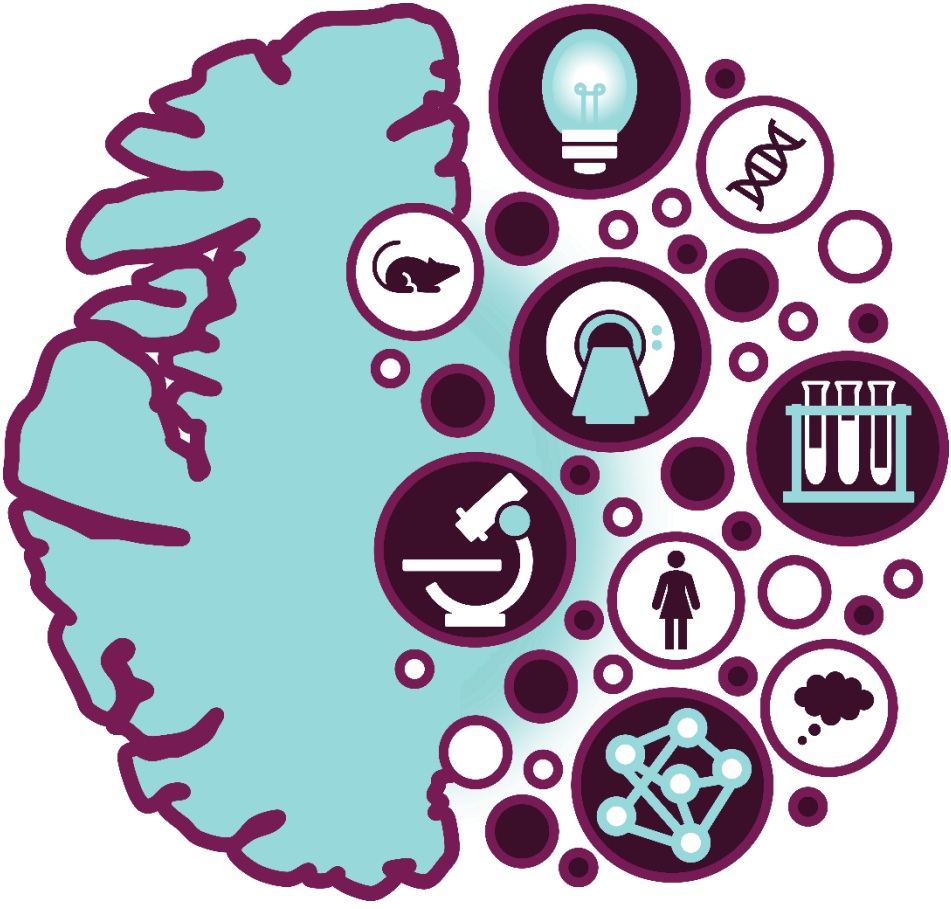
3rd Swedish Meeting for Alzheimer Research



April 10th, 2025
Aula Medica,
Stockholm

Karolinska Institutet

Cover design:

Annegret Habich (Div. Clinical Geriatrics, Karolinska Institutet)

TABLE OF CONTENTS

3rd Swedish Meeting for Alzheimer Research, 2025

Welcome to the 3rd Swedish Meeting for Alzheimer Research at Aula Medica, Karolinska Institutet (Stockholm). We are very happy to see so many attendees coming from different universities, clinics, organizations, and companies across Sweden.

This is the main national conference on Alzheimer's disease in Sweden, bringing together around 300 people from all over the country. Among them, there are world-leading Swedish researchers, as well as clinicians, industry partners and other relevant stakeholders on the topic of dementia.

This is the 3rd edition of this conference, with the first being in 2019 and the second in 2022. Uniting the Swedish Alzheimer´s disease research community in the same place only happens a few times. We truly hope you can all take this opportunity to discuss, interact, and exchange ideas and knowledge!

Center for Alzheimer Research

From left to right: Per Nilsson (Div. Neurogeriatrics), Daniel Ferreira (Director of Center for Alzheimer Research), Dorota Religa (Div. Clinical Geriatrics), Chengxuan Qiu (Aging Research Center).

Photo: Giulia Lorenzon

AULA MEDICA - IMPORTANT INFORMATION

The 3rd Swedish Meeting for Alzheimer Research is held in Aula Medica at Karolinska Institutet, Nobels väg 6, Solna (Stockholm). The lecture hall complex was completed in the summer of 2013 and is used for international events such as the Nobel lectures and large scientific symposia.

