2nd Annual Symposium of the International Graduate School ABINEP

September 02nd – 04th, 2019

Keynote Speakers

Prof. Dr. Maria J. G. T. **Vehreschild**

(Cologne, Germany)

Dr. Sanja **Mikulovic**

(Bonn, Germany)

Dr. Sonja M. **Best**

(Hamilton, USA)

Prof. Dr. Tobias H. **Donner**

(Hamburg, Germany)

Merseburg, Germany

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ESF
Europäischer Sozialfonds

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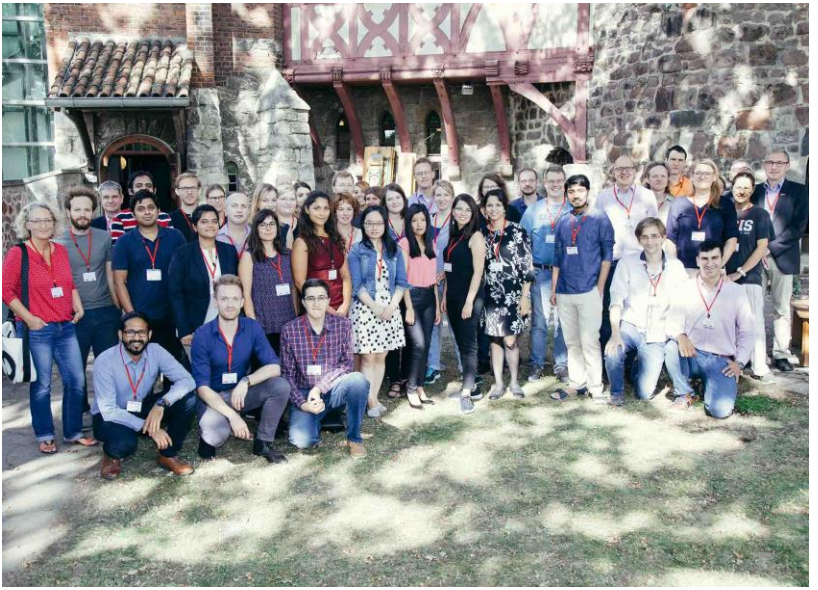

ABINEP Students

The international Graduate school (GS) on Analysis, Imaging, and Modeling of Neuronal and Inflammatory Processes (**ABINEP**) is based on the two internationally recognized biomedical research foci of the Otto-von-Guericke-University Magdeburg (OVGU), Neurosciences and Immunology, ABINEP aims at fostering cutting edge research projects in rising sub-disciplines of these research areas, which are currently supported by several German Research foundation (DFG)- and European Community (EU)-funded collaborative projects in Magdeburg including the DFG-funded Collaborative Research Centers SFBs 779 and 854 and associated graduate schools, as well as DFG TRRs 31 and 62.

The program includes scientists from the **Medical Faculty/ University Hospital Magdeburg (FME)** and the **Faculty of Natural Sciences (FNW)** of the OVGU, the **Institute for Neurobiology (LIN)** and **German Center for Neurodegenerative Diseases (DZNE)**, both located in Magdeburg, the **Helmholtz Centre of Infection Research** in Braunschweig as well as international collaborators.

Sponsors

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Special thanks to

Jens Strackeljan, Monika Brunner-Weinzierl, Volkmar Leßmann, Constanze Seidenbecher, Christiane Hedtmann and Anke Ryll for administrative support.

All ABINEP Students for contributing to organize this annual symposium.

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Foreword

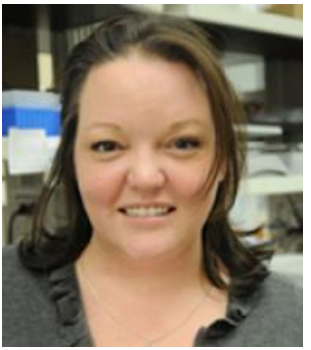
Welcome to the ABINEP Student Symposium 2019, the annual symposium for graduate students from the International Graduate School on Analysis, Imaging and Modeling of Neuronal and Inflammatory Processes.

The ABINEP Symposium provides graduate students with the opportunity to present their research and network with like-minded colleagues in a professional environment. This experience is invaluable for young graduate students, many of whom will continue on to present at national and international conferences. In addition, the ABINEP Symposium allows graduate students from across Magdeburg to learn about exciting research being conducted by their peers, whether from different institutes or from across different disciplines. We hope that the knowledge gained from this symposium will aid in stimulating new research ideas and establishing future collaborations.

The ABINEP Symposium will connect brain researchers from across Magdeburg research institutes and will include oral presentations and posters spanning four unique themes comprised of: inflammatory processes in neurodegeneration (Module 1), neurophysiology and computational modeling of neuronal networks (Module 2), infection and immunity in the context of aging (Module 3), and human brain imaging for diagnosing neurodegenerative disorders (Module 4). Attendees are also invited to a poster session with ABINEP students to highlight the outstanding presentations and projects. This would give us an opportunity for a networking session where we all can discuss the

exciting research we've been exposed to throughout the course of these two days (over a cup of coffee, of course)!
Thank you for attending our ABINEP Student Symposium, we encourage you to actively connect with your fellow research students within and outside of your discipline.

Keynote Speakers



Dr. Sonja M. Best (Hamilton, USA)
Guest speaker, Module 1

Beyond retroviruses: restriction of flavivirus replication by TRIM5α.

Ph.D. Sonja M. Best and her research team focuses on the innate immunity and pathogenesis of the flaviviruses West Nile virus (WNV) and tick-borne encephalitis virus (TBEV). They investigate the role of novel interferon (IFN) - stimulated genes (ISGs) in the antiviral response against virus infection. Especially, the role of tripartite motif (TRIM) proteins in host resistance to flavivirus replication is examining. Furthermore, Sonja Best and her team are interested in the importance of dendritic cells (DC) function to the antiviral response of the innate and adaptive immune system.

Dr. Sanja Mikulovic (Bonn, Germany)
Guest speaker, Module 2

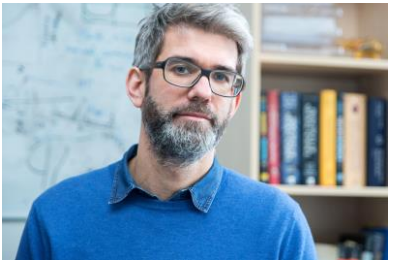
Hippocampal neuronal networks underlying cognitive, emotional and motor learning

Dr. Sanja Mikulovic is currently working as a post-doctoral researcher at the Lab of Prof. Remy in the German Centre for Neurodegenerative Diseases (DZNE) Bonn, Germany.
Her research focuses on the study of neuronal circuits that underlie motor learning and emotion-related behaviors, such as hippocampal oscillations. To this end, she applies optogenetics, 2-photon imaging and electrophysiology in vivo, as well as computational methods for automated behavioral analysis.

