the development of autoimmune disease is still undefined. Current experiments complement clinical and basic molecular and immunologic studies to investigate the possibility that a deficiency in the generation, effector function and/or survival of CD4+CD25+ Treg cells is involved in the breakdown of immune-tolerance in MS patients. The study includes the isolation and characterization of Treg cells in treatment naive patients with relapsing remitting MS and healthy persons (Collaboration Peter H. Krammer, DKFZ Heidelberg).

Future Projects and Goals

We will assess the implication of Treg cells in tumor immunity associated with paraneoplastic neurologic disorders as well as the spread of hematologic malignancies and solid tumors to the central nervous system.

Selected Publications


Structure of the group

Group leader Brigitte Wildemann
Postdoctoral fellows Juergen Haas, Andreas Hug, Andrea Viehoever
Graduate students Mirjam Korporal, Isabella Schroeder, Andrea Filser
Technician Brigitte Fritz

Contact

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Vertebrate retina development and differentiation

Joachim Wittbrodt

PhD 1991 University of Munich, Germany
Postdoctoral training at the Biocenter University of Basel, Switzerland
Junior Group Leader at the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany
At EMBL since 1999

Current Research

In a continuation of neural induction and in parallel with early patterning events in the forebrain, the optic vesicle forms as a lateral protrusion of the forebrain. The vertebrate eye is composed of neuro-ectodermal (optic cup) and surface ectodermal (lens, cornea) derivatives and it emerges from an epithelial anlage by inductive interactions beginning as early as the late stages of gastrulation. While the formation of the optic vesicle can be considered part of forebrain patterning, lens induction occurs through planar signals emanating from the anterior neural plate. These signals induce lens formation in the competent tissue of the lens placode. Most of our current knowledge of eye development is based on classical embryological experiments. Because of their transparency, rapid early development and short generation time, fish (medaka/zebrafish) are well suited for detailed study of this process.

We investigate medaka eye development following three complementary experimental strategies.

(1) The isolation and collection of genes expressed in spatially and/or temporally restricted patterns in the developing brain, with emphasis on transcription factors and signaling cascades involving TGF-ß-like genes and FGF-receptor gene families as well as on genes that are expressed in response to Six3 and Pax6 activity. In addition, novel eye genes have been identified based on their expression patterns.

(2) Functional analyses involving gain-of-function studies by ectopically expressing transgenes in the developing eye.

(3) Functional studies involving a mutagenesis screen and mutant analysis. In a collaborative screen of more than 1200 genomes, more than 100 mutants with eye phenotypes were identified, three of which completely lack eyes. We identified the mutation causing the eyeless phenotype in medaka by positional cloning and rescue analysis.

Future Projects and Goals

We will take molecular, genetic and cell biological approaches to:
- generate and identify novel early brain and eye mutants following novel mutagenesis strategies developed in the lab;
- investigate the genetic and molecular interactions leading to the establishment and patterning of the forebrain and the early eye field;
- identify genes by subtractive approaches involving mutants lacking eyes as well as medaka ES-cells transfected with candidate genes;
- study gene function and interaction of known and novel “eye genes” using novel antisense strategies.

It is our goal to understand the molecular and cellular interactions that lead to the patterning of the early brain and to eye formation.

Selected Publications


Structure of the group

Group leader Joachim Wittbrodt
Postdoctoral fellows Felix Loosli, Juan-Ramon Martinez-Morales, Rebecca Quiring
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Alan Summerfield ☎ 545471, ✉ alan@uni-hd.de

Webmaster and computer service
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74
Central Facilities

Central morphological Service Unit

Laserscanning microscopy, Calcium-Imaging, transmission electron microscopy, ultracryotomy, digital photography and image processing.

Transmission Electron Microscopy

<table>
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<tr>
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<td>Neurobiology</td>
<td>Andrea Hellwig</td>
<td>Land Baden-Württemberg</td>
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<td>Zeiss EM 10</td>
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<td>Barbara Brühl</td>
<td>Land Baden-Württemberg</td>
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Ultracryotomy

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<td>Andrea Hellwig</td>
<td>Land Baden-Württemberg</td>
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<tr>
<td>Leica Ultracut with FC-S</td>
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<td>Prof. Dr. K. Gorgas</td>
<td>Land Baden-Württemberg</td>
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Freeze Substitution

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<td>Neurobiology</td>
<td>Andrea Hellwig</td>
<td>SFB 317</td>
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Confocal Laserscanning Microscopy

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<tr>
<td>Leica TCS 4D</td>
<td>Neurobiology</td>
<td>Anja Eder</td>
<td>SFB 317</td>
</tr>
<tr>
<td>Leica TCS SP2</td>
<td>Neurobiology</td>
<td>Anja Eder</td>
<td>SFB 488</td>
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Phosphoimager

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<tr>
<td>Fuji Phosphoimager BAS 1000</td>
<td>Neurobiology</td>
<td>Mark Bajohrs</td>
<td>SFB 352</td>
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Video-Microscopy

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<th>Unit</th>
<th>Place</th>
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<th>Funding</th>
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<tbody>
<tr>
<td>Microinjection-Videoemicroscopy setup: Eppendorf Transjector, Leica microscope, Photometrix Quantix2 digital camera</td>
<td>Neurobiology</td>
<td>Dr. H.-H. Gerdes</td>
<td>SFB 317</td>
</tr>
<tr>
<td>Multi colour digital imaging setup: Olympus/Till Photonics</td>
<td>Neurobiology</td>
<td>Dr. H.-H. Gerdes</td>
<td>SFB 488</td>
</tr>
<tr>
<td>Analog imaging setup: Hamamatsu (SIT) camera system</td>
<td>Neurobiology</td>
<td>Dr. H.-H. Gerdes</td>
<td>SFB 488</td>
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<tr>
<td>Digital workstation I: Microscope: Zeiss Axioplan; Camera: Zeiss Axiocam, Software: Zeiss Axiovision</td>
<td>Neuroanatomy</td>
<td>Dr. A. Schober</td>
<td>Land Baden-Württemberg / SFB 488</td>
</tr>
<tr>
<td>Digital workstation II: Microscope: Zeiss Axiophot; Camera: Olympus DP-10, Software: Soft Imaging/Analysis 3.0</td>
<td>Neuroanatomy</td>
<td>Dr. A. Schober</td>
<td>Land Baden-Württemberg</td>
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Cell Culture

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<tr>
<td>Cell Culture</td>
<td>Neuroanatomy</td>
<td>Jutta Fey</td>
<td>SFB 488</td>
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</tbody>
</table>

The IZN is using the animal house and transgene lab of the Zentralbereich Neuenheimer Feld, and the facility of Biomolecular Chemistry of the ZMBH for syntheses and structural analyses.
IZN Teaching Program

IZN Teaching Program
Graduate College 791
"Neural Development and Degenerative Processes: Basic Research and Clinical Implications"

Lectures for student members

I. Entwicklung des Nervensystems.
R. Friedrich, H. Hutter, C. Niehrs, E. Pollerberg, K. Unsicker, V. Witzemann:
1. Gene, Faktoren und Strukturen
2. Neuronale Migration und axonales Pathfinding
3. Synapsenbildung und Elimination
4. Krankheiten als Folge gestörter Entwicklung

II. Neurodegeneration: Zelluläre und systemische Aspekte.
1. Akute Neurodegeneration
2. Chronische Neurodegeneration

III. Erregende und hemmende Neurotransmission in dem sich entwickelnden Gehirn.
D. Feldmeyer, W. Kuschinsky, U. Misgeld, W. Wisden

IV. Lernen und entwicklungsabhängige Plastizität.
D. Bartsch, W. Denk, F. Henn, H. Monyer, P. Seeburg;
1. Somatosensorischer und visueller Cortex
2. Plastizität im adulten Gehirn
3. Räumliches Lernen und der Hippocampus

Methods courses
- Zymogramme. W. Hacke
- Quantitative Autoradiographie zur Bestimmung von Funktionsgrössen im Gehirn. W. Kuschinsky
- In situ Hybridisierung und Immunhistochemie im zentralen Nervensystem. H. Monyer, W. Wisden, S. Offermanns
- Elektrophysiologische Ableitungen an Neuronen, die fluoreszierende Glutamatrezeptoren tragen. P. Seeburg
- Simultane optische und elektrophysiologische Messungen synchroner Aktivität in einfachen Netzwerken. U. Misgeld
- Elektrophysiologische Messungen an neuronalen Schaltkreisen in akuten Hirnschnitten des Neocortex. D. Feldmeyer
- Elektronenmikroskopie, neuronale Zellkultur. K. Unsicker
- Mikroinjektion von mRNA in Xenopus Oozyten. C. Niehrs
- Manipulation der neuromuskulären Synapse durch direkten Gentransfer in der Maus. V. Witzemann
- In ovo Transfektion des Nervensystems beim Huhnembryo. E. Pollerberg
- Langzeit-Schnittpräparate des Gehirns; Zwei-Photonen-Mikroskopie in lebenden Präparaten. W. Denk
- Imaging neuronaler Aktivität im Zebrafisch. R. Friedrich
- Analyse von Proteininteraktion mit Plasmon Resonanz. T. Hartmann, K. Beyreuther
- Herstellung und Analyse transgener C. elegans. H. Hutter
- Untersuchungsmethoden der Genexpression in neuralen Zellen. M. Schwaninger
- Transgene Methoden in der Maus. G. Schütz, P. Seeburg
- Verhaltenstests in der Maus für Depression, Demenz und Sucht. F. Henn
- Neurologisches Kolloquium. K. Fassbender, M. Hennerici