Aula Medica, designed by Wingårdh Architects and funded by the Erling-Persson Foundation, is situated at Karolinska Institutet Solna Campus, just across the street from the new Karolinska Hospital. The bright 1000-seat Erling Persson auditorium inside Aula Medica is built like an amphitheatre. The acoustics of the Erling Persson auditorium are exquisite and facilitate interactive discussions. Outside the venue is a 2000 square meter area suited for poster exhibition, enjoying food and beverages, and networking. Aula Medica offers good accessibility for attendees with disabilities. There are six entrances and lifts to the auditorium.

Check-in and registration desk
Check-in will be possible at the registration desk from 8:00 to 9:15.

Food and drinks
Lunch will be served during the symposium, and refreshments will be available throughout the day in between scientific sessions. We kindly ask you not to bring any food or drink (except water bottles) inside Aula Medica.

Storing luggage
There is a wardrobe and storage area for luggage at the main entrance floor, which will be guarded by personnel through the whole day. For more information, please ask at the registration desk.

Wi-fi
Free wireless Internet connection is available at Aula Medica.

Network:	KI guest
Password:	Campus22

Social media #
Please use the hashtag for the Swedish Meeting for Alzheimer Research! #SWEALZ25

Please also follow the Center for Alzheimer Research on X for future events: @CAR_Karolinska

PROGRAM, Aula Medica April 10th

TIME	
08:00 – 09:15	**Check-in at registration desk** **All attendees take their seats**
09:30 – 09:45	**WELCOME** Dean KI North Carl Johan Sundberg H.M. *Queen Silvia* Director of Center for Alzheimer Research (CAR) *Daniel Ferreira*
09:45– 10:15	**SESSION I – Epidemiology and risk factors of Alzheimer's Disease** *Chairs: Lars Lannfelt (Uppsala University), Sara Hägg (Karolinska Institutet)*
	"Blood biomarkers of Alzheimer´s disease and dementia in the community" *Giulia Grande (Karolinska Institutet)*
	"Influence of pathway-based polygenic risk for Alzheimer's disease on dementia risk and age-related cognitive decline" *Karolina Kauppi (Umeå University)*
	"Age-related risk factors biological aging and the risk for alzheimer's disease and related dementias" *Sara Hägg (Karolinska Institutet)*
	Presentation from gold sponsor: Nutricia "Latest research on medical nutrition interventions in early AD" *Nicholas Levak*
10:15 – 11:00	**SESSION II – Amyloid proteinopathy** *Chairs: Anna Månberg (Royal Institute of Technology), Hugo Lövheim (Umeå University)*
	"Identification of potential aggregation hotspots on aβ42 fibrils blocked by the anti-amyloid chaperone-like brichos domain" *Axel Abelein (Karolinska Institutet)*

	"Virus amyloid – a link between virus infection and Alzheimer's disease?" *Sofie Nyström (Linköping University)*
	"Structural features of Aβ aggregates with the Uppsala deletion" *Dag Sehlin (Uppsala University)*
	Presentation from gold sponsor: Eli Lilly
	"Eli Lilly's commitment to Alzheimer's research: Advancing progress through innovation and care" *Daniel Jaraj*
11:00 – 11:45	**Speed presentations from abstract submission** *Chair: Per Nilsson (Karolinska Institutet)*
11:45 – 12:45	**Posters and Lunch**
12:35 – 12:45	**Presentation from silver sponsor** *Chair: Daniel Ferreira*
	"Simoa® technology: Unlocking new insights in Alzheimer's disease through ultrasensitive biomarker detection" *Canan Ugur Yilmaz (Quanterix)*
12:45– 13:30	**SESSION III – Alzheimer's disease biomarkers and artificial intelligence** *Chairs: Jakob Vogel (Lund University), Sara Pudas (Umeå University)*
	"Next challenges in blood biomarkers for Alzheimer's disease" *Laia Montoliu-Gaya (University of Gothenburg)*
	"Clinical value of tau PET imaging and tau PET/tau pathology correlations" *Ruben Smith (Lund University)*
	"Synthetic MRI aging" *Rodrigo Moreno (Royal Institute of Technology)*

Presentation from gold sponsor: Olink

"Advancing neurodegeneration research through proteomics"

Anne-Li Lind

13:30 – 14:15 Posters & Coffee Break

14:15 – 14:45 A session with Alzheimerfonden

"A presentation of the Swedish Alzheimer foundation"
Liselotte Jansson (Alzheimerfonden, Secretary General)

"A conversation with an Alzheimer's patient and a relative"
Sophia Du Rietz (Alzheimerfonden, Marketing Manager)

14:45 – 15:30 SESSION IV – Neuroinflammation, retina and APOE

Chairs: Maria Lindskog (Uppsala University), Tomas Deierborg (Lund University)

