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The Korean Academy of Science and Technology

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Conference Programme

# Advances in Brain Research

7th KAST-Leopoldina Bilateral Symposium

**28 – 29 June 2023** | Halle (Saale)

## Imprint

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7th KAST-Leopoldina Bilateral Symposium

**28 – 29 June 2023**
Lecture Hall
German National Academy of Sciences Leopoldina
Jägerberg 1 | 06108 Halle (Saale) | Germany

# Programme

## Wednesday, 28 June 2023

**09:30 – 10:00** **Registration**

**10:00 – 10:30** **Opening Session**

**Welcome Remarks**
Gerald Haug ML
*President of the Leopoldina*

Ook-Joon Yoo
*President of KAST*

**Introductory Remarks by the Scientific Coordinators**
Hans Schöler ML
*Max Planck Institute for Molecular Biomedicine, Münster*

Bong-Kiun Kaang
*Department of Biological Sciences, Seoul National University*

**10:30 – 12:00** **Keynote Session**

**The Cerebral Cortex, a Delay Coupled Oscillator Network: Computations in High Dimensional Dynamic Space**
Wolf Singer ML
*Ernst Strüngmann Institute (ESI) for Neuroscience in Cooperation with the Max Planck Society, Frankfurt/Main*

**Reactive Astrocytes as the Cause of Alzheimer's Disease**
Changjoon Justin Lee
*Center for Cognition and Sociality, Institute for Basic Science (IBS), Daejeon*

**12:00 – 13:00** **Group Photo and Lunch Break**

**13:00 – 15:00** **Session 1: Progress in Understanding the Fundamental Functions of the Human Brain (I)**

**Cerebral Cortex Connectomics**
Moritz Helmstaedter
*Max Planck Institute for Brain Research, Frankfurt/Main*

**Cell-Type Specific Connectivity Mapping and Cellular Profiling**
Jinhyun Kim
*Brain Science Institute, Korea Institute of Science and Technology (KIST), Seoul*

**The Short and Long of Inhibition**
Hannah Monyer ML
*Department of Clinical Neurology, Medical Faculty of Heidelberg University*
*German Cancer Research Center (DKFZ) of the Helmholtz Association*

**Synchronization of Neuronal Networks at High Speed**
Dietmar Schmitz ML
*Charité Universitätsmedizin Berlin*

**15:00 – 15:15** **Coffee and Tea Break**

**15:15 – 16:15** **Session 1: Progress in Understanding the Fundamental Functions of the Human Brain (II)**

**Understanding Pain: Insights from the Brain and Artificial Intelligence**
Choong-Wan Woo
*Center for Neuroscience Imaging Research, Department of Biological Sciences, Sungkyunkwan University, Suwon*

**Dopaminergic Control of Compulsive Eating: Role of Dopamine D2 Receptor**
Ja-Hyun Baik
*Department of Life Sciences, Korea University, Seoul*

**16:15 – 16:30** **Coffee and Tea Break**

**16:30 – 18:30** **Session 1: Progress in Understanding the Fundamental Functions of the Human Brain (III)**

**Enhancer RNAs in Brain Plasticity**
Tae-Kyung Kim
*Department of Life Sciences, Pohang University of Science and Technology (POSTECH)*

**Neural Processing Beyond Reinstatement During Memory Retrieval in the Human Brain**
Sue-Hyun Lee
*Department of Psychology, Seoul National University*

**Modeling Human Brain Development and Disease in Stem Cell Derived 3D Culture**
Jürgen Knoblich
*IMBA – Institute of Molecular Biotechnology, Vienna, Austria*

**Discussion**

## Thursday, 29 June 2023

**09:00 – 09:05** **Welcome Remarks**

Ulla Bonas ML
*Vice-President of the Leopoldina*

**09:05 – 11:00** **Session 2: New Research Avenues – From Stem Cell Research and Organoids to Artificial Intelligence-Assisted Brain Science**

**Creation of Forebrain Assembloids to Recapitulate the Dynamic Cellular Interactions in the Human Schizophrenia Brain**
Kunyoo Shin
*Department of Biological Sciences, Seoul National University*

ML – Member of the Leopoldina

**Machine Learning and AI for the Sciences: Toward Understanding**
Klaus-Robert Müller ML
*Berlin Institute for the Foundations of Learning and Data (BIFOLD)*

**Biomedical Integrated Circuits and Systems for Brain Engineering**
Chul Kim
*Department of Bio and Brain Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon*

**Discussion**

**11:00 – 11:15** **Coffee and Tea Break**

**11:15 – 12:15** **Session 3: Advances in the Diagnosis and Treatment of Brain Disorders (I)**

**Genetic Architecture of the Restless Legs Syndrome**
Juliane Winkelmann ML
*Helmholtz Munich, Institute of Neurogenomics*
*Klinikum rechts der Isar der Technischen Universität München, Institute of Human Genetics*

**Brain Somatic Mutations in Intractable Focal Epilepsy**
Jeong Ho Lee
*Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon*

**12:15 – 13:30** **Lunch Break and Guided Tour of Leopoldina Building**

**13:30 – 15:30** **Session 3: Advances in the Diagnosis and Treatment of Brain Disorders (II)**

**Reduced Penetrance of Hereditary Movement Disorders: Elucidating Mechanisms of Endogenous Disease Protection**
Christine Klein ML
*University of Luebeck*

**Using Cerebral Organoids to Map the Impact of Prenatal Stress on Brain Development: Consequences for Psychiatry**
Elisabeth Binder ML
*Max Planck Institute of Psychiatry, Munich*

**Development of New Tools to Study Autophagy**
Jin-A Lee
*Department of Biopharmaceutical Engineering, Hannam University, Daejeon*

**Discussion**

**15:30 – 15:45** **Coffee and Tea Break**

**15:45 – 16:30** **Concluding Discussion and Closing Remarks**

Bong-Kiun Kaang
*Department of Biological Sciences, Seoul National University*

Hans Schöler ML
*Max Planck Institute for Molecular Biomedicine, Münster*

# Opening Session

## Welcome Remarks

**Gerald Haug ML**
President of the Leopoldina

**Ook-Joon Yoo**
President of KAST

## Introductory Remarks

**Hans Schöler ML**
Max Planck Institute for Molecular Biomedicine, Münster

**Bong-Kiun Kaang**
Department of Biological Sciences, Seoul National University


# Gerald Haug

**President**
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## Vita

Gerald H. Haug is the President of the German National Academy of Sciences Leopoldina.

He studied geology in Karlsruhe (1987 – 1992). For his doctorate, he moved to the University of Kiel where he received his PhD in paleoceanography in 1995. He then worked as a postdoctoral fellow at the University of British Columbia in Vancouver, Canada and at the Woods Hole Oceanographic Institution, USA. In 1998, he spent two years as a research assistant professor at the University of Southern California in Los Angeles, USA.

At the start of the 2000s, he became an 'Oberassistent' at the Swiss Federal Institute of Technology (ETH) in Zurich, where he habilitated in 2002. In 2003, he took over the post of section head at the GFZ – German Research Centre for Geosciences in Potsdam and was appointed full professor at the University of Potsdam. In 2007, he was appointed ordinary professor at ETH Zurich.

Since 2015, he has been Director of the Department of Climate Geochemistry at the Max Planck Institute for Chemistry in Mainz and a Scientific Member of the Max Planck Society. He maintains his positions at the Max Planck Institute and ETH Zürich in a part-time capacity.

# Ook-Joon Yoo

**President**
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## Vita

Prof. Ook Joon Yoo served as the Director of BioMedical Research Center and professor of Graduate School of Medical Science and Engineering at the Korea Advanced Institute of Science & Technology (KAIST). He also performs an important role in the National Science and Technology council, as a member.