76
## IZN Teaching Program

### Lectures/Courses/Seminars summer term 2001

<table>
<thead>
<tr>
<th>Type</th>
<th>Topic</th>
<th>Lecturer(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lectures</strong></td>
<td>Zellbiologie II: Molecular Medicine, 2st.</td>
<td>K. Unsicker, N.N.</td>
</tr>
<tr>
<td>ZV</td>
<td>Zellbiologie IV: Molekulare und Zelluläre Neurobiologie, 2st.</td>
<td>K. Beyreuther, R. Brandt, H.-H. Gerdes, K.A. Nave, D. Langosch, B. Sakmann, P. Seeburg, K. Unsicker</td>
</tr>
<tr>
<td>V</td>
<td>Integrierte Neuroanatomie/Neurophysiologie, 3st.</td>
<td>U. Misigeld, H. Monyer, K. Unsicker</td>
</tr>
<tr>
<td>V</td>
<td>Neurologie/Neuroradiologie/Neurochirurgie</td>
<td>W. Hacke, S. Kunze, K. Sartor, H.-M. Meinck, H. Monyer und Mitarbeiter</td>
</tr>
<tr>
<td>V/S</td>
<td>Entwicklungsneurobiologie</td>
<td>H. Simon, R. Brandt, U. Ernsberger, K. Unsicker</td>
</tr>
<tr>
<td>S</td>
<td>Molekulare Zellbiologie: Seminar zu den Grundlagen der molekularen Zellbiologie, 2st.</td>
<td>R. Brandt, H.-H. Gerdes, D. Langosch, N.N.</td>
</tr>
<tr>
<td>S</td>
<td>Einführung in die Neurowissenschaft, 2st.</td>
<td>K.A. Nave</td>
</tr>
<tr>
<td>S/U</td>
<td>Verwendung von Software und Datenbasen in der Molekularbiologie, 2st.</td>
<td>H. Simon, N.N.</td>
</tr>
<tr>
<td>FS</td>
<td>IZN Seminar 'Fortschritte in der Neurowissenschaften (für Mitarbeiter des IZN und interessierte Studenten, in englischer Sprache), 1st.</td>
<td>H. Bading, H. Monyer, K. Unsicker und die Gruppenleiter des IZN</td>
</tr>
<tr>
<td>V</td>
<td>Neurobiology Lectures mit Gastrednern (für Mitarbeiter des IZN und interessierte Studenten, in englischer Sprache), 1st.</td>
<td>R. Brandt, D. Langosch und die anderen Forschungsgruppenleiter des IZN und SFB 488</td>
</tr>
<tr>
<td>FS</td>
<td>SFB 488 Seminar 'Molekulare und zelluläre Grundlagen neuraler Entwicklungsprozesse', 2st., ganzjähr.</td>
<td>K. Unsicker und Teilprojektleiter des SFB 488</td>
</tr>
<tr>
<td>FS</td>
<td>Mitarbeiterseminar: Neuronales Zytoskelett (in englischer Sprache), 2st., ganzjähr.</td>
<td>R. Brandt und Mitarbeiter</td>
</tr>
<tr>
<td>FS</td>
<td>Mitarbeiterseminar Protein-Proteininteraktionen bei Membranproteinen (in englischer Sprache), 1st., ganzjährig</td>
<td>D. Langosch und Mitarbeiter</td>
</tr>
<tr>
<td>FS</td>
<td>Journal Club for coworkers of the Department of Neurobiology and interested students, ganzjährig</td>
<td>D. Langosch, W. Ruan</td>
</tr>
</tbody>
</table>
IZN Teaching Program

| S | Mitarbeiterseminar: TGF-Betas (in englischer Sprache), 2st. | K. Unsicker und Mitarbeiter |
| S | Journal Club für Mitarbeiter der Neuroanatomie (in englischer Sprache), im Wechsel mit Mitarbeiterseminar, 2st. | K. Unsicker und Mitarbeiter |
| S | Mitarbeiterseminar: Entwicklung der Mittelhirn dopaminergen Neurone | H. Simon und Mitarbeiter |
| S | Journal Club (in englischer Sprache), 1st.a | H. Monyer, W. Wisden und Mitarbeiter |
| S | Forschergruppen-Seminar 'Zentrale aminerge Systeme und Mechanismen', 2st. | K. Unsicker und Teilprojektleiter der Forschergruppe |
| | Praktikum: Moderne Methoden in der Neurobiologie, 3wo., ganztäg., (HF, NF, Sachgruppe III) | R. Brandt, T. Euler, H.-H. Gerdes, D. Langosch, H. Monyer |
| | Forschungspraktikum Neurobiologie, 6wo., ganztäg. | R. Brandt, H.-H. Gerdes, D. Langosch, A. Régnier-Vigouroux |
## Lectures/Courses/Seminars winter term 2001/02

### Lectures

<table>
<thead>
<tr>
<th>Type</th>
<th>Course Title</th>
<th>Audience</th>
<th>Instructor(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>V</td>
<td>Einführung zum Hauptpraktikum A2, 1st.</td>
<td>Course attendees</td>
<td>N.N.</td>
</tr>
<tr>
<td>V</td>
<td>Verwendung von Software und Datenbasen in der Molekularbiologie, 2st.</td>
<td>Course attendees</td>
<td>Simon, R. Mosbach</td>
</tr>
<tr>
<td>V</td>
<td>Entwicklungsbiologie/Embryologie, 2st.</td>
<td>Course attendees</td>
<td>Dozenten des Instituts für Anatomie und Zellbiologie</td>
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### Seminars, Courses, Colloquia

<table>
<thead>
<tr>
<th>Type</th>
<th>Course Title</th>
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</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>Einführung in die Zellbiologie für 1. Semester, 2st.</td>
<td>Course attendees</td>
<td>H.-H. Gerdes, W. Wisden,</td>
</tr>
<tr>
<td>S</td>
<td>Molekulare Zellbiologie – Begleitseminar zur Vorlesung &quot;Biologie III&quot;</td>
<td>Course attendees</td>
<td>H.-H. Gerdes, A. Régnier-Vigouroux, W. Wisden</td>
</tr>
<tr>
<td>S</td>
<td>IZN Seminar Fortschritte in den Neurowissenschaften (für Mitarbeiter des IZN und interessierte Studenten, in englischer Sprache), 1st.</td>
<td>Course attendees</td>
<td>H. Monyer, K. Unsicker und die Gruppenleiter des IZN</td>
</tr>
<tr>
<td>S</td>
<td>Neurobiology Lectures mit Gastrednern (für Mitarbeiter des IZN und interessierte Studenten, in englischer Sprache), 1st.</td>
<td>Course attendees</td>
<td>R. Brandt und die Gruppenleiter des IZN</td>
</tr>
<tr>
<td>S</td>
<td>Journal Club für Mitarbeiter der Neurobiologie (in englischer Sprache), ganzjährig, 2st.</td>
<td>Course attendees</td>
<td>Mitarbeiter der Neurobiologie</td>
</tr>
<tr>
<td>S</td>
<td>Mitarbeiterseminar: Neuronales Zytoskelett (in englischer Sprache), ganzjährig, 2st.</td>
<td>Course attendees</td>
<td>R. Brandt und Mitarbeiter</td>
</tr>
<tr>
<td>S</td>
<td>Mitarbeiterseminar: TGF-Betas (in englischer Sprache), 2st.</td>
<td>Course attendees</td>
<td>Unsicker, Mitarbeiter</td>
</tr>
<tr>
<td>S</td>
<td>Journal Club für Mitarbeiter der Neuroanatomie (in englischer Sprache), 1st.</td>
<td>Course attendees</td>
<td>Simion und Mitarbeiter</td>
</tr>
<tr>
<td>S</td>
<td>Mitarbeiterseminar: Entwicklung der Mittelhirn dopaminergen Neurone</td>
<td>Course attendees</td>
<td>Monyer und Mitarbeiter</td>
</tr>
<tr>
<td>S</td>
<td>Journal Club (in englischer Sprache), 1st.</td>
<td>Course attendees</td>
<td>H. Monyer, W. Wisden und Mitarbeiter</td>
</tr>
<tr>
<td>S</td>
<td>SFB 488 Seminar Molekulare undzelluläre Grundlagen neuraler Entwicklungsprozesse, 2st.</td>
<td>Course attendees</td>
<td>Unsicker und Teilprojektleiter des SFB 488</td>
</tr>
</tbody>
</table>

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IZN Teaching Program

79
IZN Teaching Program

<table>
<thead>
<tr>
<th>Course Code</th>
<th>Course Title</th>
<th>Instructor(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>Forschergruppen-Seminar 'Zentrale aminerge Systeme und Mechanismen', 2st.</td>
<td>K. Unsicker und Teilprojektleiter der Forschergruppe</td>
</tr>
<tr>
<td></td>
<td>Ausgewählte Themen der Zell- und Neurobiologie, 2st.</td>
<td>Dozenten des Instituts für Anatomie und Zellbiologie</td>
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<tr>
<td>K</td>
<td>Neurobiologiekolloquium mit Gastrednern (in englischer Sprache), 1st.</td>
<td>Forschungsgruppenleiter der Neurobiologie</td>
</tr>
<tr>
<td>HP: A</td>
<td>Zellbiologie A2 (Biochemie - Morphologie) 3-wöchig, ganztägig, (HF, NF, LA Sachgruppe III)</td>
<td>N.N.</td>
</tr>
<tr>
<td>HP: C</td>
<td>Laborpraktika: Moderne Methoden in der Neurobiologie, 6-wöchig, ganztägig</td>
<td>R. Brandt, H.-H. Gerdes,</td>
</tr>
</tbody>
</table>
# IZN Teaching Program

