UPCOMING VIB CONFERENCES & EVENTS

27-28 *Oct 2021*
New Horizons in Alzheimer's Disease
Virtual & Leuven - Belgium - #NHAD21

22-23 *Nov 2021*
Translational Immunology
Ghent - Belgium - #TransImmu21

10-11 *Mar 2022*
Applied Bioinformatics in Life Sciences (4th edition)
Leuven - Belgium - #ABLS22

30-31 *May 2022*
Next-Generation Protein Analysis and Detection (4th edition)
Ghent - Belgium - #NGPAD22

16-17 *Jun 2022*
Recent insights into Immuno-Oncology
Leuven - Belgium - #ImmunoOnco22

17-19 *Aug 2022*
4th International Brassinosteroid Conference
Ghent - Belgium - #BRconf2022

21-23 *Sep 2022*
The Leuven Protein Aggregation Meeting
Leuven - Belgium - #ProAgg22

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VIB conference series
Neuroscience

Hybrid edition

New Horizons in Alzheimer's Disease

27-28 OCTOBER, 2021 | LEUVEN, BE

www.vibconferences.be
#NHAD21

WELCOME

Dear conference participant,

On behalf of the organizing committee, it is our pleasure to welcome you to the hybrid edition of New Horizons in Alzheimer's Disease.

As you know Alzheimer's Disease research is accelerating with exciting new insights into molecular and cellular mechanisms. This upcoming conference brings together some of the thought leaders in the field with young investigators to stimulate discussion and interaction.

We anticipate further insights into the triangle amyloid, Tau and neuroinflammation and how these might provide novel therapeutic approaches.

The following topics will be the focus of this conference:

- Genes and environment
- Synapse and circuitry
- Seeds and spreading of disease
- Mechanisms and models of disease

To support upcoming scientists and provide them with the opportunity to present their research, we have included thirteen shorter talks in the program, which were selected from submitted abstracts, as well as offer the opportunity for further interactions at poster sessions.

On the first conference evening we'll welcome Roger M Nitsch, CEO & President of Neurimmune and inventor of aducanumab, who will give a keynote lecture on the discovery of aducanumab for the potential treatment of Alzheimer's Disease.

Next to an inspiring scientific program, you will have ample networking opportunities (both live and virtual) during the breaks, poster sessions and the conference dinner.

Finally, we would like to thank our sponsors for supporting this event. You can visit their on-site and virtual booths during the entire event.

We wish you all an inspiring and productive conference.

Organizing Committee

Wim Annaert, VIB-KU Leuven Center for Brain & Disease Research, BE
Jean-Pierre Brion, ULB Neuroscience Institute, BE
Lucía Chávez Gutiérrez, VIB Center for Brain and Disease Research, BE
Bart De Strooper, VIB-KU Leuven Center for Brain & Disease Research, BE & UK Dementia Research Institute, UK
Ilse Dewachter, Hasselt University, BE
Rosa Rademakers, VIB-UAntwerp Center for Molecular Neurology, BE
Patrik Verstreken, VIB-KU Leuven Center for Brain & Disease Research, BE
Roosmarijn Vandenbroucke, VIB-UGent Center for Inflammation Research, BE
Evy Vierstraete, Science Events Manager, VIB, BE

CORPORATE PARTNERS

The 2021 VIB Conference Series is kindly supported by the following corporate partners:

08:30 - 08:50 Registration & coffee

08:50 - 09:00 Welcome by Bart De Strooper

Session 1

GENES AND ENVIRONMENT

Chairs: Rosa Rademakers & Ilse Dewachter

09:00 - 09:30 Relevance of novel genes identified in families with neurodegenerative brain diseases
Christine Van Broeckhoven, *VIB-UAntwerp Center for Molecular Neurology, BE. Supported by SAO.*

09:30 - 10:00 Decoding microglia phenotypes in health and disease
Christopher Glass, *University of California, San Diego, US*

10:00 - 10:30 Learning from cognitively healthy centenarians to escape dementia
Henne Holstege, *Amsterdam UMC & Amsterdam Alzheimer Center, NL*

