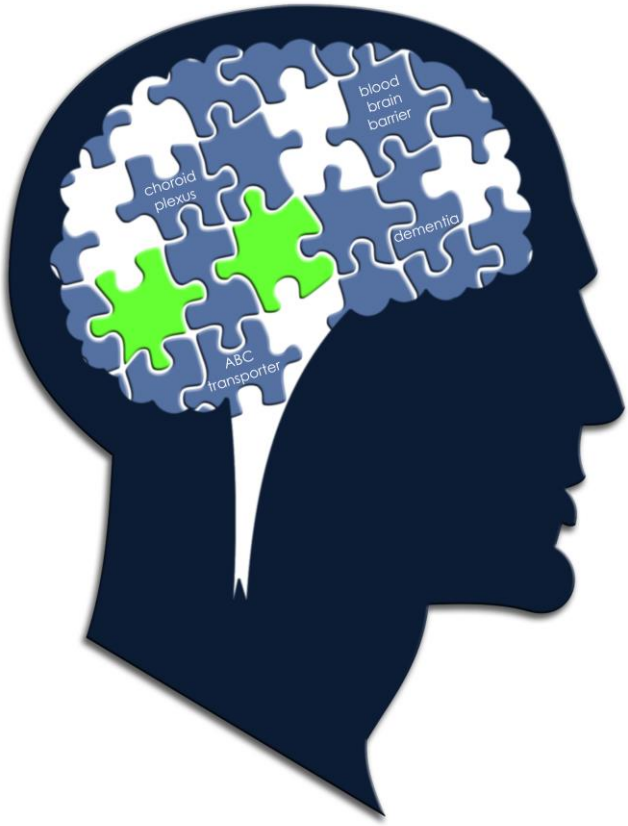
BALTIC WINTER SCHOOL 2

FOCUS on Neurodegenerative Diseases

General Information

PROGRAM

APRIL 9TH, 2021



The meeting is supported by the following project fundings:

FLPP project No. lzp-2018/1-0275 ShortAbeta (2018-2021)
JPND and Norges forskingsråd international consortia PROP-AD (2016-2021) and PETABC (2021-2024)
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EU #643417 (JPco-fuND)

BALTIC WINTER SCHOOL 2

Dear participants,

Baltic Winter School 2 (BWS2) is intended to provide the students with presentations by established researchers, PostDocs and PhD studnets and give an understanding of the common and distinct features of neurodegenerative diseases, which include, such as Alzheimer's disease, Parkinson's disease, dementia with Lewy bodies, vascular dementia, frontotemporal dementia, and mixed dementia.

This workshop welcomes discussion input from participants and seeks to identify knowledge and barriers to bridging molecular research with the broader field of neurodegenerative diseases, which can collectively guide interdisciplinary, collaborative, and innovative research.

In light of the continuing uncertainty about the evolution of the COVID-19 pandemic and its impact on travel restrictions and physical distancing requirements throughout 2021, the BWS2 organizers have decided to transform this conference as a fully online using ZOOM Platform.

Enjoy the lectures and take part at the scientific discussions

The organizers

ZOOM MEETING LINK

ZOOM Link (Meeting ID: 676 9814 6090 and Passcode: 921477)

CONTACT

If you have any further questions regarding the conference, do not hesitate to contact **Jolanta Upīte**.

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jolanta.upite@lu.lv

FRIDAY, APRIL 9TH

Session I

10:00 – 10:40 **Jens Pahnke**
(University of Oslo, Norway, University of Latvia, Latvia, University of Lübeck, Germany)

Alzheimer's and other dementias - how we develop new treatments

10:40- 11:05 **Baiba Jansone**
(Department of Pharmacology, Faculty of Medicine, University of Latvia, Latvia)

Pharmacological approaches for aging and neurodegenerative diseases

11:05 - 11:30 **Henrik Biverstål**
(Department of Physical Organic Chemistry, Latvian Institute of Organic Synthesis, Department of Neurobiology, Care Sciences and Society, Center for Alzheimer Research, Division of Neurogeriatrics, Karolinska Institutet, Sweden)

Molecular determinants to understand neurodegenerative diseases

Break (20 min)

Session II

11:50-12:10 **Kristīne Kitoka**
(Department of Physical Organic Chemistry, Latvian Institute of Organic Synthesis, Latvia)

Improved overexpression of amyloidogenic peptides mediated by solubility enhancer NT* from spider silk

12:10-12:30 **Mirjam Brackhan**
(Translational Neurodegeneration and Neuropathology Lab, University of Oslo, Norway)

Experimental approaches to solve an important research question - Is Alzheimer's disease infectious?