He began his research and teaching at the Department of Biological Science of KAIST from 1982 and he also was the Chairman of the Department. He served as the Director of Molecular Medicine Research Group supported by Ministry of Science & Technology. Besides, he was the Chairman of the Korean Bioscience and Biotechnology Association, and the President of the Korean Society for Biochemistry and Molecular Biology. Also, he served as the Executive-Vice President of the KAST during 2016 – 2019.

With his distinguished achievements as a molecular biologist, he has received diverse awards including the Order of Science and Technology Merit from Korea Government in 2015, Grand Research Award from KAIST in 2002, and Research & Development Award from KAIST in 1996.

He received his B.S. from Seoul National University and his Ph.D. in Biochemistry and Molecular Biology from the University of Chicago. His research interest covers genomics-based drug target discovery & validation as well as studies on genetic disorders.

He published more than 140 articles mostly through international journals in his research field. He also is the author of the book, BioMedical Research, which has been one of best and steady sellers for last 25 years.

Currently, he is the President of the Korean Academy of Science and Technology (KAST).


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# Hans Schöler

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## Vita

Dr. Hans Robert Schöler is director emeritus heading a group at the Max Planck Institute for Molecular Biomedicine in Münster and was full professor at the University of Münster, adjunct professor at the Hannover Medical School, distinguished professor at Konkuk University in Seoul, and adjunct professor at the University of Pennsylvania in Philadelphia. His research focuses on pluripotent and germ cells and how somatic and pluripotent cells can be converted into each other.

He received his diploma in biology and his Ph.D. in molecular biology from the University of Heidelberg. Prior to his current position, he was staff scientist at the Max Planck Institute for Biophysical Chemistry in Göttingen, led research groups at Boehringer Mannheim (now Roche) and the EMBL in Heidelberg, and as professor at the University of Pennsylvania.

One of his most important scientific achievements was the pioneering derivation of germ cells from embryonic stem cells. A renowned scientist in the field of stem cells, he is an elected member of the German Academy of Sciences Leopoldina and the North Rhine-Westphalian Academy of Sciences and Arts, as well as an associate member of the Berlin-Brandenburg Academy of Sciences and the Mainz Academy of Sciences and Literature. He was elected to the board of the ISSCR and as a member of EMBO, and recently served as president of the German Stem Cell Network (GSCN). Among numerous other awards, he received the Robert Koch prize, the Max Delbrück Medal, and the Kazemi Prize (Iran). In 2010, the Hans Schöler Stem Cell Research Center (HSSCRC) named after him was inaugurated at the Ulsan National Institute of Science and Technology (UNIST).

# Bong-Kiun Kaang

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## Vita

Bong-Kiun Kaang, Ph.D. is Distinguished Professor at School of Biological Sciences, Seoul National University (SNU). He joined SNU as a faculty member since 1994. He obtained B.S. at SNU in 1984. He obtained Ph.D. at Columbia University, in 1992 (Supervisor: Nobel Laureate Eric R. Kandel).

His research focuses on molecular mechanisms underlying synaptic plasticity. He is interested in studying how a change in synaptic efficacy leads to a functional modification of neural circuit that may represent new information and may often underlie neurological and psychiatric disorders such as Alzheimer's disease, autism spectrum disorder, drug addiction, depression and posttraumatic stress syndrome. He has used cellular, molecular, electrophysiological and behavioral techniques to understand the molecular and cellular mechanisms underlying learning and memory and brain disorders using marine snail and rodents as experimental models.

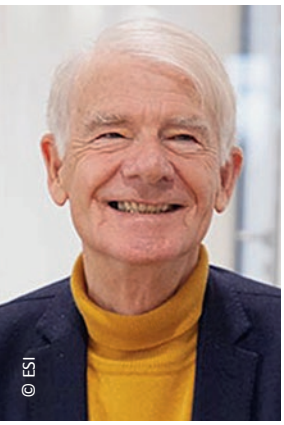
He has published 235 research and review articles in a number of journals, including *Science, Cell, Nature, Neuron,* and *Nature Neuroscience.* He is currently the Editor-in-Chief of *Molecular Brain.* He won Life Science Award (2008) from Korean Society for Molecular and Cellular Biology, Donghun Award (2012), Korean Society for Biochemistry and Molecular Biology, the Kyung Ahm Prize (2012) from the Kyung Ahm Foundation, the National Academy of Sciences Award of Korea (2016), and Korea Best Scientist & Engineer Award (2018) from the Korean Federation of Science and Technology and the Korean Government and the Hoam Samsung Prize (2021). He is currently a National Honor Scientist and a Fellow of the Korean Academy of Science and Technology.

# Keynote Session

## Speakers

The Cerebral Cortex, a Delay Coupled Oscillator Network:
Computations in High Dimensional Dynamic Space
**Wolf Singer ML**
Ernst Strüngmann Institute (ESI) for Neuroscience in Cooperation with the Max Planck Society, Frankfurt/Main

Reactive Astrocytes as the Cause of Alzheimer's Disease
**Changjoon Justin Lee**
Center for Cognition and Sociality, Institute for Basic Science (IBS), Daejeon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# Wolf Singer

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## Vita

Prof. Dr. Dr. h.c. mult. Wolf Singer studied Medicine in Munich and Paris, obtained his MD from the Ludwig Maximilian University in Munich, and his PhD from the Technical University in Munich. He is Director em. at the Max Planck Institute for Brain Research in Frankfurt, Founding Director both of the Frankfurt Institute for Advanced Studies (FIAS) and of the Ernst Strüngmann Institute for Neuroscience (ESI) and Director of the Ernst Strüngmann Forum.

His research is focused on the neuronal substrate of higher cognitive functions, and especially on the question how the distributed sub-processes in the brain are coordinated and bound together in order to give rise to coherent perception and action. These studies are performed with electrophysiological techniques in behaviorally trained monkeys and with non-invasive imaging methods in human subjects.

# The Cerebral Cortex, a Delay Coupled Oscillator Network: Computations in High Dimensional Dynamic Space


## Abstract

The cerebral cortex can be considered as a delay coupled recurrent network whose nodes are feature selective and have a propensity to oscillate. Such networks exhibit high dimensional non-linear dynamics that can be exploited for computations. Results obtained with parallel recordings of neuronal responses in the visual cortex suggest that the cerebral cortex uses this high dimensional dynamic space for the flexible encoding of relations among features (feature binding), for the acquisition and storage of information about statistical contingencies of features in the environment (priors), for the ultra-fast matching of priors with sensory evidence (predictive coding) and the segregation of stimulus specific activity vectors in high dimensional space (classification). In addition, the network dynamics allow for the generation of stimulus specific response sequences (temporal codes) and the superposition of information provided by sequentially presented stimuli (Fading memory). Simulations of such networks demonstrate the functional significance of the rich dynamics emerging from reciprocally coupled oscillators such as synchronisation, resonance, entrainment, phase shifts and reverberation. These computational principles differ from those realized in the multilayer feed forward architectures that characterize the deep learning networks currently used in AI systems. It is proposed that the remarkable differences between the performance of natural and artificial systems are mainly due to the fact that the former rely on analogue computation and exploit the temporal dimension as coding space.


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# Changjoon Justin Lee

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## Vita

Dr. C. Justin Lee is a neuroscientist specializing in the field of glioscience, concentrating on the study of astrocytes. He is currently the Managing Director of the Institute for Life Science and the Director of Center for Cognition and Sociality (CCS) at the Institute for Basic Science (IBS) from 2018. He has been on the editorial boards of the journals Molecular Brain, Molecular Pain and GLIA and is a chief editor of Experimental Neurobiology. He has also served as Professor at IBS school of UST and Adjunct Professor at UNIST.

In 2004, Dr. Lee started his professional career at the Korea Institute of Science and Technology (KIST) and established the Center for Neuroscience with Director Hee-sup Shin. He served as the Director of Center for Neuroscience at the KIST and later founded the WCI Center for Fuctional Connectomics as part of the World Class Institute Program in 2009.

