

# 12 Eibsee

THE TWELFTH EIBSEE MEETING ON

## CELLULAR MECHANISMS OF NEURODEGENERATION

November 21-24, 2012

*DZNE speakers:*

F. Bradke, D. Edbauer, C. Haass,  
M. Heneka, J. Herms, G. Höglinger,  
M. Jucker, G. Kempermann, S. Lichtenthaler,  
T. Misgeld, M. Neumann, J. Pahnke, G. Petzold,  
B. Schmid, H. Steiner, J. Tatzelt, K. Winklhofer

*guest speakers:*

A. Abeliovich (Columbia University)  
H.-U. Demuth (Probiodrug AG)  
M. Dichgans (University of Munich)  
P. Heutink (University of Amsterdam)  
C. Hoogenraad (University of Utrecht)  
M. Hübener (MPI of Neurobiology)  
M. Kerschensteiner (University of Munich)  
K.S. Kosik (University of California)  
M. Polymenidou (University of California)  
A. Quaegebeur (VIB, University of Leuven)  
D. Rubinsztein (University of Cambridge)  
M.G. Spillantini (University of Cambridge)  
H. Wekerle (MPI of Neurobiology)

*organized by:*

C. Haass (DZNE & University of Munich)



**The twelfth Eibsee Meeting  
(November 21 - 24, 2012)**

**"CELLULAR MECHANISMS OF  
NEURODEGENERATION"**

**funded by the DZNE, German Center of  
Neurodegenerative Diseases - Munich**

**The Hans und Ilse Breuer Foundation**

**SyNergy, Munich Cluster for Systems Neurology**

**\*\*\*\*\***

**organized by:  
Christian Haass  
DZNE, German Center for Neurodegenerative Diseases -  
Munich & Adolf Butenandt Institute  
Biochemistry, Ludwig-Maximilians-University Munich  
Schillerstr. 44, 80336 Munich  
Germany**

**Phone: ++49-89-2180-75471**

**Fax: ++49-89-2180-75415**

**e-mail: christian.haass@dzne.lmu.de**

**<http://www.biochemie.abi.med.uni-muenchen.de/index.html>**

## Location

### *Eibsee Hotel*

Am Eibsee 1-3

D-82491 Grainau

Phone: ++49-8821-9881-0

Fax: ++49-8821-82585

Email: [info@eibsee-hotel.de](mailto:info@eibsee-hotel.de)

[www.eibsee-hotel.de](http://www.eibsee-hotel.de)



The Eibsee Hotel at the foot of the Zugspitze



The Eibsee speakers and participants 2010

## Travelling

**by train:** take the train to Garmisch (via Munich). In Garmisch please take a cab to the hotel (about 15-20 min drive).

**by plane:** from Munich airport take the S-Bahn to Munich Central station. At the central station take the train to Garmisch (about 1 hr); from here take a cab to the hotel.

**by car:** from Munich take the highway to Garmisch. In Garmisch follow the signs to Eibsee. The hotel is at the end of the road right at the foot of the Zugspitze.

## Weather

It is fall and it may be cold already. For those who like to go on a walk: please bring your hiking boots.

## Acknowledgements

We greatly appreciate funding of the Eibsee Meeting by the Hans and Ilse Breuer foundation, the German Center for Neurodegenerative Diseases (DZNE) and SyNergy. We thank our additional sponsor Zeiss for his generous financial support.