"Astrocytes: a potential target to reduce cell-to-cell spreading in Alzheimer's disease"
Anna Erlandsson (Uppsala University)

"APOE and systemic processes"
Henrietta Nielsen (Stockholm University)

"The retina-brain nexus: Implications in Alzheimer's disease"
Malin Wennström (Lund University)

"Diagnostic potential of neuroinflammatory markers in CSF and plasma"
Petronella Kettunen (University of Gothenburg)

15:30 – 16:15 Posters & Coffee Break

16:15 – 16:55	**SESSION V – Treatment of Alzheimer's disease** *Chairs: Helena Karlström (Karolinska Institutet), Dorota Religa (Karolinska Institutet)*
	"How much should we be prepared to pay for disease-modifying treatments in Alzheimer's disease?" *Linus Jönsson (Karolinska Institutet)*
	"Swedish registry for cognitive/dementia disorders, SveDem - development of Drug module for real life data" *Dorota Religa (Karolinska Institutet)*
	"Enhanced endogenous degradation of amyloid beta as a treatment strategy for Alzheimer's disease: utilizing gene and protein therapy" *Greta Hultqvist (Uppsala University)*
	Presentation from gold sponsors: Bioarctic "Brain delivery in Alzheimer's disease" *Per-Ola Freskgård*
16:55 – 17:00	**Closing remarks** *CAR Steering committee: Chengxuan Qiu, Dorota Religa, Per Nilsson, Daniel Ferreira*

Center for Alzheimer Research at Karolinska Institutet

The Center for Alzheimer Research (CAR) is a hub for all Alzheimer research within Karolinska Institutet, meant to strengthen the synergies between independent research groups. CAR is a forum for visionary and innovative translational research to better understand, diagnose, prevent, and treat Alzheimer's disease and other dementias. The core of the research is performed at the *Department of Neurobiology, Care Sciences and Society* (NVS), which includes the divisions of Neurogeriatrics, Clinical Geriatrics, and the Aging Research Center. Yet CAR includes all researchers at Karolinska Institutet that conduct research of relevance for Alzheimer's disease and other dementias. Themes in focus within CAR are protein processing and trafficking, vascular and metabolic conditions, network- and synaptic mechanisms, inflammation, neurotrophic factors as well as lifestyle and genetic factors.

CAR organizes numerous activities to facilitate interactions between research groups within NVS and KI. Since 2020, CAR has organized weekly virtual morning coffee meetings, an imaging seminar series, and initiated a working group on sex and gender differences in dementia. CAR also organizes large, translational meetings such as the Swedish Meeting for Alzheimer Research – now for the third time.

To receive updates, follow CAR on X: @CAR_Karolinska

https://ki.se/en/nvs/center-for-alzheimer-research

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BLOOD BIOMARKERS OF ALZHEIMER´S DISEASE AND DEMENTIA IN THE COMMUNITY

Giulia Grande
Karolinska Institutet

Aims: To assess the clinical validity of Alzheimer's disease (AD) blood biomarkers for predicting incident dementia in the general population.

Methods: Six AD biomarkers (amyloid-β42/40, p-tau217, p-tau181, total tau, NfL, GFAP) were measured in 2,148 dementia-free older adults from the Swedish National Study on Aging and Care (SNAC-K), followed up to 16 years.

Results: In multi-adjusted Cox models, high baseline p-tau181, p-tau217, NfL, and GFAP were associated with increased dementia hazard, showing non-linear dose-response relationships. These biomarkers showed a good predictive performance (AUC 71–83%) for 10-year all-cause and AD dementia, with high negative (>90%) but low positive predictive values. Combining p-tau217 with NfL or GFAP improved positive prediction (up to 43%).

Conclusions: AD blood biomarkers have the potential for ruling out impending dementia in the community but might need to be combined with other biological or clinical markers to be used as screening tools.

INFLUENCE OF PATHWAY-BASED POLYGENIC RISK FOR ALZHEIMER'S DISEASE ON DEMENTIA RISK AND AGE-RELATED COGNITIVE DECLINE

Karolina Kauppi
Umeå University

Aims: To utilize pathway-based polygenic risk scores (p-PRS) of Alzheimer's Disease (AD) to investigate how genetic variations within genes with similar functions influences disease-risk and cognitive aging.

Methods: We analyzed data from 1,737 participants from the Betula project, where AD p-PRS were computed for five biological pathways: immune-, lipid-, cholesterol-, amyloid-, and tau-related processes. These were tested for associations with dementia risk and cognitive decline, together with genome-wide (GW) AD-PRS and APOE ε4 for comparisons.

