ENCEPHALON 2023

Revealing the Hidden: Advancements in Microscopy and Neurodevelopment

PROGRAM

7th December 2023
Göttingen, Germany
Max-Planck Institute for Multidisciplinary Sciences

Welcome Message from Prof. Dr. Metin Tolan

President of the University of Göttingen

Welcome to the 6th biennial Encephalon Symposium – Revealing the Hidden: Advancements in Microscopy and Neurodevelopment here in Göttingen, the city that creates knowledge. This symposium, organized by the graduate students of the GGNB doctoral program, "Cellular and Molecular Physiology of the Brain (CMPB)," promises to be an exciting journey into the cutting-edge research in Neural Development, Imaging, and Brain Physiology. As we gather here today, we come together from various corners of the world, united by our shared passion for unraveling the mysteries of the brain. The brain, with its intricate web of neurons and complex functions, remains one of the most enigmatic frontiers in science. The program offers a rich blend of talks and a vibrant poster session, providing participants and speakers ample opportunities to exchange ideas, share insights, discuss recent advancements, and foster collaborative efforts to shed light on the hidden intricacies of the brain. It is during these interactions that we often stumble upon those remarkable breakthroughs that transform our understanding of neurodevelopment and brain physiology.

I hope you enjoy forging new networks and sparking conversations, get inspired and inspire yourself by presenting your research!

Welcome Message from the Organizing Team

Dear colleagues and guests,

We are delighted to welcome you to Encephalon 2023 - Revealing the Hidden: Advancements in Microscopy and Neurodevelopment, the neuroscience symposium organized by us, the doctoral students of the CMPB.

As we all know, neuroscience is a rapidly evolving field that has made significant progress in recent years. From pioneering advancements in imaging technologies to gaining profound insights into brain development through cellular models, including the innovative use of brain-organoids in a dish. This continual progress highlights the dynamic nature of the field, constantly expanding and pushing the boundaries of our understanding of the brain.

The program promises an insightful line-up. We will have the opportunity to hear from leading experts in the field of microscopy including Prof. Stefan Hell, Dr. Benjamin Cooper, and Dr. Christophe Leterrier.

Complementing this, we are honored to host experts in neuro-development: Dr. Julia Ladewig, Prof. Britta Eickholt and Dr. Maria-Patapia Zafeiriou.

Our speakers will share their latest research findings and valuable perspectives. Between lectures, scheduled coffee breaks offer networking opportunities over a drink at your posters. The breaks should not only offer a chance for you to recharge, but they also create an environment for extended scientific discussions and exchange of creative ideas. Take advantage of these moments, connect with your colleagues, and cultivate new collaborations.

Additionally, we like to show our sincere gratitude to our sponsors, without whom this event would not have been possible.

Thank you all for being part of this community, and we wish you a productive and enjoyable symposium.

Laura and Ronja

Coordinators Encephalon and program speakers CMPB

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General Information

VENUE

Max Planck Institute for Multidisciplinary Sciences
Am Faßerg 11, 37077 Göttingen, Germany

All plenary lectures as well as the poster flash talks take place in the Manfred-Eigen Lecture Hall. Poster sessions are located in Ludwig-Prandtl Lecture Hall.

GETTING TO THE VENUE

Airport and Train

The closest airport to Göttingen is Hannover Airport. The airport is connected to Hannover main train station by local train. From there, the trip to Göttingen takes about 35 min. Göttingen can also be reached from Frankfurt International Airport with direct train connections every two hours. The trip lasts about 2-3 hours.
Find more information about the train connections here: https://www.bahn.de/p/view/index.shtml

Buses

From the train station, take bus lines 21 or 23 to the bus stop ‘’Faßberg’’, which is directly opposite the institute (approx. 15 minutes). From the city center, you can also take the bus line 22 towards Nikolausberg and get off at the "Faßberg" stop. We encourage everybody to take the public transport, as there is limited parking space.

Taxi

Taxi services can be arranged by calling one of the many Göttingen Taxi companies:

- Göttingen Taxi Zentrale: Tel. 0049 551 69300
- Hallo Taxi GmbH: Tel. 0049 551 34034
- City Taxi Göttingen GmbH: Tel. 0049 551 380840
- Night & Day Taxi GmbH: Tel. 0049 551 782828

General Information

REGISTRATION

The registration and information desk is located in the foyer of the Max Planck Institute for Multidisciplinary Sciences. The registration desk opens at 8 am.

POSTERS

Please find your stand number in the poster overview inside the booklet. All authors are kindly asked to hang up their posters at the respective poster stand boards (indicated with numbers) in the Ludwig-Prandtl Lecture Hall before the start of the first lecture on Thursday, December 7th. Posters have to stay up for the entire duration of the Symposium. Please stay by your poster during the poster session of your poster. Please remove your poster after the closing remarks (17:30) on Thursday, December 7th. All remaining posters will be disposed of by Monday, 11th December evening.

Poster sessions

The poster authors have the opportunity to explain and discuss their results during the following poster sessions:
Poster session I: 10:45 – 11:45 - even poster IDs
Poster session II: 16:30 – 17:15 - odd poster IDs

Poster prize

The best poster will be awarded with our Encephalon cup and an invite to our dinner with the speakers in the evening of the conference day. Every registered participant has the right to vote for the best poster presentation. You can find a sticker in your conference bag, please stick this next to your favorite poster.

NAME BADGES

You receive your name badge at the registration desk. Please wear it during the entire symposium. Please help us to be eco-friendly and save money by returning the reusable plastic holder of your badge at the end of the conference at the registration desk.

General Information

REFRESHMENTS & LUNCH

The lunch and coffee breaks are included in the registration fee and will be served in the foyer of the MPI NAT Faßberg Campus. Vouchers will be handed out during registration. Please do not lose them we only have 1 per person.

INTERNET

Free Wi-Fi is available at the MPI NAT. Access to the event Wi-Fi will be provided on site. If you do not have access, please contact the registration desk.

Policy on Photography

We would like to point out that during the Encephalon 2023 photos will be taken by us. These photos might be used to report about the Symposium (website, social media and press release). If you do not agree that you as a person participating in the Symposium may be photographed for the purpose described above, please inform us. You are not allowed to take pictures of presented material during talks and poster presentation unless given consent by the presenter.

General Information

CERTIFICATE OF ATTENDANCE

The certificate of attendance will be sent via mail to all the participants after the symposium.

EVALUATION

Help us to improve Encephalon by filling out our evaluation form. Shortly after the conference, the participants will receive the form via mail.

ANY MORE QUESTIONS?

If you have any remaining questions, find an organizer! They are wearing customized T-shirts, you cannot miss them!

CONTACT

Encephalon organizing team:
encephalon@uni-goettingen.de

Funding and Acknowledgments

We would like to thank the Göttingen Graduate Center for Neurosciences, Biophysics and Molecular Biosciences (GGNB) and the Max Planck Institute for Multidisciplinary Sciences for the financial, organizational and logistic support.
A special thanks to the chair of our program, Prof. Dr. Thomas Dresbach.
We thank all the speakers for accepting our invitation and sharing their knowledge.

The 6th biennial Encephalon 2023 was generously funded by our sponsors: Synaptic Systems (SYSY), ibidi®, Leica, Cell Signaling, THORLABS, ZEISS, Microsynth, SCIENCE SERVICES, SFB1286, Georg-August-Universität Göttingen, Max-Planck-Institut for Multidisciplinary Sciences.

Many thanks to all the volunteers who contributed to the symposium and finally to all the participants who joined to make the Encephalon 2023 successful!

The Encephalon 2023 organizing team

Funding and Acknowledgments

Premium sponsors

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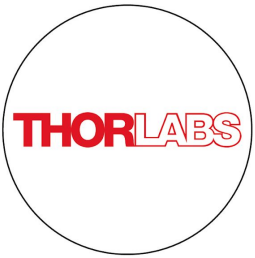

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ibidi is a global leading supplier for functional cell-based assays and advanced products for cell microscopy. Headquartered in Martinsried, Germany, the ibidi spirit of innovation, passion for quality, and steadfast commitment to our customers drives us to be at the vanguard of microscopy-based research and technology.

The ibidi product lines include various µ-Dishes, µ-Slides, and µ-Plates for the cultivation and high-resolution microscopy of cells, and also cell-based assays for investigating angiogenesis, chemotaxis, wound healing, and cells under flow.

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To complete the ibidi product family, the company also offers reagents for live cell imaging.

The ibidi customers are working in scientific institutions, industrial pharmacology, and biotechnology. The products are sold to customers worldwide.

Speakers Overview

MICROSCOPY SESSION

Prof. Stefan W. Hell: the Nobel Prize Laureate in Chemistry in 2014 for the development of STED microscopy.

Dr. Christophe Leterrier: the leader of the NeuroCyto lab and employing super-resolution microscopy methods (STORM & DNA-PAINT).

Dr. Benjamin H. Cooper: an expert in electron microscopy investigating the molecular and structural mechanisms in synaptic transmission and plasticity in the brain.

