Proteolysis at the membrane – from signaling to disease

May 13 to 16, 2024
in Kloster Seeon, Bavaria, Germany

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Organized by:

Stefan Lichtenthaler
(DZNE and Technical University Munich)

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For information and registration, please go to

www.dzne.de/secretases2024

DZNE SyNergy TUM MRI Fondation Recherche Alzheimer Stichting Alzheimer Onderzoek STOPALZHEIMER.BE

Confirmed Speakers and session chairs

Wim Annaert, KU Leuven, Belgium
Angela Bachi, CBM, CSIC-UAM and CIBERER, ISCIII , Italy
Christoph Becker-Pauly, University of Kiel, Germany
Stephen Blacklow, Harvard Medical School, USA
Carl Blobel, HSS Research Institute & Weill Cornell Medicine, USA
Paola Bovolenta, CBM CSIC, Spain
Anja Capell, University of Munich, Germany
Bart De Strooper, University College London, UK
Laura Dominguez, University of Mexico, Mexico
Stefan Düsterhöft, RWTH Aachen, Germany
Regina Fluhrer, University of Augsburg, Germany
Matthew Freeman, University of Oxford, UK
Irene Gerlach, Roche, Switzerland
Adam Grieve, University of Bristol, UK
Christian Haass, University of Munich & DZNE, Germany
Sarah Jäkel, KUM, Germany
Bernd Kasper, University of Heidelberg, Germany
Adam Lange, FMP Berlin, Germany
Thomas Langer, Max-Plank-Institute Cologne, Germany
Marius Lemberg, University of Cologne, Germany
Joanne Lemieux, University of Alberta, Canada
Song Li, University of Pittsburgh, USA
Lothar Lindemann, Roche, Switzerland
Elena Marcello, University of Milan, Italy
Paul Meakin, University of Leeds, UK
Dean Nizetic, Queen Mary University of London, UK
Stefan Rose-John, University of Kiel, Germany
Mohamed Saad, University of Adelaide, Australia
Paul Saftig, University of Kiel, Germany
Bernd Schröder, TU Dresden, Germany
Harald Steiner, University of Munich & DZNE, Germany
Kvido Strisovsky, IOCB Prag, Czechia
Jaehong Suh, Harvard Medical School, USA
David Teis, Medical University Innsbruck, Austria
Taisuke Tomita, The University of Tokyo, Japan
Michael Tomlinson, University of Birmingham, UK
Robert J Vassar, Northwestern University, USA
Elyse Watkins, University of Chicago, USA
Hoi Leong Xavier Wong, Hong Kong Baptist University, Hong Kong
Riqiang Yan, University of Connecticut, USA

Key dates of the program

Start of the meeting: Monday, May 13, 2024 at 2 pm

End of the meeting: Thursday, May 16, 2024 at 1 pm

Preliminary Program

(Program may be subject to change – final program will be available later)

Monday, May 13, 2024

14.00 – 14.15 **Welcome by the organizers**

Session 1: Proteolysis in organelles

Chair: Lucia Chavez Gutierrez

14.15 – 14.25 Chair, Introduction

14.25 – 14.45 **Thomas Langer,** Max-Planck-Institute Cologne, Germany

Proteolytic control of mitochondrial Calcium signaling

14.50 – 15.10 **Marius Lemberg,** University of Cologne, Germany

Shedding in the ER: potent driver of protein degradation

15.15 – 15.30 **David Teis,** Medical University Innsbruck, Austria

The rhomboid pseudo protease Dsc2 detects transmembrane degrons in orphaned proteins at the Golgi to target them degradation

15.35 – 16.10 Coffee break

16.15 – 16.30 **Anja Capell,** Ludwig-Maximilians-University, Germany

Proteolytic processing of TMEM106B at two sites is a prerequisite for fibril formation

Keynote lecture (Chair: Lucia Chavez Gutierrez)

16.35 – 17.05 **Christian Haass,** Ludwig-Maximilians-University and DZNE, Germany

Therapeutic modulation of TREM2 shedding

17.25 – 18.00 Flash Talks (5x 2 min talks with two slides (selected from poster abstracts))

18.00 – 18.45 Reception
18.45 – 20.15 Dinner
20.30 – 22.30 **Poster session**

Tuesday, May 14, 2024

Session 2: Intramembrane proteases

Chair: Bart De Strooper

09.00 – 09.10 Chair, Introduction

09.10 – 09.30 **Laura Dominguez,** University of Mexico, Mexico

An Effort to Decipher Gamma Secretase Mechanisms by Computational Methodologies

09.35 – 09.55 **Harald Steiner,** Ludwig- Maximilians-University and DZNE, Germany

Unravelling mysteries of γ-secretase by AI

10.00 –10.15 **Lucia Chavez Gutierrez,** KU Leuven, Belgium

Mechanistic Insights into Familial Alzheimer's Pathogenesis and Implications for Therapeutic Development

10.20 –10.35 **Wim Annaert,** KU Leuven, Belgium

Altered expression of Presenilin2 impacts endolysosomal homeostasis and synaptic signaling in Alzheimer's disease-relevant brain circuits

10.40 – 11.15 Coffee break

11.20 – 11.40 **Bernd Schröder,** TU Dresden, Germany

SPP and SPPL intramembrane proteases as regulatory switches in immune system and metabolism

11.45 – 12.00 **Regina Fluhrer,** University of Augsburg, Germany

Availability of nutrients regulates expression of the intramembrane protease Signal peptide-Peptidase-like 3 (SPPL3)

