

Review Article



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Executive Summary of 2023 International Conference of the Korean Dementia Association (IC-KDA 2023): A Report From the Academic Committee of the Korean Dementia Association

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ABSTRACT

The Korean Dementia Association (KDA) has been organizing biennial international academic conferences since 2019, with the International Conference of the KDA (IC-KDA) 2023 held in Busan under the theme ‘Beyond Boundaries: Advancing Global Dementia Solutions.’ The conference comprised 6 scientific sessions, 3 plenary lectures, and 4 luncheon symposiums, drawing 804 participants from 35 countries. Notably, a Korea–Taiwan Joint Symposium addressed insights into Alzheimer’s disease (AD). Plenary lectures by renowned scholars explored topics such as microbiome-related AD pathogenesis, social cognition in neurodegenerative diseases, and genetic frontotemporal dementia (FTD). On the first day, specific presentations covered subjects like the gut–brain axis and neuroinflammation in dementia, blood-based biomarkers in AD, and updates in AD therapeutics. The second day’s presentations addressed recent issues in clinical

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Conflict of Interest

The authors have no financial conflicts of interest.

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neuropsychology, FTD cohort studies, and the pathogenesis of non-AD dementia. The Academic Committee of the KDA compiles lecture summaries to provide comprehensive understanding of the advanced dementia knowledge presented at IC-KDA 2023.

Keywords: Alzheimer's Disease; Microbiome; Biomarkers; Frontotemporal Dementia; Social Cognition

INTRODUCTION

The Korean Dementia Association (KDA) has been organizing biennial international academic conferences since 2019, with the third conference, the International Conference of the KDA (IC-KDA) 2023, being held at the BEXCO Convention Center in Busan, Korea, on November 24–25, 2023. Under the theme ‘Beyond Boundaries: Advancing Global Dementia Solutions,’ IC-KDA 2023 attracted attention from researchers and scholars for its focus on the current state and future research directions in biomarkers and drug development for dementia.

The conference encompassed 6 scientific sessions, 3 plenary lectures, and 4 luncheon symposiums (**Table 1**). Scientific sessions covered the following 6 topics: 1) Gut-Brain Axis and Neuroinflammation in Dementia, 2) Blood-based Biomarkers for Alzheimer's Disease (AD) in Clinical Practice, 3) Update of the Treatment of Dementia, 4) Recent Issues in Clinical Neuropsychology, 5) Update of Frontotemporal Dementia (FTD) (including FTD cohort study), and 6) the Pathogenesis of Non-AD Dementia. Each session featured 3 sub-topics. The 3 plenary lectures were delivered by esteemed scholars focusing on the pathogenesis of AD related to the microbiome (Professor Keqiang Ye, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, China), social cognition in neurodegenerative diseases (Katherine P. Rankin, University of California San Francisco, USA), and genetic FTD—the FTD Prevention Initiative (Professor Jonathan Rohrer, University College London, UK).

With a total of 804 participants from 35 countries and 204 exhibited posters, IC-KDA 2023 solidified its position as a leading international academic conference in the field of dementia in Korea. In addition, this year, the first Korea–Taiwan Joint Symposium addressed insights into imaging and fluid biomarkers, as well as pharmacological and non-pharmacological interventions for AD (**Table 2**).

In parallel with the academic program, the opening ceremony featured a traditional Korean cultural performance, which attracted significant interest from domestic and international participants. In the evening, a special event at Nurimaru APEC House in Haeundae provided an opportunity for invited speakers and KDA board members to together enjoy traditional Korean music and performances, fostering academic exchange, scholarly achievements, and social connections during the conference.

This article aims to provide a comprehensive review of advanced knowledge in dementia by summarizing key events presented during IC-KDA 2023.