NEURODEVELOPMENT SESSION

Dr. Julia Ladewig: an expert in the field of stem cell biology, neurodevelopmental and degenerative disorders with innovative stem cell-based approaches.

Dr. Maria-Patapia Zafeiriou: an expert in bioengineering neural organoids and their interaction with innervated cardiac muscle.

Prof. Dr. Britta Eickholt: director of institute of biochemistry at Charité Berlin and interested in the spatial and temporal aspects of signaling events in neurons and their impact on cytoskeletal reorganization.

Prof. Stefan W. Hell

Department of NanoBiophotonics,
MPI for Multidisciplinary Sciences,
Göttingen, Germany

Talk:

“Molecule-scale resolution and dynamics in fluorescence microscopy“

Research Focus:

Recently, Prof. Hell and his lab took research on nanoscopy a step further and developed the nanoscopy with MINimal photon FLUXes technique (MINFLUX) allowing for the ultimate super-resolution down to the size of single molecules (1 nm) and their interactions.
By pushing the boundaries of microscopic imaging to limits that were thought to be impossible before, implementation of such techniques and their constant advancements will revolutionize cellular and molecular research.

Prof. Stefan W. Hell

Biography:

Prof. Stefan W. Hell is known as the Nobel Prize laureate for Chemistry in 2014 for his excellent work on circumventing the diffraction limit. Today he is the director at both the Max Planck Institute for Multidisciplinary Sciences in Göttingen, and the Max Planck Institute for Medical Research in Heidelberg, Germany.
Before Prof. Hell's work, Ernst Abbe's equation of the diffraction limit ($d = \lambda / 2NA$), formulated in 1873, has presented an insurmountable barrier for optical imaging systems, due to the physics of diffraction and the wavelength of the absorbed light. Especially in life sciences, where imaging living cells is required and light microscopy presents the only choice, the resolution was limited to around 200 nm. Thereby, small structures such as vesicles and protein complexes were prevented from being imaged separately and with high resolution.
In 2014, Prof. Hell was awarded the Nobel Prize for Chemistry, not for breaking this principle limit, but rather for overcoming and outsmarting it by the development of STimulated Emission Depletion (STED) microscopy.

Selected Publications:

Ostersehlt, L. M., Jans, D. C., Wittek, A., Keller-Findeisen, J., Inamdar, K., Sahl, S. J., ... & Jakobs, S. (2022). Dna-paint minflux nanoscopy. *Nature Methods*, *19*(9), 1072-1075.

Weber, M., von der Emde, H., Leutenegger, M., Gunkel, P., Sambandan, S., Khan, T. A., ... & Hell, S. W. (2023). MINSTED nanoscopy enters the Ångström localization range. *Nature Biotechnology*, *41*(4), 569-576.

Scheiderer, L., von der Emde, H., Hesselink, M., Weber, M., & Hell, S. W. (2023). MINSTED tracking of single biomolecules. *bioRxiv*, 2023-09.

Dr. Christophe Leterrier

NeuroCyto lab,
Institute of Neurophysiopathology
(INP CNRS-AMU),
Marseille, France

Talk:

“The functional nano-architecture of neuronal actin“

Research Focus:

Since 2017, he is leading the NeuroCyto lab, applying super-resolution microscopy techniques such as STORM & DNA-PAINT to decipher the molecular organization of neurons and how different processes such as intraneuronal protein transport and maintenance of the cytoskeleton lead to segregation into the typical compartments (axons, synapses, dendritic spines), culminating in the complex arborization and unique functions of neurons.

Dr. Christophe Leterrier

Biography:

Dr. Christophe Leterrier is the group leader of the Neurocyto Lab in the Neuropathophysiology Institute (INP, CNRS-Aix Marseille University) in Marseille, France. He studied engineering in Physics and Chemistry and received his PhD afterwards in Neuroscience from the University Pierre et Marie Curie in Paris. He worked as a postdoc in Marseille in the team of Dr. Bénédicte Dargent and subsequently became a tenured CNRS researcher.

Selected Publications:

Laine, R. F., Heil, H. S., Coelho, S., Nixon-Abell, J., Jimenez, A., Wiesner, T., ... & Henriques, R. (2023). High-fidelity 3D live-cell nanoscopy through data-driven enhanced super-resolution radial fluctuation. Nature Methods, 1-8.

Bingham, D., Jakobs, C. E., Wernert, F., Boroni-Rueda, F., Jullien, N., Schentarra, E. M., ... & Leterrier, C. (2023). Presynapses contain distinct actin nanostructures. Journal of Cell Biology, 222(10), e202208110.

Friedl, K., Mau, A., Boroni-Rueda, F., Caorsi, V., Bourg, N., Lévêque-Fort, S., & Leterrier, C. (2023). Assessing crosstalk in simultaneous multicolor single-molecule localization microscopy. Cell Reports Methods, 3(9).

Dr. Benjamin H. Cooper

Department of Molecular Neurobiology,
MPI for Multidisciplinary Sciences,
Göttingen, Germany

Talk:

“Ultrastructural approaches to investigate presynaptic functional heterogeneity and activity-dependent vesicle pool remodelling“

Research Focus:

Dr. Coopers research is focused on understanding the molecular and structural mechanisms underlying synaptic transmission and plasticity in the brain, with a particular emphasis on presynaptic proteins, ultrastructure, and morphological correlates of synaptic vesicle priming. For example, his work has revealed new details about the organization of presynaptic proteins, the structure of synaptic vesicles, and the morphology of active zones, which are specialized regions of the presynaptic membrane where neurotransmitter release occurs.

Dr. Benjamin H. Cooper

Biography:

Dr. Benjamin H. Cooper is a Project Group Leader in the Department of Molecular Neurobiology at the Max Planck Institute for Multidisciplinary Sciences in Göttingen, Germany. He completed his M.Sc and PhD studies in the Neuroscience program (IMPRS) investigating the "Membrane glycoprotein M6a: expression and regulation by stress in the brain" at the University of Göttingen. Dr. Cooper has extensive expertise in imaging and electron microscopy including high-pressure freezing (HPF) and electron tomography (ET), which are critical techniques for studying the ultrastructure of cells and tissues at high resolution. His work has provided new insights into the ultrastructure of synapses and other cellular structures involved in synaptic transmission.

Selected Publications:

Papantoniou, C., Laugks, U., Betzin, J., Capitanio, C., Ferrero, J. J., Sánchez-Prieto, J., ... & Lučić, V. (2023). Munc13-and SNAP25-dependent molecular bridges play a key role in synaptic vesicle priming. Science Advances, 9(25), eadf6222.

Banerjee, A., Imig, C., Balakrishnan, K., Kershberg, L., Lipstein, N., Uronen, R. L., ... & Kaeser, P. S. (2022). Molecular and functional architecture of striatal dopamine release sites. Neuron, 110(2), 248-265.

Papantoniou, C., Laugks, U., Betzin, J., Capitanio, C., Ferrero, J. J., Sánchez-Prieto, J., ... & Lučić, V. (2022). Synaptic vesicle-bound molecular bridges organize sequential vesicle states along parallel pathways. BioRxiv, 2022-04.

Dr. Julia Ladewig

Department of Translational Brain Research,
Central Institute of Mental Health (CIMH),
Mannheim, Germany

Talk:

“Stem cell based models to decipher human brain development in health and disease“

Research Focus:

Dr. Ladewig’s research focus includes lineage selection for young neurons, the assessment of neuronal migration and integration, direct conversion of somatic cells into neurons and cerebral organoid-based models for human malformation of cortical development.

Dr. Julia Ladewig

Biography:

After Dr. Julia Ladewig completed her studies in Biology (with distinction; 1,0*) in 2003 she spent one year abroad at the Imperial College in London where she obtained a Master of Science in Medical Ethics. Following her studies, she joined the Institute of Reconstructive Neurobiology, University of Bonn, Germany by the end of 2004 as a Junior Research Fellow. Finalizing her doctoral degree (Dr. rer. nat., Magna Cum Laude) in 2009 she continued her scientific career in Bonn as a Postdoc. In 2014, she was awarded with an independent junior research group. In 2018, she received a Group Leader position at the Hector Institute of translational Brain Research (HITBR) at the Central Institute of Mental Health in Mannheim.

Selected Publications:

Fischer, J., Fernández Ortuño, E., Marsoner, F., Artioli, A., Peters, J., Namba, T., ... & Heide, M. (2022). Human-specific ARHGAP11B ensures human-like basal progenitor levels in hominid cerebral organoids. EMBO reports, 23(11), e54728.

Jabali, A., Hoffrichter, A., Uzquiano, A., Marsoner, F., Wilkens, R., Siekmann, M., ... & Ladewig, J. (2022). Human cerebral organoids reveal progenitor pathology in EML1-linked cortical malformation. EMBO reports, 23(5), e54027.

Wilkens, R., Hoffrichter, A., Kleinsimlinghaus, K., Bohl, B., Haag, C., Lehmann, N., ... & Koch, P. (2022). Diverse maturity-dependent and complementary anti-apoptotic brakes safeguard human iPSC-derived neurons from cell death. Cell Death & Disease, 13(10), 887.