12:30-12:50 **Jolanta Upīte**
(Department of Pharmacology, Faculty of Medicine, University of Latvia, Latvia)

A novel approach for the quantification of amyloid-β plaques

QUESTIONS/DISCUSSION

CLOSING REMARKS OF THE BWS2

12:50-13:00 Closing remarks and discussion

Jens Pahnke

Translational Neurodegeneration and Neuropathology Lab

University of Oslo, Oslo, Norway

University of Lübeck, Germany

University of Latvia, Riga, Latvia

Jens Pahnke, MD, PhD is Professor of Neuropathology at the University of Oslo (UiO) and head of the Section of Neuropathology at the Oslo University Hospital (OUS) since 2014.

He is also affiliated to the University of Lübeck (UzL), the Leibniz Institute for Plant Biochemistry (IPB) in Halle/Germany and the University of Latvia in Riga.

Previously he has been working at the Universities of Greifswald, Rostock, Magdeburg and Zürich. He graduated from the University of Greifswald in 2000 as medical doctor (MD) and molecular biologist (MSc/Diploma).

The research lab focusses on the function of the blood-brain barrier for the clearance of the brain.

Recent projects investigate the infectious nature of neurodegenerative diseases: i) the PETABC JPND project wants to develop ABCC1 and ABCA7 tracer for the use in patients as early diagnostic tool, ii) the Aβ-sequence EEA project aims to assess sequence and aggregation propensity of fragments of Aβ peptides for the treatment of AD, iii) use of herbal extracts from Hypericum perforatum and Sideritis scardica for the treatment of AD.

More projects are described on the webpage of the lab: www.pahnkelab.eu

Baiba Jansone

Head of the Department of Pharmacology

Vice -President of the Latvian Society of Pharmacology

University of Latvia, Department of Pharmacology, Riga, Latvia

Baiba Jansone, PhD degree in Medicine (Pharmacology), Dr.med. is professor of Pharmacology at the Department of Pharmacology, Faculty of Medicine, University of Latvia. Main Domain of Research: behavioral testing *in vivo* with emphasis on cognitive-memory and locomotor outcomes; studies of neuroinflammation processes in diseases of the central nervous system, the analysis of the brain biomarkers.

Alzheimer's disease (AD) is a chronic, progressive and neurodegenerative disorder. AD is characterized by permanent decline in memory, learning capacity and cognitive thinking. It is a leading cause of dementia in ageing population (Chowdhury et al., 2020). Currently, there is only a symptomatic treatments for AD available that consist of cholinesterase inhibitors and the N-methyl-d-aspartate receptor antagonist such as memantine. For more than two decades no new disease-modifying treatments have been approved for AD and meanwhile the population of older people with AD continues to grow constantly. A complex neuropathologically of AD is characterized by extracellular amyloid plaques, intracellular neurofibrillary tangles, the loss of cholinergic neurons, disturbance in the other neurotransmitter systems, synaptic loss, neuroinflammation, mitochondrial dysfunction, metal dyshomeostasis, oxidative stress, hyperactivation of kinases, disturbances in neuronal Ca2+ homeostasis and dysfunction of the blood brain barrier (Pahnke *et al*., 2014; Edwards, 2019; Upīte *et al*., 2020). There is an urgent need for the new effective treatments for AD patients. Clinicaltrials.gov, a public website indicating records for the clinical trials of all diseases, includes 2490 records of AD clinical trials. Currently, there are 142 recruiting studies for AD. Numerous research approaches throughout the last years have resulted in phase I, phase II, and phase III clinical trials including agents that represent disease-modifying therapies, symptomatic cognitive enhancers as well as symptomatic agents addressing neuropsychiatric and behavioural changes.