He has received various prestige awards such as Korea Science & Technology Development Presidential Medal of Honor in 2017, Kyung-Ahm Prize in 2016, and Outstanding Researcher Award, Prime Minister of Korea in 2010.

Center for Cognition and Sociality (CCS) focuses on unraveling the mechanisms of brain function for cognition and sociality, identifying causes of psychiatric disorders and neurodegenerative diseases, and developing novel treatments through research at various levels encompassing molecules, cells, and organisms. The CCS consists of 10 laboratories in 3 groups (Cognitive Glioscience, Social Neuroscience, Brain Imaging and control and YSF Groups) according to the research topics. The CCS is conducting multidisciplinary research based on genetics, behavioral genetics, electrophysiology, optogenetics, acoustic neuromodulation, molecular neuro-imaging, brain wave analysis, synthetic biology, and glycomics.

# Reactive Astrocytes as the Cause of Alzheimer's Disease


## Abstract

Reactive astrocytes have emerged as one of the key components of the neuroinflammation and possible causes of various neurodegenerative diseases including Alzheimer's disease, Parkinson's disease and Huntington's disease. In this keynote lecture, I will present our latest works on the molecular and cellular mechanisms of how reactive astrocytes contribute to neurodegenerative diseases. Mechanistically, reactive astrocytes take up toxic protein species such as amyloid plaques to degrade and digest through autophagy/lysosome and via a series of metabolic pathways that include urea cycle and putrescine degradation pathway, resulting in final byproducts of the toxic $H_2O_2$, ammonia, and inhibitory transmitter GABA. The excessive production and release of $H_2O_2$ from severe reactive astrocytes leads to oxidative and nitrosative stress to kill the neighboring neurons, while excessive GABA causes strong tonic inhibition of neuronal activity to impair synaptic transmission, plasticity, learning, and memory. The novel concepts and tools that are proposed have been extremely valuable in developing novel therapeutic approaches to diagnose and cure the various neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease.

Session 1

# Progress in Understanding the Fundamental Functions of the Human Brain

## Co-Chairs

**Hans Schöler ML**
Max Planck Institute for Molecular Biomedicine, Münster

**Bong-Kiun Kaang**
Department of Biological Sciences, Seoul National University

## Speakers

### Cerebral Cortex Connectomics
**Moritz Helmstaedter**
Max Planck Institute for Brain Research, Frankfurt/Main

### Cell-Type Specific Connectivity Mapping and Cellular Profiling
**Jinhyun Kim**
Brain Science Institute, Korea Institute of Science and Technology (KIST), Seoul

### The Short and Long of Inhibition
**Hannah Monyer ML**
Department of Clinical Neurology, Medical Faculty of Heidelberg University
German Cancer Research Center (DKFZ) of the Helmholtz Association

### Synchronization of Neuronal Networks at High Speed
**Dietmar Schmitz ML**
Charité Universitätsmedizin Berlin

### Understanding Pain: Insights from the Brain and Artificial Intelligence
**Choong-Wan Woo**
Center for Neuroscience Imaging Research, Sungkyunkwan University, Suwon

### Dopaminergic Control of Compulsive Eating: Role of Dopamine D2 Receptor
**Ja-Hyun Baik**
Department of Life Sciences, Korea University, Seoul

### Enhancer RNAs in Brain Plasticity
**Tae-Kyung Kim**
Department of Life Sciences, Pohang University of Science and Technology (POSTECH)

### Neural Processing Beyond Reinstatement During Memory Retrieval in the Human Brain
**Sue-Hyun Lee**
Department of Psychology, Seoul National University

### Modeling Human Brain Development and Disease in Stem Cell Derived 3D Culture
**Jürgen Knoblich**
IMBA – Institute of Molecular Biotechnology, Vienna, Austria


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# Moritz Helmstaedter

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## Vita

Moritz Helmstaedter is a Director at the Max Planck Institute for Brain Research in Frankfurt, Germany. His work aims at pushing the frontiers of Connectomics, a research field occupied with mapping neuronal networks in the brain at unprecedented scale and resolution. Before joining the Max Planck Institute for Brain Research in 2014, he was a Research Group leader and Principal Investigator at the Max Planck Institute of Neurobiology in Munich (2011 – 2014).

Born in Berlin in 1978, Moritz studied medicine and physics at Ruprecht-Karls-University Heidelberg. He completed his doctoral thesis with Nobel laureate Bert Sakmann, followed by post-doctoral work with Winfried Denk, both at the Max Planck Institute for Medical Research in Heidelberg, Germany.

Additional appointments include Professor (Chair, extraordinary professor) for Neuronal Networks at Radboud University, Nijmegen, Netherlands (since 2016), member of the foundation board of the Peace Prize of the German Book Trade (since 2020) and member of the life sciences committee of Leopoldina (since 2023).

# Cerebral Cortex Connectomics


## Abstract

The mapping of neuronal connectivity is one of the main challenges in neuroscience. We use 3-dimensional electron microscopy (EM) imaging of nerve tissue at nanometer-scale resolution across substantial volumes, extending to more than one millimeter on the side, followed by AI-based image analysis to obtain dense connectivity maps, or connectomes. With these we have recently mapped local circuitry in mouse and human cortex, determined learning-related synaptic network imprints, mapped the connectomic development of inhibitory axons, and discovered a 10-fold expanded interneuron-to-interneuron network in the human cortex. We are currently screening cortical connectomes across age, disease states and experience to obtain a deeper understanding of their relevance for individual behavioral performance and brain pathology.


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# Jinhyun Kim

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## Vita

Jinhyun (Jinny) Kim, is a neuroscientist who obtained her B.S. and M.S. degrees in Biology from the Sung Kyun Kwan University, Korea in 1995 and 1997, respectively. She then pursued her interest in neuroscience and completed her PhD at the Max Planck Institute for Medical Research, Germany, in 2001. Following her doctoral studies, Dr. Kim conducted postdoctoral research at National Institutes of Health, USA, (2002 – 2007). She also worked as a Research Specialist at Janelia Research Campus, Howard Hughes Medical Institute, USA from 2008 to 2010. In 2011, Dr. Kim was appointed by the Korea Institute of Science and Technology (KIST) in Seoul, Korea, where she currently serves as the Director of the Brain Science Institute.

Her research interests focus on developing advanced imaging techniques to investigate the neural circuits underlying behavior in model organisms, including mice and mouse lemur. One of her major contributions to the field of neuroscience is the development of synaptic connectivity mapping technique (mGRASP and neuTube), which has been widely used to map neural circuits in a range of organisms, including mice, fruit flies, and zebrafish. It has helped researchers to identify previously unknown connections between neurons and to understand how neural circuits are altered in various diseases and conditions. Dr. Kim's achievements in neuroscience have been recognized with several awards and honors.

# Cell-Type Specific Connectivity Mapping and Cellular Profiling


## Abstract

The subthalamic nucleus (STN) plays an important role in controlling movement and is a target for deep brain stimulation to treat Parkinson's disease. Despite the therapeutic benefits observed in patients, the specific circuitry and cellular profile of the STN are not well understood. Using neuroanatomical techniques such as mGRASP, we construct a comprehensive connectivity map of the indirect and hyperdirect pathways in the mouse STN. Our circuit- and cellular-level connectivities reveal a topographically graded organization with three types of indirect and hyperdirect pathways (external globus pallidus only, STN only, and collateral). We confirm consistent pathways into the human STN by 7T MRI-based tractography. We identify two functional types of topographically distinct glutamatergic STN neurons (parvalbumin [PV+/-]) with synaptic connectivity from indirect and hyperdirect pathways. Glutamatergic PV+STN neurons contribute to burst firing. Our study suggest a complex interplay of information integration within the basal ganglia underlying coordinated movement control and therapeutic effects.