Dr. Maria-Patapia Zafeiriou

Department of Pharmacology and Toxicology,
University Medical Center Göttingen,
Göttingen, Germany

Talk:

“Human brain & heart organoid communication in a dish“

Research Focus:

By bioengineering different neural organoids and innervated cardiac muscle from human induced pluripotent stem cells, Dr. Zafeiriou’s group is able to study neuronal development and network dynamics in healthy and diseased tissues. This might offer the possibility to understand the molecular and cellular mechanisms of neurodegeneration, infantile epilepsy and sudden cardiac death under epilepsy.

Dr. Maria-Patapia Zafeiriou

Biography:

Dr. Maria-Patapia Zafeiriou is a Principal Investigator in the Department of Pharmacology and Toxicology at the University Medical Center in Göttingen. She studied Chemistry in the National and Kapodistrian University of Athens and successfully completed her PhD studies focusing on the investigation of pancreatic beta cell homeostasis. Afterwards, she investigated the role of TBX5, a transcription factor that is involved in the electrical signal propagation within the heart, and made important progress in the field of cardiac homeostasis. Currently, together with her group, Dr. Zafeiriou investigates how the brain and the heart communicate with each other and how cardiac dysfunction may be linked to neuronal dysregulation.

Selected Publications:

Schneider, L. V., Bao, G., Methi, A., Jensen, O., Schmoll, K. A., Setya, M. G., ... & Zafeiriou, M. P. (2023). Bioengineering of a human innervated cardiac muscle model. bioRxiv, 2023-08.

Zafeiriou, M. P., Bao, G., Hudson, J., Halder, R., Blenkle, A., Schreiber, M. K., ... & Zimmermann, W. H. (2020). Developmental GABA polarity switch and neuronal plasticity in Bioengineered Neuronal Organoids. Nature communications, 11(1), 3791.

Rathjens, F. S., Blenkle, A., Iyer, L. M., Renger, A., Syeda, F., Noack, C., ... & Zafeiriou, M. P. (2021). Preclinical evidence for the therapeutic value of TBX5 normalization in arrhythmia control. Cardiovascular research, 117(8), 1908-1922.

Prof. Dr. Britta Eickholt

Institute of Molecular Biology and Biochemistry,
Charité, Universitätsmedizin Berlin,
Berlin, Germany

Talk:

“From membrane trafficking to actin dynamics: Mechanisms controlling astrogliosis and scar formation in models of CNS injury“

Research Focus:

The research in the Eickholt lab broadly focuses on the cellular mechanism controlling the development, maturation and maintenance of neurons and astrocytes in the brain. Her lab uses a multidisciplinary approach to understand how neurons and astrocytes establish and modify their complex shapes in the healthy brain and during disease or injury. Her main expertise centers on spatial and temporal control of signaling events and cytoskeleton dynamics.

Prof. Dr. Britta Eickholt

Biography:

Dr. Britta Eickholt is Professor for ‘Molecular Biology and Biochemistry’ at the Charité – University Medicine Berlin. After a PhD in Biochemistry from Guy’s Hospital / King’s College London in 1998, she carried out a postdoc at the MRC Centre for Developmental Neurobiology in London. This is also where she started her own laboratory in 2001 as a principle investigator.

Selected Publications:

Schiweck, J., Murk, K., Ledderose, J., Münster-Wandowski, A., Ornaghi, M., Vida, I., & Eickholt, B. J. (2021). Drebrin controls scar formation and astrocyte reactivity upon traumatic brain injury by regulating membrane trafficking. Nature communications, 12(1), 1490.

Brosig, A., Fuchs, J., Ipek, F., Kroon, C., Schrötter, S., Vadhvani, M., ... & Eickholt, B. J. (2019). The axonal membrane protein PRG2 inhibits PTEN and directs growth to branches. Cell reports, 29(7), 2028-2040.

Ledderose, J. M., Benitez, J. A., Roberts, A. J., Reed, R., Bintig, W., Larkum, M. E., ... & Eickholt, B. J. (2022). The impact of phosphorylated PTEN at threonine 366 on cortical connectivity and behaviour. Brain, 145(10), 3608-3621.

Poster Flash Talks

We are looking forward to seeing you in our poster flash talk session from 10:15 to 10:45.
In this session you will have the opportunity to listen to fascinating 3-minute presentations from young motivated scientists. The students will present their research topics in a very brief and catching speech.

The poster flash talks take place in the Manfred-Eigen Lecture Hall.

Presenter	Poster ID	Poster Title
Annasara Artioli	1	Generation and characterization of basal radial glia-like cells from human induced pluripotent stem cells
Thanh Thao Do	8	In situ structural investigation of synapses with cryo-electron tomography
Nesil Eşiyok	9	Individual and combined functions of the human-specific genes NBPF14 and NOTCH2NLB during neocortical development
Ismael Fernández-Hernández	10	Adult neurogenesis in Drosophila
Nisha Hemandhar Kumar	16	Proteomics analysis in the aged brain reveals an isoform switch in physiological aging and increased protein turnover
Domonkos Nagy-Herczeg	19	The role of PLPPR3 in cytoskeleton-condensate-membrane interactions
Raquel Pérez Fernández	21	Organoid assembloids modeling the role of serotonin during human cortical development
Andrew Octavian Sasmita	22	Oligodendrocytes and neurons contribute to amyloid-beta burden in vivo
Lidiia Tynianskaia	27	Developmental characterization of iPSC-derived Callithrix jacchus cerebral organoids

Poster Sessions

If you feel intrigued by some of the presentations, we strongly invite you to visit the presenters during the poster sessions to find out more about the interesting research topics.

The poster sessions are located in the Ludwig-Prandtl Lecture Hall.

Poster Session I
Even Poster IDs
10:45-11:45

Poster Session II
Odd Poster IDs
16:30-17:15

Poster Overview

Poster ID	Poster first author	Poster Title
1	Annasara Artioli	Generation and characterization of basal radial glia-like cells from human induced pluripotent stem cells *
2	Mateo Bastidas Betancourt	Exploring the role of hominid-specific ZNF90 in brain development using rhesus macaque iPSC-derived brain organoids
3	Lena Josefine Berger	Effects of a deficient STAT1-signaling in the Tg4-42 mouse model of Alzheimer's disease
4	Cristian-Alexandru Bogaciu	Cellular dynamics of synaptic adhesion proteins: neurexins and neuroligins
5	Alexey Chizhik	Nanometer axial resolution with MIET
6	Avika Chopra	The role of RNA carrying exosomes in synaptic physiology and neurodegeneration in synucleinopathies
7	Stephan Deimel	Analyzing the subcellular compartmentalization of cAMP dynamics in Kenyon cells underlying learning and memory
8	Thanh Thao Do	In situ structural investigation of synapses with cryo-electron tomography *
9	Nesil Eşiyok	Individual and combined functions of the human-specific genes NBPF14 and NOTCH2NLB during neocortical development*

* A poster flash talk will be presented from 10:15 to 10:45.

Poster ID	Poster first author	Poster Title
10	Ismael Fernández-Hernández	Adult neurogenesis in Drosophila *
11	Merle Fricke	Amino-terminally elongated Abeta-3-x peptides can be generated by the secreted metalloprotease ADAMTS4 and deposit in the brains of a subset of Alzheimer's disease patients
12	David Garnica	Altered functional connectivity of brain networks in children with Self-limited Epilepsy of Childhood with Centrotemporal spikes (SeLECTS): An EEG/fMRI study
13	Catello Guida	Unraveling the functions of the transcription factor TBR2 in human neurodevelopment
14	Yuhao Han	Revealing the developmental dynamics, cytoskeleton organisation and AIS functional significance of neurons with axon carrying dendrite
15	Yannick Hass	Unravelling the Role of ARHGAP11A in Apical Radial Glial Cell Delamination During Human Corticogenesis
16	Nisha Hemandhar Kumar	Proteomics analysis in the aged brain reveals an isoform switch in physiological aging and increased protein turnover *
17	Angeliki Koufali	Generation of otic Bioengineered Neuronal Organoids (oBENO)
18	Frederike Maaß	Investigation of nucleoids in presynaptic mitochondria using super-resolution microscopy

* A poster flash talk will be presented from 10:15 to 10:45.

Poster ID	Poster first author	Poster Title
19	Domonkos Nagy-Herczeg	The role of PLPPR3 in cytoskeleton-condensate-membrane interactions *
20	Lisa Neuenroth	Development of Spatial and Temporal Proteomics Workflows for Pig Hearts
21	Raquel Pérez Fernández	Organoid assembloids modeling the role of serotonin during human cortical development *
22	Andrew Octavian Sasmita	Oligodendrocytes and neurons contribute to amyloid-beta burden in vivo *
23	Andrew Octavian Sasmita, Erinne Cherisse Ong	Transgenic inheritance pattern modulates plaque burden in the 5xFAD mouse model
24	Kea Aline Schmoll	Characterization of a human midbrain organoid containing dopaminergic neurons
25	Rafaela Pedro Silva	Analyses of the age-dependent challenges of the neuronal actin filament system
26	Björn Twellsieck	Cytokine/CRLF3-signalling protects insect neurons and regulates acetylcholinesterase in human cells.
27	Lidiia Tynianskaia	Developmental characterization of iPSC-derived Callithrix jacchus cerebral organoids *

* A poster flash talk will be presented from 10:15 to 10:45.