Executive Summary of IC-KDA 2023

Table 1. The program of IC-KDA 2023

	1st day		2nd day	
9:00–10:30	[Session 1] Gut-Brain Axis and Neuroinflammation in Dementia Modern Koch's Postulates Applied to a Putative Causative Link Between Oral Dysbiotic Microbiota and the Pathogenesis of Alzheimer's Disease Fecal Microbiota Transplantation in Patients with Dementia ApoE Isoform- and Microbiota-Dependent Progression of Neurodegeneration in a Mouse Model of Tauopathy	<i>Chairperson:</i> Won-Seok Choi, Hoo Won Kim, Jan Potempa Seong Hye Choi Dong-Oh Seo	[Session 4] Recent Issues in Clinical Neuropsychology Remote Memory Assessments in the Early Stage of AD Predictive Utility of Machine Learning Approach with Neuropsychological Test in AD Spectrum Digital Neuropsychological Assessments for Frontotemporal Dementia	<i>Chairperson:</i> So Young Moon, Ju Hee Chin, David Berron Seyul Kwak Adam Staffaroni
10:50–12:10	Plenary Session I Pathogenesis and Early Diagnosis of Neurodegenerative Disease Plenary Session II Update on Blood Biomarkers for Alzheimer's Disease	<i>Chairperson:</i> Kunho Lee, Keqiang Ye Cancelled Kaj Blennow	Plenary Session III Social Cognition in Neurodegenerative Diseases Plenary Session IV Creating a Worldwide Platform Trial for Genetic Frontotemporal Dementia – The FTD Prevention Initiative	<i>Chairperson:</i> Dong Won Yang, Katherine Rankin <i>Chairperson:</i> Jee Hyang Jeong, Jonathan Rohrer
12:10–13:00	Luncheon Symposium	<i>Chairperson:</i> Jae-Hong Lee	Luncheon Symposium	<i>Chairperson:</i> Yong Soo Shim
13:00–14:00	Poster Session 1		Poster Session 2	
14:00–15:30	[Session 2] Blood-based Biomarkers for AD in Clinical Practice Implementation of High-performance Blood Biomarkers in Routine Clinical Care for the Evaluation of Individuals with Cognitive Impairment Plasma Biomarkers of Neurodegenerative Diseases toward Clinical Practice (MagQu) AlzOn: The Real-World Example of Blood-based Biomarker Test Utility in Clinical Practice	<i>Chairperson:</i> SangYun Kim, Seong-Ho Koh, Joel Braunstein Charles Yang Sungmin Kang	[Session 5] Update of FTD (Including FTD Cohort Study) North American FTD Registry (ALLFTD) Korean FTD Registry (LEAF-FTD) Chinese FTD Registry	<i>Chairperson:</i> Jonathan Rohrer, Eun-Joo Kim, Howard Rosen Eun-Joo Kim Qin Chen
15:50–17:20	[Session 3] Update of the Treatment of Dementia Advances in AD Experimental Therapeutics Gene Therapy Neuromodulation for Gliopathy in Alzheimer's Disease	<i>Chairperson:</i> Kee Hyung Park, Sang Won Seo, Alireza Atri Jae Young Lee Tae Kim	[Session 6] Pathogenesis of Non-AD Dementia Molecular Mechanism of Neuroinflammation in Non-AD Pathology Molecular Mechanism of α -Synuclein in Non-AD Dementia Identifying the Early Events in ALS Pathogenesis	<i>Chairperson:</i> Yong Jeong, Yun Kyung Kim, Hoon Ryu Seung-jae Lee Jeehye Park

IC-KDA: International Conference of the Korean Dementia Association, AD: Alzheimer's disease, FTD: frontotemporal dementia, ALS: amyotrophic lateral sclerosis.

Table 2. Korea-Taiwan Joint Symposium

	2nd day	
08:30–09:30	Korea-Taiwan Joint Symposium-1 Can Fluid Biomarker Testings Change the Diagnosis and Management of Dementia? Alzheimer's Disease Biomarkers: Towards a New Era in the Diagnosis and Treatment of AD Based on Blood Biomarkers What is the Role of Brain Imaging in the Diagnosis of Dementia?	<i>Chairperson:</i> SangYun Kim, Jong-Ling Fuh, Yung-Shuan Lin, Seong Ho Koh Jung-Lung Hsu
09:30–10:30	Korea-Taiwan Joint Symposium 2 What is the Appropriate Use of Amyloid Imaging Under the Situations that DMT Drugs Have Been Developed? How Can I Choose the Right Pharmacological Therapy for Alzheimer's Disease?	<i>Chairperson:</i> Dong Won Yang, Chaur-Jong Hu, Kee Hyung Park Li-Kai Huang
10:30–10:50	Korea-Taiwan MOU	Dong Won Yang, Young Chul Yoon, Cheng-Sheng Chen, Ming-Chyi Pai

AD: Alzheimer's disease, DMT: disease-modifying therapy.

SESSION 1. GUT-BRAIN AXIS AND NEUROINFLAMMATION IN DEMENTIA

In this session, three experts presented the complexities of bacterial involvement, microbiota transplantation, and neurodegeneration progression in AD.