Henrik Biverstål

Department of Physical Organic Chemistry, Latvian Institute of Organic Synthesis

Department of Biosciences and Nutrition, Karolinska Institutet, Stockholm, Sweden

Dr. Henrik Biverstål is a part of the laboratory of protein misfolding and assembly, BioNut department at Karolinska Institutet, Sweden and is an expert in structural biology and biophysics. Since 2009, he has extensively studied amyloid-forming peptides involved in neurodegenerative diseases and their interaction with molecular chaperones. He is also affiliated with the Nuclear Magnetic resonance group at the Latvian Institute of Organic Synthesis (LIOS) in Riga. Latvia.

Medical conditions associated with amyloid formation, such as Alzheimer's disease (AD), type 2 diabetes mellitus and Parkinson's disease (PD), have one thing in common, namely the presence of deposits of abnormally aggregated proteins in the body. These aggregates consist of a protein or peptide such as Amyloid-β in AD, IAPP (also called amylin) in type 2 diabetes mellitus and α-synuclein (ASN) in PD. What causes these diseases is not fully understood. However, it is believed that the transition of monomeric disease-causing protein or peptide into β-sheet rich oligomers and fibers is an important event.

Recent advancements in cryo-EM and solid-state NMR have made it possible to study the molecular structure of patient-derived brain material from AD patients and solve most of the disease's structure of amyloid fibers and oligomers at atomic resolution.

I will go through the latest discoveries of the molecular structure and function of amyloid fibers and oligomers. After that, I will also give examples of how this could help find new therapies for these devastating diseases.

Kristīne Kitoka

Department of Physical Organic Chemistry, Latvian Institute of Organic Synthesis, Riga, Latvia

Kristīne Kitoka is a Research Assistant at the Latvian Institute of Organic Synthesis. In 2020, she graduated from University of Latvia wth a master's degree in Chemestry. Currently, she is on her 1st year of PhD in Chemestry at the University of Latvia. Her research is focused on proteins and peptides linked to Alzheimer's disease. She is studying their structural and biophysical features by Nuclear magnetic resonanse spectroscopy.

Amyloidogenic peptides and proteins are associated with several neurodegenerative disorders, e.g. Alzheimer's disease and Parkinson disease. These peptides are found in a form of insoluble aggregates in brain tissues. Over the past decades, scientists have made enormous efforts to understand the detailed pathways of their self-assembly. Unfortunately, even now, the understanding of processes and driving forces remain scarce. Studies of amyloidogenic peptides are limited due to failure to produce large amounts of pure peptides. Recently gained knowledge of how spiders manage the storage of their silk allowed us to design a modified variant of the N-terminal (NT) domain of their silk proteins NT*. With NT* we have overcome issues with aggregation and low yields of amyloidogenic peptides and proven the usefulness of NT* as solubility tag.

Mirjam Brackhan

Translational Neurodegeneration and Neuropathology Lab, University of Oslo, Oslo, Norway

Mirjam Brackhan, PhD completed her degree in veterinary medicine in 2013 at the University of Veterinary Medicine Hannover. In 2016, she obtained her PhD in neuroscience investigating epileptogenesis-associated brain inflammation as a nuclear imaging biomarker and treatment target for epilepsy prevention at the University of Veterinary Medicine Hannover and Hannover Medical School. On completion of her PhD, she took up a post-doctoral position in the Pahnke laboratory at the University of Oslo where she conducts research on the propagation behavior of peripheral amyloid-β as well as the role of role of blood-brain barrier carrier proteins in Alzheimer's disease.

Cerebral deposition of amyloid-β (Aβ), a cleavage product of the amyloid precursor protein (APP), is a major hallmark of Alzheimer's disease. Accumulating evidence suggests that Aβ can misfold and aggregate into seeds that in turn cause other Aβ peptides to misfold as known from prion diseases. Recent findings of premature cerebral Aβ deposition in both mice after peripheral inoculation with brain extracts containing Aβ, and humans following treatment with cadaveric human growth hormone raised concerns that Aβ seeds may be transmissible between individuals. However, proof that Aβ seeds actually reached the brain from the inoculation site is lacking. Thus, we generated stable isotope labelled APP-transgenic mouse brain extract, injected it intraperitoneally into young APP-transgenic mice and investigated the spatiotemporal distribution of labelled Aβ by highly sensitive mass spectrometry.