Poster Abstracts

1. Generation and characterization of basal radial glia-like cells from human induced pluripotent stem cells

Annasara Artioli[1,2,3], Ammar Jabali[1,2,3], Andrea Rossetti[1,2,3], Anne Hoffrichter[1,2,3], Yannick Hass[1,2,3], Fabio Marsoner[1,2,3], Philipp Koch[1,2,3], Julia Ladewig [1,2,3]

[1]Central Institute of Mental Health (ZI), University of Heidelberg/Medical Faculty Mannheim, Mannheim, Germany
[2]Hector institute for Translational Brain Research (gGmbH), Mannheim, Germany
[3]German Cancer Research Center (DKFZ), Heidelberg, Germany

Keywords: Neurodevelopment, hiPSCs, basal radial glia

Abstract: Important steps during primate evolution led to the development of a structurally and functionally complex human brain, which distinguishes Homo sapiens from all other species and still represents a challenge to investigate. The expansion of basal radial glia cells (bRGC), a primate-specific progenitor population, is thought to contribute to the increase in cortical size and complexity of the human brain. Until recently, we gained our knowledge about bRGC from human fetal cortex ex vivo studies. However, these are limited due to the lack of tissue availability. In addition, bRGC can be generated and studied in the context of human pluripotent stem cell (PSC)-derived cerebral organoids. In this project, we set out to develop a protocol for the generation and expansion of PSC-derived bRGC as homogenous 2D cell cultures. More specifically, we identified culture conditions composed of a mix of small molecules that mimics the in vivo neural stem cell niche of bRG in vitro. Following immunohistochemistry and transcriptional analyses we could confirm the bRGC identity of our neural cultures. Live-cell imaging analyses revealed the hallmark feature of bRGC proliferative behaviour, known as mitotic-somal-translocation, in our in vitro cultures. Moreover, bRGC can give rise to different cortical layer neurons and astrocytes upon differentiation. Finally, co-culture of bRGC with forebrain-type organoids indicate their preference to infiltrate and proliferate in the outer subventricular zone and to give rise to neurons and glia. By that, our 2D protocol provides new possibilities to study bRG cell behaviour and human brain development in vitro.

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Annasara Artioli will give a Flash Talk (10:15 to 10:45).

2. Exploring the role of hominid-specific ZNF90 in brain development using rhesus macaque iPSC-derived brain organoids

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Keywords: Brain organoids, hominids, electroporation, RNAseq

Abstract: Previous studies on the role of human-specific genes in brain development have highlighted their effect on the brain progenitors´ proliferative capacity and division plane, proving that early brain developmental stages set the ground for the cognitive uniqueness and complexity of the human brain. However, cross-species comparative analyses of transcriptomic datasets so far have lacked both the sequencing depth that bulk-RNAseq can still provide and the anatomical precision and correlation that single cell approaches offer. Additionally, no well-established pipeline has been used to compare progenitor cell populations of different primate species to uncover underlying differential regulatory networks or enriched functional modules. Using our data mining approach, we found a set of potential candidate genes that may explain part of the evolutionary divergence previous studies have remarked at the level of brain progenitor cells. Finally, we used our lately established organoid electroporation protocol to ectopically express the hominid-specific ZNF90 on rhesus macaque iPSC-derived brain organoids to confirm its role during early stages of hominid brain development.

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3. Effects of a deficient STAT1-signaling in the Tg4-42 mouse model of Alzheimer's disease

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Keywords: Alzheimer's disease, Inflammation, STAT proteins

Abstract: Next to amyloid-β (Aβ) plaques and neurofibrillary tangles, a chronic inflammatory environment is one of the key features characterizing Alzheimer's disease (AD) that has become increasingly important throughout the last years. A central factor in this inflammatory cascade is STAT1 ("Signal Transducer and Activator of Transcription 1") due to its crucial role in microglial activation and triggering other inflammatory responses. We aim to characterize the contribution of STAT1 to AD pathogenesis in the well-established Tg4-42 AD mouse model by introducing a global STAT1 knock-out. Immunohistochemical analyses with respect to astro- and microgliosis, neurodegeneration, neurogenesis, and phagocytosis were conducted on brain samples from Tg4-42, Tg4-42/STAT1-KO, and WT mice. On a transcriptional level, we conducted quantitative real-time PCR analyses of genes related to inflammation, neurodegeneration, and neurogenesis. Strong astro- and microgliosis was observed in the CA1 region of adult Tg4-42 mice, which, in the case of astrocytes, is significantly reduced in Tg4-42/STAT1-KO mice, validating complementary qPCR results. Regarding neurodegeneration, we confirmed a significant reduction in the number of pyramidal neurons in the CA1 region in Tg4-42 and Tg4-42/STAT1-KO mice by around 40-50% compared to age-matched WT controls. Although Tg4-42 mice do not display an overt extracellular plaque pathology, we could demonstrate substantial amounts of intraneuronal and phagocytosed Aβ, predominantly in the distal CA1 region, in both lines of interest already visible at 3 months of age. In summary, our study addresses the effects of a global knock-out of STAT1 on AD pathology regarding inflammation, neuron loss, and phagocytosis in a multi-level analysis.

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4. Cellular dynamics of synaptic adhesion proteins: neurexins and neuroligins

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Keywords: endocytosis, recycling, pre/post-synapse

Abstract: Neurexins and neuroligins are pre/post-synaptically-expressed adhesion molecules, synthesized as heparan sulfate proteoglycans (HSPG). They have a key role in the specification of synapse identity and connectivity, by the stabilization of axo-dendritic contacts. The current literature shows evidence for cellular trafficking of both neurexins and neuroligins, but the precise mechanisms have not been sufficiently studied. A previous study of our group revealed that a major extracellular matrix (ECM) protein, Tenascin-R, undergoes frequent endocytosis, and returns later to the surface, preferentially near synapses, through a long-loop recycling pathway (Dankovich et al., 2021). We therefore tested this pathway for neurexins and neuroligins. We could follow their recycling in simple systems (PC12 cells), and we could also validate the findings in primary hippocampal neurons. Frequent endocytosis and re-surfacing of neurexins and neuroligins might represent a way of renewing the glycosylation of these proteins, without needing to synthesize their peptide chains, thereby saving energy.

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5. Nanometer axial resolution with MIET

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Keywords: Fluorescence microscope, high resolution imaging

Abstract: The Metal-Induced Energy Transfer Imaging (MIET) is a fluorescence-based technique used for the axial localization of a fluorophore with nanometer precision. This method relies on energy transfer from an excited molecule to plasmons in a metal film. This energy transfer induces a uniform modulation of the molecule's excited state lifetime within the first 200 nm of the surface. If the molecule is situated within this range, the measured lifetime can be converted into the axial position of the molecule with nanometer accuracy. MIET is compatible with live cell and multicolor imaging and can be integrated with other high-resolution methods to improve lateral resolution.

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6. The role of RNA carrying exosomes in synaptic physiology and neurodegeneration in synucleinopathies

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Keywords: Parkinson's disease, exosomes, miRNA

Abstract: Alpha-synuclein (aSyn) is a key player in Parkinson's disease (PD) and other synucleinopathies as it accumulates in pathognomonic inclusions in the brain. Currently, the prevailing hypothesis is that aSyn pathology may spread throughout the brain in a prion-like manner, but the precise molecular mechanisms involved in the spreading are still unclear. Several studies have shown that aSyn can be released from cells packaged into exosomes. Exosomes are small extracellular vesicles (EVs), 30-200nm in size carrying proteins, nucleic acids, and metabolites, thereby regulating homeostasis. Exosomes hold great potential as biomarkers in the diagnosis of PD and other disorders, as they may reflect molecular alterations characteristic of the disease. In this project, we would like to characterize the transfer of miRNAs from astrocytes to neuronal synapses via exosomes in transgenic mouse models of synucleinopathy, and to further study the dysregulation of the synaptic RNAome as an early event in PD. Based on our results so far, we can conclude that exosomes are transported from astrocytes to neurons under physiological conditions. These exosomes that are transported contain small RNAs including miRNAs. We are currently working on the identification of differential gene expression of miRNAs in A30P when compared with wild-type mouse models which are currently being sequenced.