# PROGRAM

\*\*\*\*\*

## Wednesday, November 21

Arrival, Hiking, Opening Lecture

- 14:30 The traditional “scientific walk“ around the lake (if weather permits)
- 17:00 – 17:15 Welcome** (C. Haass)
- 17:15 – 18:15 Key Note Lecture**  
D. Rubinsztein, University of Cambridge, UK  
Autophagy and neurodegeneration
- 18:15 – 19:00 Announcement of the Hans & Ilse Breuer Award 2013** (R. Bergfeld/C. Haass)

*19:15 Cocktails*

*20:00 Dinner*

## Thursday, November 22

### **9:30 – 10:25 Amyloid production, toxicity and spreading I**

*Chair: E. Mandelkow*

#### **Invited speaker**

- 9:30 – 9:55 H.-U. Demuth, Probiobdrug AG, Halle, Germany  
Prion-like behavior and tau-dependent cytotoxicity of  $\beta$ -amyloid oligomers seeded by pyroglutamylated  $\beta$ -amyloid – and its therapeutic prevention

#### **Short talks**

- 9:55 – 10:10 M. Jucker, DZNE & University of Tübingen, Germany  
Modeling cerebral beta-amyloidosis
- 10:10 – 10:25 J. Tatzelt, DZNE & University of Munich, Germany  
The heat shock response is modulated by and interferes with toxic effects of scrapie prion protein and amyloid-beta

*10:25 – 11:05 Coffee Break/Poster Session*

### **11:05 – 12:00 Glio-vascular dysfunction**

*Chair: U. Lindauer*

#### **Invited speaker**

- 11:05 – 11:30 A. Quaegebeur, VIB, University of Leuven, Belgium  
Oxygen sensors, neuroprotection and metabolism: unexpected liasons with therapeutic opportunities for neurodegeneration

#### **Short talks**

- 11:30 – 11:45 M. Dichgans, ISD & University of Munich, Germany  
Histone deacetylases as a target for stroke prevention
- 11:45 – 12:00 G. Petzold, DZNE & University of Bonn, Germany  
Glial and vascular dysregulation in vascular dementia and Alzheimer’s disease

*12:30 – 13:30 Lunch*

*13:30 – 15:30 Time for recreation*

**15:30 – 16:30 Role of inflammation**

*Chair: T. Misgeld*

**Short talks**

- 15:30 – 15:45 H. Wekerle, MPI Neurobiology, Munich, Germany  
Brain inflammation and autoimmunity in MS: a chicken/egg dilemma?
- 15:45 – 16:00 M. Heneka, DZNE & University of Bonn, Germany  
Multiple level interactions between neurodegeneration and neuroinflammation in Alzheimer's disease
- 16:00 – 16:15 M. Kerschensteiner, University of Munich, Germany  
How neuroinflammation causes axon degeneration
- 16:15 – 16:30 K. Winklhofer, DZNE & University of Munich, Germany  
Mechanisms of stress protection and their role in neurodegenerative diseases

*16:30 – 17:10 Coffee Break/Poster Session*

**17:10 – 18:35 ALS and FTLN: Genes and mechanisms**

*Chair: G. Kleinberger*

**Invited speaker**

- 17:10 – 17:35 M. Polymenidou, University of California, San Diego, USA  
Misregulated RNA processing in Amyotrophic lateral sclerosis (ALS)

**Short talks**

- 17:35 – 17:50 M. Neumann, DZNE & University of Tübingen, Germany  
FET proteins in ALS and FTD: molecular neuropathology and animal models
- 17:50 – 18:05 B. Schmid, DZNE Munich, Germany  
TDP-43 loss of function analysis in zebrafish
- 18:05 – 18:20 D. Edbauer, DZNE Munich, Germany  
Loss of fused in sarcoma (FUS) promotes pathological tau splicing
- 18:20 – 18:35 C. Haass, DZNE & University of Munich, Germany  
Cellular mechanisms of FTLN and ALS

*19:00 Dinner*

**Friday, November 23**

**9:00 – 10:25 In vivo imaging of neuronal function and dysfunction**

*Chair: U. Müller*

**Invited speaker**

- 9:00 – 9:25 C. Hoogenraad, University of Utrecht, The Netherlands  
Control of neuronal polarity and plasticity - the role of dynamic cargo trafficking