Modern Koch's Postulates Applied to Bacterial Pathogenesis of Alzheimer's Disease (Jan Potempa, Jagiellonian University, University of Louisville School of Dentistry, Poland/USA)

Professor Potempa provided an overview of the pathogenesis of AD with respect to the microbiome. In the 19th century, Robert Koch established criteria for evaluating the causation of infectious diseases, which have been updated with modern methods.¹ Applying these to *Porphyromonas gingivalis*, a bacterium linked to AD, revealed its potential role in AD pathogenesis. DNA and gingipain antigens from *P. gingivalis* were identified in the brains of AD patients, correlating with tau and ubiquitin pathology. Gingipains were found in age-matched controls, but at lower levels. Oral infection of mice with wild-type *P. gingivalis* led to brain colonization and increased A β 1–42 plaques, with gingipains contributing to neurotoxicity.² Targeting gingipains with inhibitors in a murine model reduced bacterial load, blocked A β 1–42 production, and alleviated neuroinflammation, suggesting a causal link between chronic periodontitis and AD. The findings propose gingipain inhibitors as potential treatments for *P. gingivalis*-associated neurodegeneration in AD.

Fecal Microbiota Transplantation in Patients with Dementia (Seong Hye Choi, Inha University College of Medicine, Republic of Korea)

In her presentation, Professor Choi presented the clinical effects of fecal microbiota transplantation in patients with dementia. Fecal microbiota transplantation (FMT) for *Clostridioides difficile* infection (CDI) has shown cognitive improvements, suggesting a link between the gut microbiome and brain function.³ In a study with ten dementia patients and severe CDI who underwent FMT, cognitive function significantly improved, compared to a control group receiving antibiotics. Evaluations using the Mini-Mental State Examination (MMSE) and Clinical Dementia Rating scale–Sum of Boxes (CDR–SB) demonstrated notable enhancements in the FMT group. Analysis of fecal samples revealed changes in gut microbiota composition, including the enrichment of *Proteobacteria* and *Bacteroidetes*. Metabolic pathways related to alanine, aspartate, and glutamate also increased after FMT. These findings indicate the potential benefits of FMT in delaying cognitive decline in dementia patients, highlighting the significant interaction between the gut microbiome and cognitive function.

ApoE Isoform- and Microbiota-Dependent Progression of Neurodegeneration in a Mouse Model of Tauopathy (Dong-oh Seo, Washington University in St. Louis, USA)

Dr. Seo elucidated the connection between microbiota, neuroinflammation, and tau-mediated neurodegeneration, a key feature of AD. Notably, apolipoprotein E (ApoE)-mediated neuroinflammation plays a role in tau-mediated neurodegeneration,⁴ a hallmark of AD progression. While there is growing evidence of the gut microbiota influencing neuroinflammation in an ApoE genotype-dependent manner, a definitive causal link to tau-mediated neurodegeneration has been lacking. Dr. Seo addressed this gap by presenting experimental results involving tauopathy expressing human ApoE isoforms raised under germ-free conditions, or subjected to gut microbiota perturbation with antibiotics. Both manipulations demonstrated a sex- and ApoE isoform-dependent reduction in gliosis,

tau pathology, and neurodegeneration.⁵ These findings uncover mechanistic insights and translational implications for the intricate relationships between microbiota, neuroinflammation, and tau-mediated neurodegeneration.

PLENARY SESSION 1: PATHOGENESIS AND EARLY DIAGNOSIS OF NEURODEGENERATIVE DISEASE (Keqiang Ye, Shenzhen Institute of Advanced Technology and Chinese Academy of Sciences, China)

The research by Keqiang Ye on asparagine endopeptidase (AEP) has unveiled crucial insights into its role in cancer progression and neurodegenerative diseases, including AD and Parkinson's disease (PD). In this plenary lecture, Professor Ye highlighted the role of C/EBP β /AEP as a transcription factor activated by chronic inflammation within the scope of neurodegenerative diseases.⁶ This pathway hastens the advancement of AD, while also impacting longevity. The overexpression of C/EBP β in the brain, simulating aging, reduces the lifespan in mouse, and correlates with diminished cognitive abilities and heightened neuro-excitation. In human, this gene's expression increases with age, and reaches its peak in those aged 60 to 84. Notably, the expression levels of AEP genes in nerve cells correlate with lifespan—individuals who live longer generally exhibit lower levels of these genes.⁷ His work further delves into the regulatory functions of AEP in aging, and its pathological role in the cleavage of amyloid precursor protein, tau, or α -synuclein. This process results in amyloidogenic aggregation in neurodegenerative mouse models. Elimination of AEP in these models has been shown to lessen the pathologies of AD and PD, suggesting its usefulness in early diagnosis, and highlighting its potential as a novel target for treating and diagnosing neurodegenerative diseases.