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7. Analyzing the subcellular compartmentalization of cAMP dynamics in Kenyon cells underlying learning and memory

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Keywords: Drosophila, cAMP, Learning, Memory

Abstract: In the Drosophila central brain, the mushroom body (MB) mediates olfactory learning and memory. During classical conditioning, odor inputs are conveyed by projection neurons (PNs) to the Kenyon cells (KCs) of the MB, and the coincidence of the activation of dopaminergic neurons (DANs) by the reinforcement (punishing or rewarding) along with this odor input leads to an alteration in the plasticity of the synapses with the mushroom body output neurons (MBONs) and thus behavior. Based on the innervation pattern by MBONs and DANs, the lobes of the MB can be subdivided into functional compartments. Here, the second messenger cAMP plays a crucial role in the regulation of several cellular processes, including synaptic plasticity, mediated by the adenylyl cyclase rutabaga (Rut) and its counterpart the phosphodiesterase dunce (Dnc). While it is established that Dnc maintains spatial specificity between the lobes of the MB, the influence on compartmentalization within the lobes, especially on the single neuron level remains unknown. We want to elucidate this influence by addressing two objectives: The localization of phosphodiesterase Dnc within single neurons and its influence on cAMP dynamics to understand the role of KC synaptic boutons as individual functional units in learning and memory.

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8. In situ structural investigation of synapses with cryo-electron tomography

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Keywords: synapse, cryo-electron tomography, ultrastructure

Abstract: Neurons communicate at specialized terminals called synapses, where hundreds of molecules work together in harmony to ensure proper and efficient signal transmission, which is crucial for normal brain functions. Aberrant synaptic signalling is involved in “synaptopathies”, a group of neurodevelopmental and neurodegenerative diseases such as autism and Parkinson’s disease. This highlights the need to understand the organization and interactions of molecular complexes at the synapse. Cryo-electron tomography (cryo-ET) offers a close-to-native preservation of biological specimen and the unique possibility to capture both the cellular context and the molecular details, and thus can be utilized to advance structural understanding of the synapse. However, methodological challenges (synapse targeting, sample thickness) still limit the use of cryo-ET in synapse imaging. Our laboratory is developing a pipeline to produce high-quality cryo-tomograms of intact synapses of cultured neurons, employing several techniques such as cryo-fluorescent microscopy to aid targeting and cryo-focused ion beam milling to create thin, electron-transparent sample. The workflow consists of complimentary strategies and can be adapted to address different biological questions.

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Thanh Thao Do will give a Flash Talk (10:15 to 10:45).

9. Individual and combined functions of the human-specific genes NBPF14 and NOTCH2NLB during neocortical development

Nesil Eşiyok[1], Neringa Liutikaite[1], Christiane Haffner[2], Wieland B. Huttner[2], Michael Heide[1,2]

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Keywords: brain development, human-specific genes, neocortex

Abstract: The neocortex is the most recently evolved brain structure and the seat of higher cognitive abilities. Different primate species show strong diversity in neocortex size and its degree of folding culminating in the large and highly folded human neocortex. The basis for this is established during fetal neocortex development and is primarily controlled by genes that are specifically expressed in cortical neural stem and progenitor cells (cNPCs). Human-specific genes have received increasing attention as potential major contributors to human neocortex expansion and folding. Previously, we identified 15 human-specific genes enriched in cNPCs. Among these genes, NBPF14 is of special interest, as its signature protein domain–the Olduvai domain–is associated with brain size. Interestingly, NBPF14 is found to be co-expressed and co-evolved with another human-specific gene–NOTCH2NLB, which has been suggested to maintain the proliferative state in apical progenitors. Here we studied the individual and combined functions of NBPF14 and NOTCH2NLB during neocortex development by (i) microinjection of mRNA into single apical progenitors of mouse embryos and (ii) targeted electroporation of expression plasmids into chimpanzee cerebral organoids. We found that (i) NOTCH2NLB alone leads to an increase in the number of apical progenitors; (ii) NBPF14 alone produces more basal progenitors by inducing delamination of apical progenitors; and (iii) co-expression of NOTCH2NLB and NBPF14 maintains the apical progenitor pool, while expanding basal progenitors in both species. These findings suggest that NBPF14 and NOTCH2NLB regulate the correct balance between proliferation and differentiation of apical progenitors – one key mechanism of human neocortex expansion.

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10. Adult neurogenesis in Drosophila

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Keywords: Neuron regeneration, aging, drugs, Drosophila

Abstract: Promoting adult neurogenesis in the aging brain has the potential to rejuvenate neural circuits and restore cognitive functions. We have implemented methods to capture and genetically control adult-born neurons in the genetically conserved and easily scalable model system Drosophila melanogaster. Adult neurogenesis proceeds at low rates in physiologic conditions in adult flies, while enhanced regeneration is triggered upon injury and oral administration of small molecules. By leveraging this novel platform, our current efforts are aimed at identifying clinically-relevant compounds promoting functional neurogenesis in vivo in the aging brain. Ultimately, this approach has the potential to expedite the development of regenerative therapies to treat otherwise irreversible neurodegenerative conditions, affecting an increasingly growing aging population and bearing a significant socioeconomic impact.

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Ismael Fernández-Hernández will give a Flash Talk (10:15 to 10:45).

11. Amino-terminally elongated Abeta-3-x peptides can be generated by the secreted metalloprotease ADAMTS4 and deposit in the brains of a subset of Alzheimer's disease patients

Merle Fricke[1], Christina Lehnen[1], Hans-Wolfgang Klafki[1], Barbara Morgado[1], Sandra Lehmann[2], Carolina Münch[2], Thomas Liepold[3], Jens Wiltfang[1], Olaf Jahn[1], Sascha Weggen[2], Oliver Wirths[1]

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Keywords: Alzheimer's disease, Amyloid-beta, ADAMTS4

Abstract: The aggregation and deposition of amyloid-beta (Abeta) peptides in the brain is thought to be the initial driver in the pathogenesis of Alzheimer's disease (AD). In addition to full-length Abeta peptides starting with an aspartate residue in position 1, both N-terminally truncated and elongated Abeta peptides are produced by various proteases from the amyloid precursor protein (APP), and have been detected in brain tissues and/or body fluids. We had demonstrated recently that the particularly abundant N-terminally-truncated Abeta4-x peptides are generated by ADAMTS4, a secreted metalloprotease that in the brain is exclusively expressed in oligodendrocytes. We employed a previously developed electrochemical sandwich immunoassay and immuno-precipitation (IP) followed by mass spectrometry to determine Abeta-3-40 levels in the supernatants of a variety of cell lines, in addition to a detailed immunohistochemical analysis of human brain samples. In this study, we describe another ADAMTS4 cleavage site in APP N-terminal to Asp(1) between residues Glu(-4) and Val(-3), resulting in the release of N-terminally elongated Abeta-3-40 peptides, which serve as a component in a promising Abeta-based plasma biomarker assay. These elongated Abeta-3-40 peptides were detected in supernatants of various cell lines, and ADAMTS4 enzyme activity promoted the release of Abeta-3-x peptides. In addition, extracellular and vascular localization of N-terminally elongated Abeta-3-x peptides was identified in a subset of AD patient cases with immunohistochemistry. The results indicated that ADAMTS4 facilitates the generation of N-terminally elongated Abeta-3-x peptides, which were also identified in parenchymal and vascular deposits in brain samples of a subset of AD patients.

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12. Altered functional connectivity of brain networks in children with Self-limited Epilepsy of Childhood with Centrotemporal spikes (SeLECTS): An EEG/fMRI study

David Garnica[1], Stuart D.W. Smith[2], Dagmar Weise[3], Josefin Hennecke[3], Daniel van de Velden[1], Manuel Hewitt[1], Carsten Schmidt-Samoa[4], Peter Dechent[4], Knut Brockmann[3], Niels K. Focke[1]

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Keywords: Rolandic epilepsy, EEG, fMRI, FC, Power, IEDs

Abstract: Objective: Study power and functional connectivity (FC) during rest and language tasks in children with Self-limited Epilepsy with Centrotemporal Spikes (SeLECTS - Rolandic epilepsy). Method: Retrospectively, source-reconstructed resting-state EEG from 37 children with SeLECTS and 37 controls were compared, with additional comparisons between recent-onset and longer-duration SeLECTS cases, and epochs without and with interictal epileptiform discharges (IEDs). Prospectively, 9 children with SeLECTS and 17 controls were examined using fMRI during rest and language tasks: phonological processing and verbal working memory. Participants also underwent cognitive testing. Results: Retrospective EEG results revealed increased power in patients across all comparisons. FC analysis highlighted increased focal, predominantly left-sided beta and decreased theta without IEDs when compared to controls. In epochs with IEDs, a prominent right-sided FC increase in delta emerged. FMRI data indicated no significant BOLD differences post-correction, but SeLECTS patients demonstrated diminished performance in verbal comprehension, reading, and writing tests. Additionally, distinct FC-fMRI alterations were identified during rest and language processing. A significantly negative correlation was found between IED frequency and processing speed. Conclusions: SeLECTS children exhibit abnormal power and FC patterns, especially in recent-onset cases and in EEG epochs with and without IEDs. This suggests a relationship between IED frequency and disease evolution. Marked FC abnormalities highlight multifocal functional disorganization, consistent with prior suggestions of network perturbations linked to IEDs, visible even at early disease phases. Significance: Analyzing power and FC in children with epilepsy provides insight into disease progression, the impact of IEDs on brain function, cognitive development constraints, and the potential need for IED treatment.