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# Hannah Monyer

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## Vita

Hannah Monyer was born in Romania and went to Germany at the age of 17. She finished high-school in Heidelberg and studied medicine at the University of Heidelberg. After five years of training in child psychiatry and pediatric neurology in Mannheim and Lübeck, she went to Stanford/USA as a postdoctoral fellow with Dennis Choi. Subsequently she did a second postdoc with Peter Seeburg at the University of Heidelberg, and was then a junior group leader at the same university. Since 1999 she is Head of the Department of Clinical Neurobiology at the Medical Faculty of Heidelberg University and since 2009 also professor at the German Cancer Research Center (DKFZ) of the Helmholtz Association. In her research on synaptic plasticity, learning and memory she has used a large array of techniques employing molecular biology, electrophysiology, optogenetics and behavioral approaches. For her achievements she has obtained numerous prizes, including the most prestigious German award for scientists, the Leibniz Prize, the Guy-Lussac-Humboldt Prize, the Tsungming Tu Prize of the Ministry of Science and Technology Taiwan, the Prize of the Berlin-Brandenburg Academy of Sciences and the Lautenschläger Research Prize of the Heidelberg University. She is a member of the Heidelberg Academy of Sciences, of EMBO, of the German National Academy of Sciences Leopoldina and of the Academia Europaea.

# The Short and Long of Inhibition

## Abstract

GABAergic neurons play an essential role in governing the timing of principal neuron firing. My lab has focused for long on studying functional properties of GABAergic neurons in mice by taking advantage of genetic modifications that would reduce the recruitment of defined GABAergic neurons preferentially in the hippocampal formation, and investigate the consequences thereof for spatial coding and memory.

Neocortical GABAergic neurons have long been considered “interneurons”, that is their range of inhibition is confined to local networks. We discovered that this is not the case: a subpopulation are GABAergic “projection” neurons that inhibit preferentially GABAergic neurons thereby causing disinhibition in the target area. The functional study of these neurons, be that in the slice preparation or in freely mice has been heavily aided by the use of optogenetic approaches. I will discuss ongoing projects in the lab that focus on GABAergic projection neurons in health and disease.

Finally, I will present and discuss work focusing on the medial and lateral entorhinal cortex and their participation in spatial- and non-spatial coding. Here too I will highlight data on GABAergic neurons (i.e. fast-spiking cells), raising the question as to their coding in simple and complex environments.


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# Dietmar Schmitz

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## Vita

Dietmar Schmitz, born in 1968 in Lennestadt, studied medicine at the University of Cologne and received his doctorate in 1997. As a postdoctoral fellow, he conducted research at the University of California (San Francisco/CA, USA). In 2002, he established his research as an assistant professor with funding from the Emmy-Noether program at the Charité and Humboldt-University. Since 2005, he has been Professor of Neurosciences and Director of the Neuroscience Research Center. He is speaker of the Cluster of Excellence NeuroCure. He has also been spokesperson of the German Center for Neurodegenerative Diseases in Berlin (DZNE) and the Einstein Center for Neurosciences. He was a member of the Young Academy of the BBAW and the Leopoldina (2004 – 2009). Since 2017, he has been a member of the German National Academy of Sciences Leopoldina and the Berlin-Brandenburg Academy of Sciences and Humanities.

Among the numerous prizes and honors that have recognized his achievements are the First Einstein Professorship, the Bernard Katz and Humboldt award, and the Schilling Research Prize of the German Neuroscience Society (2005).

His research questions include how the central nervous system encodes experience and information in synapses and neuronal networks. In close collaboration with clinical colleagues, he also focuses on the analysis of neuropsychiatric diseases.

# Synchronization of Neuronal Networks at High Speed


## Abstract

One of the most intriguing open questions in neuroscience is how the brain captures and stores information in such an efficient and long-lasting way. To do so, it has to perform a tremendous task: it has to process a continuous input from our sensory organs and at the same time it must be able to store memories, sometimes even for a lifetime. What are network-level foundations of this long-term information storage capacity? In a concert between the hippocampal formation and cortical areas specific forms of memories are established. Differential roles of synchrony of neuronal networks are thought to be important for both the encoding as well as the consolidation of memory traces. I will consider how brain rhythms at the network level contribute in processes of information storage and by what means they participate. Furthermore, I examine memory consolidation at the system level during processes of sleep.


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# Choong-Wan Woo

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## Vita

Choong-Wan (Wani) Woo is the director of the Computational Cognitive Affective Neuroscience (Cocoan) Lab. His research focuses on understanding how the human brain represents, processes, and regulates pain and emotions using machine learning and computational modeling. He received his dual Ph.D. in the Department of Psychology and Neuroscience and the Institute of Cognitive Sciences from the University of Colorado Boulder (Ph.D. advisor: Tor D. Wager), M.A. in clinical psychology, and B.S. in Biological Sciences from Seoul National University.

He has received many awards including the Top 100 R&D achievements from the government (2022), Kim Chan Award from the Korean Pain Research Society (2022), Outstanding Academic Achievement Award from the Korean Society for Human Brain Mapping (2021), Jaeil Kim Young Scholar Paper Award from the Korean Psychological Association (2019).

Currently, he is an associate director of the IBS Center for Neuroscience Imaging Research, an assistant professor in the Department of Biomedical Engineering at Sungkyunkwan University (SKKU), and also the BK21-FOUR funded department of Intelligent Precision Healthcare Convergence (IPHC) at SKKU.

# Understanding Pain: Insights from the Brain and Artificial Intelligence


## Abstract

One in five adults suffers from chronic pain yet we do not fully grasp the mechanisms of pain. Despite almost 30 years of using fMRI to study pain, good brain models of pain are still lacking. In this talk, I will present our previous findings from 10 years of modeling pain in the brain, highlighting the limitations of current models. Then, I will introduce new research directions emerging from recent advances in personalized brain mapping and artificial intelligence, with the aim of developing better neurocomputational models of pain to help individuals suffering from chronic pain.


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# Ja-Hyun Baik

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## Vita

Dr. Baik earned a Ph.D. degree in Molecular and Cellular Pharmacology in 1992 from University Paris 6 (Pierre et Marie Curie), Paris, France. She trained as a postdoctoral fellow at IGBMC (Institut de Genetique et de Biologie Moleculaire et Cellulaire, Director: Dr. Pierre Chambon), CNRS, Strasbourg, France from 1992 to 1995 studying the in vivo function of dopamine D2 receptors. In 1996, she established an independent research group at Medical Research Center, College of Medicine, Yonsei University, Seoul, Korea. Then in 2003, Dr. Baik moved to Dept. of Life Sciences, College of Life Sciences and Biotechnology, Korea University, Seoul, Korea and from 2006, is currently serving as a full professor.

Research in the Dr. Baik's laboratory is focused on understanding the dopamine reward circuit involved in the neuropsychiatric disorders such as addiction, maladaptive eating behaviors, and depression. Research in her laboratory employs a variety of techniques including anatomical, physiological as well as optogenetic and behavioral analysis in wild-type and genetically-engineered mouse models.

# Dopaminergic Control of Compulsive Eating: Role of Dopamine D2 Receptor


## Abstract

Dopamine regulates emotional and motivational behavior and the dopamine reward system would be the most prominent system in control of appetite and motivational feeding behavior. Motivation toward the palatable food involves reward learning and conditioning processes and pathological overeating is associated with dysregulation of reward-related behavioral components such as impulsivity and compulsivity. Dysfunctional dopaminergic neurotransmission, especially involving dopamine D2 receptor (D2R), has been proposed to be a mechanism underlying these maladaptive behaviors. We observed that D2R knockout mice consumed significant amounts of palatable food in the aversive context, displaying compulsive eating behavior. We demonstrated that D2R-expressing neurons from the central nucleus of the amygdala critically contribute to regulate impulsive and compulsive eating behavior. I will present recent findings obtained in our laboratory in the analysis of role of dopamine system in compulsive eating. These studies may provide a basis for the development of new approaches to the management of neuropsychiatric and metabolic disorders associated with maladaptive eating behaviors. [Supported by Bio & Medical Tech. Dev. Program (2016M3A9D5A01952412) of the MSIP, South Korea]


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## Vita

Prof. Kim is a Professor at Pohang University of Science and Technology (POSTECH), Korea. He is also the director of POSTECH Brain Research Center (BRC) and Biological Research Information Center (BRIC). His research field of interest is epigenetic mechanisms underlying brain functions and diseases. He discovered a novel class of regulatory RNAs, termed as enhancer RNAs (eRNAs) which has been shown to be an integral component of enhancer-mediated control of gene transcription.