Additionally, Dr. Ye presented the innovative Single Molecule Array (SIMOA) technique for detecting serum biomarkers, which opens new possibilities for early disease detection and future therapeutic strategies. The advanced SIMOA method for measuring serum biomarkers holds promise for early identification, thereby facilitating the development of future treatments.

PLENARY SESSION 2: UPDATE ON PLASMA BIOMARKERS IN ALZHEIMER'S DISEASE (Kaj Blennow, University of Gothenburg, Sweden)

Plenary Session 2 was canceled, owing to health issues affecting the scheduled speaker.

SESSION 2: BLOOD-BASED BIOMARKERS FOR AD IN CLINICAL PRACTICE

The development of disease-modifying therapies (DMTs) for AD emphasizes the need for accurate and accessible diagnostic tools. During this session, three speakers provided a comprehensive exploration of the latest advancements in blood-based biomarkers for AD, and their practical application in routine clinical care for patients with cognitive impairment.

Implementation of High-Performance Blood Biomarkers in Routine Clinical Care for the Evaluation of Individuals with Cognitive Impairment (Joel Braunstein, C2N, USA)

The presentation by Dr. Braunstein was focused on blood biomarkers in individuals with cognitive impairment with AD. The PrecivityAD2™ blood test by C2N Diagnostics addresses this need, offering an analytically and clinically validated multianalyte assay with algorithmic assessment (MAAA). This high-throughput mass spectrometry-based test quantifies key AD biomarkers, including A β 42/40 ratio and p-tau217/np-tau217 ratio, aiding in early AD diagnosis and identifying amyloid pathology. The discussion outlined the rationale behind the PrecivityAD2™ test, designed as a diagnostic aid for AD, and its predecessor, the PrecivityAD® blood test. These tests showed the significant reliability of measuring brain amyloid plaques in individuals aged 55 and older with cognitive impairment.^{8,9} His presentation also addressed the integration of blood biomarkers into routine clinical care, emphasizing diagnostic accuracy, clinical usefulness, and economic considerations in shaping the future role of blood biomarkers in cognitive care and management.

Plasma Biomarkers of Neurodegenerative Diseases toward Clinical Practice (MagQu) (Charles Shieh-Yueh Yang, MagQu, Taiwan)

Professor Yang presented plasma biomarker assay for AD using immunomagnetic reduction (IMR), which is commercialized by MagQu. Clinical trials evaluating plasma amyloid β peptides and total tau proteins using the IMR assay have been successfully completed. The international multi-centered trials validated the IMR plasma biomarker assay against clinical diagnoses, brain atrophy, amyloid positron emission tomography (PET), and amyloid neuropathology at autopsy.^{10,11} The results demonstrate that plasma A β 1–42/A β 1–40 or A β 1–42 \times T-Tau levels align closely with clinical diagnoses, distinguishing normal controls from patients with amnesic mild cognitive impairment (MCI) or AD. Plasma T-Tau levels show a negatively moderated correlation with brain volumes, and that A β 1–42/A β 1–40 levels moderately correlate with amyloid PET standardized uptake values ratios (SUVRs). The IMR assay predicts amyloid neuropathology, and provides insights into the progression of cognitive decline. Since 2020, the IMR assay for AD biomarkers in plasma has been approved for clinical use in Taiwan, aiding in assistant diagnoses and treatment monitoring. The IMR assay is entering *in vitro* diagnostic markets in Taiwan, Korea, the Middle East, China, and the United States.

AlzOn: The Real-World Example of Blood-based Biomarker Test Utility in Clinical Practice (Sungmin Kang, PeopleBio, Republic of Korea)

The presentation of Sungmin Kang introduced blood-based diagnosis of protein misfolding diseases based on multimer detection system (MDS) and the first commercial blood biomarker test for AD in Korea, which received product approval from the Ministry of Food and Drug Safety (MFDS) in 2018, and successfully passed on new Health Technology Assessment (nHTA) in 2021. AlzOn, an enzyme-linked immunosorbent assay based on MDS, serves as a blood-based biomarker test for AD, detecting and measuring plasma β -amyloid (A β) oligomerization—the core and earliest pathological change in AD. Approved for aiding AD diagnosis, AlzOn boasts over 85% accuracy in detecting ongoing AD pathology, and has been validated in various clinical studies.^{12,13} Widely accessible, it is employed in over 500 hospitals, including 35 tertiary hospitals and major medical checkup centers in Korea. In primary care, AlzOn is a first-line blood test, complementing neuropsychological tests for cognition assessment. In secondary and tertiary hospitals, it aids in enriching AD diagnosis. Due to the practical constraints of costly and invasive ‘golden-standard’ biomarkers, AlzOn

offers a simple, inexpensive option for routine clinical use and differential diagnosis in dementia cases. Its ability to reflect peripheral amyloidosis enhances its clinical utility, making it valuable for proactive AD risk factor testing in medical check-up centers.