10:30 - 10:40 *Selected Talk* Stem-cell-derived human microglia transplanted in mouse brain to study human disease
Poster #32
Nicola Fattorelli, *VIB-KU Leuven Center for Brain & Disease Research, BE*

10:40 - 10:50 Microbiota-derived short chain fatty acids modulate microglia and promote Aβ plaque deposition
Poster #99
Sabina Tahirovic, *German Center for Neurodegenerative Diseases (DZNE), DE*

10:50 - 11:20 Coffee

11:20 - 11:50 Molecular basis of familial Alzheimer's disease: insights into disease mechanisms and implications for therapeutics
Lucía Chávez Gutiérrez, *VIB Center for Brain and Disease Research, BE. Supported by SAO.*

11:50 - 12:20 Modulation of Amyloid Deposition and Neuroinflammation by the Microbiome
Sangram S. Sisodia, *Department of Neurobiology, University of Chicago, US*

12:20 - 12:50 Glial disease and aging confer competitive disadvantage: A basis for cell replacement as a therapeutic strategy in neurodegenerative disorders
Steven A. Goldman, *University of Rochester, Medical Center, US & University of Copenhagen, DK*

12:50 - 13:00 *Selected Talk*: New regulators of amyloid ß-peptide toxicity in Alzheimer's disease
Poster #73
Francisco Muñoz, *Universitat Pompeu Fabra, ES*

13:00 - 13:05 *Company pitch*: 3D light sheet microscopy of entire mouse brain
Veerle Lemmens, *Imaging Specialist BeNeLux Miltenyi Biotec, BE*

13:05 - 13:45 Lunch

13:45 - 14:30 On-site Poster Session

Session 2

SYNAPSE AND CIRCUITRY

Chairs: Patrik Verstreken & Jean-Pierre Brion

14:30 - 15:00 Novel insights into the role of the APP family in maintaining neural circuit function, with implications for AD therapy
Marc Aurel Busche, *UK Dementia Research Institute at UCL, UK*

15:00 - 15:30 SYNGO: defining the synapse and synaptic pathways in brain disease
Matthijs Verhage, *Vrije Universiteit & Amsterdam University Medical Center, NL*

15:30 - 16:00 Neural Basis of a Silent Alzheimer's Disease Phase
Inna Slutsky, *Tel Aviv University, IL*

16:00 - 16:30 Coffee

16:30 - 16:40 *Poster #58* *Selected Talk*: Lowering Synaptogyrin-3 expression rescues Tau-induced memory defects and synaptic loss in the presence of microglial activation
Pablo Largo Barrientos, *VIB-KU Leuven Center for Brain & Disease Research & KU Leuven, Department of Neurosciences, Leuven Brain Institute, Mission Lucidity, BE*

16:40 - 16:50 *Poster #93* *Selected Talk*: Astrocytes and functional network disruptions at early stages of amyloid pathology
Disha Shah, *VIB-KU Leuven Center for Brain & Disease Research, BE*

16:50 - 17:00 *Poster #89* *Selected Talk*: *In vivo* assessment of synaptic pathology in dementia with SV2A-PET
Eric Salmon, *University of Liege / GIGA Cyclotron Research Centre, BE*

17:00 - 17:30 Gamma oscillations: mechanisms, function and human diseases
Li-Huei Tsai, *The Picower Institute for Learning and Memory & MIT, US*

17:30 - 18:00 Imaging synaptic changes in Alzheimer's disease
Tara Spires-Jones, *The University of Edinburgh & UK Dementia Research Institute, UK*

18:00 - 19:00 Walk to Kinepolis Leuven, followed by a welcome drink

19:00 - 20:00 The discovery of aducanumab for the potential treatment of Alzheimer's disease
Roger M Nitsch, *CEO & President, Neurimmune, CH*

20:15 - 22:30 Conference dinner at Kinepolis Leuven

08:30 - 09:00 Welcome coffee

Session 3

SEEDS AND SPREADING OF DISEASE

Chairs: Ilse Dewachter & Roos Vandenbroucke

09:00 - 09:30 Fluid biomarkers and their relation to Alzheimer brain pathology
Mathias Jucker, *The Hertie Institute for Clinical Brain Research (HIH) & German Center for Neurodegenerative Diseases (DZNE), DE*