Results: Dementia risk was best predicted by APOE ε4, followed by GW AD-PRS. Several p-PRS were also significant. Cognitive decline was instead stronger predicted by the immune and tau p-PRS than the GW PRS, and APOE was only predictive of decline in those later developing dementia.

Conclusions: While APOE ε4 is specifically linked to dementia risk, other AD risk genes, in particular immune-related genes, also impact normal cognitive aging.

AGE-RELATED RISK FACTORS BIOLOGICAL AGING AND THE RISK FOR ALZHEIMER'S DISEASE AND RELATED DEMENTIAS

Sara Hägg
Karolinska Institutet

Aging is the most important risk factor for Alzheimer's disease and related dementias (ADRD). During the lifespan, cellular and molecular changes of aging manifest at tissue, organ and whole-body level, increasing the susceptibility for ADRD. For example, systemic inflammation is associated with both ADRD and aging, especially via glia dysfunction, through chronic low-grade inflammation processes. Metabolic disturbances and glucose intolerance are seen both in aging and ADRD, and more evidence of communalities exist.
In my talk, I will describe characteristics of biological aging, how these processes are linked to ADRD, and present some recent data from our ongoing studies in support for accelerated biological aging as a risk factor for ADRD.

LATEST RESEARCH ON MEDICAL NUTRITION INTERVENTIONS IN EARLY AD

Nicholas Levak
Nutricia – Gold Sponsor

Aim: Prodromal Alzheimer's disease is marked by cognitive decline and nutritional deficiencies that may accelerate disease progression. Souvenaid targets synaptic health by providing nutrients essential for neuronal membrane synthesis.

Method: We synthesized data from LipiDiDiet (24- and 36-month RCTs) and the MIND-ADmini study (multimodal lifestyle ± Souvenaid).

Results: In LipiDiDiet, Souvenaid reduced cognitive decline (NTB memory, $p<0.05$) and slowed CDR-SB worsening by ~45% at 36 months. MRI also showed less hippocampal atrophy. Data from the MIND-ADmini pilot study suggest combining Souvenaid with lifestyle changes may yield synergistic cognitive benefits.

Conclusion: Long-term Souvenaid use appears to slow disease progression in prodromal AD. Nutritional support complements lifestyle interventions, reinforcing a multifaceted approach to early-stage AD.

TRÄFFAR DU PATIENTER MED ALZHEIMERS SJUKDOM?

Även nutritionsåtgärder kan påverka livskvaliteten för patienter och anhöriga positivt. Souvenaid är ett kosttillägg för kostbehandling av patienter i ett tidigt skede av Alzheimers sjukdom.

Souvenaid visar signifikant effekt vs kontroll vid kostbehandling av patienter i tidigt skede av Alzheimers sjukdom.

Smaker: cappuccino, jordgubb och vanilj

Ny analys av data från LipidiDiet-studien är tillgänglig.
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IDENTIFICATION OF POTENTIAL AGGREGATION HOTSPOTS ON AMYLOID FIBRILS BLOCKED BY THE ANTI-AMYLOID CHAPERONE-LIKE BRICHOS DOMAIN

Axel Abelein
Karolinska Institutet

Aims: Protein misfolding can generate toxic intermediates, which underlies Alzheimer's and Parkinson's disease (AD/PD), where the surface of amyloid fibrils has been suggested to act as a catalyzer for generation of potentially toxic species. Here, we aim to specifically target "aggregation hotspots" on the fibril surface by utilizing molecular chaperones, such as the BRICHOS domain.

Methods: We apply a combined approach of high-resolution structural techniques together with aggregation kinetics experiments.

Results: Here, we identify a site on the AD-associated fibrils, which is efficiently sensed by BRICHOS, suggesting that this site acts as a catalytic aggregation hotspot. Further, we recently found a similar inhibitory effect of BRICHOS on PD-related protein aggregation, where BRICHOS prevents surface-catalyzed secondary nucleation, binds to oligomeric species and reduces related toxicity.

Conclusions: In summary, these findings provide an understanding how toxic nucleation events can be targeted by molecular chaperones, which might facilitate the development of new treatment approaches against protein misfolding diseases.

VIRUS AMYLOID – A LINK BETWEEN VIRUS INFECTION AND ALZHEIMER'S DISEASE?

Sofie Nyström
Linköping University

Misfolding and amyloid deposition of Aβ and Tau proteins expressed in our brains are hallmarks of Alzheimer's disease (AD). Mutations in these proteins are also the most prominent risk factors for disease. However, an absolute majority of patients do not carry known disease mutations. Also, mechanisms initiating misfolding are largely unknown.