SESSION 3. UPDATE OF THE TREATMENT OF DEMENTIA

In this session, three speakers presented cutting-edge perspectives on treatments for dementia patients, which included recent advancements in AD experimental therapeutics, emphasizing the drug development pipeline, and the practical application of monoclonal antibodies targeting amyloid plaques, the potential of gene therapy for neurodegenerative diseases, highlighting opportunities and challenges in its development and innovative neuromodulation for gliopathy as a therapeutic potential in AD.

Advances in AD Experimental Therapeutics (Alireza Atri, Banner Sun Health Research Institute [AZ] & Harvard Medical School [MA], USA)

Professor Atri offered a comprehensive overview of the latest advancements in experimental therapeutics for AD. Currently, most treatments for AD primarily offer symptomatic relief, yielding initial benefits; however, patients will still experience a progressive decline.¹⁴ A disease-modifying treatment would slow the disease progression of the patient.¹⁵ It will cover the current AD drug development pipeline, emphasizing the most recent data on efficacy and safety.¹⁶ The focus will extend to crucial considerations, such as patient selection, risk assessment, and the detection, monitoring, and management of amyloid-related imaging abnormalities (ARIA).¹⁷ He pointed out in particular the process from clinical trials to the practical implementation of monoclonal antibodies targeting amyloid plaques, such as aducanumab, lecanemab, and donanemab, providing valuable insights for both researchers and practitioners in the field. He emphasized that we are now moving beyond the beginning of AD therapeutics and anti-amyloid treatment.

Gene Therapy for Neurodegenerative Diseases (Jae young Lee, ToolGen, Republic of Korea)

Gene therapy has the capacity to target both the symptoms and the fundamental pathologies of neurodegenerative diseases. Introduction of viral vectors into the central nervous system enables the delivery of genes that can either restore lost functions, or encode neurological growth factors and metabolic enzymes. Concurrently, the potential of genome editing techniques like CRISPR offers significant promise in directly addressing the mutations responsible for these pathologies.

In this presentation, Professor Lee reviewed recent developments in gene therapy for neurodegenerative diseases, delving into its potential as a crucial therapeutic modality.^{18,19}

The discussion encompassed both opportunities and challenges associated with gene therapy in the context of neurological diseases, emphasizing the need to address hurdles in its development.

Neuromodulation for Gliopathy in Alzheimer's Disease (Tae Kim, GIST, Republic of Korea)

Professor Kim's presentation focused on neuromodulation for gliopathy in AD. Recognizing the increasing evidence of glial cells contribution in AD progression, novel therapeutic

strategies, specifically non-invasive neuromodulation techniques, have emerged as promising interventions to address glial pathophysiology. Professor Kim presented groundbreaking research concentrating on astrocytic GABA in AD, unveiling the presence of astrocytic GABA in sleep-promoting areas of AD models. Acoustic stimulation at 40 Hz demonstrated a reduction in astrocytic GABA levels, correlating with observed sleep disturbances. Additionally, the research indicated that neuronal activity induces astrocytic volume expansion, leading to a secondary increase in calcium influx, potentially offering a protective effect on brain pathology.^{20,21} These findings suggest that the benefits of gamma entrainment may originate from cascading secondary responses initiated by astrocytic changes. Overall, the research implicates the potential of 40 Hz acoustic neuromodulation in inducing glial alterations, providing a promising therapeutic pathway to ameliorate AD pathology.

SESSION 4. RECENT ISSUES IN CLINICAL NEUROPSYCHOLOGY

Leveraging mobile devices like smartphones and tablets presents opportunities to enhance case identification, enable remote assessments, and moreover, allow unsupervised follow-up in both clinical and research contexts. Also, machine learning approach provides a new approach to utilizing neuropsychological test performances. In the neuropsychology session, three speakers presented recent issues related to digital cognitive assessment and the utilization of a machine learning approach in patients with dementia.