**Short talks**

- 9:25 – 9:40 F. Bradke, DZNE Bonn, Germany  
Cytoskeletal mechanisms of axonal growth and regeneration
- 9:40 – 9:55 M. Hübener, MPI of Neurobiology, Munich, Germany  
Imaging cortical activity in behaving mice under physiological and neuropathological conditions
- 9:55 – 10:10 J. Herms, DZNE Munich, Germany  
Pharmacological inhibition of BACE1 impairs the formation of dendritic spines
- 10:10 – 10:25 T. Misgeld, DZNE & Technical University of Munich, Germany  
New tools to study axon degeneration in mice

*10:25 – 11:05 Coffee Break/Poster Session*

**11:05 – 12:15 Amyloid production, toxicity and spreading II**

*Chair: S. Weggen*

**Invited speaker**

11:05 – 11:30 M. Spillantini, University of Cambridge, UK  
Axonopathy in a cellular model of progressive tau pathology

**Short talks**

11:30 – 11:45 J. Pahnke, DZNE & University of Magdeburg, Germany  
ABC transporters in neurodegeneration and neuroregeneration

11:45 – 12:00 H. Steiner, DZNE & University of Munich, Germany  
Modulation of  $\gamma$ -secretase activity by the lipid environment

12:00 – 12:15 S. Lichtenthaler, DZNE & Technical University of Munich, Germany  
Secretases in Alzheimer's disease: functional characterization by proteomics

*12:30 – 13:30 Lunch*

*13:30 – 15:30 Time for recreation*

**15:30 – 16:25 Translational research**

*Chair: J. Schulz*

**Invited speaker**

15:30 – 15:55 A. Abeliovich, Columbia University, New York, USA  
Modeling Alzheimer's disease by directed conversion of patient skin cells

**Short talks**

15:55 – 16:10 G. Höglinger, DZNE & Technical University of Munich, Germany  
Gene-environment interactions in tauopathies

16:10 – 16:25 G. Kempermann, DZNE Dresden, Germany  
A systems genetics approach to adult neurogenesis

*16:25 – 17:05 Coffee Break/Poster Session*

**17:05 – 18:15 Translational research (continued)**

*Chair: M. Dichgans*

**Invited speakers**

17:05 – 17:30 P. Heutink, University of Amsterdam, The Netherlands & DZNE Tübingen, Germany  
Molecular genetics of FTD

17:30 – 17:55 K.S. Kosik, University of California, Santa Barbara, USA  
Genomic and transcriptomic studies of FAD and familial tauopathies

**Special event**

17:55 – 18:15 Antioquia Colombia: A genetic crucible of Alzheimer's disease (film report by K.S. Kosik)

*18:30 Dinner*

**Saturday, November 24**

*Departure*

## The twelfth Eibsee Meeting on Cellular Mechanisms of Alzheimer's Disease

November 21-24, 2012 - Poster Session

### Topic 1: Amyloid & tau: toxicity and spreading: Thursday, Nov. 22, 2012, 10:25 - 11:05

- No. 1: S. Meister<sup>1</sup> (Breuer stipend), S. Baches<sup>2</sup>, S. Weggen<sup>2</sup>, C.U. Pietrzik<sup>1</sup>, <sup>1</sup>University of Mainz, <sup>2</sup>University of Düsseldorf: Nanoparticulate flurbiprofen affects A $\beta$  generation in an *in vitro* blood-brain barrier model
- No. 2: L. Ye<sup>1</sup>, S.K. Fritschl<sup>1</sup>, U. Obermüller<sup>1</sup>, Y. S. Eisele<sup>1</sup>, M. Staufenbiel<sup>2</sup>, M. Jucker<sup>1</sup>, <sup>1</sup>DZNE & University of Tübingen, <sup>2</sup>Novartis Institutes for Biomedical Research, Basel: Clearance of A $\beta$  seeds in mouse brain
- No. 3: P. Glöckner<sup>1</sup> (Breuer stipend), J. Uney<sup>2</sup>, T. Arendt<sup>1</sup>, U. Ueberham<sup>1</sup>, <sup>1</sup>University of Leipzig, <sup>2</sup>University of Bristol: Validation of a gene therapeutic tool targeting neuronal cell cycle activation as a critical event in the pathological cascade of AD
- No. 4: J.M. Decker<sup>1</sup>, K. Hochgräfe<sup>1,3</sup>, A. Sydow<sup>3</sup>, E. Mandelkow<sup>1,2,3</sup>, E.-M. Mandelkow<sup>1,2,3</sup>, <sup>1</sup>DZNE Bonn, <sup>2</sup>CAESAR Research Center, Bonn, <sup>3</sup>Max-Planck-Unit for Neurol. Research, Hamburg: Impairment and reversibility of mossy fiber plasticity in pro-aggregant full-length human Tau transgenic mice
- No. 5: F.J.A. Dennissen\*, N. Kholod, H.W.M. Steinbusch, N.P. Dantuma, F.W. van Leeuwen, Department of Neuroscience, Maastricht University, \*current address DZNE Bonn: Hydrolysis of the mutant ubiquitin (UBB+1) associated with neurodegenerative disorders by UCH-L3