Epidemiology and biomarker studies have lately connected virus infection to increased risk of AD later in life. Proteins from different virus families form amyloid in vitro and in vivo. Amyloids are resistant to degradation and can reside for extended time in the body. We hypothesize that amyloid formation of virus protein during virus infections earlier in life is a culprit of AD.

We have found that by adding in vitro formed virus amyloids to Aβ in our model systems, we can accelerate formation and deposition of amyloid. This pinpoints a potentially crucial and hitherto unexplored connection between virus infection and disease progression.

STRUCTURAL FEATURES OF AB AGGREGATES WITH THE UPPSALA DELETION

Dag Sehlin
Uppsala University

The recently discovered Uppsala APP mutation results in a 6 amino acid deletion in the mid region of amyloid-β (AβUpp). This leads to increased formation and enhanced aggregation of AβUpp, resulting in early onset Alzheimer's disease in mutation carriers. Here we have investigated the evolution and structural properties of Aβ pathology in mouse models expressing AβUpp, either alone or in combination with Aβwt. Cryo-EM, immunostaining, ELISA and in vivo antibody PET imaging analyses demonstrated that AβUpp forms diffuse parenchymal plaques that are resistant to lecanemab treatment and does not induce a glial response. Mice expressing both AβUpp and Aβwt showed accelerated formation of distinct Aβwt pathology, potentially initiated by the rapidly aggregating AβUpp and accompanied by abundant gliosis. Taken together, we find that the Uppsala APP mutation forms aggregates of a distinct structure that does not induce gliosis, but retains the ability to seed Aβwt.

ELI LILLY'S COMMITMENT TO ALZHEIMER'S RESEARCH: ADVANCING PROGRESS THROUGH INNOVATION AND CARE

Daniel Jaraj
Eli Lilly – Gold Sponsor

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SIMOA® TECHNOLOGY: UNLOCKING NEW INSIGHTS IN ALZHEIMER'S DISEASE THROUGH ULTRASENSITIVE BIOMARKER DETECTION

Canan Ugur Yilmaz
Quanterix – Silver Sponsor

Simoa® ultrasensitive technology enables biomarker measurement at sub-femtomolar levels in blood and other accessible biofluids, addressing the need for minimally invasive and accurate diagnostic tools. Over the past decade, Simoa® assays have improved diagnostic accuracy and prognostic power across multiple diseases, with the greatest impact in neurodegeneration. Traditional methods like cognitive assessments, imaging, and cerebrospinal fluid analysis often lack precision, are costly, or require invasive procedures.

Simoa® has been widely adopted in clinical trials for neurological disease-modifying therapies, including Alzheimer's and ALS. Additionally, the first plasma-based assays for pTau181 and serum NfL have reached clinical use, with Simoa® pTau181-LDT receiving FDA approval.

This talk will highlight Simoa® technology's sensitivity, its role in detecting neurodegeneration biomarkers (pTau's, BD-Tau, GFAP, and NfL), and its applications in Alzheimer's and neuroinflammation research.

NEXT CHALLENGES IN BLOOD BIOMARKERS FOR ALZHEIMER'S DISEASE

Laia Montoliu-Gaya
University of Gothenburg

Blood biomarkers, particularly phosphorylated tau (p-tau), are becoming essential not only for diagnosing Alzheimer's disease (AD) but also for patient selection and monitoring in anti-amyloid therapies. In this presentation, we will explore the key challenges and future directions for advancing the application of blood-based biomarkers in AD. First, we will discuss the potential of tau blood biomarkers as reliable tools for the biological staging of AD, providing insights into brain neuropathology and disease progression with implications for clinical decision-making. Next, we will examine how tau blood biomarkers are influenced by brain co-pathologies and comorbidities, a crucial factor in accurately interpreting biomarker results and minimizing confounding variables. Finally, we will highlight the promise of dried blood spots as a remote collection method that could expand access to biomarker testing in diverse populations and facilitate screening and repeated sampling. By addressing these key aspects, we aim to provide the audience with a comprehensive understanding of the current state of tau blood biomarkers and the challenges that lie ahead in their clinical implementation.