12.05 – 12.20 **Adam Grieve,** University of Bristol, UK

Sharpening the cell surface signalling through intramembrane proteolysis

12.25 – 12.40 **Discussion on intramembrane aspartyl proteases**

12.40 – 13.45 Lunch

14.00 – 14.45 Scientific Walk

Session 3: TSPANs and ADAM10

Chair: Paul Saftig

15.00 – 15.10 Chair, Introduction

15.10 – 15.25 **Elena Marcello,** University of Milan, Italy

The Cyclase-Associated Protein 2: a novel binding partner of ADAM10 in the synapse

15.30 – 15.50 **Michael Tomlinson,** University of Birmingham, UK

Six scissors: ADAM10 regulation by TspanC8 tetraspanins

16.55 – 16.15 **Steve Blacklow,** Harvard Medical School, USA

Structural basis for membrane-proximal proteolysis of substrates by ADAM10

16.20 – 17.00 *Coffee Break*

17.05 – 17.20 **Stefan Lichtenthaler,** DZNE and TUM, Germany

In vivo substrates and functions of the a-secretase ADAM10

17.25 – 17.35 **Discussion on ADAM10 and TSPANs**

17.40 – 18.00 Flash Talks (selected from poster abstracts))

18.30 – 20.15 *Dinner*

20.30 – 22.30 **Poster session**

Wednesday, May 15, 2024

Session 4: Rhomboids and iRhoms

Chair: Colin Adrain

09.00 – 09.10 Chair, Introduction

09.10 – 09.30 **Matthew Freeman,** University of Oxford, UK

Revealing the iRhom2/ADAM17 complex

09.35 – 09.50 **Song Li,** University of Pittsburgh, USA

Inhibition of iRhom1 by CD44-targeting nanocarrier for improved cancer immunochemotherapy

09.55 – 10.15 **Carl Blobel,** HSS Research Institute, USA

IRhoms: key regulators of ADAM17-dependent signaling

10.20 – 10.35 **Stefan Düsterhöft,** RWTH Aachen, Germany

Structure-function analysis of the iRhom-ADAM17 complex and its interactome

10.40 – 11.10 *Coffee break*

11.15 – 11.35 **Joanne Lemieux,** University of Alberta, Canada

Examining the role of rhomboid protease in bacterial pathogenicity

11.40 – 12.00 **Kvido Strisovsky,** IOCB Prag, Czechia

Rhomboid protease RHBDL2 is a calcium activated suppressor of EGFR signaling in human keratinocytes

12.05 – 12.20 **Adam Lange,** FMP Berlin, Germany

The opening dynamics of the lateral gate regulates the activity of rhomboid proteases

12.25 – 12.40 **Discussion on Rhomboids and iRhoms**

12.40 *Lunch*

Session 5: Metalloproteases

Chair: Stefan Rose-John

15.00 – 15.10 Chair, Introduction

15.10 – 15.25 **Taisuke Tomita,** The University of Tokyo, Japan

Soluble form of Lingo2, an autism spectrum disorder-associated molecule, functions as an excitatory synapse organizer in neurons

15.30 – 15.50 **Paola Bovolenta,** University of Madrid, Spain

Lack of shedding at the membrane in Alzheimer disease

15.55 – 16.15 **Hoi Leong Xavier Wong,** Hong Kong Baptist University, Hong Kong

MT1-MMP: New Therapeutic Target for Metabolic Disorders

16.20 – 16.35 **Mohamed Saad,** University of Adelaide, Australia

Targeting metalloproteinases as a novel therapeutic strategy for pancreatitis

16.40 – 17.10 Coffee break

17.15 – 17.35 **Christoph Becker-Pauly,** University of Kiel, Germany

Degradome of the part-time sheddase meprin β

Session 6: Beta-Secretases

Chair: Robert Vassar

17.40 – 17.50 Chair, Introduction

17.50 – 18.10 **Riqiang Yan,** University of Connecticut, USA

The role of BACE1 in glial cells for Alzheimer's pathogenesis

18.15 – 18.30 **Elyse Watkins,** University of Chicago, USA

High-dose BACE inhibition alters sleep architecture and reduces slow-wave sleep

19.00 Dinner, afterwards Bar and Bowling

Thursday, May 16, 2024

Session 7: Beta-Secretases

Chair: Robert Vassar

09.00 – 09.15 **Sarah Jäkel,** KUM, Germany

Oligodendrocyte secretases can contribute to plaque pathology in Alzheimer's disease

09.20 – 09.35 **Dean Nizetic,** Queen Mary University of London, UK

Cerebral organoid models of Alzheimer's disease as a tool to study the AD-pathogenesis-modulating effects of β-secretase-2

09.40 – 09.55 **Jaehong Suh,** Harvard Medical School, USA

Physiological function of BACE1 in motor coordination and its potential as therapeutic target for spinocerebellar ataxia

10.00 – 10.20 **Angela Bachi,** CBM, CSIC-UAM and CIBERER, ISCIII, Italy

BACE2 orchestrates tumor-microenvironment mechanical and metabolic interactions

10.25 – 11.10 Coffee break

11.15 – 11.35 **Paul Meakin,** University of Leeds, UK

BACE1: A novel driver of Cardiometabolic disease

Session 8: Clinical Trials Targeting gamma-Secretase

Chair: Bart De Strooper

11.40 – 11.55 **Lothar Lindemann / Irene Gerlach,** Roche, Switzerland

RG6289 – A Novel Gamma Secretase Modulator in Clinical Development for Alzheimer's Disease

12.00 – 12.15 **Bernd Kasper,** University of Heidelberg, Germany

The role of gamma secretase inhibitors in the treatment of desmoid tumors

12.20 – 12.35 **Discussion on BACE and gamma-secretase**

12.35 – 12.45 **Poster Awards**

13.00 – 14.15 Short Lunch or Lunch package

13.30 Departure 1 to Munich airport

14.30 Departure 2 to Munich airport and main station Munich