### Topic 2: ALS and FTLN: Thursday, November 22, 2012, 16:30 – 17:10

- No. 6: E. Bentmann<sup>1</sup>, M. Neumann<sup>2</sup>, S. Tahirovic<sup>1</sup>, R. Rodde<sup>1</sup>, D. Dormann<sup>1</sup>, C. Haass<sup>1</sup>, <sup>1</sup>DZNE & University of Munich, <sup>2</sup>Institute of Neuropathology, University of Zurich: Requirements for stress granule recruitment of Fused in Sarcoma (FUS) and TAR DNA-binding Protein of 43kDa (TDP-43)
- No. 7: D. Dormann<sup>1</sup>, T. Madl<sup>2,3,4</sup>, C.F. Valori<sup>5</sup>, E. Bentmann<sup>1</sup>, S. Tahirovic<sup>6</sup>, C. Abou-Ajram<sup>1</sup>, E. Kremmer<sup>3</sup>, O. Ansorge<sup>7</sup>, I.R.A. Mackenzie<sup>8</sup>, M. Neumann<sup>5,9</sup>, C. Haass<sup>1,6</sup>, <sup>1</sup>University of Munich, <sup>2</sup>University of Graz, <sup>3</sup>Helmholtz Center Munich, <sup>4</sup>Technical University of Munich, <sup>5</sup>University Hospital Zurich, <sup>6</sup>DZNE Munich, <sup>7</sup>John Radcliffe Hospital, Oxford, <sup>8</sup>Vancouver General Hospital, <sup>9</sup>University of Tübingen: Arginine methylation modulates Transportin-mediated nuclear import of FUS
- No. 8: S. Rothhämel, C. Haass, B. Schmid, DZNE & University of Munich: Zebrafish as a model to study the neurodegenerative disease FTLN/ALS
- No. 9: L. Hasenkamp (Breuer stipend), A. Hruscha, M. Teucke, C. Haass, B. Schmid, DZNE & University of Munich: Fusion (Fus) in zebrafish: physiological function of a neurodegeneration related gene
- No. 10: K. Strecker<sup>1</sup> (Breuer stipend), A. Hruscha<sup>1</sup>, E. Kremmer<sup>2</sup>, B. Schmid<sup>1</sup>, C. Haass<sup>1</sup>, <sup>1</sup>DZNE & University of Munich, <sup>2</sup>Institute of Molecular Immunology, Helmholtz Center Munich: Linking neurodegeneration to vascular dysfunction: TDP-43 loss of function causes vessel patterning defects