Prof. Dr. Maria J. G. T. Vehreschild (Cologne, Germany)
Guest speaker, Module 3

Microbiota-based infection prevention – A clinical perspective

Prof. Dr. Maria J.G.T. Vehreschild is the head of the AG Clinical Microbiology Research at the University Hospital Cologne. Prof. Maria J.G.T. Vehreschild and her team focus on the influence of the human microbiome on different clinical pictures. Currently, she is working on a clinical and scientific program for intestinal flora transmission in recurrent *C. difficile* infection. The working group was able to set up a clinical and scientific program for intestinal flora transmissions at the university of cologne. In collaboration with the translational research platform of CECAD they have successfully treated patients with recurrent *C. difficile* infections without endoscopic support, simply by administering cryopreserved intestinal flora. Another research focus of her group is the analysis of preventative and therapeutically approach to handle the rising problem of colonization and infection with multidrug-resistant pathogens in patients.



Prof. Dr. Tobias H. Donner (Hamburg, Germany)
Guest speaker, Module 4

Understanding Variability in Brain and Behavior

Dr. Donner's research focuses on the understanding of the neuromodulation of cortical dynamics and decision computations; in particular how specific neuromodulatory systems remodel the cortical network dynamics underlying decisions. With his group, he tries to investigate this process at different level of analysis of human brain function: quantitative analysis of behaviour, computational modelling of the underlying algorithmic and neural processes, multimodal neuroimaging (fMRI and MEG) measurements of these processes, and pharmacological intervention to pinpoint the role of the specific neurotransmitter systems involved.

ABINEP Institutes

BMMR = Biomedizinische Magnetresonanz
DZNE = Deutsches Zentrum für Neurodegenerative Erkrankungen
FME = Medizinische Fakultät
FNW = Fakultät für Naturwissenschaften
HZI = Helmholtz-Zentrum für Infektionsforschung
IBIO = Institut für Biologie
IBZ = Institut für Biochemie und Zellbiologie
IEIM = Institut für Experimental Internal Medicine
IEP = Institute of Experimental Physics
IfP = Institute of Psychology
IHG = Institut für Humangenetik
IIN = Institut für Inflammation und Neurodegeneration
IKND = Institut für Kognitive Neurologie und Demenzforschung
IMMB = Institut für Medizinische Mikrobiologie und Krankenhaushygiene
IMKI = Institut für Molekulare und Klinische Immunologie
IPA = Institut für Pathologie
IPHY = Institut für Physiologie
IPSY = Institut für Psychologie
IPT = Institut für Pharmakologie und Toxikologie
LIN = Leibniz-Institut für Neurobiologie
KGHI = Universität für Gastroenterologie, Hepatologie und Infektiologie
KHAE = Universitätsklinik für Hämatologie und Onkologie
KHNO = Universitätsklinik für Hals-Nasen-Ohrenheilkunde, Kopf-und Halschirurgie
KNEU = Universität für Neurologie
KNEP = Universitätsklinik für Nieren –und Hochdruckkrankheiten, Diabetologie und Endokrinologie
KOBI = Cognitive Biology Group at IBIO
KORT = Orthopädische Universitätsklinik
KPNE = Universitätsklinik für Pneumologie
OVGU = Otto-von-Guericke Universität
UKMD = Universitätsklinikum Magdeburg

ABINEP Fellows and Supervisors

Module 1: Neuroinflammation: Inflammatory Processes in Neurodegeneration

(Students Names are in *Italics* and Supervisor(s) Names are in **Bold**)

1) Ms. Sarah Schreier

Prof. Dr. rer. nat. Daniela Dieterich (OVGU, FME, IPT)

Prof. Dr. rer. nat. Andrea Kröger (OVGU, FME, IMMB)

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2) *Mr. Timothy French*

Prof. Dr. rer. nat. Ildiko Dunay (OVGU, FME, IIN)

PD Dr. rer. nat. Björn Schott (LIN)

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3) Ms. Ayse Malci

Prof. Dr. rer. nat. Eckart Gundelfinger (LIN)

Prof. Dr. rer. nat Michael Naumann (OVGU, FME, IEIM)

Prof. Dr. rer. nat. Constanze Seidenbecher (LIN)

4) Ms. Rituparna Bhattacharjee

PD Dr. rer. nat. Eike Budinger (LIN)

PD Dr. med. Jürgen Goldschmidt (LIN)

Dr. rer. nat. Xu Wang (OVGU, FME, IMMB)

Dr. rer. nat. Nishanth Gopala (OVGU, FME, IMMB)

Prof. Dr. med. Dirk Schlüter (MHH)

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5) Ms. Carla Marcia Cangalaya Lira

Prof. Dr. rer. nat. Klaus-Dieter Fischer (OVGU, FME, IBZ)

Prof. Dr., Ph.D. Alexander Dityatev (DZNE)

Dr., Ph.D. Stoyan Stoyanov (DZNE)

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Module 2: Neurophysiology and Computational Modeling of Neuronal Networks

(Students Names are in *Italics* and Supervisor(s) Names are in **Bold**)

1) Mr. Babak Khodaie

Prof. Dr. rer. nat. Volkmar Leßmann (OVGU, FME, IPHY)

Dr. rer. nat. Elke Edelmann (OVGU, FME, IPHY)

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2) Mr. Ehsan Kakaei

Prof. Dr., Ph.D. Jochen Braun (OVGU, FNW, IBIO)

Prof. Dr. rer. nat. Oliver Speck (OVGU, FNW, BMMR)

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3) Ms. Evangelia Pollali

Prof. Dr. sc. nat. Oliver Stork (OVGU, FNW, IBIO)

Dr. rer. nat. Thomas Munsch (OVGU, FME, IPHY)

4) Mr. Vivekanandhan Viswanathan

Prof. Dr. rer. nat. Frank Ohl (OVGU, FNW, IBIO, LIN)

Dr. rer. nat. Andreas Schulz (LIN)

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5) Mr. Babak Saber Marouf

Dr., Ph.D. Motoharu Yoshida (DZNE, LIN)

Prof. Dr., Ph.D. Magdalena Sauvage (LIN)

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Module 3: Immunosenescence: Infection and Immunity in the Context of Aging

(Students Names are in *Italics* and Supervisor(s) Names are in **Bold**)

1) Ms. Lisa Osbelt

Prof. Dr. med. Thomas Fischer (OVGU, FME, KHAE)

Prof. Dr. med. Dirk Schlüter (MHH)

Prof. Dr. Till Strowig (HZI)

OA Dr. med. Enrico Schalk (OVGU, FME, KHAE)

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2) Ms. Ann-Kathrin Meinshausen

Prof. Dr. rer. nat. Jessica Bertrand (OVGU, FME, KORT)

Prof. Dr. med. Christoph Lohmann (OVGU, FME, KORT)

Prof. Dr. rer. nat. Dietmar Pieper (HZI)

Dr. Eva Medina (HZI)

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Dr. rer. nat. Julia Boehme (OVGU, FME, IMMB, HZI)

Prof. Dr. Till Strowig (HZI)

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4) Ms. Aneri Tusharbhai Shah

Prof. Dr. rer. nat. Ingo Schmitz (OVGU, FME, IMKI, HZI)