CLINICAL VALUE OF TAU PET IMAGING AND TAU PET/TAU PATHOLOGY CORRELATIONS

Ruben Smith
Lund University

Tau PET imaging has been used in research for over a decade and was approved for clinical use in the EU in 2024 as a biomarker for Alzheimer's Disease. This presentation will discuss recent evidence on the clinical added value of incorporating tau PET into the diagnostic process in Memory Clinics. It will also cover data comparing the established flortaucipir visual read algorithm to the BioFINDER visual read algorithm for determining tau positivity.
Additionally, the prognostic value of tau PET imaging will be explored, along with its correlation to neuropathology using [^{18}F]flortaucipir PET. The data presented comes from a large [^{18}F]flortaucipir multi-cohort study (Ossenkoppele *et al.* Nat Med 2022), the AVID A16 end-of-life study with [^{18}F]flortaucipir and [^{18}F]RO948 tau PET scans from the Swedish BioFINDER-2 study.

SYNTHETIC MRI AGING

Rodrigo Moreno
Royal Institute of Technology

Aims: I will introduce the methods we have proposed to simulate MRI aging from MRI scans of healthy and Alzheimer's subjects.

*Methods: W*e use deep learning-based diffeomorphic registration for the simulation. The advantage of our approach is that the generated images are anatomically plausible by construction. If longitudinal data is available, we use diffeomorphic registration for the simulation of intermediate images. If a single image is available, we first generate with AI age-resolved image templates to extract aging trajectories for healthy and disease subjects. Such trajectories are then moved to the subject space with parallel transport.

Results: The methods perform better than AI generative models. The quality of the images was assessed by a radiologist.

Conclusions: Diffeomorphic registration is appropriate for aging simulation. Possible applications include filling gaps in longitudinal data, simulation of clinical scenarios and disentanglement of aging and disease.

ADVANCING NEURODEGENERATION RESEARCH THROUGH PROTEOMICS

Anne-Li Lind
Olink – Gold Sponsor

The aim of this talk is to provide an overview of how proteomics is utilized to identify biomarkers and develop therapies for Alzheimer's disease. We will explore pivotal studies that uncover biomarker candidates for the detection and differential diagnosis of Alzheimer's disease, to track disease progression, and to evaluate the mechanisms of action of new treatments. Key findings from each study will be highlighted to demonstrate that proteomics is a powerful tool for advancing our understanding of Alzheimer's disease pathophysiology and informing treatment strategies.

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Olink is committed to accelerating proteomics together with the scientific community and providing deeper understanding of real-time biology in human health and disease. This is enabled through the ground-breaking Proximity Extension Assay (PEA) technology, a uniquely scalable proteomics solution that empowers seamless transition from large-scale biomarker discovery to the development and validation of protein signatures with clinical utility.

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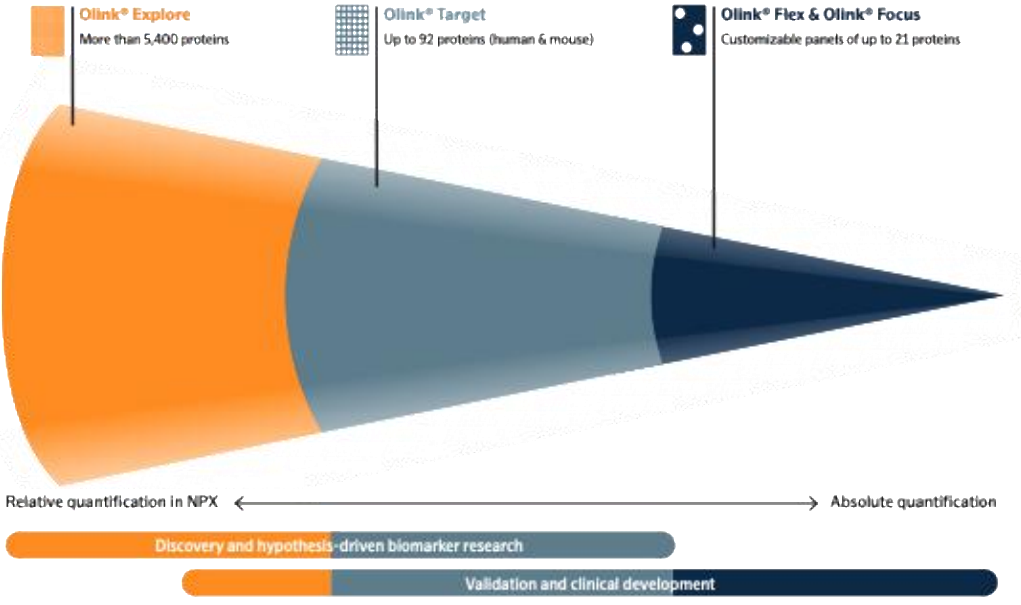
Olink Insight, an open-source proteomics knowledge hub, further enhances the smooth transition of PEA across the biomarker discovery-to-implementation process, offering researchers a set of bioinformatic and biostatistical tools for streamlined study planning and data analysis, as well as various layers of curated data for accelerated insights into proteomics data.