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13. Unraveling the functions of the transcription factor TBR2 in human neurodevelopment

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Keywords: TBR2, EOMES, Neurodevelopment, Preplate, Subplate

Abstract: The human brain is remarkably complex, both structurally and functionally and clearly represents the organ with the greatest progression during evolution. The human neocortex is greatly expanded and exhibits increased complexity. The developmental mechanisms underlying the evolutionary changes are, however, poorly understood. With the advent of efficient gene editing technologies in human cells in combination with the ability to generate human pluripotent stem cells (PSC) and organotypic PSC-derived brain organoids we are now technologically equipped to decipher the molecular basis of the changes between our brain and that of our ancestors. In this project we apply gene editing in PSC and thereof derived organoids to study the function of TBR2, a transcription factor selectively expressed in IPs and functionally required for SVZ neurogenesis, during early cortical development. Using CRISPR/Cas9 mediated gene editing we generated PSC-TBR2-knockout (KO) lines. Following validation we applied a standardized forebrain-type organoid protocol. When analysing the transgenic organoids and isogenic controls we found that TBR2 is impacting on the proliferation of progenitor cells and their differentiation into cells positive for the neuronal markers TBR1 and SATB2. Furthermore, our data suggests a role of TBR2 in the development of the cortical pre- and subplate. By that our data suggest that transgenic organoids represent a powerful tool to map gene function in brain development, to correlate genetics to functional phenotypes and to complement the long tradition of KO-models in developmental biology and neuroscience.

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14. Revealing the developmental dynamics, cytoskeleton organisation and AIS functional significance of neurons with axon carrying dendrite

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Keywords: AcD enruons, AIS, Cryo-ET

Abstract: Most principal neurons have a singular soma-derived axon that begins with the axon initial segment (AIS), an important structure to maintain axo-dendritic polarity and generate action potentials (APs). However, in a subset of cells, known as axon carrying dendrite (AcD) neurons, the axon emanates from a basal dendrite. This dendritic axon origin provides a privileged route for AP initiation at the AIS. In turn, the AcD neurons can evade peri-somatic inhibition to participate circuits that produce sharp-wave ripples, a process involved in memory consolidation. Despite the physiological significance, the cell biology of AcD neurons remains unclear. Here, we investigated the development, cytoskeleton organisation, and AIS functionality in AcD neurons. We found that during AcD neuron development, a single precursor neurite give rise to the axon and then the AcD, and the dendrite before axon-AcD branching point inherit axon-like microtubule organisations. Like soma-derived AIS, the AIS in AcD neurons possesses similar cytoskeleton structures and functions as a trafficking barrier to maintain specific molecular compositions in the axon. However, it does not undergo selfremodelling to compensate abnormal activity level, and receives less inhibitory inputs. To gain further insights, we are establishing Cryo-CLEM procedures to reconstruct the native cytoskeletal structures of AcD neurons.

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15. Unravelling the Role of ARHGAP11A in Apical Radial Glial Cell Delamination During Human Corticogenesis

Yannick Hass[1,2,3], Anne Hoffrichter[1,2,3], Fabio Marsoner[1,2,3], Ammar Jabali[1,2,3], Nesil Esiyok[4], Wieland B. Huttner[5], Michael Heide[4,5], Julia Ladewig [1,2,3]

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Keywords: radial glia, brain organoids, corticogenesis

Abstract: During corticogenesis, apical radial glial cells (aRG) form a pool of neural progenitors in the ventricular zone. With progression of brain development, aRG delaminate from the ventricular surface to produce basal progenitors, which reside in the basally located subventricular zone where they generate cortical neurons. This process of delamination can be regulated by an actomyosin-dependent constriction of the apical endfeet of aRG and downregulation of adherens junctions, or asymmetric cell division, regulated by the orientation of the cleavage plane. However, the exact mechanisms regulating delamination remain poorly understood. Here, we test whether ARHGAP11A, a RhoGTPase-activating protein highly expressed in aRG, might play a role in the process of delamination. To this end, we used CRISPR/Cas9-mediated gene editing to generate human induced-pluripotent stem cell (hiPSC) ARHGAP11A-knockout (KO) lines. Following validation, we applied a standardised forebrain-type organoid protocol. When analysing the KO organoids and their isogenic controls, we found that in ARHGAP11A-KO organoids aRG delaminate pre-maturely, which results in a greater abundance of neurons compared to the isogenic control at early timepoints. Moreover, preliminary data indicate that this delamination might be driven by actin-dependent changes in the structure of the ventricular surface. Hence, our data suggest that ARHGAP11A is a suppressor of pre-mature delamination of aRG and support the validity of using human forebrain-type organoids as a model to study early brain development and corticogenesis.

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16. Proteomics analysis in the aged brain reveals an isoform switch in physiological aging and increased protein turnover

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Keywords: aging, proteogenomics, protein turnover

Abstract: Brain aging is a complex process involving tissue deterioration and increased cellular diversity, leading to functional impairment and vulnerability to diseases. Despite technological advancements, understanding the intricate molecular processes remains limited, particularly when integrating mRNA and protein datasets. In this study, we analyzed mRNA levels, protein levels, and protein turnover in young and aged adult mice. Our findings revealed increased protein lifetimes in aged brains and highlighted pathways associated with neurodegenerative diseases. By comparing mRNA and protein measures, we observed shifts in neuronal homeostasis. Additionally, we identified novel protein isoform sequences based on our mRNA dataset which reveals an age specific expression. Integrating these datasets unveiled differential effects on mRNA levels, protein translation, and degradation with age, implicating specific pathways in physiological aging and neurodegeneration. Our integrated proteogenomic approach underscores the potential of targeting these pathways for anti-aging interventions.

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Nisha Hemandhar Kumar will give a Flash Talk (10:15 to 10:45).

17. Generation of otic Bioengineered Neuronal Organoids (oBENO)

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Keywords: hiPSC, otic, organoids, inner ear

Abstract: Over 5% of the global population suffers from sensorineural hearing loss. Although some patients benefit from electrical cochlear implants no therapy to date can ensure functional restoration. Human pluripotent stem cells (iPSCs) derived inner ear organoid models are powerful tools that can be used to decipher mechanisms of disease and develop novel therapeutic strategies. However, current protocols show low efficiency, with 20% of the tissues developing hair cells and spiral ganglion neurons. We have developed an inner ear organoid model by patterning our previously established Bioengineered Neuronal Organoid (BENO) model. Human iPSC embedded in collagen hydrogel are differentiated by the addition of small molecules and growth factors modulating BMP, TGF, WNT, and RA pathways. On day 20, gene expression revealed a 10-, 27-, and 8-fold increase in otic progenitor genes PAX8, PAX2, and FBOX2 compared to iPSC, respectively (N=3 independent experiments, n=4-5 tissues). By day 40, mRNA levels for hair cell-specific markers ATOH1 and MYO7A were 8.2-fold and 3.2-fold higher than in iPSC, respectively (N=3, n=4-5). On day 60 ATOH1 mRNA levels decreased (6.8-fold higher than iPSC, N=3, n=4-5), while MYO7A transcripts were increased (7.3-fold higher than iPSC, N=3, n=4-5), highlighting the otic fate induction of sensory cells. Wholemount immunofluorescence (N=3, n=3) validated the qPCR findings. PAX8 positive otic progenitors developed into MYO7A/ATOH1 positive hair cell-like cells (in 74/82 organoids) and BRN3A/PV positive spiral ganglion neuron-like cells around vesicular structures after 60 days in culture. We additionally identified BRN4-positive periotic mesenchyme-like cells near sensory neurons and SOX2-positive supporting cells around hair-like cells. By day 90, OTOF/RIBEYE-positive cells confirmed functional ribbon synapses. In conclusion, we established an efficient inner ear organoid protocol for disease modeling and therapeutic screening.

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18. Investigation of nucleoids in presynaptic mitochondria using super-resolution microscopy

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Keywords: Mitochondria, Neurons, Nucleoids

Abstract: Neurons consume a lot of energy in the form of ATP which is mainly produced by oxidative phosphorylation in mitochondria. 13 proteins of the electron transport chain are encoded in the mitochondrial DNA (mtDNA) which is packaged with the mitochondrial transcription factor A (TFAM) into compact nucleoid structures. Unpublished data could demonstrate that axonal mitochondria often lack nucleoids but in presynapses the amount of mitochondria containing nucleoids is increased suggesting a functional role of nucleoids in presynaptic mitochondria. Therefore, this project aims to elucidate the role of nucleoids in presynaptic mitochondria using super-resolution microscopy.