Prof. Dr. med. Peter Mertens (OVGU, FME, KNEP)

Dr. rer. nat. Xenia Gorny (OVGU, FME, KNEP)

Prof. Dr. rer. nat. Dunja Bruder (OVGU, FME, IMMB, HZI)

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5) Ms. Isabel Bernal

Prof. Dr. rer. nat. Dunja Bruder (OVGU, FME, IMMB, HZI)

Prof. Dr. med. Ali Canbay (OVGU, FME, KGHI)

Prof. Dr. rer. nat. Lothar Jänsch (HZI)

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6) Ms. Ulrike Pfohl

Prof. Dr. med. Christoph Arens (OVGU, FME, KHNO)

Prof. Dr. rer. nat. Michael Naumann (OVGU, FME, IEIM)

Prof. Dr. med. univ. Dr. sc. nat. Johannes Haybaeck (OVGU, FME, IPA)

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Module 4: Human Brain Imaging for Diagnosing Neurocognitive Disorders

(Students Names are in *Italics* and Supervisor(s) Names are in **Bold**)

1) Ms. Beatrice Barbazzeni

Prof. Dr. med. Emrah Düzel (OVGU, FME, IKND, DZNE)

Prof. Dr. rer. nat. Oliver Speck (OVGU, FNW, BMMR)

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2) Mr. Sharavanan Ganesan

Prof. Dr. phil. Stefan Pollmann (OVGU, FNW, IPSY)

Prof. Dr. Elena Azañón (OVGU, IPSY)

---

3) Ms. Camila Silveira Agostino

Prof. Dr. rer. nat. Tömme Noesselt (OVGU, FNW, IPSY)

Prof. Dr.-Ing. Hermann Hinrichs (OVGU, FME, KNEU)

4) Ms. Julia Rogge

Prof. Dr. med. Markus Ullsperger (OVGU, FNW, IPSY)

PD Dr. rer. nat. Gerhard Jocham (Heinrich-Heine-University Düsseldorf)

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5) Mr. Stefan Repplinger

Dr. phil. Tino Zähle (OVGU, FME, KNEU)

Prof. Dr. med. Hans-Jochen Heinze (OVGU, FME, KNEU)

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Program

ABINEP Symposium 2019
of the International Graduate School ABINEP

Sep 02nd-04th, 2019 | Merseburg, GER

Program September 02, 2019

13:00-13:30	**Welcome Lunch**
13:30-13:45	**Welcome by Prof. Dr. Volkmar Leßmann**
Session I:	**Module 3 -** Immunosenescence: Infection and Immunity in the Context of Aging *Chairs: Lisa Osbelt, Julia Rogge*
13:45-14:55	*Guest speaker-* **Prof. Dr. Maria J.G.T Vehreschild** *Microbiota-based infection prevention – A clinical perspective*
14:55-15:10	**Lisa Osbelt** *Influence of the microbiota composition on the individual susceptibility towards infections*
15:10-15:25	**Coffee Break**
15:25-15:40	**Aneri Shah** *Role of Y-box binding protein 1 in activation of NF-κB signaling pathway downstream*
15:40-15:55	**Ann-Kathrin Meinshausen** *The terminal complement pathway identifies prosthesis infection in periprosthetic tissue samples*
15:55-16:10	**Alexander Pausder** *Impact of immunomodulating substances on pneumococcal colonization of the respiratory tract in murine allergic asthma*
16:10-16:25	**Ulrike Pfohl** *Uncovering the role of mutant SMAD4R361H in colorectal cancer using patient-derived 3D models*
16:30-17:30	**Poster Session**
17:30-18:30	**'PhD students and Guest speakers only' round table (Modules 3 & 4)**
19:00	**Dinner**

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Program September 03, 2019 – Part I

09:00-09:05	**Welcome**
Session II:	**Module 4-** Human Brain Imaging for Diagnosing Neurocognitive Disorders *Chairs: Beatrice Barbazzeni, Ayse Malci*
09:05-10:15	*Guest speaker-* **Prof. Dr. Tobias H. Donner** *Understanding Variability in Brain and Behavior*
10:15-10:30	**Beatrice Barbazzeni** *Cognitive Training Based on EEG-Neurofeedback to Improve Working Memory in Healthy Volunteers*
10:30-10:50	**Coffee Break**
10:50-11:05	**Camila Agostino** Predicting occluded trajectories using temporal information as predictor
11:05-11:20	**Stefan Repplinger** *Into the Deep – Intracranial Recordings from the Human Substantia Nigra*
11:20-11:35	**Sharavanan Ganesan** *Single target visual search training in simulated central vision loss - A pilot study*
11:35-12:30	**Future Perspectives: ABINEP Lecture/Workshops 2020 (Organizers only)**
12:30-13:30	**Lunch**

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Program September 03, 2019 – Part II

12:30-13:30	**Lunch**
Session III:	**Module 2-** Neurophysiology and Computational Modeling of Neuronal Networks *Chairs: Evangelia Pollali, Rituparna Bhattacharjee*
13:30-14:40	*Guest speaker-* **Dr. Sanja Mikulovic** Hippocampal neuronal networks underlying cognitive, emotional and motor learning
14:40-14:55	**Evangelia Pollali** *The GAD65 KO mouse model of reduced GABAergic synthesis: changes in hippocampal network oscillations and single cell properties*
14:55-15:15	**Coffee Break**
15:15-15:30	**Babak Saber Marouf** *Role of TRPC Channels in Temporal Bridging and Spatial Navigation in the Hippocampal-Entorhinal Circuit*
15:30-15:45	**Ehsan Kakaei** *Spontaneous versus physical reversals of kinetic depth (KDE): a whole-brain fMRI study*
15:45-16:00	**Babak Kodaie** *Modulation of spike timing-dependent LTP at Schaffer collateral-CA1 synapses along the longitudinal axis of the mouse hippocampus*
16:00-16:15	**Vivekanandhan Viswanathan** *A rat model of reward conditioning using optogenetic VTA stimulation*
16:20-17:20	**'PhD students-Guest speakers only' round table (Modules 1 & 2)**
17:30-19:00	**Get Together – Guided Tour**
19:00	**Dinner**

ABINEP Symposium 2019
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Sep 02nd-04th, 2019 | Merseburg, GER

Program September 04, 2019

09:00-09:10	**Welcome**
Session IV:	**Module 1-** Neuroinflammation: Inflammatory processes in Neurodegeneration *Chairs: Ayse Malci, Vivekanandhan Viswanathan*
09:10-10:20	*Guest speaker-* **Dr. Sonja Best** *Beyond retroviruses: restriction of flavivirus replication by TRIM5α.*
10:20-10:35	**Ayse Malci** *Neuroplastin-plasma membrane Ca2+ ATPase complexes: Are they new players in Ca2+ signaling and synaptic plasticity?*
10:35-10:50	**Coffee Break**
10:50-11:05	**Rituparna Bhattacharjee** *Early events leading to Experimental Cerebral Malaria (ECM) associated brain pathology*
11:05-11:20	**Carla Marcia Cangalaya Lira** *Cytoskeleton-dependent mechanisms of the microglia-extracellular matrix-neuron interaction during neuroinflammatory processes*
11:20-11:35	**Sarah Schreier** *Cell specific regulation of antiviral response in astrocytes during CNS infection*
11:35-11:50	**Timothy French** *Neuronal impairment following chronic Toxoplasma gondii infection is aggravated by intestinal nematode challenge in an IFN-γ-dependent manner.*
11:50-12:00	*Goodbye Words* **Prof. Leßmann**
12:00-13:10	**Photograph session + Lunch**
13:20	**Departure**