09:30 - 10:00 New cell model for FTD tauopathy
Karen Duff, *UK Dementia Research Institute at UCL, UK*

10:00 - 10:30 Seeding and speading in tauopathies: mechanisms and therapeutic approaches
Luc Buée, *University of Lille, Inserm, CHU-Lille, FR*

10:30 - 10:35 *Company pitch*: WuXi AppTec: Your partner for Alzheimer's Disease drug discovery
Kris Rutten, *Director, WuXi AppTec, NL*

10:35 - 11:05 Coffee

11:05 - 11:15 *Poster #54* *Selected Talk*: Heterotypic Abeta interactions facilitate amyloid assembly and modify amyloid structure
Frederic Rousseau, *Switch Laboratory, VIB-KU Leuven Center for Brain & Disease Research, BE*

11:15 - 11:25 *Poster #74* *Selected Talk*: Disassembly of Tau fibrils by the human Hsp70 disaggregation machinery generates small seeding-competent species
Eliana Nachman, *VIB-KU Leuven Center for Brain & Disease Research, BE*

11:25 - 11:35 *Poster #70* *Selected Talk*: Conformational strain diversity in misfolded amyloid beta peptides and potential repercussions in Alzheimer's pathology
Rodrigo Morales, *The University of Texas Health Science Center at Houston, US*

11:35 - 12:05 The Glymphatic System
Maiken Nedergaard, *University of Rochester, Medical Center, US & University of Copenhagen, DK*

12:05 - 12:35 The cellular phase of Alzheimer's disease
Bart De Strooper, *VIB-KU Leuven Center for Brain & Disease Research, BE & UK Dementia Research Institute, UK*

12:35 - 13:15 Lunch

13:15 - 14:00 Virtual Poster Session

Session 4

MECHANISMS AND MODELS OF DISEASE Chairs: Lucía Chávez Gutiérrez & Wim Annaert

14:00 - 14:30 Beyond microglia: Temporal sequencing of perturbations in human cellular communities to establish the causal chain leading to aging-related cognitive decline
Philip L. De Jager, *Division of Neuroimmunology & Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University Medical Center, US*

14:30 - 15:00 Impaired SorLA maturation and trafficking as a new mechanism for SORL1 missense variants in Alzheimer disease
Anne Rovelet-Lecrux, *University of Rouen, Inserm UMR1245, FR*

15:00 - 15:30 Direct neuronal reprogramming to study aging and age-related neurodegeneration
Jerome Mertens, *Salk Institute for Biological Studies, US & University of Innsbruck, AT*

15:30 - 15:40 *Poster #103* *Selected Talk*: Combining pathogenic Tau pathways generates a super toxic Tau
Valerie Uytterhoeven, *VIB-KU Leuven Center for Brain & Disease Research, BE*

15:40 - 15:50 *Poster #90* *Selected Talk*: Generation of non-human primate models of Alzheimer's disease
Hiroki Sasaguri, *RIKEN Center for Brain Science, JP*

15:50 - 16:20 Coffee break

16:20 - 16:30 *Poster #27* *Selected Talk*: Microglial contributions along the ATN axis in AD in preclinical models
Ilse Dewachter, *Hasselt University, BE*

16:30 - 16:40 *Poster #110* *Selected Talk*: Developing human cellular models to understand biological mechanisms linked to AD genetic risk
Jessica Young, *University of Washington, US*

16:40 - 17:10 Systemic regulation of brain function at the vasculature
Tony Wyss-Coray, *Stanford University, US*

17:10 - 17:40 Redefining Microglia States and Function in Alzheimer's Disease
Beth Stevens, *FB Kirby Neurobiology Center; Boston Children's Hospital & Broad Institute Member, US*

17:40 - 18:10 Update on fluid biomarkers for Alzheimer's disease
Henrik Zetterberg, *University of Gothenburg, SE & UK Dementia Research Institute, UK*

18:10 - 18:25 Poster prize ceremony and closing remarks by Bart De Strooper

POSTER ABSTRACTS

Abstracts ordered by first author. Presenting authors are highlighted in orange.
Posters marked with a 🎤 were selected for a short talk.