Jolanta Upīte

Department of Pharmacology, Faculty of Medicine, University of Latvia, Riga, Latvia

Jolanta Upīte, is Researcher and PhD candidate of Pharmaceutical Sciences at the Department of Pharmacology, Faculty of Medicine, University of Latvia. Main Domain of Research: molecular mechanisms of neurodegenerative and inflammatory processes in Alzheimer's disease.

Accumulation of amyloid-β (Aβ) plaques is a hallmark of Alzheimer's disease. To characterize the Aβ pathology in vivo models, a wide range of techniques has been applied over the past decades. One of the most commonly used methods for quantification of Aβ are high-resolution scans and imaging systems. Various imaging systems offers additional possibility to write scripts – an adjustment of method for quantification. These improvements offer a new analytic tool to quantify Aβ plaques and can be useful for a several therapeutic approaches, e.g. method for continuous systemic infusion for targeted delivery of test substances into specific sites are Alzet® pumps. Until now, no data are available how to examine Aβ and distribution of test substances in the brain using Alzet® pumps. Our aim was to develop an improved methodology to quantify Aβ plaques (number, size and etc.) and precise distribution of experimental compound infused by Alzet® pumps in the brain tissue. Our analytic tool provides quantification of Aβ to analyse plaque numbers, size and coverage, calculating the region of the lost brain tissue, after the removal of Alzet® pump cannula. The results demonstrated that this new analytic tool is beneficial to analyse long-term continuous intracerebral experimental compound infusions using Alzet® pumps. This method helps to generate reliable data for Aβ characterization and distribution of experimental compounds.

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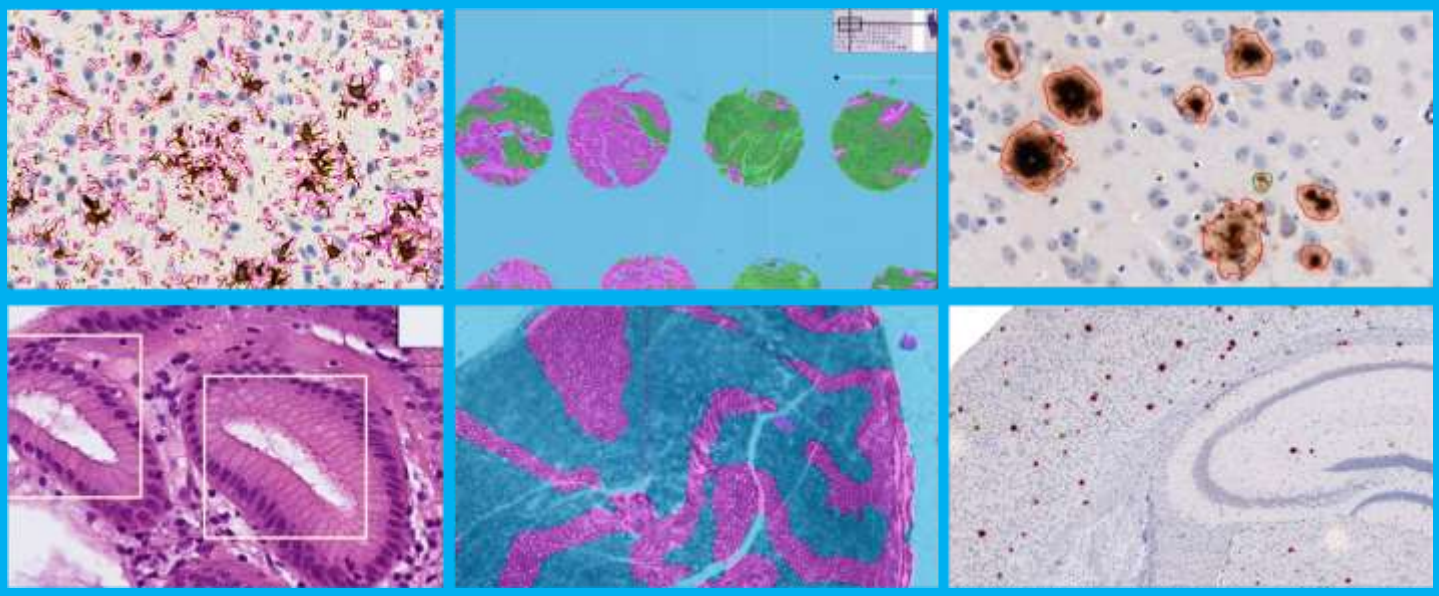

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