ABINEP Symposium 2019
of the **International Graduate School ABINEP**

Sep 02nd-04th, 2019 | Merseburg, GER

Program September 02, 2019 – Poster Session

16:30-17:30 **Poster Session**

Julia Rogge
Beta-lateralisation builds up over time throughout a delay
Evangelia Pollali
The GAD65 KO mouse model of reduced GABAergic synthesis: changes In hippocampal network oscillations and single cell properties
Ulrike Pfohl
Uncovering the role of mutant SMAD4R361H in colorectal-tumor-derived 3D cultures (PD3D®)

Keynote Speaker Talks

Beyond retroviruses: restriction of flavivirus replication by TRIM5α.

Dr.Sonja Best

TRIpartite Motif (TRIM) proteins belong to a large family of proteins, many of which are inducible by type I interferon and serve to suppress virus infection through direct interactions with viral proteins to disrupt viral replication. Primate TRIM5α is a consequential inhibitor that suppresses lentivirus replication (e.g HIV-1) in a highly host species- and virus species-specific fashion to limit cross-species transmission of these viruses. Importantly, the antiviral effects of TRIM5α are thought to function exclusively in the context of lentivirus infection. Our research interests center on the flaviviruses, which include significant pathogens that have emerged into human populations from primates (e.g. dengue virus, Zika virus, yellow fever virus), prompting us to determine whether TRIM5α could also function to inhibit flavivirus replication. Surprisingly, this work has revealed a new function for TRIM5 as a potent restriction factor for replication of specific flaviviruses. The mechanisms of restriction and its implications for flavivirus emergence and evolution will be discussed.

Hippocampal neuronal networks underlying cognitive, emotional and motor learning

Dr. Sanja Mikulovic

Hippocampal neuronal networks play a pivotal role in movement control, cognitive and emotional information processing. Theta oscillation (4-12 Hz) is one most prominent rhythms of the brain. Emerging research evidence points to the existence of several theta subtypes related to movement, cognition and emotion. Theta frequency has been shown to predict the intensity of subsequent locomotion, but also the processing of emotion-related stimuli. However, little is known about neuronal circuits underlying di- ferent types of theta rhythms. Here, I present the role of oriens-lacunosum/moleculare expressing Chrna2 receptor (OLMα2) interneurons in regulating specific type of theta activity and controlling cogn- tive and emotional information processing. Furthe- more, I will present the role of different excitatory and inhibitory cell types involved in motor- versus aversion-related learning. We used a combination of optogenetics and local field potential recordings to study the role of OLMα2 interneurons in regulating hippocampal oscillations, cognitive and emotional information processing. We furthermore use 2 Pho- ton Calcium imaging to study the involvement of di- ferent cell types in motor, appetitive and aversive learning. We show that ventral hippocampus OLM cell stimulation in vivo generates cholinergicdepenent type 2 theta oscillations in both anesthetized and freely behaving mice. We further show that type 2 theta can coexist with movement-driven type 1 theta activity. Theta

oscillations induced by OLMα2 cell stimulation were directly related to a considera- ble increase in risk-taking behavior in a predatory odor innate anxiety test. We further show that OLMα2 interneurons control cognitive and emotional learning. Finally, I will show the involvement of different hippocampal cell types related to motor, appetitive and aversive learning. Conclusion: I propose that different, and in some cases overlapping, neuronal networks underlie diverse oscillatory subtypes and different forms of learning.

Microbiota-based infection prevention – A clinical perspective

Prof. Dr. Maria J.G.T Vehreschild

Commensal bacteria play a major role in the regulation of homeostasis, but may also turn into pathogens, particularly in the immunocompromised patient. The introduction of antibiotics must be considered a milestone in the history of human medicine and is currently necessary to treat these infections. The global threat of emerging antibacterial resistance has, however, created an increasing awareness of the associated complications and limitations of this treatment approach. In this setting, the exploration of alternatives to antibiotic treatment and prophylaxis is gaining considerable traction. In this presentation, microbiota-based alternatives, including refined antimicrobial stewardship, phages, antibodies, probiotics and fecal microbiota transfer products will be presented and discussed in their capacity restore and/or protect the microbiota and thus maintain colonization resistance.

Understanding Variability in Brain and Behavior

Prof. Dr. Tobias H. Donner

Variability is a pervasive feature of neural activity and behavior. Several theories postulate that variability is fundamental for adaptive brain function. I propose that understanding the sources and functional role of neural variability requires partitioning the variability of observed behavior. One partition is, in fact, only "apparent variability": it is caused by dynamic variations in systematic decision biases (not decision noise), which often remain hidden. Only the second partition is "genuine variability", which results from the inherent noisiness of cortical neurons.

To support this claim, I will present our recent work on perceptual decision-making under uncertainty. We find that a large portion of the variability in perceptual choice behavior can be explained by dynamic trial-to-trial modulations of decision biases: apparent variability. Those bias modulations are induced by the history of previous choices as well as by phasic arousal transients during decision formation. They are implemented by systematic modulations of the underlying cortical activity states. In another line of work, we show that the level of genuine variability in perceptual choice is controlled by a major neuromodulatory system – the norepinephrine system – likely through altering the balance between excitation and inhibition in cortical networks. This line of work points to an adaptive function of noise in perceptual inference. I conclude that pinpointing the factors governing

apparent behavioral variability and identifying control mechanisms for genuine behavioral variability will enable a deeper understanding of brain function.