TAU-MISSORTING BASED LOSS OF MICROTUBULES IN HUMAN MODEL SYSTEMS

Mhd Aghyad Al Kabbani[1,2]

[1]Institute of Human Genetics, Uniklinik Köln, Germany, DE; [2]Center of Molecular Medicine Cologne, DE

TAU is a neuronal microtubule-associated protein that is missorted and aggregated in an array of diseases known as tauopathies, including Alzheimer disease (AD). Microtubules are essential for neuronal function, but in AD neuronal microtubules are lost, the cause is unclear. TTLLs are a class of enzymes that regulate microtubule dynamics and stability via specific post translational modifications of microtubules, of which polyglutamylation leads to subsequent recruitment of SPASTIN and other microtubule severing enzymes.

In AD-paradigms in cell and animal models, missorted TAU recruits TTLL6 to the dendrites, inducing microtubule polyglutamylation and SPASTIN-mediated microtubule loss. In this study, we aim to study the interrelationship between TAU and different TTLLs and their role in microtubule loss in TAU-missorting based, human-disease relevant systems, and test the therapeutic potential of manipulating TTLLs and related proteins such as SPASTIN.

We will use iPSC-derived human neurons, primary mouse neurons and TAU transgenic mice expressing human disease-relevant TAU (P301L-TAU or all 6 human TAU-isoforms) to investigate the activities of TAU, SPASTIN and TTLLs in disease paradigms. We will manipulate TAU, SPASTIN and TTLLs via overexpression/knockdown and study the subsequent effects on microtubules, TAU and neuronal cell physiology.

We will provide first evidence of the disease relevance and druggability of several TTLLs, opening up novel therapeutic approaches for AD and related tauopathies.

PICALM REDUCTION EXACERBATES TAU PATHOLOGY IN A MURINE TAUOPATHY MODEL

Kunie Ando[1], Robert De Decker[1], Cristina Vergara[1], Zehra Yilmaz[1], Salwa Mansour[1], Valérie Suain[1], Kristel Sleegers[2], Marie-Ange de Fisenne[1], Sarah Houben[1], Marie-Claude Potier[3], Charles Duyckaerts[3,4], Toshio Watanabe[5], Luc Buée[6], Karelle Leroy[1], Jean-Pierre Brion[1]

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Genome wide association studies (GWAS) have identified *PICALM* as one of the most significant susceptibility loci for late-onset Alzheimer disease (AD) after *APOE* and *BIN1*. PICALM is a clathrin adaptor protein and plays critical roles in clathrin-mediated endocytosis and in autophagy.

In this study, we confirmed a significant reduction of soluble PICALM protein and autophagy deficits in the *post-mortem* human brains of FTLD-tau-*MAPT* (P301L, S364S and L266V). We generated a novel transgenic mouse line named Tg30xPicalm+/- by crossing Tg30 tau transgenic mice with Picalm haploinsufficient mice to test whether Picalm reduction may modulate tau pathology. While Picalm haploinsufficiency did not lead to any motor phenotype or detectable tau pathology in mouse brains, Tg30xPicalm+/- mice developed markedly more severe motor deficits than Tg30 by the age of 9 months. Tg30xPicalm+/- had significantly higher pathological tau levels in the brain, an increased density of neurofibrillary tangles compared to Tg30 mice and increased abnormalities of autophagy markers.

Our results demonstrate that Picalm haploinsufficiency in transgenic Tg30 mice significantly aggravated tau pathologies and tau-mediated neurodegeneration, supporting a role for changes in Picalm expression as a risk/sensitizing factor for development of tau pathology and as a mechanism underlying the AD risk associated to PICALM.

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The Belgian Alzheimer Foundation is a proud sponsor of the conference New Horizons in Alzheimer's Disease. Our foundation supports Belgian Basic and Clinical Research of Alzheimer's Disease and related dementia. In 2020 the foundation invested € 3,2 million in 17 research projects.

Each year in February we send invitations to all Belgian universities and research institutions to submit research proposals. These proposals are evaluated by a peer-reviewing system driven by our Scientific Advisory Board, so that the best projects are rewarded with a grant.

Standard Grant Applications for a 3-years award period are fixed at € 250.000 and Pilot Grant Applications for a 2-years award period are fixed at € 100.000.