Unsupervised Remote Memory Assessments in the Early Stages of Alzheimer's Disease (David Berron, German Center for Neurodegenerative Diseases [DZNE], Germany)

Dr. Berron presented remote assessment for the early stage of AD. He explored the mobile application of a set of digital remote and unsupervised memory assessments to detect MCI in AD. He demonstrated that longitudinal digital remote memory assessments conducted over a year could capture changes in memory among individuals with MCI.²² Additionally, he showed that these cognitive changes corresponded to alterations observed in established in-clinic cognitive assessments.

Predictive Utility of Machine Learning Approach with Neuropsychological Test in AD Spectrum (Seyul Kwak, Pusan National University, Republic of Korea)

The presentation by Professor Kwak focused on how complex patterns of test performances could be harnessed for specific predictive purposes using machine learning. Based on the nonlinear modeling of a large-scale dataset, he demonstrated how multiple scores of detailed neuropsychological batteries (CERAD-K) can be utilized to predict the clinical outcomes of dementia in more than 2,600 older adults with varying cognitive statuses (no impairment, mild cognitive impairment, and dementia with AD). He presented the findings that linear models demonstrated superior performance with a relatively smaller sample size, whereas nonlinear models with low and high complexity exhibited improved accuracy with a larger dataset.²³ Notably, the nonlinear models showed a gradual increase in predictive accuracy, in particular when the sample size exceeded 500, emphasizing their effectiveness in exploiting complex patterns within the dataset. He suggested that nonlinear models, particularly with sufficient data, can predict levels of functional impairment, offering a valuable augmentation to the summary index of neuropsychological batteries, especially in estimating dementia-related functional status.

Digital Neuropsychological Assessments for Frontotemporal Dementia (Adam Staffaroni, University of California San Francisco, USA)

In the presentation, Professor Staffaroni introduced digital neuropsychological assessments for FTD, a neurodegenerative condition characterized by cognitive, behavioral, language, or motor impairments. These digital assessments aimed to quantify deficits within the domains affected by FTD, offering a valuable tool for both clinical care improvement and remote evaluations. He showed that the use of digital tools enhanced clinical practices, while also addressing recruitment barriers for observational research and FTD clinical trials.²⁴ The presentation highlighted various existing digital technologies for FTD assessment, encompassing tablet-based testing solutions, and smartphone applications.

PLENARY SESSION 3. SOCIAL COGNITION IN NEURODEGENERATIVE DISEASES (Katherine P. Rankin, University of California San Francisco, USA)

The neuropsychological evaluation of socioemotional cognition has received less attention in the field of dementia. However, patients with behavioral variant FTD (bvFTD), semantic variant primary progressive aphasia (svPPA), and right temporal lobe degeneration often exhibit deficits in socioemotional behavior. This highlights the need to expand our perspective beyond traditional cognitive domains to encompass their behavioral symptoms. Professor Rankin found the explanation in neural circuits in intrinsically connected networks. She showed how the salience network, semantic appraisal network, and default mode network are related to behavioral dysfunction in neurodegenerative diseases.²⁵ Moreover, Professor Rankin introduced neuropsychological tests to evaluate social cognition, such as the revised self-monitoring scale,²⁶ and social interaction vocabulary test.²⁷ Additionally, she discussed the importance of considering language and cultural factors when applying these assessments internationally.

PLENARY SESSION 4. CREATING A WORLDWIDE PLATFORM TRIAL FOR GENETIC FRONTOTEMPORAL DEMENTIA – THE FTD PREVENTION INITIATIVE (Jonathan Rohrer, University College London, UK)

Professor Rohrer introduced the Frontotemporal Dementia Prevention Initiative (FPI), a global endeavor targeting familial forms of FTD, integrating ongoing cohort studies worldwide.²⁸ Collaborators include ALLFTD (US),²⁹ GENFI (Europe and Canada), DINAD (Australia), FTDeNZ (New Zealand), ReDLat (South America), South-East Asia FTD Consortium, FTLD-J (Japan), and networks in India, China, and the LEAF-FTD study in Korea. The overall aim of FPI is to facilitate clinical trials of new therapies to prevent FTD, establishing uniform standards, an international FTD research participant database, and responsible data sharing. The FPI involves over 300 researchers and 3,000 participants worldwide. Key achievements included clinical rating scale development, validation of multimodal biomarkers for trials, and fluid biomarker validation,³⁰ notably plasma neurofilament light chain.^{31,32} Ongoing studies explored genomics and digital biomarkers,³³ culminating in a global platform trial for testing novel FTD therapies, initially focusing on

MAPT gene mutations. He emphasized future studies to refine outcome measures and extend trials across all FTD forms..