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19. The role of PLPPR3 in cytoskeleton-condensate-membrane interactions

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Keywords: cytoskeleton, actin, LLPS, membrane, filopodia

Abstract: Liquid-liquid phase separation (LLPS) is a biophysical process, in which aqueous biomolecules in a solution condensate into separate aqueous phases. Cells exploit condensate formation to efficiently and reversibly generate membrane-less compartments. These compartments can catalyze biochemical reactions, including cytoskeleton remodeling, act as liquid scaffolds that reshape membranes and function as signaling domains that support intracellular information transfer. However, the way interaction sites between condensates and membranes organize cellular biochemistry dynamically, and how such organization governs cellular physiology remain poorly understood. This project builds upon our precious findings on the physico-molecular nature of condensate-membrane contact sites and a condensate-forming domain of PLPPR3 (Phospholipid Phosphatase-Related 3), a membrane protein involved in neuronal branching and filopodia formation. We will explore functions of PLPPR3 that shape membranes and assemble actin networks compatible with neuronal filopodia formation. We have proven the phase separating nature of PLPPR3 in vitro using purified PLPPR3 and in cell lines using expression methods with overexpression method and using the Cry2 technique, and PLPPR3 membrane bending was shown with giant unilamellar vesicles (GUVs) We study the actin recruitment into PLPPR3 phases both in vitro and in cell lines. In the future, we plan to implement the techniques used on cell lines into experiments with neurons. There we will explore the role of PLPPR3 post-translational modifications (PTM), intracellular signaling and actin polymerization on protrusive membrane formation during axon branching. Our studies will provide fundamental mechanistic insights into how the cytoskeleton together with membrane-bound and membrane-less compartments organise neuronal morphogenesis.

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Domonkos Nagy-Herczeg will give a Flash Talk (10:15 to 10:45).

20. Development of Spatial and Temporal Proteomics Workflows for Pig Hearts

Lisa Neuenroth[1], Jumana Jaber[1,2], Verena Ebner[1], Stephan E. Lehnart[1,2,3,4], *Christof Lenz*[1,2,3,4,5]

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Keywords: Proteomics, Pigs, PCT-SP3-DIA MS, Cardiomyopathies

Abstract: Cardiomyopathies, including myocardial infarction, dilated/hypertrophic cardiomyopathies (CM), and heart failure (HF), are characterized by various cellular defects, such as protein aggregation and fibrosis. Understanding these complex phenotypes and uncovering the underlying cellular and molecular mechanisms necessitates advanced systems biology and multi-omics approaches. While transgenic mice and human-induced pluripotent stem-cell-derived cardiomyocytes (hiPSC-CMs) serve as standard models, they differ significantly from native human cardiac biology. Pig models offer human-like physiology and enable spatially-resolved proteomics studies, but the lack of reproducible, medium-throughput proteome analysis workflows has been a challenge. In recent developments, our group introduced an automated pressure-cycling technology (PCT) single-pot solid-phase-enhanced sample preparation (SP3) workflow for data-independent analysis (DIA)-MS. This approach significantly enhances the analysis of cardiac biopsies obtained from live WT pigs. The use of specific detergents, including 2% SDS, showed superior results over urea-based methods, leading to up to a 90% increase in the recovery of selected cardiac proteins of interest. The PCT-SP3-DIA proteomics workflow enables quantitative analysis of approximately 6,000 protein groups from a mere 0.5 mm³ tissue volume, with a throughput of 12 samples per day. This approach paves the way for reproducible proteomics data, even from small 0.5 mm³ biopsies, offering the potential for spatially-resolved proteome mapping. Currently, these techniques are being applied to investigate a novel pig disease model.

Lead contact: Lisa Neurenroth

21. Organoid assembloids modeling the role of serotonin during human cortical development

Raquel Pérez Fernández[1,2,3], Marco T. Siekmann[1,2,3], Martin Kubitschke[4], Lutz Wallhorn[4], Ammar Jabali[1,2,3], Anne Hoffrichter[1,2,3], Philipp Koch[1,2,3], Olivia Andrea Masseck[4], Julia Ladewig [1,2,3]

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Keywords: Serotonin, corticogenesis, raphe , assembloids

Abstract: The development of the human cortex involves the coordination of several processes including cell proliferation, migration, differentiation, and connectivity. Alterations in these events can lead to pathological conditions such as psychiatric disorders. The neurotransmitter serotonin (5-HT) has been shown to play a significant role in this context, although its molecular effects are poorly understood. Interestingly, the developing cortex initially receives 5-HT from the maternal placenta prior to endogenous innervation from the serotoninergic neurons in the raphe nuclei. We used human induced pluripotent stem cell-derived cortical progenitors, cortical organoids (CO), and cortical-raphe assembloids to investigate serotonin's role during early human corticogenesis. When cortical progenitors and CO were exposed to 5-HT, we observed increased proliferation of progenitor populations, including apical (aRG) and basal radial glial cells (bRG). Agonist and antagonist experiments revealed that 5- HT signalling is mediated via cell type specific receptor subtypes: 5-HTR2C in aRGs, and 5-HTR2A in bRGs To mimic the interaction between 5-HT neurons and the developing cortex more accurately, we establish cortical-raphe assembloids. To that end, we developed raphe-type organoids (RO), composed of progenitors expressing raphe-nuclei markers. Upon differentiation, RO exhibited a considerable presence of serotonergic neurons. Moreover, by introducing the genetically encoded serotonin sensor sDarken, we detected serotonin release in RO. Combining CO and RO led to widespread invasion of serotonergic afferents in CO and increased progenitor proliferation in CO regions innervated by serotonergic afferents. Our data suggest that organoid assembloids provide a valid platform to explore serotonin's role in corticogenesis and investigate related diseases.

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Raquel Pérez Fernández will give a Flash Talk (10:15 to 10:45).

22. Oligodendrocytes and neurons contribute to amyloid-beta burden in vivo

Andrew Octavian Sasmita[1], Constanze Depp[1], Taisiia Nazarenko[1], Ting Sun[1], Xuan Yu[1], Sophie Siems[1], Erinne Cherisse Ong[1], Bastian Bues[2], Riqiang Yan[3], Klaus-Armin Nave[1]

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Keywords: Alzheimer's disease, oligodendrocytes, light-sheet

Abstract: In Alzheimer's disease (AD) and its mouse models, amyloid-β (Aβ) production has primarily been attributed to excitatory neurons (ExNs), despite emerging evidence that other cell types, such as inhibitory interneurons or glial cells, might contribute to Aβ production. Cultured oligodendrocytes (OLs) are capable of generating detectable levels of Aβ in vitro. Since OL lineage cells are abundantly present in the nervous system, we aimed to investigate if oligodendrocytes, much like neurons, contribute to amyloid-beta plaque burden in vivo. Reanalysis of single-cell resolution datasets revealed the expression of amyloid-beta-processing machinery in mouse and human OLs. Next, we generated triple mutant mouse models combining OL- and forebrain ExN-specific deletion (OL cKO and ExN cKO) of BACE1 on the knock-in APPNLGF background. We then utilized quantitative light-sheet microscopy and biochemical techniques to analyze mutant mice. By performing volumetric analysis of light-sheet data, we showed that plaque burden in OL cKO hemibrains was reduced by ~30% with the strongest decrease seen in the alveus, a white matter tract where OLs predominate. Surprisingly, the forebrain ExN-specific cKO showed >95% plaques reduction even in subcortical regions. Via amyloid-beta immunoassay, it was revealed that there was still a substantial amount of soluble amyloid-beta still produced in the ExN cKO even without significant plaque production. Moreover, we corroborated the previously observed non-linear relationship between amyloid-beta production and plaque production by showing that heterozygous APPNLGF mice do not develop 50% of homozygous mice, but rather 10%, hinting at a threshold amyloid-beta concentration that is not reached for plaque deposition. OLs actively contribute to amyloid-beta burden in vivo while forebrain ExNs remain the major producer of amyloid-beta. Our findings challenge the neuronal-centric view held in AD research with implications for anti-amyloid therapies.

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Andrew Octavian Sasmita will give a Flash Talk (10:15 to 10:45).

23. Transgenic inheritance pattern modulates plaque burden in the 5xFAD mouse model

Andrew Octavian Sasmita[1], Erinne Cherisse Ong[1], Taisiia Nazarenko[1], Maik Thalmann[2], Lena Spieth[1], Stefan Berghoff[1], Constanze Depp[1], Klaus-Armin Nave[1]

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Keywords: Alzheimer's disease, transgene, light-sheet

Abstract: The 5xFAD mouse model is one of the most commonly used mouse models of amyloidosis or more specifically, Alzheimer's disease (AD). Sex dimorphism has been reported in many transgenic AD mouse models, but even after stratification of mouse cohorts by sex, the variability of amyloid burden remain staggeringly high. As this line is bred heterozygously, here, we present a jarring relationship between the parental source of the transgene and the amyloid burden that ensued. We performed in toto amyloid plaque staining with the Congo red dye and imaged whole hemispheres via light sheet microscopy. We grouped our gender-matched data based on whether the mice inherited their transgene paternally or maternally. Mice that inherit their transgenes paternally develop a much higher amyloid burden, especially within cortical regions where amyloid plaque numbers are twice as many. We further stratified our data based on the parental and grandparental source of the transgene. We saw even more clustering of our data when taking the grandparental origin into account, albeit not as strongly as the direct parental source. This suggests that this transgenic inheritance pattern persists through generations of breeding, highlighting the importance of mouse pedigree in 5xFAD mouse, or perhaps, transgenic mouse research in general. As mice that inherit the transgene would naturally be gestated within 5xFAD mothers, we analyzed offspring of heterozygous breeding pairs. The amyloid burden of the heteroyzgous offspring still clustered into two separate populations, suggesting that it is unlikely that the distinct amyloid plaque populations are the result of maternal immune priming. We provided a novel outlook on the relationship between the 5xFAD transgenic source and amyloid plaque burden in vivo. We believe that epigenetic analysis of these mice would remain valuable.