## Lectures/Courses/Seminars summer term 2002

### Lectures

<table>
<thead>
<tr>
<th>Code</th>
<th>Course Title</th>
<th>Instructor(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZV</td>
<td>Zellbiologie II: Molecular Medicine, 2st.</td>
<td>K. Unsicker, N.N.</td>
</tr>
<tr>
<td>ZV</td>
<td>Zellbiologie IV: Molekulare und Zelluläre Neurobiologie, 2st.</td>
<td>H. Bading, K. Beyreuther, H.-H. Gerdes, K.A. Nave, B. Sakmann, P. Seeburg, K. Unsicker</td>
</tr>
<tr>
<td>V</td>
<td>Integrierte Neuroanatomie/Neurophysiologie, 3st.</td>
<td>U. Misgeld, H. Monyer, K. Unsicker</td>
</tr>
<tr>
<td>V</td>
<td>Makroskopische und Mikroskopische Anatomie, Entwicklungsgeschichte, Neuroanatomie, 10st. (Begleitvorlesung zu den Kursen für Makroskopische, Mikroskopische und Neuroanatomie)</td>
<td>W. Kriz, K. Unsicker, S. Mense, K. Tiedemann, K.H. Endlich, D. Hock</td>
</tr>
<tr>
<td>V</td>
<td>Neurologie/Neuroradiologie/Neurochirurgie</td>
<td>W. Hacke, S. Kunze, K. Sartor, H.-M. Meinck, H. Monyer und Mitarbeiter</td>
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</table>

### Seminars, Courses, Colloquia

<table>
<thead>
<tr>
<th>Code</th>
<th>Course Title</th>
<th>Instructor(s)</th>
</tr>
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<tbody>
<tr>
<td>V/S</td>
<td>Begleitseminar zum GP C</td>
<td>H.-H. Gerdes, U. Ernsberger, T. Euler, R. Friedrich</td>
</tr>
<tr>
<td>S</td>
<td>Die Entwicklung des Neurosystems von Modellorganismen: Systemische, zelluläre und molekulare Aspekte, 2st.</td>
<td>C.E. Pollerberg mit H. Hutter und U. Ernsberger</td>
</tr>
<tr>
<td>S/U</td>
<td>Verwendung von Software und Datenbasen in der Molekularbiologie, 2st.</td>
<td>H. Simon, N.N.</td>
</tr>
<tr>
<td>FS</td>
<td>IZN Seminar: Fortschritte in den Neurowissenschaften für Mitarbeiter des IZN und interessierte Studenten, in englischer Sprache, 1st.</td>
<td>H. Bading, H. Monyer, K. Unsicker und die Gruppenleiter des IZN</td>
</tr>
<tr>
<td>V</td>
<td>Neurobiology Lectures mit Gastrednern für Mitarbeiter des IZN und interessierte Studenten, in englischer Sprache, 1st.</td>
<td>U. Ernsberger, W. Wisden und die anderen Forschungsgruppenleiter des IZN und SFB 488</td>
</tr>
<tr>
<td>S</td>
<td>SFB 488 Seminar: 'Molekulare und zelluläre Grundlagen neuraler Entwicklungsvorgänge', 2st., ganzjähr.</td>
<td>K. Monyer und Mitarbeiter</td>
</tr>
<tr>
<td>FS</td>
<td>Mitarbeiterseminar: Gene Regulation by Nuclear and Cytoplasmic Calcium Signals in Neurons (in englischer Sprache), ganzjähr.</td>
<td>H. Bading und Mitarbeiter</td>
</tr>
<tr>
<td>FS</td>
<td>Mitarbeiterseminar: Neuronales Zytoskelett (in englischer Sprache), 2st., ganzjähr.</td>
<td>R. Brandt und Mitarbeiter</td>
</tr>
<tr>
<td>S</td>
<td>Mitarbeiterseminar: TGF-Betas (in englischer Sprache), 2st.</td>
<td>K. Unsicker und Mitarbeiter</td>
</tr>
<tr>
<td>S</td>
<td>Journal Club für Mitarbeiter der Neuroanatomie (in englischer Sprache), im Wechsel mit Mitarbeiterseminar, 2st.</td>
<td>K. Unsicker und Mitarbeiter</td>
</tr>
<tr>
<td>S</td>
<td>Mitarbeiterseminar: Entwicklung der Mittelhirndopaminergen Neurone</td>
<td>H. Simon und Mitarbeiter</td>
</tr>
</tbody>
</table>
### IZN Teaching Program

#### Lectures/Courses/Seminars winter term 2002/03

<table>
<thead>
<tr>
<th>Code</th>
<th>Course Description</th>
<th>Participants</th>
</tr>
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<tbody>
<tr>
<td>S</td>
<td>Journal Club (in englischer Sprache), 1st.</td>
<td>H. Monyer, W. Wisden and Mitarbeiter</td>
</tr>
<tr>
<td>S</td>
<td>Forschergroupen-Seminar ‘Zentrale aminerge Systeme und Mechanismen’, 2st.</td>
<td>K. Unsicker and Teilprojektleiter der Forscherguppe</td>
</tr>
<tr>
<td>V</td>
<td>Verwendung von Software und Datenbasen in der Molekular Biologie, 2st.</td>
<td>H. Simon, R. Mosbach</td>
</tr>
<tr>
<td>S</td>
<td>Einführung in die Biologie (für 1. Semester), 2st.</td>
<td>O. Bräunling, F. Ciccolini</td>
</tr>
<tr>
<td>S</td>
<td>Entwicklungsneurobiologie</td>
<td>H. Bading, H.-H. Gerdes, H. Simon, K. Unsicker, K.-A. Nave</td>
</tr>
<tr>
<td>S</td>
<td>Molecular Mechanisms of Organogenesis, HF</td>
<td>J. Wittbrodt</td>
</tr>
<tr>
<td>FS</td>
<td>IZN Seminar: Progress in Neurosciences (for members of the IZN and interested students, in English), 1st.</td>
<td>H. Bading, H. Monyer, K. Unsicker and the groupleaders of the IZN</td>
</tr>
<tr>
<td>Course</td>
<td>Description</td>
<td>Instructors</td>
</tr>
<tr>
<td>--------</td>
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</tr>
<tr>
<td>S</td>
<td>Neurobiology Lectures with invited speakers (for members of the IZN and interested students, in English), 1st.</td>
<td>U. Ernsberger, W. Wisden and the group leaders of the IZN</td>
</tr>
<tr>
<td>LS</td>
<td>Journal Club Neurobiology (in English), 2st.</td>
<td>Members of Neurobiology</td>
</tr>
<tr>
<td>FS</td>
<td>Mitarbeiterseminar: Neuronal Plasticity (in English), 2st.</td>
<td>H. Bading and Mitarbeiter</td>
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<tr>
<td>FS</td>
<td>Mitarbeiterseminar: Neuronal Cytoskeleton (in English), 2st.</td>
<td>R. Brandt and Mitarbeiter</td>
</tr>
<tr>
<td>FS</td>
<td>Mitarbeiterseminar: Neural Stem Cells (in English), 2st.</td>
<td>F. Ciccolini and Mitarbeiter</td>
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<tr>
<td>FS</td>
<td>Mitarbeiterseminar: Sekretion von Neuropeptiden (in English), 2st.</td>
<td>H.-H. Gerdes and Mitarbeiter</td>
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<tr>
<td>FS</td>
<td>Mitarbeiterseminar: TGF-Betas (in English), 2st.</td>
<td>K. Unsicker and Mitarbeiter</td>
</tr>
<tr>
<td>LS</td>
<td>Journal Club für Mitarbeiter der Neuroanatomie (in English), 2st.</td>
<td>K. Unsicker and Mitarbeiter</td>
</tr>
<tr>
<td>FS</td>
<td>Mitarbeiterseminar: Entwicklung der Mittelhirndopaminergen Neurone</td>
<td>H. Simon and Mitarbeiter</td>
</tr>
<tr>
<td>FS</td>
<td>Progress Report der Arbeitsgruppe (in English), 2st.</td>
<td>H. Monyer, W. Wisden and Mitarbeiter</td>
</tr>
<tr>
<td>LS</td>
<td>Journal Club (in English), 3st.</td>
<td>H. Monyer, W. Wisden and Mitarbeiter</td>
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<tr>
<td>S</td>
<td>SFB 488 Seminar 'Molekulare und zelluläre Grundlagen neuraler Entwicklungsprozesse', 2st.</td>
<td>K. Unsicker and Teilprojektleiter des SFB 488</td>
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<tr>
<td>FS</td>
<td>Forschergruppen-Seminar 'Zentrale aminerge Systeme und Mechanismen', 2st.</td>
<td>K. Unsicker and Teilprojektleiter der Forschergruppe</td>
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<tr>
<td>HP-E</td>
<td>Cellbiology E2 (Biochemistry - Morphology) 3-weekly, full day. (HF, NF, LA Sachgruppe III)</td>
<td>H. Bading, O. Bräunling, H.-H. Gerdes, A. Régnier-Vigouroux, W. Wisden</td>
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<tr>
<td>HP-L</td>
<td>Laborpraktika: Moderne Methoden in der Neurobiologie, 6-wöchig, ganztägig</td>
<td>H. Bading, F. Ciccolini, H.-H. Gerdes, W. Wisden</td>
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<tr>
<td>HP-L</td>
<td>Anti-tumour immunity in the brain</td>
<td>A. Régnier-Vigouroux</td>
</tr>
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</table>
Publications of IZN members, 2001-2002

Hilmar Bading

Peer-reviewed publications


Reviews


Roland Brandt

Peer-reviewed publications

Francesca Ciccolini

Peer-reviewed publications

  Characterisation of neurosphere-derived neuronal precursor cells from E14 mouse striatum.
  J. Physiol. 523P, pp. 197 P.
  Localised and global spontaneous calcium events during neural precursor differentiation.
  J. Physiol. 527P, pp. 103P.
  Induction of pRb degradation by the human papillomavirus type 16 E7 protein is essential to efficiently overcome p16INK4a-imposed G1 cell cycle arrest.
  J. Virol. 75: 4705-12.
- Ciccolini, F. (2001)
  Identification of two distinct types of multipotent neural precursors that appear sequentially during CNS development.
- Ciccolini, F., Svendsen, C.N. (2001)
  Neurotrophin responsiveness is differentially regulated in neurons and precursors isolated from the developing striatum.
  Local and global spontaneous calcium events regulate neurite outgrowth and onset of GABAergic phenotype during neural precursor differentiation.