SESSION 5. UPDATE OF FTD (INCLUDING FTD COHORT STUDY)

As advancements in comprehending frontotemporal lobar degeneration (FTLD) pave the way for potential disease-modifying treatments, the establishment of a data registry for FTD patients becomes crucial to amplify clinical trial efficiency and extend opportunities for research participation. In this session, three speakers presented FTD cohort studies from different countries. These studies encompassed clinical trials, the utilization of clinical rating scales, and the validation of multimodal biomarkers, collectively contributing to the global effort to advance understanding of FTD, and facilitate the development of effective treatments.

North American FTD Registry (ALLFTD) (Howard Rosen, University of California San Francisco, USA)

Professor Rosen introduced the North American FTD registry (ALLFTD). The ARTFL-LEFFTDs Longitudinal Frontotemporal Lobar Degeneration (ALLFTD) consortium, established in 2014, has significantly advanced the development of such treatments for FTLD. With over 4,000 visits across 28 North American sites involving 2,500 participants, ALLFTD has highlighted the value of clinical rating scales, cognitive tests, MRI-based volumetrics, and Neurofilament Light Chain (NfL) as crucial markers for disease progression. Notable achievements include the creation of mutation-specific multimodal models, streamlining the efficiency of clinical trials. ALLFTD has also identified novel clinical and fluid-based measures potentially tracking disease evolution and individual vulnerability to neurodegeneration.^{31,34} Furthermore, the consortium has piloted mobile-phone-based applications,³³ aiming to enhance clinical trial efficiency and broaden research participation opportunities. This substantial progress signifies a crucial step toward developing effective treatments for this devastating disorder.

Korean FTD Registry (LEAF-FTD) (Eun Joo Kim, Pusan National University Hospital, Republic of Korea)

Professor Kim introduced the Longitudinal study of early onset dementia and family members (LEAF), a Korean cohort focusing on early onset dementia, initiated in April 2021, with participation from 31 centers across Korea. Within LEAF, LEAF-FTD constitutes one of the sub-studies alongside LEAF-AD and LEAF-Other early onset dementia. LEAF-FTD is specifically aimed at enrolling patients diagnosed with bvFTD, svPPA, non-fluent variant agrammatic primary progressive aphasia, FTD-MND (FTD with motor neuron disease), corticobasal syndrome, and progressive supranuclear palsy syndrome. Currently, LEAF-FTD has enrolled nearly 80 patients, encompassing both sporadic and familial cases of FTD. The cohort is collecting neuropsychological tests, various behavior scales, brain MRI, amyloid PET, blood samples, and whole exome sequencing data. These data will further enhance our understanding of the characteristics of FTD patients in Korea.

Familial FTD in China: Progress and Prospects (Qin Chen, West China Hospital of Sichuan University, China)

Professor Chen presented cross-sectional reports of Chinese FTD patients with gene mutations and updated status of the longitudinal study by the Chinese Familial

Frontotemporal Lobar Degeneration Consortium (CFFC). The CFFC was initiated in October 2022 with seven top teaching hospitals, and has expanded to over 20 centers. Comprehensive electronic searches to review the current status of Chinese FTD patients revealed genetic mutations in 5.13%–27.9% of Chinese FTD patients, predominantly *MAPT*, *GRN*, *TBKI*, *CHCHD10*, *C9orf72*, *VCP*, and *SQSTM1*. To date, the CFFC has enrolled 26 pedigrees with *MAPT* mutations, 11 with *GRN* mutations, and 9 with *C9orf72* repeat expansions. The CFFC has also endeavored to create a behavioral assessment scale for Chinese bvFTD patients, to develop voice-based digital biomarkers for various PPA types, and to participate in international phase III clinical trials for familial FTD. The high prevalence of *MAPT* mutations in Chinese FTD patients has suggested genetic heterogeneity, emphasizing the need for longitudinal studies with larger sample sizes to model biomarker trajectories for early diagnosis and intervention.

SESSION 6. PATHOGENESIS OF NON-AD DEMENTIA

This session focused on the pathogenesis of non-AD dementia. Professor Ryu discussed chronic traumatic encephalopathy (CTE), revealing AD-like signatures through multiomic analyses of post-mortem brain tissues. Professor Lee explored α -synuclein's role in non-AD dementia, proposing a model where A β -activated microglia induce compound proteinopathies. Finally, Professor Park investigated early ALS pathways using a MATR3 S85C KI mouse model, providing valuable insights into ALS prevention and intervention.