ABINEP Fellows

Talks and Posters

Influence of the microbiota composition on the individual susceptibility towards infections

Osbelt L [1,2,3,4], Schalk E [1,3], Schlüter D [1,2], Thomas F [1,3], Strowig T [1,4]

[1]ESF International Graduate School on Analysis, Imaging and Modelling of Neuronal and Inflammatory Processes
[2]Microbial Immune Regulation, Helmholtz Centre Infection Research, Braunschweig
[3]Clinic for Oncology and Hematology, Otto-von-Guericke University, Magdeburg, Germany
[4]Institute for Medical Microbial Microbiology and Hygiene, Otto-von-Guericke University, Magdeburg, Germany

Infectious diseases caused by multidrug-resistant gram-negative bacteria (MRGN) are a major problem during the therapy of hematological-oncological patients associated with prolonged hospital stays and increasing mortality rates (1), (2). In healthy humans, the microbiota, a complex community of bacteria, archaea, fungi and eukaryotes colonizing all body surfaces provides colonization resistance against invading pathogens. There is evidence that the susceptibility towards infection as well as the development and course of mucositis, colitis and GvHD is also associated with changes in the microbiome of patients (3-5). During this project, we aim to investigate the role of the microbiome composition and its ecological factors regarding the susceptibility to infections and persistence of MRGN in cytostatic-treated mice and leukemic patients.
To address these questions, we characterized the microbiome composition of healthy and drug-

treated mice and humans in multiple ways including sequencing and culture-depending approaches. Inoculation of stool samples with MRGN *K.pneumoniae* lead to various outcomes. As expected, drug treated samples could be successfully colonized, whereas untreated mice showed a relatively high degree of colonization resistance. Strikingly, in vitro inoculation of human feces with *K. pneumoniae* has resulted in large donor-specific differences (>1000x) in the *in situ* growth of the pathogen. Different factors seem to contribute to the observed variations, including variations of short-chain fatty acid (SCFA) levels, pH-value, bacterial composition and species richness. In future, we would like to unravel the complex interplay between pH-value, SCFA concentrations and bacterial species conferring resistance against MRGN colonization to facilitate the development of patient-specific microbiota-based decolonization strategies.

Role of Y-box binding protein 1 in activation of NF-κB signaling pathway downstream

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The immune system constitutes the first line of defense against invading pathogens. Phagocytic cells like monocytes/macrophages combat and clear pathogens and coordinate immune responses via the secretion of cytokines like tumor necrosis factor (TNF), IL-1, IL-6, IL-8 and IL-12. The cold-shock Y-box binding protein 1 (YB-1) is important for monocyte/macrophage differentiation and phagocytic function. Macrophage polarization is impaired when YB-1 is genetically deleted in monocytes/macrophages, i.e. *Ybx1*$^{\Delta LysM}$. Mechanism of phagocytosis also involves activation of intracellular signaling cascades, amongst others leading to the activation of NF-κB. To test for the crosstalk between YB-1 and NF-κB signaling in the orchestration of monocyte and macrophage function, we established two systems: lentiviral transduced YB-1 knockdown monocytic THP-1 cells and bone marrow-derived macrophages *Ybx1*$^{\Delta LysM}$. Both systems show a prominent role of YB-1 in the activation of the NF-κB subunit p65. Imaging flow cytometry in-

dicated reduced nuclear translocation of NF-κB p65 in YB-1 knockdown cells after TNF stimulation compared to controls. Expression of Tumor necrosis receptor-associated factor-2 (Traf-2), which is required for NF-κB activation upon TNF stimulation, was significantly reduced in the absence of YB-1. This suggests YB-1 may play an important role in the recruitment of Traf-2 to the receptor or alternatively YB-1 may regulate Traf-2 expression.

The terminal complement pathway identifies prosthesis infection in periprosthetic tissue samples

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Low-grade infections cannot be easily distinguished from aseptic complications frequently leading to false negative diagnoses and late onset of antibacterial therapy. Therefore, there is a great need to establish biomarkers for early detection of low-grade infections. In this study, we proved anti-α-defensin, anti-C3, anti-C5 and anti-C9 as potential biomarkers for infection in a cohort of septic revision cases. Here we included 78 patients with septic and aseptic revision surgeries. CRP values and WBC count were evaluated. Patient characteristics, number of prior revision surgeries and comorbidities were recorded. Periprosthetic tissue was stained immunhistologically with different antibodies. The CRP values were significantly increased in the septic cohort, but no changes were observed in leucocyte count. Interestingly, we found a strong increase in the terminal complement system component C9 (p=.0004) in the septic periprosthetic tissue. The predictive value of α-defensin staining was not statistically significant (p= .09). Analyzing the synovial fluid of aseptic and septic patients, the presence of C9 in the septic group was not signifi-

cantly higher compared to the aseptic group. After that we investigate the specificity C9 detection using different joint related diseases such as chondrocalcinosis (CC), rheumatoid arthritis (RA) and metallosis. The median of C9 staining in the CC group was significant lower than the infection group. Similar results have been observed in RA and the metallosis group. We found a strong predictive value of anti-C9 staining for tissue infection, suggesting that C9 deposition could be a novel biomarker for the identification of periprosthetic joint infections using tissue biopsies.

Impact of immunomodulating substances on pneumococcal colonizationof the respiratory tract in murine allergic asthma

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Streptococcus pneumoniae colonizes the human nasopharynx and is the predominant pathogen in the upper airways of asthmatic patients. Asthma was identified as a risk factor for severe pneumococcal disease. The transfer of secretory immunoglobulins into the mucosal lumen by the polymeric immunoglobulin receptor (pIgR) is an essential mechanism of mucosal host defense in the respiratory tract. The identification of immunomodulating agents that enhance epithelial *Pigr* gene expression might have therapeutic implications. To analyze the influence of immunomodulating substances on pneumococcal colonization of the respiratory tract in a murine model of allergic asthma. *Pigr* gene expression in lung, trachea and nasal-associated lymphoid tissue (NALT) of naïve, LPS-, IFN-gamma- and IL-4-treated mice was analyzed by q-PCR. Mice were infected with *Streptococcus pneumoniae* and respiratory bacterial burden was determined at dif-

ferent time points. Mice were intranasally treated with house dust mite extract (HDM) once a week over 3 weeks. HDM-triggered immune responses were assessed by flow cytometric analyses of leukocyte subsets in spleen, lung and bronchoalveolar lavage (BAL). *Pigr* gene expression gradually decreases from the upper to the lower respiratory tract. LPS-treatment caused increased *Pigr* gene expression in the lung. IFN-gamma- and IL-4-treatment led to decreased *Pigr* gene expression in the trachea while lung and NALT showed no alterations. The upper respiratory tract was colonized by *S. pneumoniae* up to 9 days post infection. HDM-treatment triggered airway eosinophilia. Basal *Pigr* gene expression is site-specific and can be partly modulated by proinflammatory stimuli. A pneumococcal colonization model of the upper respiratory tract was established. HDM-treatment led to an allergic phenotype in the airways. Other important aspects of murine asthma will be investigated.

Uncovering the role of mutant SMAD4^{R361H} in colorectal cancer using patient-derived 3D models

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SMAD4, one of the most frequently mutated genes in colorectal cancer (CRC), is associated with a decreased overall survival of CRC patients and is suspected to modulate chemoresistance. The aim of the present study is to generate CRISPR-engineered SMAD4^{R361H} CRC organoids from patient-derived SMAD4^{wt} cells as a model to study the effects of this mutation on drug response *in vitro.* We have engineered isogenic organoids (SMAD4^{R361H}) from SMAD4^{wt} organoids using CRISPR-Cas9 genome-editing to investigate the mechanism of drug re-

sistance. Single clones were isolated and genotyped by locus specific PCR to confirm the particular R361H point mutation. We successfully established four isogenic clones. SMAD4^{wt}, SMAD4^{R361H} mutated organoids directly obtained from the same tumor as well as SMAD4^{R361H}-engineered organoids were subjected to a semi-automated *in vitro* drug screening, allowing for a direct comparison of their respective drug sensitivities. Native SMAD4^{R361H} and engineered organoids were more resistant to small molecules (e.g. EGFR-inhibitors) in comparison to SMAD4^{wt} organoids. Interestingly, engineered organoids were more sensitive to the MEK-inhibitor trametinib in comparison to SMAD4^{wt} organoids. Results clearly show that SMAD4^{R361H} modulates the therapy response *in vitro*, underlining their prominent role in discovering the connection between genotype and phenotype in complex PD3D models. While this approach is not limited to studying the role of the R361H mutation, it has a broad range of applications in understanding cancer biology, intratumor heterogeneity, drug response and may eventually lead to new clinical insights, including design of new therapeutic strategies.