Reviews

  Calcium signalling: an overview.

Uwe Ernsberger

Peer-reviewed publications

  Reduction of endogenous TGF-ß does not affect phenotypic development of sympathoadrenal progenitors into adrenal chromaffin cells.
  BMP growth factors and Phox2 transcription factors can induce synaptotagmin I and neurexin I during sympathetic neuron development.
  Mech. Dev. 10: 149-159.
  Development of chromaffin cells depends on MASH1 function.
  Development 12: 4729-4738.

Reviews

- Ernsberger, U. (2001)
  The development of postganglionic sympathetic neurons: coordinating neuronal differentiation and specification.
  Generation of neuroendocrine chromaffin cells from sympathoadrenal progenitors: Beyond the glucocorticoid hypothesis.
  Gene expression from precursor to mature neuron.
  In „Molecular Biology of the Neuron“, 2nd ed; Davies, W., Morris, B., eds; Oxford University Press, Oxford, UK, in press

Siegfried Mense

Peer-reviewed publications

  Tetrodotoxin-resistant conductivity and spinal effects of
cutaneous C-fibre afferents in the rat. Neuroscience Res. 39: 413–419.


Reviews and book contributions


Hannah Monyer

Peer-reviewed publications


Publications of IZN members, 2001-2002


Book Chapters, Reviews


Andrei Rozov

Peer-reviewed publications


Publications of IZN members, 2001-2002

Reviews

  Genomic control of receptor function.

Horst Simon

Peer-reviewed publications

  Fate of midbrain dopaminergic neurons is controlled by engrailed-1 and –2.
  J. Neurosci. 21 (9) 3126-34.
- Thuret, S., Gassmann, M., Lloyd, K., Klein, R., Dyck, R.H., Simon, H.H.
  Expression of the neuregulin receptor, ErbB4, is not required for normal development of the substantia nigra.
  Submitted.
- Simon, H.H., Scholz, C., Döderlein, G.
  Genome Sequencing Data: Fast, one step cloning of defined genomic DNA Fragments from identified TIGR BAC clones.
- Thuret, S., Kaestner, K., Simon, H.H.
  The expression of the forkhead transcription factor, HNF3α, is highly restricted in the mammalian brain to the midbrain dopaminergic neurons.
  Submitted.
- Alberi, L., Scholz, C., Thuret, S., Logan, C., Simon, H.H.
  The engrailed transcription factors are cell autonomously required for the survival of the midbrain dopaminergic neurons.
  Submitted.

Reviews

  The midbrain dopaminergic neurons: Determination of their developmental fate by transcription factors.
  Ann. N.Y. Acad. Sci. in press.

Jacqueline Trotter

Peer-reviewed publications

  The AN2 protein is a novel marker for the Schwann cell lineage expressed by immature and non-myelinating Schwann cells.
  J. Neurosci. 21, 920-933.
  Isolation of enteric glia and establishment of transformed enteroglial cell lines from the myenteric plexus of adult rat.
  Neurogastroenterol. Motil. 13, 95-106.
  AN2/NG2 protein-expressing glial progenitor cells in the murine CNS: isolation, differentiation and association with radial glia.
  Glia 34: 213-228.
  Process outgrowth of oligodendrocytes is promoted by interaction of Fyn kinase with the cytoskeletal protein Tau.
  Overexpression of the myelin proteolipid protein leads to accumulation of cholesterol and proteolipid protein in endosomes/lysosomes: implications for Pelizaeus-Merzbacher disease.
  The proteoglycan NG2 is complexed with AMPA receptors by the PDZ protein GRIP in glial progenitor cells: implications for glial-neuronal signalling.
  J. Biol. Chem. in press.

Reviews

- Stegmüller, J., Schneider, S.S., Hellwig, A., Garwood, J.G., Trotter J.
  AN2, the mouse homologue of NG2, is a surface antigen on glial precursor cells implicated in control of cell migration.
  J. Neurocytology, special issue on NG2, invited review.
Publications of IZN members, 2001-2002

Kerry L. Tucker

Peer-reviewed publications


Reviews


Klaus Unsicker

Peer-reviewed publications

Publications of IZN members, 2001-2002

  Molecular mechanisms underlying the cooperative effect of glial cell line-derived neurotrophic factor and transforming growth factor beta in neurons.
  Growth differentiation factor-15/Macrophage inhibitory cytokine-1 (GDF-15/MIC-1) immunoreactivity in oxidatively stressed, apoptotic macrophages of human atherosclerotic carotid arteries.
  J. Leucocyte Biol., in press.
  TGF-ß2 is released from PC12 cells via the regulated pathway of secretion.
  Morphological alterations in the amygdala and hippocampus of mice during aging.
  Eur. J. Neuroscience 16: 2434-2440
  Growth/differentiation factor-15 prevents low potassium induced cell death of cerebellar granule neurons by differential regulation of Akt and ERK pathways.
  J. Biol. Chem., in press (online as M20037200).
  Age-related decline in the catecholaminergic innervation of the amygdala and dentate gyrus in mice.
  Development of adrenal chromaffin cells is largely normal in mice lacking the receptor tyrosine kinase c-Ret.
  Functions of FGF-2 and FGF-5 in astroglial differentiation and blood brain barrier permeability: Evidence from mouse mutants.
  J. Neuroscience, in press.

Submitted
  In profilin 2 mutant mice refractory stress response and lack of maternal behavior correlates with deregulated neuronal membrane recycling.
  Science, submitted.
  TGF-ßs are essential for the development of midbrain dopaminergic neurons in vitro and in vivo.
  J. Neuroscience, submitted and revised.
  Dopamine differentially regulates functional coupling and connexin43 expression in cortical and striatal neonatal rat astroglial cultures.
  Loss of leukemia inhibitory factor receptor ß causes severe deficits in the pre- and postganglionic sympathetic nervous system.

Reviews/Book Chapters
- Schober, A., Krieglstein, K., Unsicker, K. (2001)
  Neurotrophins, the chromaffin system, and preganglionic sympathetic neurons.
  In: Neurobiology of the Neurotrophins (I. Mocchetti, ed.), pp. 189-204. FP Graham Publishing Co, Johnson City, TN.
- Schober, A., Unsicker, K. (2001)
  Growth and Neurotrophic Factors regulating development and Maintenance of Sympathetic Preganglionic Neurons.
  Int. Review Cytol. 205: 37-76.
  TGF-ß and the regulation of neuron survival and death.
  From the neural crest to chromaffin cells: Introduction to a session on chromaffin cell development.
  Ann. NY Acad. Sci., Volume .,The chromaffin cell: transmitter
Publications of IZN members, 2001-2002

biosynthesis, storage, release, actions, and informatics” (O’Connor, D., Eiden, L., eds), in press.


William Wisden

Peer-reviewed publications


Special Reviews


General Reviews/book chapters


Symposia and Seminars
<table>
<thead>
<tr>
<th>Name</th>
<th>Group</th>
<th>Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mascha Blatow</td>
<td>Monyer group</td>
<td>Synaptic plasticity and Ca$^{2+}$ - buffers in a new type of interneuron</td>
</tr>
<tr>
<td>Lorena Esposito</td>
<td>Ernsberger group</td>
<td>Segregating neuronal and endocrine development in the sympathoadrenal system</td>
</tr>
<tr>
<td>Anne Herb</td>
<td>Monyer group</td>
<td>Molecular and functional characterization of NMDA receptor subunit composition</td>
</tr>
<tr>
<td>Istvan Katona</td>
<td>Monyer group</td>
<td>Molecular determinants controlling network activity</td>
</tr>
<tr>
<td>Nina Lüdemann</td>
<td>Brandt group</td>
<td>NL6 – a novel antibody which recognizes a glycosylated epitope on neurofilament protein M</td>
</tr>
<tr>
<td>Heike Peterziel</td>
<td>Unsicker group</td>
<td>Release of TGF-ß2 via the regulated pathway of secretion</td>
</tr>
<tr>
<td>Jörg Piontek</td>
<td>Brandt group</td>
<td>Organization of neuronal signaling complexes by gravin</td>
</tr>
<tr>
<td>Rana Roy</td>
<td>Langosch group</td>
<td>Does SNARE-transmembrane segment play a role in membrane fusion?</td>
</tr>
<tr>
<td>Amin Rustom</td>
<td>Gerdes group</td>
<td>Selective delivery of secretory cargo in Golgi-derived carriers reveals cognate sorting principles in polar and non-polar cells</td>
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<tr>
<td>Bernhard Reuss</td>
<td>Unsicker group</td>
<td>GFAP and Connexin 43 are region-specifically reduced in the brain of FGF-2 / FGF-5 double-mutant mice</td>
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<td>Thorsten Salm</td>
<td>Gerdes group</td>
<td>Recruitment of myosin Va to SG – a matter of time?</td>
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<tr>
<td>Paola Sgadò, Simon group</td>
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<td>Pbx1, an atypical homeodomain transcription factor, and the midbrain dopaminergic neurons</td>
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<tr>
<td>Neelam Shahani, Simon group</td>
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<td>MINUS: A negative regulator of microtubule assembly in neurons (?)</td>
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<tr>
<td>Alfred Strandl</td>
<td>Monyer group</td>
<td>Point mutations in AMPA receptors that affect short-term plasticity in GABAergic interneurons</td>
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<td>Jens Strelau</td>
<td>Unsicker group</td>
<td>Expression of GDF-15/MIC-1 in the perinatal, adult and injured rat brain</td>
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<td>Karsten Theilen, Pollerberg group</td>
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<td>The L1 cytoplasmic domain regulates neuronal migration, signaling, and cytoskeletal interactions</td>
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<td>Sandrine Thuret, Simon group</td>
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<td>Identification of genes expressed in the dopaminergic neurons of the substantia nigra and ventral tegmentum</td>
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<td>Peter Trudrug, Mense group</td>
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<td>Effects of chronic pathophysiological alterations on the behaviour and spinal cord immunohistochemistry in rats</td>
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<td>Bill Wisden</td>
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<td>Defining the role of neuronal circuits: fast, reversible regulation of selected cell types</td>
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<td>Stephan Oberle, Unsicker group</td>
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<td>Neurotrophic factors regulating development and maintenance of preganglionic sympathetic neurons</td>
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<td>Rüdiger Rudolf, Gerdes group</td>
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<td>Motorizing maturation? „On the role of myosin Va in the life of a secretory granule“</td>
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<td>Daniel Gherbassi, Simon group</td>
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<td>How are the midbrain dopaminergic axons directed towards the basal ganglia?</td>
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<td>Siegfried Mense</td>
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<td>Abnormal discharges in spinal neurones as an explanation for chronic pain in patients with spinal cord injury</td>
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<td>Mikhail Filippov, Monyer group</td>
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<td>Investigation of Connexin26 gene expression using reporter mice</td>
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<td>Peer Wulff, Wisden group</td>
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<td>Selective neuronal silencing</td>
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Symposia and Seminars