Molecular Neuropathology of Chronic Traumatic Encephalopathy (CTE) Reveals Alzheimer's Disease-like Signatures (Hoon Ryu, KIST, Republic of Korea)

Professor Ryu introduced CTE, which is a progressive neurodegenerative disorder linked to repetitive head injuries, featuring distinct neuropathological characteristics.³⁵ Although intraneuronal tau aggregates are key diagnostic features of CTE, the underlying tauopathy mechanism remains unclear. He presented the results of recent research employing multiomic analyses on post-mortem brain tissues from CTE patients, which revealed significant downregulation of gene signatures associated with MAP Kinase and calcium signaling pathways. The altered expression of protein phosphatases (PP) suggests shared pathological mechanisms with AD. Experimental validation using cell lines and animal models has confirmed a direct link between reduced PPP3CA/PP2B phosphatase activity and an increase in phosphorylated tau. This finding suggests that PP-dependent neurodegeneration might offer a potential biomarker and therapeutic target for modulating CTE-associated tauopathy.

Molecular Mechanism of α -Synuclein in Non-AD Dementia (Seung-Jae Lee, Seoul National University, Republic of Korea)

Professor Lee presented the interconnection of compound proteinopathies in dementia. His study showed that intracerebral transplantation of A β -activated microglia induced cognitive and motor deficits, along with compound proteinopathies like tauopathy and synucleinopathy, gliosis, and neuroinflammation. Notably, these features extended beyond the injection site, mirroring the progressive spread observed in neurodegenerative diseases.^{36,37} This protocol offered a model for neurodegenerative diseases, particularly the post-A β phase of AD. Unlike cross-seeding mechanisms requiring physical interactions between different aggregate proteins, he proposed a new mechanism that involves A β oligomers activating microglia, creating an inflammatory microenvironment that fosters the aggregation of downstream proteins like tau and α -synuclein. This alternative perspective

emphasized environmental changes promoting protein aggregation, providing valuable insights into the complex interplay of neuropathological features in AD.

Identifying the Early Events in ALS Pathogenesis (Jeehye Park, University of Toronto, Canada)

Professor Park elucidated early molecular pathways in amyotrophic lateral sclerosis (ALS), a condition marked by severe motor impairment, muscle atrophy, and paralysis, highlighting the pressing need to unravel the disease's early stages for effective interventions.^{38,39} Despite insights gained from ALS studies, understanding the initiation and development of the disease, particularly its mechanisms in the early phases, has remained elusive. Leveraging a MATR3 S85C knock-in (KI) mouse model that closely mirrors the human ALS genotype, Professor Park discerned early events in the disease, and explained how the ALS-linked mutation in MATR3 alters RNA splicing. This study, unraveling features of early-stage ALS development, holds promise for advancing prevention and intervention strategies, presenting a transformative approach to mitigate ALS's devastating impact.

KOREA-TAIWAN JOINT SYMPOSIUM

In the first session, Dr. Yung Shuan Lin from Taipei Veterans General Hospital, Taiwan, commenced proceedings by examining the potential impact of fluid biomarker testing on reshaping the landscape of dementia diagnosis and management. Subsequently, Professor Seong-Ho Koh from Hanyang University Guri Hospital, Republic of Korea, expounded upon the latest advancements in AD Biomarkers, with particular emphasis on the promising potential of blood biomarkers in heralding a new era in the diagnosis and treatment of AD. Dr. Jung Lung Hsu from New Taipei Municipal TuCheng Hospital, Taiwan, elucidated the pivotal role of brain imaging in dementia diagnosis. A subsequent session concentrated on diverse facets of AD diagnosis, treatment, and prevention strategies. Professor Kee Hyung Park from Gachon University College of Medicine, Republic of Korea, initiated discourse by examining the judicious utilization of amyloid imaging within the milieu of DMT development. Professor Park's presentation delved into the integral role of amyloid imaging in informing treatment decisions and optimizing patient outcomes. Following Professor Park's presentation, Dr. Li-Kai Huang from Taipei Medical University Shuang-Ho Hospital, Taiwan, delved into the intricacies surrounding the selection of pharmacological therapy for AD. Dr. Huang's discourse aimed to elucidate the multifaceted considerations inherent in tailoring the most appropriate pharmacological interventions to individual patients, encompassing factors such as disease stage, comorbidities, and treatment efficacy. Wrapping up the session, Professor Seong Hye Choi from Inha University College of Medicine, Republic of Korea, presented findings from the South Korean Study to Prevent Cognitive Impairment and Protect BRAIN Health through Lifestyle Intervention (SUPERBRAIN). Professor Choi's research emphasized the significance of lifestyle interventions in mitigating cognitive decline, providing invaluable insights into holistic approaches for managing AD.

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