He started his independent research career in 2010 as an Assistant Professor in the Department of Neuroscience at UT Southwestern Medical Center and was promoted to an Associate Professor with tenure in 2017.

He received the B.S. degree in Biology at the Korea University, Korea in 1993 and the Ph.D. degree in Biochemistry at Rutgers University- Robert Wood Johnson Medical School, NJ, USA in 2000 (Advisor: Dr. Danny Reinberg, Ph.D.). He then moved to Harvard Medical School for his postdoctoral training in the laboratory of Dr. Michael Greenberg in 2002.

He has received various awards and fellowships such as Lefler Postdoctoral Fellowship (2002, Harvard Medical School), Jane Coffin Childs Postdoctoral Fellowship (2003), Reagent's Research Scholar Award (2010, UT Southwestern Medical Center), The Klingenstein Fellowship Award (2012), Junior Faculty Award (2012, Association of Korean Neuroscientists), and SFARI Pilot Award (2018, Simons Foundation for Autism Research). After returning to Korea, he also received a research fund from Samsung Science & Technology Foundation (SSTF) in recognition of high impact potential of his research in broad field of Neuroscience.

# Enhancer RNAs in Brain Plasticity


## Abstract

Long non-coding RNAs (lncRNAs) have emerged as an essential component of gene regulatory networks. Their genome-wide characteristics and expression patterns have highlighted the critical role of lncRNAs in regulating protein-coding genes and have indicated their potential involvement in various human diseases. Recent research has shed light on the complex regulatory mechanisms of lncRNAs that operate at multiple levels. In our previous work, we discovered a novel class of lncRNAs, known as enhancer RNAs (eRNAs), that are dynamically expressed from active neuronal enhancers. Unlike other lncRNAs, eRNAs are rapidly and transiently induced and are tightly regulated by external stimuli, such as neuronal activity. Epigenomic analyses in various cell types have unequivocally demonstrated that eRNAs are a hallmark of active enhancers. This characteristic of eRNAs has allowed us to investigate their molecular function in gene expression and brain function, as well as the dynamic coordination mechanisms of enhancer clusters that ensure the robust induction of target genes in response to various stimuli. Taken together, our findings suggest that transcription at enhancers and eRNAs represents a new layer of complexity in the molecular architecture of many human diseases.


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## Vita

Dr. Lee received her B.S. degree in Physics from the Korea Advanced Institute of Science & Technology (KAIST) in 2003, and her Ph.D. degree, with a major in Neurobiology from Seoul National University in 2008. During her graduate career in Dr. Kaang's laboratory, she studied the neural mechanism of memory reconsolidation using animal models. To extend the fundamental biological knowledge to memory paradigms closer to real-world human experience, Dr. Lee joined Dr. Baker's laboratory at National Institute of Mental Health (NIMH) / NIH as a postdoctoral fellow. There, she investigated neural representations throughout the major visual processing pathways during perception and mental imagery, and goal-dependent representations during working memory, using human functional brain imaging (fMRI) combined with behavioral tasks.

In 2015, Dr. Lee began her career as an independent researcher in the Department of Bio and Brain Engineering at KAIST, where she focused on the neural processes underlying long-term memory retrieval process, retrieval-induced memory strengthening, and interaction between emotional and memory processes. She served as Assistant and Associate Professor at KAIST from 2015 to early 2023.

In 2023, Dr. Lee joined the Department of Psychology at Seoul National University as an Associate Professor. Her long-term research goal is to elucidate how human memories are stored, recalled, and updated throughout life, and how these memory processes interact with our emotional processes. Dr. Lee has made significant contributions to the research that determines information processing underlying human memory.

# Neural Processing Beyond Reinstatement During Memory Retrieval in the Human Brain


## Abstract

Memory retrieval enables individuals to relive past experiences or stimuli. During retrieval, it is thought that the same neural populations that were active during the initial experience are reactivated. Recent neuroimaging studies investigating neural activation in the sensory cortex support this idea, showing that cortical responses can be utilized to decode the identity of retrieved items based on the activation observed during perception. However, retrieval processing in the brain is not solely a matter of replaying stored information; rather, it involves dynamic information processing. In the first part, I will focus on retrieval-induced processing beyond reinstatement of memory. Our findings suggest that the retrieval signal itself can trigger changes of memory traces such as memory strengthening in the human hippocampus. We demonstrate a retrieval-induced strengthening process of associative memory traces in CA3/DG, resulting in the long-lasting maintenance of memory. In the second part, the neural basis underlying the confidence of false memories that were never stored in the brain but are assumed to be experienced is examined. Our results demonstrate that false memory confidence is critically based on the reinstatement of high-level semantic gist of stored memories in the prefrontal cortex. Taken together, these findings suggest that our memory traces are dynamically reorganized in the brain to efficiently guide and support our behaviors.


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# Jürgen Knoblich

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## Vita

Juergen Knoblich's laboratory is interested in the biology of neural stem cells. In the fruitfly, they have identified the molecular mechanism that allows neural stem cells to divide asymmetrically. They have demonstrated that defects in this mechanism lead to brain tumor formation. More recently, they have established a 3D culture system that recapitulates the early steps of human brain development in cell culture allowing brain pathologies and human specific developmental events to be studied in unprecedented detail.

Jürgen Knoblich began his scientific career as a graduate student at the Max Planck Institute in Tübingen under the guidance of Christian Lehner. He moved to San Francisco for his postdoc in the Jan lab at UCSF in 1994. In 1997, Jürgen Knoblich became a group leader at the Institute of Molecular Pathology (IMP) in Vienna, Austria. In 2004, he moved to the newly founded Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA) as a senior scientist. He became deputy director of IMBA in 2005 and director in 2018. Since 2021, he holds a professorship in synthetic biology at the Medical University of Vienna.

Jürgen Knoblich has received a number of awards including the Wittgenstein prize, the Schroedinger award, the FEBS anniversary award and the Hans Krebs medal. He is a member of the European Molecular Biology Organisation (EMBO), the Austrian Academy of Sciences, the Pontifical Academy of Sciences, the Board of Directors of ISSCR (International Society for Stem Cell Research, and the editorial boards of Current Biology, Current Opinion in Cell Biology and the Journal of Cell Biology.

# Modeling Human Brain Development and Disease in Stem Cell Derived 3D Culture


## Abstract

The human brain is unique in size and complexity, but also the source of some of the most devastating human diseases. While many of these disorders have been successfully studied in model organisms, recent experiments have emphasized unique features that can not easily be modeled in animals. We use cerebral organoids to recapitulate those features in vitro and to test their role in human disease. Cerebral organoids derived from patients suffering from neuro-developmental disease can recapitulate the developmental defects leading to those diseases and allow us to disentangle the mechanistic complexity of disorders like Epilepsy and Autism. Our new data demonstrate that by studying those defects, we can gain unique insights into the development of the human cortex that cannot be made in rodent model organisms.