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24. Cellular dynamics of synaptic adhesion proteins: neurexins and neuroligins

Kea Aline Schmoll[1,2], Ole Jensen[3], Jürgen Brockmöller[3], Wolfram-Hubertus Zimmermann[1,2], Maria-Patapia Zafeiriou[1]

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Keywords: midbrain, organoid, dopamine, neuronal, hiPSC

Abstract: Parkinson's Disease (PD) is an incurable neurological disease affecting 1% of the population above 60 years of age. The main pathological hallmark of this disease is the degeneration of dopaminergic neurons in the substantia nigra in the midbrain, leading to lack of dopamine in the human forebrain. Although in vivo experiments in rodent models have been instrumental for the identification of the pathological hallmarks of PD, the underlying cause remains unknown rendering treatment impossible. Human induced pluripotent stem cells (hiPSCs) derived organoids offer new opportunities to investigate and treat neurological diseases. To decipher the molecular mechanisms underlying the pathophysiology of PD, we aimed to generate a human organoid containing ventral midbrain dopaminergic (mDA) neurons, based on a previously established model, the bioengineered neuronal organoid (BENO) (Zafeiriou et al., 2020). The midbrain BENO (mBENO) is generated from hiPSCs embedded in collagen hydrogel, patterned into ventral midbrain by growth factors and small molecules over a timecourse of 30 days. On D62 mBENOs were analysed for floor plate (LMX1a, FOXA2), midbrain (EN1) and mDA neuron (TH) markers. Real-time PCR analysis a six-fold higher expression of TH, a 180-fold higher expression of EN1, a seven-fold higher expression for LMX1a and a 24-fold higher expression for FOXA2 compared to undifferentiated hiPSCs (n=4). Wholemount immunofluorescence analysis validated the high abundance of mDA neurons marked by FOXA2 and TH. Finally, we quantified the dopamine content of mBENO via liquid chromatography mass spectrometry and detected 0.86 ± 0.25 pmol/mg of tissue by D62 of differentiation (n=4), which was significantly higher than BENO (0.05 ± 0.01 pmol/mg). In conclusion, mBENO represents a novel human midbrain organoid model enriched in ventral dopamine producing neurons. In the future, we will explore the mBENO potential in modelling PD by patient and transgenic lines or as mDA source.

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25. Analyses of the age-dependent challenges of the neuronal actin filament system

Rafaela Pedro Silva[1], Patricia Kreis[1], Till Mack[1], Marieluise Kirchner[2], Fan Liu[3], Janine Kirstein[4], Britta J. Eickholt[1]

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Keywords: Actin, dendritic spine, aging, neurodegeneration

Abstract: Dendritic spines are specialized protrusions arising from the dendritic shaft that convey input from neighboring neurons, coordinating higher functions such as memory and cognition. Besides transmembrane and cytoplasmic proteins, spines are composed of a dense cytoskeletal network. Dendritic spines are often shrinked or depleted in aging and Alzheimer's disease (AD). The morphological changes at the spine are accomplished by the remodeling of its structural framework – the actin cytoskeleton. The actin binding protein (ABP) Drebrin (Dbn) regulates cytoskeletal functions during neuronal development and is thought to contribute to structural and functional synaptic changes associated with aging and AD. Interestingly, decreased protein levels of Dbn have been reported to be associated with mild cognitive impairment and AD. We previously identified Dbn phosphorylation at S647 to increase protein stability and stress resilience at the spines. Long-term depression (LTD) defined as a long-lasting weakening of a synapse has been suggested to be altered in age-related memory deficits. Our ongoing work shows that induced chemical LTD (cLTD) in cortical neurons rapidly decreases both Dbn protein levels, which is triggered by phosphorylation. We aim to characterize posttranslational modifications observed during cLTD, and use Dbn as an entry point to characterize the actin interactome in synaptosomes isolated from aged and AD model mouse brains. This work will provide mechanistic and physiological insights into the functional role of the actin cytoskeleton to provide neuronal protection upon stress in neurodegeneration and with the progression of aging.

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26. Cytokine/CRLF3-signalling protects insect neurons and regulates acetylcholinesterase in human cells.

Björn Twellsieck[1], Ida-Marie Tiedeken[1], Ralf Heinrich[1]

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Keywords: Neuroprotection, Apoptosis, Neuropharmacology

Abstract: Previous studies demonstrated that the protective effects of Erythropoietin (EPO) are sufficient to protect locust neurons from apoptosis in cell culture under hypoxic conditions. These antiapoptotic effects were mediated via the evolutionary conserved Cytokine Receptor Like Factor 3 (CRLF3) receptor and potentially other tissue protective EPO receptors, but not via the classical EPO receptor as it exists in mammalia. Using the EPO splice variant EV-3, which binds only to CRLF3 rather than the classical EPO receptor, neuroprotection was also observed in human cells. Furthermore, treatment with EPO resulted in CRLF3-mediated downregulation of proapoptotic acetylcholinesterase (AChE) in locusts. These findings prompted us to investigate whether other cytokines could also bind to CRLF3 and if similar downregulation of AChE occurred in mammalian cells. Our approach involved immunohistochemistry and spectrophotometry to assess cell viability following treatment with EPO-related cytokines and subsequent exposure to adverse chemical (rotenone) or environmental (hypoxia) conditions. Our results suggest that other cytokines can indeed bind to the CRLF3 receptor, conferring cell-protective effects. These findings support the hypothesis that the CRLF3 receptor serves as a conserved, multi-cytokine binding receptor within the type 1 cytokine receptor family.

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27. Developmental characterization of iPSC-derived Callithrix jacchus cerebral organoids

Lidiia Tynianskaia[1], Cesar Mateo Bastidas Betancourt[1], Nesil Eşiyok[1], Neringa Liutikaite[1], Michael Heide[1]

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Keywords: Common marmoset, cerebral organoids

Abstract: The common marmoset (Callithrix jacchus) is a New World primate widely employed as a model organism for neuroscientific research, due to its evolutionary proximity to human. However, the usage of marmosets as a research model is restricted by ethical considerations and technical limitations. Cerebral organoids represent one of the most promising in vitro instruments to study the primate brain in a technically simple and ethically justifiable way. In this study, we generated this organoid type from marmoset induced pluripotent stem cells (iPSCs). We developed a unified protocol enabling us to generate cerebral organoids from different primate species including human and common marmoset. To the best of our knowledge, our group was the first one to achieve this. In order for marmoset cerebral organoids to become a well-established in vitro model for brain research extensive characterization is required. Here, we compare human and marmoset organoids to elucidate similarities and differences in their maturation and developmental rates on a molecular level.

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Lidiia Tynianskaia will give a Flash Talk (10:15 to 10:45).

Organizing Team

The Encephalon 2023 is organized by the PhD students of the GGNB program “Cellular and Molecular Physiology of the Brain” (CMPB).

Name	Affiliation
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Thank You Message from the Organizing Team

Dear Colleagues and Guests,

As we stand on the threshold of the Encephalon Symposium, our hearts are filled with gratitude and we would like to express our appreciation to our guests. Your involvement in our symposium is instrumental in making this event a success, and we hope that you will all take away new insights and ideas that will help you in your own research.

A special thank you to our sponsors for their invaluable support. Including our Premium Sponsors, who are available at the symposium: Synaptic Systems; Ibidi; Leica; Cell Signaling. Our Basic sponsors: Thorlabs; Zeiss; Microsynth; Science Services and other Sponsors: SFB 1286; Georg-August-Universität Göttingen; and Max-Planck-institute for Multidisciplinary Sciences.

And in the end, our heartfelt gratitude goes to all the people who played a role in making this symposium possible. Who spent hours, days, and even months to make this symposium happen. Your unwavering commitment has turned challenges into triumphs. Thank you for making this journey extraordinary.

With heartfelt appreciation,

Laura and Ronja

Coordinators Encephalon and program speakers CMPB

Organizing Team

From left:Thomas Dresbach;Dawei Wang;Nikos Mougios;Laura v. Agen;Kristina Jevdokimenko; László Albert;Víctor M. Palacios; Luca Büschgens;Matea Krizman;Sarthak Banerjee;Mrinalini Ranjan;Ronja Rehm;Frederieke S. Moschref;Leonie C. Schadt;Xiaoyi Mao

From left:Dawei Wang;Thomas Dresbach;Kristina Jevdokimenko;Laura v. Agen;Nikos Mougios; Frederieke S. Moschref;Matea Krizman;Ronja Rehm;Leonie C. Schadt;László Albert;Luca Büschgens

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