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ASTROCYTES: A POTENTIAL TARGET TO REDUCE CELL-TO-CELL SPREADING IN ALZHEIMER'S DISEASE

Anna Erlandsson
Uppsala University

Glial cells, including astrocytes are closely associated with Alzheimer's disease pathogenesis, but their role in disease progression is still unclear. Our results demonstrate that astrocytes engulf and process, but fail to fully degrade amyloid-beta and tau aggregates. The protein aggregates are instead stored as large deposits in the astrocytes, which induce severe cellular stress. Importantly, we have shown that stressed astrocytes spread pathogenic protein aggregates to nearby cells via different routes, including tunneling nanotubes and extracellular vesicles. Our recent data demonstrate that astrocytes with tau deposits secrete tau species with exceptional seeding capacity that induce pathology in healthy neurons. During my presentation, I will provide an overview of our results, both published and unpublished, on glial-mediated spreading mechanisms that may contribute to Alzheimer's disease progression.

APOE AND SYSTEMIC PROCESSES

Henrietta Nielsen
Stockholm University

Aims: APOE4 is the strongest genetic risk factor for sporadic Alzheimer's disease (AD). We aim to elucidate the biological underpinnings of the increased risk in APOE4-carriers in the peripheral compartment.

Methods: We use lipidomics, proteomics, ELISA, Western blot and in vitro culture systems and employ primary human hepatocytes, human-derived cell lines, patient plasma and CSF, APOE-TR and FRGN humanized-liver mice to study various aspects of the peripheral compartment and how a peripheral APOE4 phenotype may dictate brain processes and function.

Results: Plasma apolipoprotein E (apoE) levels are reduced in APOE4-carriers in Scandinavian cohorts but initial studies of African-Americans do not support this outcome. APOE-TR mice and FRGN humanized-liver mice w/o APOE4 exhibit similar plasma apoE levels, reduced in APOE4 mice, as humans and appear to be linked to behavior and cognition irrespective of APOE genotype. The human hepatic lipidome and proteome appear to differ in an APOE4-dependent manner – the relevance is still to be elucidated.

Conclusions: Peripheral APOE4-related processes resulting in an altered hepatic lipidome and proteome with implications to the plasma lipid and protein profiles may have important effects on the brain and its functions and mediate some of the APOE4-promoted risk of neurodegenerative disease.

THE RETINA-BRAIN NEXUS: IMPLICATIONS IN ALZHEIMER'S DISEASE

Malin Wennström
Lund University

Aims: Immunostaining studies suggest that hyperphosphorylated tau (p-tau) accumulates in the retina of patients with Alzheimer's disease (AD), potentially explaining visual impairment and offering new diagnostic opportunities. This study aimed to identify specific p-tau phosphorylation sites in the retina and determine which of these correspond to tauopathy in the brain.

Methods: Mass spectrometry was used to identify the retinal and brain p-tau species in matched retinal and hippocampal homogenates from cases with high or low amyloid-beta (Aβ) load.

Results: P-tau was detected at sites 181, 199/202, 231, 396 + 403/404, and 403/404 in the retina. Several of the p-tau species were elevated in cases with high Aβ load, and specifically p-tau 231 and 396+403/404 correlated with neurofibrillary tangle burden and the corresponding p-tau speices in the hippocampus.

Conclusions: These findings link retinal and brain tau pathology, suggesting retinal tau—particularly p-tau231 and p-tau396+403/404—as potential biomarkers for Alzheimer's disease (AD) and contributors to the visual impairment associated with AD.

DIAGNOSTIC POTENTIAL OF NEUROINFLAMMATORY MARKERS IN CSF AND PLASMA

Petronella Kettunen
University of Gothenburg

We investigated inflammatory markers in 152 controls (HC) and patients with Alzheimer's disease (AD) subcortical small-vessel disease (SSVD) and mixed dementia (MIX) and correlations with white matter hyperintensities (WMHs), blood-brain barrier (BBB) dysfunction and cognition.

We analyzed 17 inflammatory cytokines and matrix metalloproteinases (MMPs) in CSF and plasma from the Gothenburg MCI study.

Proinflammatory markers were elevated in CSF in AD and MIX, while antiinflammatory markers were reduced in AD and SSVD compared to HC. Many CSF MMPs were elevated in AD compared to HC. Several CSF markers correlated with WMHs, BBB damage and cognitive functions. While fewer associations were found between plasma markers and patient variables, ROC analyses identified markers in both CSF and plasma with moderate capacity of separating patient groups.