Session 2

# New Research Avenues – From Stem Cell Research and Organoids to Artificial Intelligence-Assisted Brain Science

## Welcome

**Ulla Bonas ML**
Vice-President of the Leopoldina

## Co-Chairs

**Hans Schöler ML**
Max Planck Institute for Molecular Biomedicine, Münster

**Bong-Kiun Kaang**
Department of Biological Sciences, Seoul National University

## Speakers

Creation of Forebrain Assembloids to Recapitulate the Dynamic Cellular Interactions in the Human Schizophrenia Brain
**Kunyoo Shin**
Department of Biological Sciences, Seoul National University

Machine Learning and AI for the Sciences: Toward Understanding
**Klaus-Robert Müller ML**
Berlin Institute for the Foundations of Learning and Data (BIFOLD)

Understanding Pain: Insights from the Brain and Artificial Intelligence
**Chul Kim**
Department of Bio and Brain Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon

# Ulla Bonas

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## Vita

Professor Dr. Ulla Bonas studied Biology at the University of Cologne from 1974 to 1980. In 1984, she completed her PhD thesis in Genetics at the University of Cologne with a dissertation entitled *In-vitro cloning of a transposable element in the chalcone synthase gene of Antirrhinum majus.* From 1985 to 1987, she worked as a postdoc at the University of California, Berkeley, supported by fellowships from DAAD, DFG and the Max-Planck society. From 1988 to 1993, she was the Leader of an Independent Research Group at the Institute for Gene Biology Research in Berlin. In 1992, she habilitated in Genetics at the Free University of Berlin with a thesis on *Molecular genetic analysis of the interaction between Xanthomonas campestris* pv. *vesicatoria and the plant.* From 1993 to 1998, Ulla Bonas was a Groupleader (Directeur de Recherche; permanent) at the CNRS Institute of Plant Sciences in Gif-sur-Yvette, France. From 1998 until 2021, she was a Full Professor of Genetics at the Martin Luther University Halle-Wittenberg, Halle, Germany. Her research was focused on the genetic and molecular analysis of pathogenicity and plant disease resistance in the *Xanthomonas*/plant interaction.

Ulla Bonas is a member of the European Molecular Biology Organization (EMBO) and in 2011 received the prestigious Gottfried Wilhelm Leibniz Price of the German Research Foundation (DFG). Since 2008, she is a member of the German National Academy of Sciences Leopoldina, and since 2015, she is Vice-President of the Leopoldina.


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# Kunyoo Shin

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## Vita

Dr. Kunyoo Shin is an Associate Professor in the School of Biological Sciences at Seoul National University. He received his PhD from the Department of Biological Chemistry at the University of Michigan Medical School (under the guidance of Ben Margolis) and conducted his postdoctoral research at Harvard University (with Andy McMahon) and Stanford University (with Phil Beachy).

Dr. Shin established his independent research group in the Institute for Stem Cell and Regenerative Medicine at Stanford University as an Instructor. In 2014, he moved his laboratory to the Department of Cell and Developmental Biology at OHSU (Oregon Health & Science University). Prior to his current position at Seoul National University, he was an Associate Professor in the Department of Life Sciences at POSTECH (Pohang University of Science and Technology).

Dr. Shin's laboratory is interested in the signaling networks that operate in stem cell regulation during tissue homeostasis and regeneration, and in various diseases including cancers. Particularly, his lab is interested in understanding how such signaling networks exert their effects in the maintenance of tissue integrity and tumor initiation/growth through the regulation of tissue stem cell physiology. Recently, his laboratory's research is focused on the development of stem cell based, novel concept of human organoids to precisely model a variety of complex human diseases including cancers and neurodevelopmental diseases. Using newly established human organoids from various tissues and organs, his laboratory currently studies the complex signaling networks that control tissue dynamics through cell-cell interactions in various human diseases for the ultimate development of better therapeutic options.

# Creation of Forebrain Assembloids to Recapitulate the Dynamic Cellular Interactions in the Human Schizophrenia Brain


## Abstract

In this study, we created human forebrain assembloids that represent a six-layered structure with a mature laminar organization of the cortical layers and functional connectivity by spatially reconstituting neuronal progenitor cells with a reelin-expressing neuronal layer and non-neuronal glial cells. Brain assembloids derived from schizophrenia patients were also created by reconstituting patient-specific schizophrenia brain organoids with patient-derived glial cells. These assembloids exhibited weakened structures of the cortical layers and altered transcriptomes of the neurons and glial cells, which are mutually dependent, with reduced synapse connectivity. Combining integrated modular analysis of gene expression in post-mortem schizophrenia brain tissue and assembloids, we identified increased expression of TP53 and NFATC4, which function as master transcriptional regulators that reprogram the transcriptome involved in the cellular dynamics of neuronal progenitor cells, leading to premature neurogenesis at the early stage of brain development. Using combinatorial, mix-and-match assembloids derived from patients, we discovered the neuron-dependent, transcriptional plasticity of glial cells and their altered signalling feedback with neurons, in which neuronal UCN and PTPRF elicited the expression of WNT11 and THBS4 in astrocytes and microglia, respectively, to alter the neuronal transcriptome associated with neuronal response to various stimuli and synthetic processes of biomolecules. Thus, this study elucidates the nature of the dynamic cellular interplay between neurons and glial cells in human schizophrenia brains and suggests an innovative model system to study various human neurological diseases, understanding the pathogenesis of which requires the platform that is capable of representing the mature human brain with multiple cell types.


# Klaus-Robert Müller

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## Vita

Klaus-Robert Müller has been a professor of computer science at Technische Universität Berlin since 2006; at the same time he is directing rsp. co-directing the Berlin Machine Learning Center and the Berlin Big Data Center and most recently the Berlin Institute for the Foundations of Learning and Data (BIFOLD).

He studied physics in Karlsruhe from1984 to 1989 and obtained his Ph.D. degree in computer science at Technische Universität Karlsruhe in 1992. After completing a postdoctoral position at GMD FIRST in Berlin, he was a research fellow at the University of Tokyo from 1994 to 1995. In 1995, he founded the Intelligent Data Analysis group at GMD-FIRST (later Fraunhofer FIRST) and directed it until 2008. From 1999 to 2006, he was a professor at the University of Potsdam. From 2012 he has been Distinguished Professor at Korea University in Seoul. In 2020/2021 he spent his sabbatical at Google Brain as a Principal Scientist.

Among others, he was awarded the Olympus Prize for Pattern Recognition (1999), the SEL Alcatel Communication Award (2006), the Science Prize of Berlin by the Governing Mayor of Berlin (2014), the Vodafone Innovations Award (2017), Pattern Recognition Best Paper award (2020), Digital Signal Processing Best Paper award (2022). In 2012, he was elected member of the German National Academy of Sciences-Leopoldina, in 2017 of the Berlin Brandenburg Academy of Sciences, in 2021 of the German National Academy of Science and Engineering and also in 2017 external scientific member of the Max Planck Society. From 2019 on he became an ISI Highly Cited researcher in the cross-disciplinary area.

His research interests are intelligent data analysis and Machine Learning in the sciences (Neuroscience (specifically Brain-Computer Interfaces, Physics) Chemistry) and in industry.

# Machine Learning and AI for the Sciences: Toward Understanding


## Abstract

In recent years, machine learning (ML) and artificial intelligence (AI) methods have begun to play a more and more enabling role in the sciences and in industry. In particular, the advent of large and/or complex data corpora has given rise to new technological challenges and possibilities. In his talk, Müller will touch upon the topic of ML applications in the sciences, in particular in neuroscience, medicine and physics. He will also discuss possibilities for extracting information from machine learning models to further our understanding by explaining nonlinear ML models. Finally, Müller will briefly discuss perspectives and limitations.


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# Chul Kim

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## Vita

Chul Kim (IEEE Senior member) is an Assistant Professor in the Department of Bio and Brain Engineering and the Program of Brain and Cognitive Engineering at Korea Advanced Institute of Science and Technology (KAIST), Daejeon, South Korea. He received the Bioengineering Ph.D. degree in 2017 from UC San Diego, La Jolla, CA, USA, where he was a postdoctoral fellow from 2017 to 2019. From 2009 to 2012, he was with SK HYNIX, South Korea, where he designed power management circuitry for dynamic random-access memory. His current research interests include the design of energy-efficient integrated circuits and systems for fully wireless invisible brain-machine interfaces and wearable sensors.