Sandrine Thuret, Simon group
Identification and characterization of genes expressed by the midbrain dopaminergic neurons

Sergei Kuznetsov, Gerdes group
Motor proteins in fast axonal transport

Uwe Ernsberger
Cholinergic differentiation in sympathetic neurons – revising a classical model of neuronal diversification

Antonio Caputi, Monyer group
Generation and analysis of Calretinin-EGFP transgenic mice

Amin Rustom, Gerdes group
“Piggy-back” transport of Xenopus hyaluronan synthase via the secretory pathway to the plasma membrane

Christine Winterstein, Trotter group
 Trafficking of myelin proteins and lipids

Zsófia Sebő, Brandt group
Functional analysis of a tau-mutant (R406W) and its role in the neurodegenerative disease FTDP-17

Andrei Rozov
Presynaptic mechanisms of short-term synaptic enhancement

Elke Fuchs, Monyer group
Changing AMPA-receptor function in GABAergic interneurons

Nina Lüdemann, Brandt group
NL6 – a new antibody to analyse development of human neurons

Srinivasa Subramaniam, Unsicker group
GDF-15/MIC-1 protects cultured rat cerebellar granule neurons from cell death via the phosphatidylinositol-3 kinase pathway

Irina Coserea, Monyer group
Excitotoxicity in transgenic mice models

Isabel Aller, Wisden group
Gene-specific deletions in cerebellar granule cells

Sheriar Hormuzdi, Monyer group
Cx36 – Orchestrating synchrony in specific inhibitory circuits

Oliver von Bohlen und Halbach, Unsicker group
Morphological alterations in the hippocampus and amygdala of aged mice

Roberto Bruzzone, Monyer group
The molecular and functional diversity of connexins in the vertebrate retina

Peter Vanhoutte, Bading group
Glutamate receptor trafficking triggers changes in neuronal network properties

Uwe Ernsberger /Ernsberger- Unsicker cooperation
Reconsidering sympathoadrenal beliefs

Lavinia Bhatt, Simon group
Genes essential for survival of the midbrain dopaminergic neurons

Christine Bark, Monyer group
Ultrastructural analysis of the connexin 36-EGFP mouse in the olfactory bulb

Lavinia Alberi, Simon group
Cell autonomous requirement of the Engrailed genes for the survival of the midbrain dopaminergic neurons

Bernhard Reuss, Unsicker group
Reduced levels of GFAP and a leaky blood brain barrier in mice deficient for FGF-2 and FGF-5 alone or in combination

Ulrich Hoheisel, Mense group
The significance of purinergic and vallinoid receptors for the induction of muscle pain
Symposia and Seminars

SFB 488 Friday Seminars

2001

Roland Brandt
Cytoskeletal mechanisms of neuronal morphogenesis

Dirk Feldmeyer
Cajal-Retzius Zellen im Neokortex: Neue Ergebnisse zur Morphologie und Physiologie

Rainer Friedrich
Dynamics of odor processing in the zebrafish olfactory bulb

Chaya Kalcheim
Regulation and function of the interaction between BMP and noggin during neural crest and somite development

Clemens Kiecker
A gradient of Wnt signalling regulates anteroposterior neural patterning in Xenopus

Corinna Klein
Linking up with the cytoskeleton: The role of Fyn and Tau during early events of myelination

Rüdiger Klein
Distinct requirements for TrkB and TrkC signaling for target innervation of sensory neurons

Dr. Thomas Lemberger
Brain-specific disruption of CREB function leads to neuronal death and neurodegeneration

G. Elisabeth Pollerberg
The role of microtubule-associated protein MAP1B in steering growth cones

Friedrich Reinhard
Presenilin complex formation

Daniel Spergel
GABA and Glutamate Receptor-Mediated Signaling in Hypothalamic GnRH Neurons

Mathias Treier
Signaling pathways regulating pituitary organogenesis

Klaus Unsicker
Recent developments in the development of the neuroendocrine progeny of sympathoadrenal cells

Irene Wacker
C. elegans zag-1, a zinc finger homeobox transcription factor involved in axon guidance

Jochen Wittbrodt
Molecular and genetic mechanisms controlling vertebrate eye development

2002

Evi Albers
Vesicular traffic in myelinating oligodendrocytes

Stefan Berger
Analysis of corticosteroid signaling in the brain by gene targeting

Dirk Feldmeyer
Cajal-Retzius cells in the neocortex of the reeler mutant mouse

Sheriar Hormuzdi
Characterization of gap junction-communicative neuronal circuits

Katrin Huber
Development of the sympathoadrenal lineage

Nina Lüdemann
NL6 - a new antibody to analyze glycosylation and development of human neurons

Stefan Offermanns
Regulation of RhoA in neurons: The role of specific RhoGEFs

Christoph Peter
Construction of structurally intact but functionally silent AChR complexes: A tool to analyze activity-dependent synapse formation

Oliver Schlicker
GABAA receptors on the move

Peter Soba
APP and Notch signaling

Karsten Thelen
Two members of the IgCAM family, L1 and DM-GRASP, modulate neuronal migration and axonal pathfinding

Wei Wu
Dkk2 and Dkk1 function antagonistically during Wnt signalling
Symposia and Seminars

Heidelberg Neurobiology Lectures
2001

Christian Behl, München
The Female Sex Hormone Estrogene and Intracellular Signaling in Neuroprotection

Christian Kaltschmidt, Witten/Herdecke
Signaling via NF-κB in the nervous system

Arthur Konnerth, München
Neurotrophin-evoked excitation in central neurons

Andrew Matus, Basel
Analysis of synaptic plasticity using GFP-labeled proteins of the actin cytoskeleton

T.R. Raju, Bangalore, India
Neuronal Plasticity - Progressive and regressive changes in the CA3 Pyramidal Neurons of the Hippocampus

Christine Richter-Landsberg, Oldenburg
Stress response in oligodendrocytes: Implications for neurodegenerative diseases

Estelle Sontag, Texas, USA
Protein phosphatase 2A: The Trojan Horse of cellular signaling

Walter Stuehmer, Göttingen
Visualizing the Last Steps in Exocytosis

2002

Matthias Bähr, Göttingen
Molecular basis of neural repair strategies

Jürgen Bolz, Jena
Wiring Molecules for the Assembly of Cortical Circuits

Heiko Braak, Frankfurt
Neuropathological staging of idiopathic Parkinson’s disease and some speculative considerations pertaining to its pathogenesis

Christian Brösamle, Baltimore
Myelination in the vertebrate brain – more than axonal insulation

Nils Brose, Göttingen
Dynamic Regulation of Active Zone Function in Neurotransmitter Release

Wolfgang Driever, Freiburg
Genetic analysis of the isthmic organizer and dopaminergic differentiation in zebrafish

Eberhard Fuchs, Göttingen
Stressful experiences: Their effects for brain structure and function

Martyn Goulding, La Jolla
Wiring Up Interneurons in the Spinal Cord: The Connection Between Embryo and Adult

Reinhard Köster, Pasadena
Intravital characterization of neuronal migration

Hans-Christian Pape, Magdeburg
Neural correlates of fear behavior and fear memory in the amygdala

Christoph Schuster, Tübingen
Molecular Mechanisms of Long-Term Neuronal Plasticity: Insights from a Glutamatergic Model Synapse

Cornelius Schwarz, Tübingen
Connecting Two Different Worlds. The Functional Architecture of the Cerebro-cerebellar Pathway

Werner Sieghart, Wien
Structure and function of GABAA receptor subtypes

Steven Skaper, Harlow, UK
Neurotrophins and neuro-immune system interactions

Kerry Tucker, Basel
A green mouse: Using GFP to study peripheral nervous system development