Beta-lateralisation builds up over time throughout a delay

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Decision making requires the perception and processing of surrounding stimuli. Brain activation studies (electroencephalography [EEG]) report a gradual decrease of beta-power (12-25 Hz) which lateralizes throughout such tasks (Fischer, Nigbur, Klein, Danielmeier, & Ullsperger, 2018) and peaks over (pre-)motor areas just before a movement is executed (Donner, Siegel, Fries, & Engel, 2009). This pre-movement signal potentially serves as a neural representation of the decision formation process and we try to distinguish it from a mere motor execution signal. We predict beta-lateralisation (BL) slopes to reflect stimulus evidence strength as well as faster responses and fewer errors with increasing strength. BL is further expected to peak at decision formation irrespective of the response time. Two variations of the random dot motion (RDM) paradigm were presented to 30 young healthy humans (12 females) during 64-channel EEG recordings. They indicated their choices about left- or rightward motion with the corresponding button press, either upon decision or

after a delayed cue. Dot-stimuli varied in evidence strength between trials. Reactions are slower and accuracy lower with decreasing evidence strength. Strikingly, BL rises gradually towards a peak just before the response in the immediate as well as the delayed version of the task. Specifically, BL onset latency at around 400ms after stimulus onset does not differ between immediate and delayed responses. Contrary to our hypothesis, BL slope is not modulated by evidence strength. The onset of BL before the imperative response cue in the delayed task variant makes it potentially suitable as a readout of decision making and motor preparation, not just motor execution.

Cognitive Training Based on EEG-Neurofeedback to Improve Working Memory in Healthy Volunteers

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Working memory (WM) has been associated with brain oscillatory activity, attention and motivation to learn while encoding new stimuli. We investigated whether providing individuals online feedback about their ongoing brain oscillatory activity over several sessions can improve WM performance. We focused on brain oscillations, called alpha suppression, that are associated with the anticipation of monetary reward for correct performance in a WM trial. Thus, to improve WM in healthy volunteers, we combined WM training with EEG-Neurofeedback (NF) to enhance alpha suppression in a monetary-rewarded delayed match-to-sample task (DMST). Individuals were trained over five-days in double-blinded experiment. We investigated i) whether alpha suppression enhancement increases attention and whether monetary-reward increases motivation to learn while performing the DMST and ii) whether NF training facilitates the performance of different cognitive tasks. In Reward and No Reward conditions, participants were trained to suppress alpha receiving a real-time NF or a control NF (CO) of

their brain activity. Preliminary results show that while performing the DMST, the accuracy was significantly different from the first to the last training day in both groups only for the Reward condition ($P < .05$). Both groups showed a significant difference in RTs for both reward conditions ($P < .05$). Differently, while performing different cognitive tasks the accuracy level did not reach a significant difference when comparing training days and groups. Moreover, a significant difference in alpha suppression between training days has been found in the NF group only for the reward condition ($P < .05$).

Predicting occluded trajectories using temporal information as predictor

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Predicting trajectories and positions of occluded object is a core cognitive ability. Recent studies report even low-level visual cortex (V1) to be instrumental in the anticipation of upcoming apparent motion, when only the beginning of a sequence of events is presented. However, it remains unclear, if continuous motion is governed by the same mechanisms. Here, we investigate how the prediction of trajectories of occluded moving stimuli affects fMRI-responses focusing on low-level visual areas. We hypothesized that similar regions in V1 should be activated for the continuous and occluded yet predicted trajectory. In the training phase participants (n=20) were familiarized with speed trajectory associations (stimulus moving from left to the center and, then to the top (high/low velocity) or bottom (low/high velocity) of the screen, i.e. speed predicted trajectory). In the test phase, the vertical movement was occluded and participants judged where and when the stimulus would end, based on the speed of the horizontal. Results revealed that participants were always accurate in predicting the association between speed and direction (up-fast, down-slow, p=0.76; up-slow, down-fast, p=0.24), and in estimating time dis-

placement (fast-slow discrimination ability: p=0.05; 0.03). Preliminary fMRI-results (n=3) revealed that V1 also activates when the stimulus is occluded. Activation in the upper and lower portions of the calcarine fissure were seen when the occluded stimulus would end in the bottom or top of the screen, respectively. Together, the pattern of the results suggests that participants could be imagining the trajectories and lower-visual areas become responsive to this extrapolation.

Into the Deep – Intracranial Recordings from the Human Substantia Nigra

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Goal directed human behavior presupposes an implicit cost-benefit calculations determining the most appropriate action to reach a certain goal. The corresponding neural processes are represented in the basal ganglia. Via cortico-basal ganglia-thalamo-cortical loops, the instantiation and inhibition of actions are mediated. Dopaminergic substructures of the basal ganglia – namely the substantia nigra (SN) and ventral tegmental area (VTA) – play a crucial role in the maintenance of the balance between go and no-go signaling. A dysbalance between those extremes leads to severe neurological disorders. The neuroscientific investigation of this essential mechanism of human behavior mostly relies on animal research or indirect measurements using neuroimaging techniques such as fMRI. In our project, we bridge the gap between invasive electrophysiology in animals and noninvasive imaging in humans. For this purpose, we intraoperatively record from intracranial microelectrodes during implantation for Deep Brain Stimulation. Directly assessing the activity in the SN of patients suffering from Parkinson's disease, we elucidate its function with different paradigms. In a first

study, we show that activity in the SN is effort-sensitive. In a second study, we provide insights about the processing of social feedback in the SN. A third study highlights the SN as coding the predictability of sounds during acoustic stimulation. We provide direct evidence for the general role of the SN in approach and avoidance behavior in humans even in the absence of reward.

Single target visual search training in simulated central vision loss – A pilot study

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Patients with age-related macular degeneration (AMD) have poor central vision with an eccentric preferred retinal location (PRL). AMD patients have shown poor performance in visual search due to lack of memory-guided search with inefficient saccadic exploration. Saccades redirected to the new PRL, i.e., saccadic re-reference (SR), develops slowly after months of oculomotor adaptation following the PRL development. Recent studies on healthy participants with simulated central vision loss (sCVL) have shown that a predetermined retinal location, i.e., forced retinal location (FRL), can be induced and redirect saccades to FRL within few hours of training. But, these studies had manual target detection responses or poor choice of targets and distractors. To avoid these limit ations, a novel visual search training was administered to determine the hours of training required to produce FRL use in normal subjects with sCVL. Participants (N=5) were subjected to a single target search training ('X' in the presence of 'O's) during experimentally induced gaze-contingent scotoma of radius 1.75° for 5 days – an hour/day. FRL was defined as an area centered just below fixation. The average reaction time to search for a target in

the presence of distractors reduced with the training. A one-way repeated measures ANOVA on the reaction time showed a significant main effect of hours of training ($F(4,16) = 9.21$, $p < 0.001$). Our results from the pilot study show that 5 hours of training is enough to induce an FRL in healthy individuals. However, to investigate SR to FRL after training demands further research.