He received a Gold Prize in the 16th Humantech Thesis Prize Contest from Samsung Electronics, South Korea, in 2010, and the 2018 Shunichi Usami Ph.D. Thesis Design Award from the Bioengineering Department, UC San Diego. He was the recipient of a 2017 – 2018 IEEE Solid-State Circuits Society Predoctoral Achievement Award. He served as a Guest Editor of *IEEE Transactions on Biomedical Circuits and Systems* (TBioCAS) for the special issue of ISCAS2020. Since 2020, he has served as an Associate Editor of TBioCAS, and technical program committee for *IEEE Custom Integrated Circuits Conference* (CICC) 2022. Prof. Kim was the co-editor of High-density integrated electrocortical neural interfaces: Low-noise low-power system-on-chip design mythology (Academic Press, 2019).

# Biomedical Integrated Circuits and Systems for Brain Engineering


## Abstract

Despite tremendous progress over the years, current brain engineering systems such as brain-machine interfaces are relatively bulky, highly invasive, and limited in their effectiveness. To improve performance of current brain engineering systems, it is necessary to dramatically increase spatial resolution and coverage across the brain without constraining the mobility of the subject. This calls for innovative approaches to high-density integrated neural recording and stimulation using non-invasive or minimally invasive microelectrode and custom silicon integrated circuits at extreme energy and area efficiency. In this talk, I will introduce various biomedical miniaturized and energy-efficient integrated circuits and systems for neural recording and stimulation, wireless power delivery and data communication, and wearable devices.

Session 3

# Advances in the Diagnosis and Treatment of Brain Disorders

## Co-Chairs

**Hans Schöler ML**
Max Planck Institute for Molecular Biomedicine, Münster

**Bong-Kiun Kaang**
Department of Biological Sciences, Seoul National University

## Speakers

### Genetic Architecture of the Restless Legs Syndrome
**Juliane Winkelmann ML**
Helmholtz Munich, Institute of Neurogenomics
Klinikum rechts der Isar der Technischen Universität München, Institute of Human Genetics

### Brain Somatic Mutations in Intractable Focal Epilepsy
**Jeong Ho Lee**
Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon

### Reduced Penetrance of Hereditary Movement Disorders: Elucidating Mechanisms of Endogenous Disease Protection
**Christine Klein ML**
University of Luebeck

### Using Cerebral Organoids to Map the Impact of Prenatal Stress on Brain Development: Consequences for Psychiatry
**Elisabeth Binder ML**
Max Planck Institute of Psychiatry, Munich

### Development of New Tools to Study Autophagy
**Jin-A Lee**
Department of Biopharmaceutical Engineering, Hannam University, Daejeon


# Juliane Winkelmann

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## Vita

Professor Juliane Winkelmann is Director of the Institute of Neurogenomics at Helmholtz Munich and Director of the Institute of Human Genetics at the Klinikum Rechts der Isar. Since 2015 she holds the chair of Neurogenetics and since 2023 the chair of Human Genetics at the Technical University of Munich. Previously, she was a professor of neuroscience at Stanford University in California, USA.

She is a specialist in neurology and human genetics and conducts research on the genetic basis of rare and common diseases with a focus on movement and sleep disorders. Multi-omics technologies and joint analysis with digital data enable accurate diagnosis and individualized therapy for patients, and prediction prevents disease occurrence.

She has received national and international awards for her research in genomics, including the Outstanding Scientific Achievement Award from the American Sleep Research Society and the Sleep Science Award from the American Academy of Neurology. She is a member of the Leopoldina.

# Genetic Architecture of the Restless Legs Syndrome


## Abstract

Restless legs syndrome (RLS) is a prevalent chronic neurological disorder with severe mental and physical health consequences. A better understanding of the underlying pathophysiology is needed to improve treatment options. To this end, we performed a meta-analysis of genome-wide association studies (GWAS) to identify new molecular targets including >110,000 cases and >1,400,00 controls of European ancestry. This increased the number of known risk loci from 22 to > 160. Using the summary statistics of the meta-analysis, we performed gene annotation, pathway, and gene set enrichment analyses with a range of bioinformatics tools. We also studied the genetic correlation between RLS and neurological disorders and additional traits of interest. Our study confirmed *MEIS1* as the strongest genetic risk factor for RLS. Functional studies provided evidence for highly intronic conserved elements with an allele-dependent function during embryonic development in the forebrain. In addition, rare coding variants and intermediate effect and frequency variants demonstrate the full spectrum of genetic variation contributing to RLS. The genetic factors highlight molecules linked to axon guidance, synapse formation, and neuronal specification. Enrichment analyses and genetic correlation analyses also converged on pathways linked to neurodevelopment. Finally, loci containing the genes of a receptor and its physiological substrate suggested completely new targets for therapeutic development.


# Jeong-Ho Lee

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## Vita

Prof. Lee is a KAIST Endowed chair professor and Chief Scientific Officer (CSO) at SoVarGen. He was also a member of Young-Korean Academy of Science and Technology (Y-KAST). He is recognized for his research investigating genetic mutations occurring in a subset of cells in the brain, a phenomenon referred to as brain somatic mutation (or mosaicism). Particularly, Prof. Lee studies the genetic mutations in stem cells in the brain that result in developmental brain disorders. These mutations can cause dysfunction of the entire brain, resulting in epilepsy and tumor formation. His work has also influenced scientific thinking about tumorigenesis and has helped lay the foundation for studying somatic mosaicism in neuropsychiatric and neurodegenerative diseases such as Alzheimer's disease. Based on his findings, he co-founded SoVarGen which develops new RNA therapeutics and diagnostic tools for neurological disorders with somatic mutations.

Prof. Lee has been recognized by numerous awards, including the Innovators in Science Award of The New York Academy of Science & Takeda 2020, the Kyung-Am award of the Kyung-Am Foundation 2020, the KAISTian of the Year in 2018, the Pediatric Epilepsies Award of Citizens United for Research in Epilepsy (CURE) 2015.

# Brain Somatic Mutations in Intractable Focal Epilepsy


## Abstract

Mutations occur during cell division in all somatic lineages due to the unavoidable DNA replication errors or DNA damage. Because neural stem cells continue to undergo cell division throughout human life, somatic mutations in human brain can arise during development and accumulate with the aging process. Although somatic diversity is an evident feature of the brain, the extent of somatic mutations affecting the neuronal structure and function and their contribution to neurological disorders remain largely unexplored. Over the last decade, we have provided the molecular genetic evidence that brain somatic mutations arising from neural stem cells (NSCs) indeed lead to the structural and functional abnormalities of the brain observed in neurodevelopmental disorders, brain tumors, and neurodegenerative disorders. In this symposium, I will present our recent findings of brain somatic mutations and the related molecular pathogenesis in childhood intractable focal epilepsy.


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## Vita

Dr. Christine Klein is a Professor of Neurology and Neurogenetics. She studied medicine in Hamburg, Heidelberg, Luebeck, London, and Oxford (UK) and did internships in Stockholm (Sweden), Rennes (France), Wollongong (Australia) and Vitebsk (Belarus). She moved to Boston from 1997 – 1999 for a fellowship in Molecular Neurogenetics with Dr. X.O. Breakefield and completed her neurology training at Luebeck University in 2004, followed by a series of summer sabbaticals in movement disorders with Dr. A.E. Lang in Toronto, Canada in 2004 – 2015. She was appointed Lichtenberg Professor at the Department of Neurology of Luebeck University in 2005, where her research has focused on the clinical and molecular genetics of movement disorders and its functional consequences. In 2009, Dr. Klein was appointed Schilling Professor of Clinical and Molecular Neurogenetics at the University of Luebeck and became Director of the newly founded Institute of Neurogenetics in 2013.