Michael Wegner, Erlangen
Sox10 Function in PNS and CNS Development

Michael Weller, Tübingen
Biological relevance and therapeutic modulation of cytokine activity (Apo2L/TRAIL, TGF-β) in malignant glioma
Symposia and Seminars

Graduate College 791
“Neural Development and Degenerative Processes: Basic Research and Clinical Implications”

Winter Term 2002/2003

Karsten Thelen / G.E. Pollerberg
Neuronal migration and axonal pathfinding

Christof Niehrs
Molecular mechanisms of early antero-posterior patterning

Rainer Friedrich
Organization and development of the peripheral olfactory system

Hannah Monyer
Elektrische und exzitatorische Synapse während der Entwicklung

Harald Hutter
Axon guidance signals: Molecules and Mechanisms

Veit Witzemann
Formation of synapses at the neuromuscular junction - a change of the neurocentric view

Dirk Feldmeyer
Neuronal networks in the neocortex – structural and functional properties

Klaus Unsicker
Development of the nervous system and related malformations

Seminars of the DFG ‘Forschergruppe’ FOR 302/2-1, 2001

Michael Aggensteiner, Leipzig
Klonierung und Quantifizierung der entwicklungsabhängigen Genexpression von p42IP4 im Rattenhirn

Eva Grundström, Uppsala
On Pathophysiological Mechanisms in Amyotrophic Lateral Sclerosis

Brigitte Kieffer, Illkirch
Opioid receptors: from genes to mice

Reinhard Müller, Leipzig
Untersuchungen zur 6-Phosphofructo-1-kinase in humanen Fibroblasten

Beate Niesler, Heidelberg
Genetic variability of the human serotonin receptor HTR3 genes and cloning of alternatively spliced isoforms

Flora de Pablo, Madrid
Antia apoptotic signalling of the insulin/insulin receptor system in early neural development

John Peters, Dundee
Physiology and Pharmacology of Native and Recombinant 5-HT3 Receptors

Dmitry Poteryaev, Helsinki
The role of GDNF family receptors alpha in Ret-mediated oncogenesis and neuronal function

Enrique de la Rosa, Madrid
Programmed cell death during early neural development: its physiological regulation by intrinsic and extrinsic signals

Norman Saunders, Tasmania, Australia
Barriers in the developing brain, control of its internal environment

Katharina Schindowski, Frankfurt
Mechanismen der apoptotischen Zelltodes an peripheren Zellen in der Alzheimer Demenz
Seminar Developmental Neurobiology, Summer Term 2001

Tobias Wolfram
Turning Blood into brain

Christine Jakoby
Neuralrohrsegmentierung

Esther Zanin
The control of neuronal cell shape

Simone Giese
Die Entstehung einer Synapse: Differenzierung von Synapsen im ZNS

Susanne Fritsch
The formation of neuromuscular synapses

Ida Kollmar
How developing neurons balance their economies

Florian Stindl
Signal-processing machines at the postsynaptic density.

Sandra Dischinger
Die Entstehung einer Synapse II: Präsynaptische Differenzierung

Vanessa Schubert
Neuronenwanderung während der ZNS-Entwicklung

Yasmin Issa
Die Entstehung einer Synapse III: Postsynaptische Differenzierung

Winter Term 2002/03

Isabel Brachmann
Oligodendroglial development

Holger Baldauf
Retino-tectal projection

Lothar Blüm
Entwicklung des Geruchssinns

Andreas Wippel
Tangentiale Zellwanderung im zentralen Nervensystem

Yong-Boum Kim
Specifying neuronal identity by combinatorial RNA splicing

Jan-Marik Weislogel
Isolation of neural stem cells in the mammalian CNS

Christina Bauch
Festlegung der Neuralrohrachsen während der Embryogenese

Neurobiology Seminars 2002

John Creemers, Department for Human Genetics, Leuven
Intracellular Trafficking and Pathophysiology of Proprotein Convertases

Oliver Dick, MPI für Hirnforschung, Frankfurt
Localization and function of cytomatrix-proteins at retinal synapses

Thomas Dresbach, Leibnitz-Institut für Neurobiologie in Magdeburg
Golgi-derived precursor organelles in assembly of neurotransmitter release sites

Lara Gnügge, University Freiburg, Department of Developmental Biology
The making of GFP transgenic zebrafish for pancreas tracking and mutant characterization

Javeed Jiqbal, Hans-Knöll-Institute For Natural Products Research, Department of Cell and Molecular Biology, Jena
Genotyping and Gene expression profiling in HPV 16 immortalized cell lines with cDNA microarrays
Symposia and Seminars

Symposia

SFB 488 Christmas Symposium 2001 - Saturday, 01.12.2001, ZMBH

Session 1: Neural Induction, pattern formation, and cell determination
(Chair: G. E. Pollerberg)

Christof Niehrs  Role of dkk1 in embryonic head induction
Judith Stegmüller / Jacqueline Trotter  Identification of intracellular binding partners of the AN2/NG2 proteoglycan.
Klaus Unsicker  Development of sympathoadrenal progenitor cells and their preganglionic innervation

Session 2: Axon growth and pathfinding
(Chair: Christof Niehrs)

Roland Brandt  Cytoskeletal mechanisms of neuronal morphogenesis
Hans-Hermann Gerdes  Membrane traffic in neuronal cell systems
Stefan Offermanns  Mechanisms of RhoA activation in neuronal cells
Dusan Bartsch  Conditional overexpression of the minibrain kinase in mouse brain

Session 3: Neuronal differentiation
(Chair: Klaus Unsicker)

Gunter Merdes / Renato Paro  Notching up APP in Drosophila
Peter Seeburg  Genetic approaches to understand GnRA pulsatility in hypothalamic GnRA neurons

Session 4: Molecular bases of synapse formation
(Chair: Hannah Monyer)

Hannah Monyer  Functional importance of gap-junction coupling in the postnatal brain
Ulrich Misgeld  The developmental switch of neuronal GABAergic responses from excitation to inhibition
Veit Witzemann  Factors required for AChR clustering at the neuromuscular junction
Daniel Gau / Günther Schütz  Phosphorylation of CREB Ser-142 regulates light-induced phase shifts of the circadian clock

SFB 488 Christmas Symposium 2002 - Saturday, 30.11.2002, ZMBH

Session 1:
Chair: H. Bading

A1 C. Niehrs  A Wnt morphogen gradient controls anteroposterior patterning of the early neural plate in Xenopus
A6 K. Unsicker  TGFßs as master regulators of neuron survival and death
B5 S. Offermanns  Mechanisms of RhoA activation in neuronal and non-neuronal cells
B6 R. Kuner  Molecular mechanisms governing nociceptive transmission at spinal synapses

Session 2:
Chair: H. Monyer

J. Kuhse  Developmental expression and localization of NMDA-receptor subunits in primary cultures of rat spinal cord neurons: effects of agonist and antagonist administration
B2 H.-H. Gerdes  Dendritic membrane traffic
D8 W. Wisden  Developing a transgenic method to regulate reversibly the activity of specific neuronal types
D9 U. Misgeld  D1 tone modulates synaptic inhibition in substantia nigra

Session 3:
Chair: J. Kirsch

B4 K. Thelen  Role of NrCAM and DM-GRASP in guidance of retinal ganglion cell axons
Th. Euler  Direction-selective calcium signals in retinal starburst amacrine cells
D6 T. Lemberger  Brain-specific CREB mutants and neurodegeneration
D3 H. Monyer  To mnemonists in the literature of the 20th century
Symposia and Seminars

SFB 488 Symposium
„Neural and Non-Neural Stem Cells“
Heidelberg, October 26./27., 2001

Friday, Oct 26, 2001
Session 1 - Chair: Klaus Unsicker
Oliver Brüstle
Embryonic stem cells: Applications in reconstructive neurobiology

Anna Wobus
Embryonic stem cell differentiation: Modulation by genetic modification and extracellular signals

Cedric Kempermann
Genetic and functional aspects of adult neurogenesis

Key Note Lecture
Helen M. Blau
The evolving concept of a stem cell: entity or function?

Saturday, Oct 27, 2001
Session 2 - Chair: Roland Brandt
Margot Mayer-Pröschel
Gliogenesis in the mammalian spinal cord: from the embryo to the adult

Magdalena Götz
Glial cells generate neurons: cellular and molecular mechanisms of neurogenesis in the vertebrate CNS

Clive N. Svendsen
Human neural precursor cells grown as neurospheres are regionally specified

Session 3 - Chair: Horst Simon
Angela Gritti
Neural stem cells in the adult brain: the SVZ-RMS pathway

Rudolf Götz
Signalling pathways for survival and differentiation of neural cells

Karen J. Chandross
Adult mammalian bone marrow gives rise to neural-like cells in the brain

Georg Kuhn
Neural stem cell activity in the adult brain: The balance of proliferation and apoptosis

Session 4 - Chair: Peter Seeburg
Anthony D. Ho
Non-hematopoietic tissues from hematopoietic stem cells?

Albrecht Müller
Developmental potentials of somatic stem cells: unique or all the same?