The GAD65 KO mouse model of reduced GABAergic synthesis: changes in hippocampal network oscillations and single cell properties

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Mice with targeted disruption of the gene for glutamic acid decarboxylase (GAD65 KO mice) display a postnatal deficit in γ-aminobutyric acid (GABA) synthesis, increased fear and anxiety. In the current study I examine GABAergic network activities and single cell properties in the ventral hippocampus (vHP) that may be involved in the emergence of this phenotype. For this reason, I performed local field potential recordings from acute slices including vHP and examined the spontaneous sharp-wave ripples (SW-R), the carbachol-induced gamma oscillations from Cornu Ammonis 1 (CA1) and 3 (CA3) and the synaptic plasticity of the circuit CA3-CA1. I found that the power and the peak frequency of gamma oscillations were significantly increased both in CA3 and CA1 subregions of GAD65 KO mice in comparison to wild-types (WT). In line, SW-R activity was altered and propagation failure from CA3 to CA1 was observed. Additionally, I performed patch clamp recordings in CA1 pyramidal neurons in order to investigate possible alterations

in single cells properties, that may contribute to the network alterations. These experiments, revealed unaltered intrinsic properties of CA1 pyramidal cells but moderate changes in their excitatory and inhibitory post-synaptic currents, that were dependent on the network oscillations. These findings suggest that reduced GABA availability in GAD65 KO mice may trigger long-term alterations in vHP network oscillations, which in turn may underlie the fear- and anxiety- phenotype of GAD65 KO mice. Augmented network oscillations in the vHP might be a risk factor for the development and persistence of fear memories and stress-related disorders.

Role of TRPC Channels in Temporal Bridging and Spatial Navigation in the Hippocampal–Entorhinal Circuit

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Working memory is a (part of) brain system that provides temporary storage and processing of essential information for different cognitive tasks. One of the intrinsic neurophysiological mechanisms to maintain the working memory is persistent activity of single cell during delay period. We hypothesize that hippocampus and entorhinal cortex use persistent firing by recruiting TRPC 4 and TRPC 5 channels. This allows these structures to retain necessary information and further process memory and behavior. To study the role of TRPC4 channels in hippocampus (mainly CA1), shRNA technique will be used to silence the TRPC4 channels in hippocampus. In the next step, the role of TRPC4 channels in spatial working memory will be studied using T-maze forced alternation task. After behavioural task, in-vivo electrophysiological recording will be started using implanted tetrode on CA1 during T-maze task to study the effect of TRPC4 silencing on electrophysiological characteristics of CA1 cells.

Modulation of spike timing-dependent LTP at Schaffer collateral-CA1 synapses along the longitudinal axis of the mouse hippocampus

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For many decades, the diversity along the hippocampal dorso-ventral axis has been neglected. Recent evidences showed that CA1 pyramidal cells are heterogeneous with respect to neuromodulation and input and output fibers. Furthermore, there is a gradient in plasticity related receptors along the dorso-ventral axis.
Our current focus is to test differences in the modulation of timing-dependent long-term potentiation (t-LTP) at Schaffer collateral (SC) -CA1 synapses along the dorso-ventral axis using spike timing dependent plasticity (STDP) with different low-repeat paradigms. After adding APV, our 6x 1:1 t-LTP was not impaired in dorsal and ventral slices, but dependent on NMDARs in the intermediate region. The 6x 1:4 t-LTP was not impaired in presence of APV. Further experiments were carried out to examine the role of dopamine in t-LTP along the dorso-ventral gradient. For the 6x 1:1 protocol we observed no D2 receptor effect on t-LTP in dorsal and intermediate slices. However, 6x 1:4 t-LTP was dependent on functional D2 signaling in the intermediate, but not in the dorsal slices. We addressed the inhibitory control of t-LTP along the dorso-

ventral axis. Our data revealed that the 6x 1:4 t-LTP remains intact in the absence of any GABAergic antagonists in both the intermediate and dorsal region, while 6x 1:1 t-LTP was impaired under these conditions. However, inhibition of $GABA_A$ and $GABA_B$ receptors did not reduce dorsal 6x 1:1 and 6x 1:4 t-LTP magnitude, but impaired t-LTP in the intermediate region.

Our data suggest that SC-CA1 t-LTP is differentially modulated and requires distinct Ca^{2+} sources for its induction along the dorso-ventral axis. Furthermore, the observed differences are critically dependent on subtle changes in the stimulation pattern used for induction of t-LTP.

A rat model of reward conditioning using optogenetic VTA stimulation

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To survive in an ever changing world, organisms have to adapt to changing stimulus-outcome contingencies. A major driving force for such adaptation is reward. In the mammalian brain, rewards are processed by the mesolimbic dopamine system, which—through the encoding of reward-prediction error —facilitates neuronal plasticity. Here we present a novel paradigm to measure the effects of reward conditioning through its influence on the acoustic startle response. We transduced the VTA of TH::Cre rats with ChR2 and implanted an optical fiber into the VTA, allowing specific stimulation of dopamine neurons. After two weeks of expression time, rats underwent a baseline startle measurement and seven consecutive sessions of optogenetic self-stimulation (US). Animals could only operate the selfstimulation nose poke in the presence of a visual cue (CS), but not in the absence of the cue. Following this operant conditioning, animals underwent a second startle test to assess the influ-

ence of visual cue presentation on startle. To compare our results to previous studies, we also include rats that underwent electrical, instead of optogenetic, self-stimulation. In both groups we find a reduction in startle amplitude following the presentation of the paired CS.

Neuroplastin–plasma membrane Ca^{2+} ATPase complexes: Are they new players in Ca^{2+} signaling and synaptic plasticity?