Dr. Klein has published >500 scientific papers and has an h-factor of 105 with >45,000 citations. She is Deputy Editor of 'Movement Disorders' and 'Science Advances', was President of the German Neurological Society (~11,500 members) in 2019/2020, and is the current Chair-elect of the European Section of the International Parkinson and Movement Disorder Society (MDS-ES) and lead of the Monogenic Network of the Global Parkinson's Genetics Program (https://gp2.org). She was elected a member of the National Academy of Sciences Leopoldina in 2021. Twelve of her former doctoral students or mentees have been promoted to the level of assistant, associate, or full professor.

# Reduced Penetrance of Hereditary Movement Disorders: Elucidating Mechanisms of Endogenous Disease Protection


## Abstract

Given the identification of a surprisingly large number of carriers of allegedly pathogenic variants remaining free of disease or developing it late in life, reduced penetrance represents a central question in medical genetics and personalized medicine. Formally, 'penetrance' is defined as the conditional probability of being affected with disease X given a specific pathogenic genotype. Taking this concept one step further, on may propose different 'levels of penetrance' not only in carriers of pathogenic variants in a single gene but also across different genes causing a similar or identical condition.

Recent large-scale sequencing efforts allow us to assess penetrance of putatively pathogenic variants and gene variants from the reverse perspective – based on large numbers of presumably non-diseased individuals – and to discover protective alleles. Generally speaking, there is a preoccupation with disease causes and susceptibility, whereas the concepts of protection against disease, delay of its age at onset (AAO), or attenuation of its severity have thus far been largely neglected within the research community. Hereditary forms of parkinsonism will serve as examples to illustrate the discovery and effect of modifiers of penetrance. For example, affected and unaffected PINK1/PRKN monoallelic variant carriers can be distinguished by heteroplasmic mtDNA variant load. AAO of carriers of the retrotransposon insertion causing X-linked dystonia-parkinsonism is modified by at least three different genetic mechanisms. Finally environmental and lifestyle factors may impact penetrance of pathogenic variants causing hereditary movement disorders.


# Elisabeth Binder

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## Vita

Elisabeth Binder has studied Medicine at the University of Vienna, Austria and Neuroscience at Emory University in Atlanta, GA, USA. Following a postdoctoral training at the Max-Planck Institute of Psychiatry in Munich, Germany, she returned to Emory University as an Assistant Professor in the Departments of Psychiatry and Behavioral Sciences and Human Genetics. In 2007, she was appointed as research group leader at the Max Planck Institute of Psychiatry within the Minerva Program of the Max Planck Society.

Since August 2013, Elisabeth Binder is the director of the Department of Translational Research in Psychiatry at the Max Planck Institute of Psychiatry, now renamed Department Genes and Environment. She also holds an appointment as Adjunct Professor in the Department of Psychiatry and Behavioral Sciences at Emory University School of Medicine. Her main research interests are the identification of molecular moderators of the response to environmental factors, with a focus on early adverse environment and gene x environment interactions. Her method portfolio includes different omics approaches, with a focus on gene regulation, evaluated both in large human cohorts, often with deep multimodal phenotyping as well as in induced pluripotent stem-cell derived models, including cerebral organoids. She studies the convergent molecular mechanisms that influence trajectories to psychiatric disease or well-being to ultimately use this information for novel prevention and treatment strategies.

# Using Cerebral Organoids to Map the Impact of Prenatal Stress on Brain Development: Consequences for Psychiatry


## Abstract

Risk for psychiatric disorders is shaped by both, genetic as well as environmental factors. While the field has made tremendous advances in mapping genetic risk, the molecular and cellular mechanisms of how environmental factors alter risk trajectories is much less understood. The advent of induced pluripotent stem cell derived systems, including cerebral organoids, now allows to model aspects of human brain development, and importantly also responses to “environmental” challenges. Early adverse exposures, including prenatally, have been shown to result in long-lasting consequences on neural circuit function and stress hormone regulation and ultimately in an increased risk for psychiatric disorders later in life. This presentation will focus on one possible mediator, stress hormones, i.e glucocorticoids (GCs).

Using data from human cerebral organoids and single cell sequencing this presentation illustrates how exposure to GCs during brain development alters transcriptional and epigenetic profiles in a cell-type specific way and converges on relevant transcription factors that promote specific types of neural progenitors (ZBTB16) and shifts neuronal developmental trajectories from dorsal (excitatory) to ventral (inhibitory) pattern, possibly with lasting consequences on excitatory/inhibitory balance. Furthermore, especially in neurons, transcripts altered by GC exposure are enriched for genes associated with neurodevelopmental and psychiatric disorders in genetic studies. This underscore a convergence of genetic and environmental risk factors onto the same molecular pathways. Such molecular and cellular understanding of environmental risk can promote pathomechanistic understanding, which consequences on diagnoses and treatments.


# Jin-A Lee

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## Vita

Jin-A Lee a Professor in the Department of Biological Science & Biotechnology at Hannam University, where she has been since 2009. From 2009 to present she served as Assoiate Editor of Molecular Brain or Scientific Reports. In 2017 – 2018 she has been a visiting faculty at Johns Hopkins Medical School, and University of Pennsylvania, US. She received a B.S. from Ewha Womens University in 1999, and an M.S. from the Seoul National University at Seoul. She received his Ph.D. in Neurobiology from the Seoul National University in 2005. From 2005 to 2008 she worked at Gladstone Institute of Neurological Disorders of UCSF, as a Post-doc, and a Senior Scientist.

Her research interests span both neuroscience and stem cells. Much of her work has been on improving the tools for stduying and understanding of autophagy associated with several neurological disorders. She recently developed sensors to monitor autophagy in live cells and in vivo mouse model, and the decongugases to study selective autophagy. She has also investigated cellular pathogenic mechanisms of various neurological disorders using patient-specific iPSC-derived neuronal model. Professor Lee is the author of over a hundred papers on neuroscience and autophagy. She holds ten patents deriving from her research. She has also given numerous invited talks and tutorials.

# Development of New Tools to Study Autophagy

## Abstract

ATG8 is an ubiquitin-like protein that is conjugated with a lipid, phosphatidylethanolamine (PE), and playscritical roles in autophagy in a lipidated form. During selective autophagy, cargo-bound receptors interact with lipidated mammalian ATG8 proteins (mATG8s) using an LC3 interacting region (LIR) motif, which is a critical step in the selective sequestration of the cargo into an autophagosome. mATG8s consist of six paralogs that are divided into an LC3 family (LC3A-C) and a GABARAP family (GABARAP, -L1, and -L2). To date, dozens of LIRs have been identified in various receptors and other autophagy-related proteins; however, their selectivity toward each member of the mATG8s and the functional significance of each LIR-mATG8 interaction in autophagy/selective autophagy remain elusive. Furthermore, although recent studies show that ATG8 proteins possess lipidation-independent functions in autophagy and non-autophagy in yeast, animal, and mammalian cells, there is no proper tool (method) to distinguish the function of lipidated versus delipidated forms of each mATG8 protein. In the current study, we developed a new and powerful method to characterize selective mATG8 in live cells. In this talk, I will present recent our progress about development of a new tool to study mATG8s.

# List of Participants

## Academy Representatives

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The **Korean Academy of Science and Technology** is an authoritative academic organization comprised of Korea's leading science and technology scholars. It was established as a purely private organization in 1994 to lay the foundation of promoting Korea's science and technology community. KAST supports policy research and advisory activities of scholars in science and technology for the development of basic science in Korea and the creation of a healthy R&D eco-system. It also performs science education and cultural activities to nurture future talent. Additionally, through exchanges and cooperation with overseas academies, KAST plays a crucial role in science and technology private diplomacy, and works towards ensuring that science and technology contribute to the common good of humankind.

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