Wolfgang M. Franz
Selection of ventricular-like cardiomyocytes from ES cells in vitro

SFB 488 Symposium
‘Frontiers in Developmental Neuroscience’
Heidelberg, June 14./15, 2002

Friday, June 14
Session 1: Induction and patterning I - Chair: Klaus Unsicker
Yoshiki Sasai, Kyoto
Molecular control of neural specification in frog and mouse ectoderm

Christof Niehrs, Heidelberg
Molecular mechanism of embryonic head induction by Dickkopf1

Wolfgang Wurst, München
Mesoderm - Brain development: From embryonic to adult physiology

Session 2: Patterns and migration - Chair: Christof Niehrs
David Wilkinson, London
Control of terminal differentiation of neuronal cell fate in the vertebrate brain

Arnon Rosenthal, Palo Alto
Control of morphogenesis of neural crest and cranial structures

Renato Paro, Heidelberg
Notching up the Amyloid Precursor Protein (APP) in Drosophila

François Guillemot, Illkirch
Common and divergent functions of proneural genes in specification of neural cell types

Saturday, June 15, 2002
Session 3: Visual system and neural crest – Chair: Renato Paro
Matthias Carl, Heidelberg
Genetic and molecular analysis of vertebrate eye development

Chaya Kalcheim, Jerusalem
Cell intrinsic and environmental factors regulating the onset of neural crest migration

Jean-François Brunet, Paris
Phox2b, master gene of a neural circuit

Hermann Rohrer, Frankfurt/Main
Molecular control of noradrenergic neuron development

Carmen Birchmeier, Berlin
The role of the Neuregulin signaling system in development of the peripheral nervous system

Session 4: Migration, synapse formation and glia – Chair: Chaya Kalcheim
Michael Frotscher, Freiburg
How does reelin control granule cell migration in the dentate gyrus?

Eduardo Soriano, Barcelona
Mechanisms of Reelin action in cortical development

Christian Klämbt, Münster
Glia cell migration in Drosophila

Session 5: Formation of networks and plasticity – Chair: Peter Seeburg
Matthew Dalva, Boston
A role for EphB in synapse development: regulating NMDA receptor localization and function

Hilmar Bading, Heidelberg
Dynamics of simple neuronal networks

Klaus Willerich, Bonn
Analysis of glial and neuronal connexins in transgenic mouse mutants

Hannah Morsley, Heidelberg
Functional role of GAP junction coupling in the developing and the adult brain
# Symposia and Seminars

IZN Retreat St. Odile, Alsace

April 5 - April 7, 2001

**Thursday, April 5, 2001**

Introduction: Klaus Unsicker: Neuro-Development in Heidelberg

Session I: From molecules to cells (1) Chair: Hannah Monyer
- Jan Rohde (Langosch group): Assembly and function of integral membrane proteins
- Hans-Hermann Gerdes: Membrane traffic in neuronal cell systems
- Evi Albers (Trotter group): From cell migration to membrane traffic: current topics in myelin biology

**Friday, April 6, 2001**

Session II: From molecules to cells (2) Chair: Peter Seeburg
- Uwe Ernsberger: To build a neuron
- Heinz Steffens: The Na+-channel blocker tetrodotoxin: (Mense group) a tool in systemic neuroscience research?
- Ulrich Misgeld: Regulation of chloride transport in neurons

Session III (2 talks): From molecules to systems (1) Chair: Ulrich Misgeld
- Peter Seeburg: RNA editing in mammals: developmental deficiencies revealed by genetic interference
- Dirk Feldmeyer: Excitatory neurotransmission in the neocortex

Session IV (2 talks): From molecules to systems (2) Chair: Roland Brandt
- Klaus Unsicker: Autonomic motoneurons in the spinal cord: how similar to, how different from somatic motoneurons?
- Horst Simon: Specification of the midbrain dopaminergic neurons

Session V (3 talks): From molecules to systems (3) Chair: Hans-Hermann Gerdes
- Harald Hutter: Axon guidance genes in C. elegans: help from the genome sequence
- Erich Greiner: Genetic dissection of tailless function in developing and adult mouse brain
- Jochen Wittbrodt: From eye to brain: optic vesicle morphogenesis, retinal patterning and projection

**Saturday, April 7, 2001**

Session VII (3 talks): from molecules to systems to cognition Chair: Klaus Unsicker
- Hannah Monyer: GABAergic interneurons: their role in rhythmicity and synchronicity of neuronal networks
- Herta Flor: Cortical plasticity: mechanisms and functional significance
- Roland Brandt: From tubules to cognition

**Session VI (3 talks): from molecules to systems (4) Chair: Harald Hutter**
- William Wisden: Homeostatic regulation of gene expression in the developing brain
- Anne Régnier-Vigouroux: Anti-tumour immunity in the brain: an impossible talk?
- Brigitte Wildemann: The diagnostic and pathogenetic implications of lymphocytic gene rearrangements in malignant lymphomas of the nervous system and multiple sclerosis

Discussion: Neurophilosophy - Future of Heidelberg Neuroscience
- Hilmar Bading:
IZN Retreat
Kloster Schöntal, May 7 – 8, 2002
Neurosciences at the IZN: Where to go
Concepts and Techniques

Tuesday, May 7
Session 1
Chair: H. Monyer
Klaus Unsicker | IZN: Past, Presence, and Future Directions
Hilmar Bading | From molecules to networks: my concepts
Klaus Unsicker | From systems to molecules: a top-to-bottom approach
Ad Aertsen | From Neurons to Networks and Back -- Recurrent Approaches in Neural Dynamics

Session 2
Chair: K. Unsicker
Joachim Kirsch | Forming inhibitory synapses
Andreas Draguhn | Analysis of high-frequency network oscillations in the rodent hippocampus in vitro

Session 3
Chair: H. Bading
Jörg Hoheisel | Analysis of Genetic Variations in Cancer Tissue by Complex DNA and Antibody Microarrays
Winfried Denk | Multiphoton imaging in neurosciences
Rainer Friedrich | Network dynamics and odor processing in the olfactory bulb
Special Lecture - Peter Ruppersberg
Venture capital and biotech companies in the crisis

Wednesday, May 8:
Session 4
Chair: U. Misgeld
Hannah Monyer | From molecules to networks to mind: my concepts
Bill Wisden | Selective neuronal silencing: a review of possible approaches

Horst Simon | Differentiation of the midbrain dopaminergic neurons
Session 5
Chair: J. Trotter
Markus Schwaninger | Molecular and genomic approaches in stroke research
Rainer Spanagel | Neurobiological bases of drug addiction
Siegfried Mense | Plans and ideas for studying mechanisms of muscle pain in vivo

Session 6
Chair: H. Hutter
Christoph Cremer | Lightoptical Nanoscopy
Philipp Bastiaens | Imaging RTK signal initiation, propagation and termination in cells
Francesca Ciccolini | A new strategy for isolating neural stem cells
Uwe Ernsberger | To build a neuron - conceptually

Session 7
Chair: G. E. Pollerberg
O. von Bohlen und Halbach | NO visualization
Peter Vogel | Antiapoptotic interventions and outcome following global cerebral ischemia due to cardiocirculatory arrest
Wolfgang Ketsch | Characterization of KCC2 by its cation dependence
Peter Vanhoutte | NMDA receptor-induced unsilencing of synaptic contacts triggers change in neuronal network properties
Graduate Workshop: Live Cell Imaging

September 24-30, 2001
GFP-based multi-color imaging - automated quantitative image analysis - microinjection

Organizers:
- Hans-Hermann Gerdes (Heidelberg)
- Brian Storrie (Blacksburg)

Instructors:
- Tanja Kögel
- Amin Rustom
- Rüdiger Rudolf

External speakers

Vicky Allan
Using transmitted light microscopy to study organelle movement in vivo and in vitro

Philipp Bastiaens
Spatial organisation of tyrosine kinase and phosphatase activities

Jan de Mey
Living cells in depth: analysing cellular processes by ultrafast 4D recording of two fluorescent tagged proteins and high throughput deconvolution

Hans-Hermann Gerdes
The use of GFP to monitor protein secretion

Roland Eils
4D imaging reveals new insights into cellular and nuclear dynamics

Jan Ellenberg
4D imaging and fluorescence photobleaching to study nuclear envelope structure and function in live cells.

Chris Hawes
Expression of fluorescent proteins in plant cells for the study of organelle dynamics

Jennifer Lippincott-Schwartz
Dissection of intracellular protein trafficking pathways using FRAP and FLIP

Rainer Pepperkok
Using GFP to study structure and function in the secretory pathway

Tullio Pozzan
Imaging second messengers in living cells

Ernst Stelzer
The truth behind confocal microscopy

Brian Storrie
Imaging Golgi apparatus biogenesis through expression of dominant mutations
ZMBH Forum 2001

“Genes, Proteins and Brain Disease”
Heidelberg, May 17 to 19, 2001

Thursday, 17.05.2001
Keynote Lecture:
Colin L. Masters (Melbourne)
Amyloid proteins in neurodegenerative diseases: 17 years from Sequenator to clinic

Friday, 18.05.2001
Session I (Chair: Tobias Hartmann)

Steven Younkin (Jacksonville)
Plasma A beta as a premorbid biomarker and surrogate phenotype for typical late onset Alzheimer’s Disease

Lars Lannfelt (Huddinge)
Genetics and pathophysiology of Alzheimer’s disease

Hilkka Soininen (Kuopio)
Risk genes of Alzheimer’s disease – approach of genome wide search

Rudolph E. Tanzi (Charlestown)
Alzheimer’s Disease: Resolving a Complex Genetic Picture

Michel Goedert (Cambridge)
Tau gene mutations and neurodegeneration

Session II (Chair: Gerd Multhaup)

Peter St. George-Hyslop (Toronto)
Biology and Genetics of the Presenilins and of their Partners

Sangram S. Sisodia (Chicago)
Function and Dysfunction of Presenilin 1

Bart De Strooper (Leuven)
The secretases as drug targets in the fight against Alzheimer’s Disease

Martin Citron (Thousand Oaks)
β-secretase – a target for the treatment of Alzheimer’s Disease

Ronald K. Taylor (Hanover)
Characterization of a novel family of polytopic aspartyl proteases that contribute in diverse ways to the pathogenesis of human disease

Wieland Huttner (Dresden)
Neurogenesis and the cell biology of neuroepithelial cells

Saturday, 19.05.2001
Session III (Chair: Klaus-Armin Nave)

Adriano Aguzzi (Zuerich)
Molecular Biology of Prion Diseases

Christian Haass (Munich)
Amyloid β-Peptide and Synuclein, two major players in Neurodegeneration

Ta Yuan Chang (Hanover)
Cholesterol Mutants at Dartmouth

Session VI (Chair: Klaus Unsicker)

Tobias Hartmann (Heidelberg)
The role of lipids in Alzheimer Amyloid Precursor processing

Thomas Bayer (Bonn)
What can we learn from transgenic mice to understand the pathology of Alzheimer’s disease?