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Neuroplastins, type 1 transmembrane proteins with extracellular Ig-like domains, play a crucial role in synapse formation and stabilization. Our lab had shown that in neuroplastin-deficient mutant mice synaptic plasticity is reduced. Also, the protein levels of the four plasma membrane Ca^{2+} ATPases (PMCA) were found to be reduced. We and others have shown that neuroplastin binds PMCA to regulate Ca^{2+}-extruding activity in the plasma membrane. Thus, we are interested in the role of neuroplastin-PMCA-modulated synaptic Ca^{2+} signaling in activity-induced plastic changes of synapses. Ca^{2+}-dependent extracellular signal-regulated kinases (ERK) activation is well-known to be important for synaptic plasticity. Thus, we propose that the dysfunction of neuroplastin-PMCA complexes during pathophysiologically relevant conditions such as neuroinflammation should result in impaired plas-

tic capacity of neurons. Therefore, we hypothesize that neuroinflammatory conditions may alter the normal function of neuroplastin-PMCA-mediated calcium clearance, and in turn, impair downstream signaling cascades (Ca^{2+}-dependent ERK activation). Our preliminary results show that ERK phosphorylation and PMCA abundance are drastically altered in brain samples derived from neuroplastin-deficient mice. Furthermore, we monitored by immunoblot, STED microscopy as well as FLIM/FRET-based biosensors the activation of ERK and the dynamics of Ca^{2+} signals in synapses of cultured hippocampal neurons. We assessed the contribution of neuroplastin and PMCA to the activity-dependent plastic mechanisms using overexpression and extracellular peptides targeting neuroplastin and PMCA. In future, neuroplastin-PMCA driven signaling cascades will be studied under pathophysiological conditions by checking a potential relevance of the complex dysfunction in neuroinflammation models.

Early events leading to Experimental Cerebral Malaria (ECM) associated brain pathology.

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Cerebral malaria (CM) is a complex neurological syndrome of human malaria caused by the parasite *Plasmodium falciparum*. Experimental cerebral malaria (ECM), induced by *Plasmodium berghei* ANKA (*Pb*A), is the widely used rodent disease model to study CM. To understand the early events of the disease before the onset of clinical symptoms, one group of *Pb*A-infected mice was treated with pyrimethamine (anti-malarial drug) starting at day 5 post infection (p.i.) (asymptomatic stage) while the control group received phosphate buffered saline (PBS). SPECT imaging of control mice showed accumulation of radiolabelled-infected red blood cells throughout the brain with significant increase in the olfactory bulb, cortical and brainstem regions beginning at day 5 p.i. It is noteworthy that impairment of neurogenesis and disturbance of the

rostral migratory stream (RMS) were also detectable at day 5 p.i. which progressed until day 7 p.i. where the RMS was completely disrupted. Further immunohistochemistry analysis showed widespread brain pathology particularly in the olfactory bulb and the brain stem regions. Concomitantly, the chemokine and cytokine responses in these areas were also enhanced. Interestingly, anti-malarial treatment before the onset of clinical symptoms, was able to prevent the brain pathology to a greater extent and fostered recovery of the RMS. Taken together our study identifies the early events underlying ECM progression and suggests that early treatment before the onset of clinical symptoms would aid in complete recovery and may prevent the neurological sequelae.

Cytoskeleton-dependent mechanisms of the microglia-extracellular matrix-neuron interaction during neuroinflammatory processes

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Neuroinflammation is a common feature in dementias. Microglia functions and their ability to survey the neuropil can be impaired during neuroinflammation. Cytoskeleton dysfunction and overexpression of small GTPases in microglia, as well as upregulation in the extracellular matrix (ECM), have been reported in neurodegenerative diseases and dementia. Moreover, there is evidence that the enzymatic digestion of ECM, antibodies against specific ECM glycoepitopes and the treatment with inhibitors of small GTPases can restore the synaptic transmission/plasticity in dementia/ neuroinflammatory conditions. Thus, the perisynaptic ECM and cytoskeleton-dependent mechanisms are likely to play a crucial role in the interaction between microglia and synapses. In order to investigate these phenomena, we aim to study how ECM components and actin cytoskeleton regulate microglia-neurons interactions during inflammation. We will perform time-lapse studies of microglia interactions with

neurons and ECM, and the effects of this interaction on synapse formation/elimination under normal physiological conditions and in neuroinflammation. Moreover, we will investigate the role of small GTPases and actin cytoskeleton-regulated processes in microglia interactions with neurons and ECM. To perform these studies, we are using conditional knockout models of cytoskeletal regulators, and chondroitinase ABC injection/knockdown of specific ECM components for ECM attenuation. Microglia activation and interaction with synapses in vivo are studied using a single cell/spine photoablation with two-photon microscopy. Phagocytic functions of microglia are also evaluated by in vivo injection of fluorescently labeled A□42 and ex vivo analysis of intramicroglial localization of A□42/synaptic markers in fixed tissue by confocal microscopy and flow cytometry-based assays.

Cell specific regulation of antiviral response in astrocytes during CNS infection

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Tick-borne encephalitis virus (TBEV) is an important vaccine-preventable human pathogen. Patients can undergo severe meningo-encephalitis and sequelae from cognitive disorders and paralysis. The innate immune system plays an important role in the antiviral control of TBEV infection. The transcription factor IRF-7 is responsible for the induction of interferon β (IFN-β) and regulates a positive feedback loop to enhance antiviral immune response. In this work, we analyzed the impact of IRF-7 on astrocytes during a subclinical infection of Langat virus (LGTV), a live-attenuated member of TBEV. In comparison to WT mice, significantly more astrocytes are infected in IRF-7$^{-/-}$mice. Furthermore, an increased IFN-β production in the brain of LGTV infected IRF-7$^{-/-}$mice were detected. These findings suggest that the susceptibility of astrocytes to LGTV is regulated by IRF-7 and the production of IFN-β in astrocytes is independent of the positive feedback loop of the type I IFN system. To determine the role of astrocytes in antiviral response against TBEV, we will analyze protein expression by mass spectrometry (MS) using cell-type-specific

labeling of nascent proteins with a non-canonical amino-acid and click chemistry.

Neuronal impairment following chronic *Toxoplasma gondii* infection is aggravated by intestinal nematode challenge in an IFN-γ-dependent manner

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It has become increasingly evident that the immune and nervous systems are closely intertwined, relying on one another during regular homeostatic conditions. Prolonged states of imbalance between neural and immune homeostasis, such as chronic neuroinflammation, are associated with a higher risk for neural damage. *T. gondii* is a highly successful neurotropic parasite that causes persistent subclinical neuroinflammation, which is strongly associated with psychiatric and neurodegenerative disorders. Here, we investigated if co-infection with *H. polygyrus*, an intestinal nematode with an immunomodulatory capacity, may reshape the course of *T. gondii* infection-induced neuroinflammation and related neuronal alterations. We found that the acute nematode co-infection resulted in a significant increase in the recruitment of immune cells that exhibit Th1 effector functions and enhanced production of Th1 type (IL-12, IFN-γ, iNOS) as well as pro-inflammatory (TNF, IL-1β, IL-6) molecules in the brains of mice. The enhanced cerebral Th1 immune response was also associated with

enhanced *T. gondii* removal but exacerbated the inflammation-related decrease of gene expression of synapse-associated proteins. Notably, synaptic proteins EAAT2 and $GABA_A\alpha1$, involved in the excitatory/inhibitory balance in the CNS, were strongly affected. These synaptic alterations were partially recovered by reducing neuroinflammation indirectly via antiparasitic treatment and in particular, by application of IFN-γ-neutralizing antibody. Our results suggest that an acute enteric nematode co-infection is able to modulate neuroimmune responses to *T. gondii* by altering neuronal function as well as promoting parasite elimination via IFN-γ.

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