Our findings indicate that neuroinflammatory markers may have a good potential to help diagnose patients in the future.

HOW MUCH SHOULD WE BE PREPARED TO PAY FOR DISEASE-MODIFYING TREATMENTS IN ALZHEIMER'S DISEASE?

Linus Jönsson
Karolinska Institutet

Aims: The aim of our study was to estimate the value-based price for lecanemab, the first amyloid-targeting disease modifying therapy (DMT) for Alzheimer's disease (AD).

Methods: We developed a Markov model with states defined by disease severity and care setting. The model was populated by integrated clinical and economic data from the SveDem registry linked to other sources. We included patients with biomarker-confirmed AD, and fitted flexible parametric survival models for transitions between model states. Progression from the MCI state was estimated based on data from the NACC study. Costs and quality-adjusted life-years (QALYs) gained over a 10-year time horizon was estimated for standard of care (SOC) without DMT, and for patients receiving DMT resulting in a 31% reduction in disease progression as evidenced in registrational clinical trials of lecanemab.

Results: Treatment with DMT over 3 years was estimated to resulted in 0.16 QALYs gained and a net costs increase of 87,200 SEK due to administration and monitoring, before considering the cost of drug. The value-based price was estimated to 32,300 SEK per year of treatment.

Conclusions: The future price of AD DMT is European countries is unknown, however treatment is unlikely to be cost-effective in Sweden at the levels of current list prices in the United States. Our results are in line with previous estimates of the cost-effectiveness of AD DMT.

SWEDISH REGISTRY FOR COGNITIVE/DEMENTIA DISORDERS, SVEDEM – DEVELOPMENT OF DRUG MODULE FOR REAL LIFE DATA

Dorota Religa
Karolinska Institutet

Aims: The Swedish registry for cognitive/dementia disorders, SveDem, is a national quality registry since 2007. The aim of the project is to use unique properties of SveDem to prepare Drug module.

Methods: First step - add Mild Cognitive Impairment (MCI) group. Secondly discussion with other quality registry occurred. Lastly the relevant list of variables needs to include medical and laboratory parameter.

Results: All 58 cognitive clinics are connected to SveDem. Totally 136 974 person are registered in SveDem. Long-term data of 5-10 years in the large population of people with AD is already available. The population of MCI is now included. Drug module was built based on chosen variables and can be expanded when new drugs are registered and come to the clinics.

Conclusions: SveDem has already built the possibility for follow-ups in Drug module and can start when needed. Follow-up of new medications will not replace the basic and follow-up registration that is already available in SveDem.

ENHANCED ENDOGENOUS DEGRADATION OF AMYLOID BETA AS A TREATMENT STRATEGY FOR ALZHEIMER'S DISEASE: UTILIZING GENE AND PROTEIN THERAPY

Greta Hultqvist
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In sporadic cases of Alzheimer's disease (AD), the degradation and clearance of amyloid beta (Aβ) are impaired, leading to its accumulation and aggregation. Neprilysin, the primary enzyme responsible for Aβ degradation, is regulated by the peptide hormone somatostatin. Both neprilysin and somatostatin are significantly downregulated in AD. We have explored the use of somatostatin as a therapeutic approach to enhance neprilysin levels in the brain, thereby promoting Aβ degradation. Our research employs both protein-based therapies, utilizing transporters designed in our laboratory for high and uniform brain delivery, and AAV-based gene therapy, optimized for CNS targeting and neuronal expression. In transgenic mouse models of AD, these approaches have demonstrated significant reductions in brain Aβ levels, suggesting a novel therapeutic strategy for AD.

BRAIN DELIVERY IN ALZHEIMER'S DISEASE

Per-Ola Freskgård
Bioarctic – Gold Sponsor

The development of large molecules with therapeutic targets within the brain faces a major challenge; the blood-brain barrier (BBB). This severely limits the ability of biotherapeutics to access the brain, and preclinical studies in mice and non-human primates have shown that the brain concentrations of therapeutic antibodies are much less than 0.1% of their blood concentrations. BioArctic have developed a proprietary Brain Transporter (BT) platform to overcome this challenge in neuroscience drug discovery. BT technology facilitates transport across the BBB using receptor-mediated transcytosis, whereby large circulating biotherapeutics bind to an endogenous receptor on the endothelial cells that form the BBB and are then actively transported into the brain. This leads to an increased, faster and broader brain distribution, which will improve the likelihood of achieving clinical benefit in patients with neurological disorders.


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We are immensely thankful for your hard work, and we hope this Meeting will reflect all your enthusiasm and passion for science and collaboration.

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