Thomas Jentsch (Hamburg)
Role of intracellular C1--channels - lessons from mouse models and human disease
Symposia and Seminars

Workshop on Molecular Cell Biology
The Hebrew University of Jerusalem and
The University of Heidelberg
May 8 – May 12, 2002
ZMBH, INF 282, SR 001

Thursday, May 9
Session I: Genes and Development
Klaus Unsicker
Generation of neural crest-derived neuroendocrine cells and their integration into a neural circuitry
Uri Gat
The Wnt pathway in the development of hair and other skin appendages

Session II: Transcriptional and Subcellular Signalling
Christof Niehrs
Molecular mechanism of embryonic head induction by dickkopf1
Avihu Klar
Plasmin modulates the axonal guidance properties of F-spondin
Roland Brandt
Mechanisms of neuronal degeneration in the tau pathologies
Oded Behar
The role and mechanism of action of Semaphorin 3A in axon guidance
Renato Paro
Chromatin and Epigenetics
Zeiev Paroush
Transcriptional repression in Drosophila development
Peter Seeburg
Synaptic activity-induced conversion of intronic to exonic sequences

Friday, May 10
Session III: Transduction Processes from Membrane to Nucleus
Blanche Schwappach
Quality control in the heteromultimeric assembly of ion channels and receptors
Thomas Lemberger
Disruption of CREB function in brain leads to progressive neurodegeneration
Nissim Ben Arie
Math 1 in neurogenesis
Gudrun Rappold
Functional disruption of a Rho-GTPase activating gene on chromosome 3p25 causes severe mental retardation
Ulrich Misgeld
Developmental change of GABA response and chloride transport in neurons

Session IV: Molecular and Physiological Aspects of Nervous System Function
Hermona Soreq
The molecular neurobiology of acetylcholinesterase variants: from stressful insults to antisense intervention
Hannah Monyer
Molecular determinants for oscillatory and synchronous network activity
Yifat Prut
Neuronal networks: from structure to function
Yael Stern-Bach
Neuronal functioning of glutamate ion channels
Israel Steiner
Herpes simplex virus type I (HSV-1) latency: the many functions of the HSV-1 latency associated gene

Saturday, May 11
Session IV: Molecular and Physiological Aspects of Nervous System Function, cont’d
Guy Bloch
Per gene expression in the honey bee
Michael Brandeis
Cell cycle-associated genes
Rainer Spanagel
The role of per genes in drug addiction
Guest Scientists

Theses
Guest Scientists 2001-2002

Guest Scientists 2001-2002

Group Hilmar Bading, Neurobiology
- Giles Hardingham, Department of Preclinical Veterinary Studies, Royal School of Veterinary Studies, Edinburgh University-Summerhall, Edinburgh, England (02/02 - 09/02, part-time)

Group Roland Brandt, Neurobiology
- Pavol Zelina, Slovak Academy of Sciences, Bratislava, Slovakia (07/01 – 08/01)

Group Uwe Ernsberger, Neuroanatomy
- Ulla Amtmann, Clinical Neurobiology, Neurology, University Heidelberg (05/01)
- L. Paraoanu, Biology, Techn. Univ. Darmstadt (06-07/01)
- N. Dünker, Anatomy, University Homburg, Homburg (10/01)

Group Hans-Hermann Gerdes, Neurobiology
- Dr. Ivanka Markovic, School of Medicine, Institute of Biochemistry, Belgrad (08-10/02)

Group Siegfried Mense, Neuroanatomy
- Prof. D.G. Simons, MD, Physical Med. & Rehabilitation, Emory University, Atlanta, Ga, USA (05/01, 09/02)

Group Hannah Monyer, Clinical Neurobiology
- Prof. Dr. Roberto Bruzzone, Institut Pasteur, Paris (06/02 - 2 years)

Group Klaus Unsicker, Neuroanatomy
- Urmas Arumäe, PhD, Institute of Biotechnology, University of Helsinki, Helsinki, Finland (10/02)
- Cesar Berrios, Dept. Biology, University of Puerto Rico, San Juan, Puerto Rico (03-06/02)
- Nicole Dünker, PhD, Neuroanatomy, Universität Göttingen, Göttingen, Germany (09/02)
- Anke Lackmann, PhD, Neuroanatomy, Universität Göttingen, Göttingen, Germany (12/02)
- Beata Legutko, PhD, Pharmacology, Polish Academy of Sciences, Krakow, Poland (07/02)
- Azita Parvaneh Tafreshi, PhD, Research Centre for Genetic Engineering and Biotechnology, University of Teheran, Teheran, Iran (07/01 – 06/02)
- Dmitry Poteryaev, PhD, Institute of Biotechnology, University of Helsinki, Helsinki, Finland (12/01 – 05/02)
- Elena Roussa, PhD, Neuroanatomy, Universität Göttingen, Göttingen, Germany (04/02)
- Nicole Dünker, PhD, Neuroanatomy, Universität Göttingen, Göttingen, Germany (09/02)
- Anke Lackmann, PhD, Neuroanatomy, Universität Göttingen, Göttingen, Germany (12/02)
- Beata Legutko, PhD, Pharmacology, Polish Academy of Sciences, Krakow, Poland (07/02)
- Azita Parvaneh Tafreshi, PhD, Research Centre for Genetic Engineering and Biotechnology, University of Teheran, Teheran, Iran (07/01 – 06/02)
- Dmitry Poteryaev, PhD, Institute of Biotechnology, University of Helsinki, Helsinki, Finland (12/01 – 05/02)
- Elena Roussa, PhD, Neuroanatomy, Universität Göttingen, Göttingen, Germany (04/02)
Diploma and Doctoral Theses

1. Diploma Theses

**Group Roland Brandt, Neurobiology**

Julia Leschik (2000)
Expression von GFP-markiertem Tau-Protein und PHF-ähnlichen Tau-Phosphomutanten in Hippocampus-Schnittkulturen

Zsófia Sebő (2001)
Funktionale Analyse einer Tau-Mutanten (R406W), die in der neurodegenerativen Krankheit FTDP-17 auftritt

Carlos Bas Orth (2002)
Analyse der Funktion des Kinase verankernden Proteins Gravin in Nervenzellen

Sonja Grosskinsky (2002)
Charakterisierung neuer "Alzheimer-diagnostischer Antikörper" und Antikörper gegen weitere neuronale Zytoskelett-Antigene

**Group Hans-Hermann Gerdes, Neurobiology**

Oliver Schlicker (2001)
Untersuchung zum Transport von GABA-A-alpha1 und alpha2 GFP-Fusionsproteinen

**Group Jacqueline Trotter, Neurobiology**

Christine Neuber (2003)
Vesikeltransport und Sortierung von Proteinen und Lipiden in myelinisierenden Oligodendrozyten

Christine Winterstein (2003)
Mögliche Interaktionspartner der AN2/NG2-positiven Zellen, vermittelt über die LNS-Domänen

**Group Horst Simon, Neuroanatomy**

Christian Scholz (2002)
Die Entwicklung der dopaminergen Neurone im Mittelhirn des Huhns

2. Doctoral Theses

**Group Roland Brandt, Neurobiology**

Jochen Eidenmüller (2001)

Thomas Fath (2002)
Die Rolle des Mikrotubuli-assoziierten Proteins Tau in neurodegenerativen Erkrankungen

Jörg Piontek (2002)

**Group Hans-Hermann Gerdes, Neurobiology**

Rüdiger Rudolf (2001)
Bildung, Transport und Exozytose sekretorischer Granula und die funktionelle Beteiligung von Myosin Va

Thorsten Salm (2001)
Maturierungsabhängige Assoziation von Myosin Va mit sekretorischen Granula

**Group Siegfried Mense, Neuroanatomy**

Thomas Blüm (2001)
Fibroblasten Wachstumsfaktor-2 moduliert die Impulsaktivität spinaler Neurone

**Group Hannah Monyer, Clinical Neurobiology**

Elke C. Fuchs (2002)
Generierung transgener Mauslinien zur Untersuchung der AMPA-Rezeptor-Funktionen in GABAergen Interneuronen.
Diploma and Doctoral Theses

**Group Horst Simon, Neuroanatomy**

Sandrine Thuret (2002)
Identification and Characterization of Genes Expressed by the Midbrain Dopaminergic Neurons

**Group Jacqueline Trotter, Neurobiology**

Brigitte Schauwienold (2001)
Klonierung und Charakterisierung von BS1, einem Mitglied der RUN-Familie

Corinna Klein (2001)
Signaltransduktion zum Zytoskelett in Oligodendrozyten während der Myelinisierung

Judith Stegmüller (2002)
Molekulare Analyse des Proteoglykans NG2/AN2 und Identifizierung von seinen intrazellulären Bindungspartnern in glialen Zellen

**Group Klaus Unsicker, Neuroanatomy**

Heike Specht (2001)
Subzelluläre Lokalisation und Mechanismen der Sekretion von transformierenden Wachstumsfaktoren & in neuronalen Zellen