## **Topic 2: ALS and FTL D: Thursday, November 22, 2012 (continued)**

- No. 11: C.M. Lang (Breuer stipend), K. Fellerer, A. Capell, C. Haass, DZNE & University of Munich: Membrane orientation and subcellular localization of transmembrane protein 106B (TMEM106B), a major risk factor for frontotemporal lobar degeneration
- No. 12: B. Schwenk<sup>1</sup>, D. Orozco<sup>1</sup>, S. Hogg<sup>1</sup>, S. Tahirovic<sup>1</sup>, C.M. Lang<sup>1</sup>, A. Capell<sup>1</sup>, C. Haass<sup>1</sup>, S.F. Lichtenthaler<sup>2</sup>, D. Edbauer<sup>1</sup>, <sup>1</sup>DZNE & University of Munich, <sup>2</sup>DZNE & Technical University of Munich: Characterization of TMEM106b in primary neurons
- No. 13: J. Götzl, C. Lang, K. Fellerer, C. Haass, A. Capell, University of Munich: Phenotypical characterization of progranulin knockout mice with a focus on lysosomal dysfunction

## **Topic 3: Protease function: Friday, November 23, 2012, 10:25 – 11:05**

- No. 14: M. Voss (Breuer stipend), U. Künzel, C. Haass, R. Fluhrer, DZNE & University of Munich: Signal peptide peptidase-like protease 3 (SPPL3) is an unconventional GxGD protease
- No. 15: D. Fleck<sup>1</sup> (Breuer stipend), F. v. Bebbler<sup>1</sup>, C. Galante<sup>1</sup>, E. Kremmer<sup>2</sup>, B. Schmid<sup>1</sup>, C. Haass<sup>1</sup>, M. Willem<sup>1</sup>, <sup>1</sup>DZNE & University of Munich, <sup>2</sup>Helmholtz Center Munich: Dual cleavage of Neuregulin 1 type III by BACE1 and ADAM17 liberates its EGF-like domain and allows paracrine signaling
- No. 16: P.-H. Kuhn, S. Lichtenthaler et al., DZNE & Technical University of Munich: Secretome protein enrichment with click sugars unravels substrates of alpha- and beta-secretase in primary cortical neurons

## **Topic 4: Parkinson's disease, Huntington's disease and Prion disorders: Friday, November 23, 2012, 16:25 – 17:05**

- No. 17: M. Patra<sup>1</sup> (Breuer stipend), A.K. Müller-Rischart<sup>1</sup>, M. Funke<sup>1</sup>, C. Schweimer<sup>1</sup>, F. Kopp<sup>2</sup>, A. Roidl<sup>2</sup>, E. Wagner<sup>2</sup>, J. Tatzelt<sup>1</sup>, K.F. Winklhofer<sup>1</sup>, <sup>1</sup>DZNE & University of Munich, <sup>2</sup>Pharmaceutical Biotechnology, University of Munich: The role of PARKIN as a possible tumor suppressor gene
- No. 18: M. Funke, A.K. Müller-Rischart, J. Tatzelt, K.F. Winklhofer, DZNE & University of Munich: The Parkin co-regulated gene PACRG has a neuroprotective activity
- No. 19: M.S. Hipp<sup>1</sup>, S.-H. Park<sup>1</sup>, A. Konagai<sup>1</sup>, R.R. Kopito<sup>2</sup>, F.U. Hartl<sup>1</sup>, <sup>1</sup>Max Planck Institute of Biochemistry, Martinsried, <sup>2</sup>Stanford University: Interference of polyQ expanded proteins with proteasomal degradation
- No. 20: M. Spadaro<sup>1</sup>, U.K. Resenberger<sup>1</sup>, V. Sakthivelu<sup>1</sup>, V. Ruf<sup>1</sup>, S. Kutzi<sup>1</sup>, M. A. Tranulis<sup>2</sup>, H.A. Kretschmar<sup>3</sup>, K.F. Winklhofer<sup>1</sup>, J. Tatzelt<sup>1</sup>, <sup>1</sup>DZNE & University of Munich, <sup>2</sup>Norwegian School of Veterinary Science, Oslo, <sup>3</sup>Center for Neuropathology and Prion Research, University of Munich: Stress-protective and neurotoxic signalling of the prion protein: the role of the intrinsically disordered N-terminal domain