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International ALZHEIMER'S DISEASE & DEMENTIA CONFERENCE

15-16 JUNE 2022

VIRTUAL EVENT

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BOOK OF ABSTRACTS

INTERNATIONAL ALZHEIMER'S DISEASE & DEMENTIA CONFERENCE

15-16 JUNE

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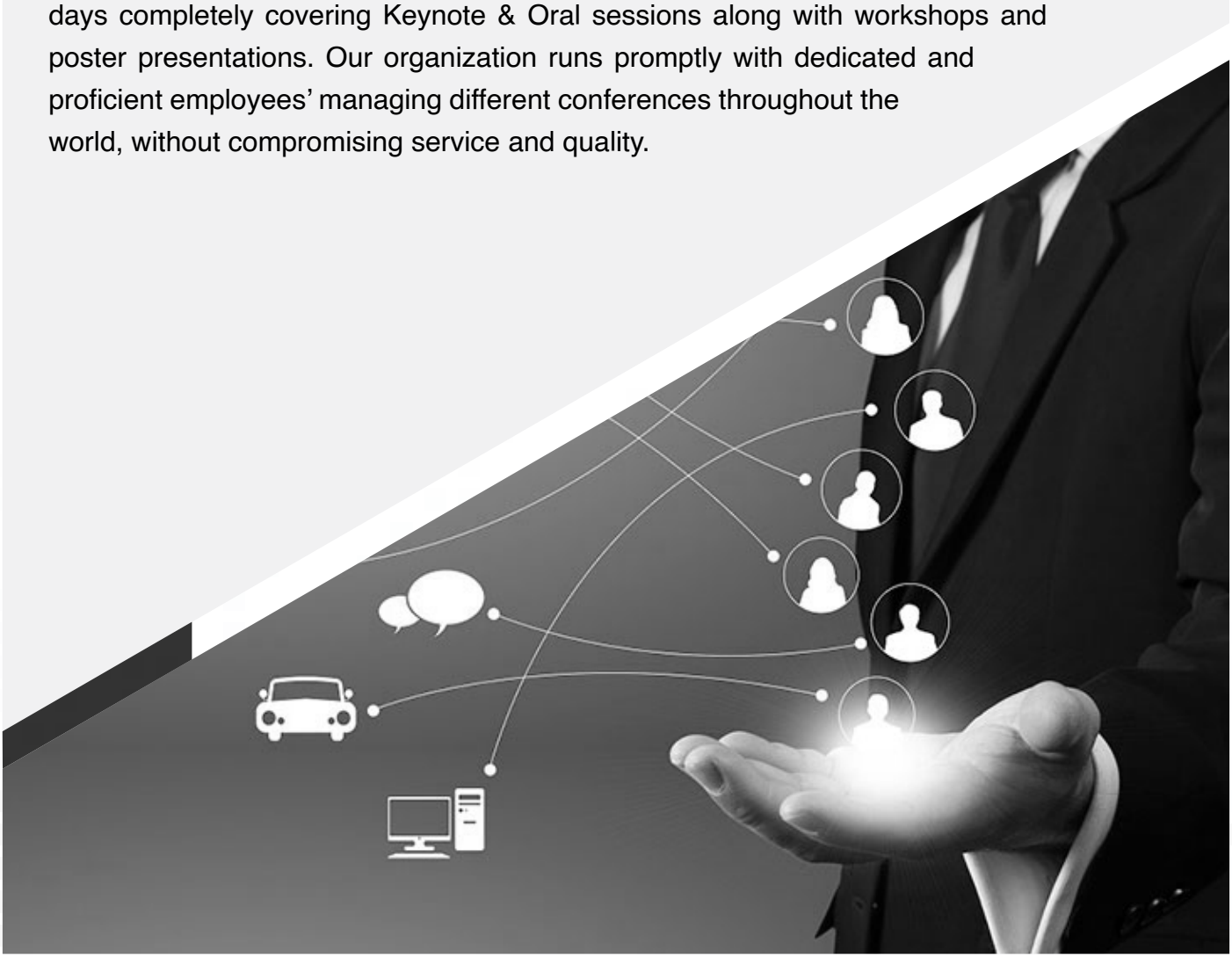
ABOUT MAGNUS GROUP

Magnus Group (MG) is initiated to meet a need and to pursue collective goals of the scientific community specifically focusing in the field of Sciences, Engineering and technology to endorse exchanging of the ideas & knowledge which facilitate the collaboration between the scientists, academicians and researchers of same field or interdisciplinary research. Magnus group is proficient in organizing conferences, meetings, seminars and workshops with the ingenious and peerless speakers throughout the world providing you and your organization with broad range of networking opportunities to globalize your research and create your own identity. Our conference and workshops can be well titled as 'ocean of knowledge' where you can sail your boat and pick the pearls, leading the way for innovative research and strategies empowering the strength by overwhelming the complications associated with in the respective fields.

Participation from 90 different countries and 1090 different Universities have contributed to the success of our conferences. Our first International Conference was organized on Oncology and Radiology (ICOR) in Dubai, UAE. Our conferences usually run for 2-3 days completely covering Keynote & Oral sessions along with workshops and poster presentations. Our organization runs promptly with dedicated and proficient employees' managing different conferences throughout the world, without compromising service and quality.



ABOUT DEMENTIA 2022

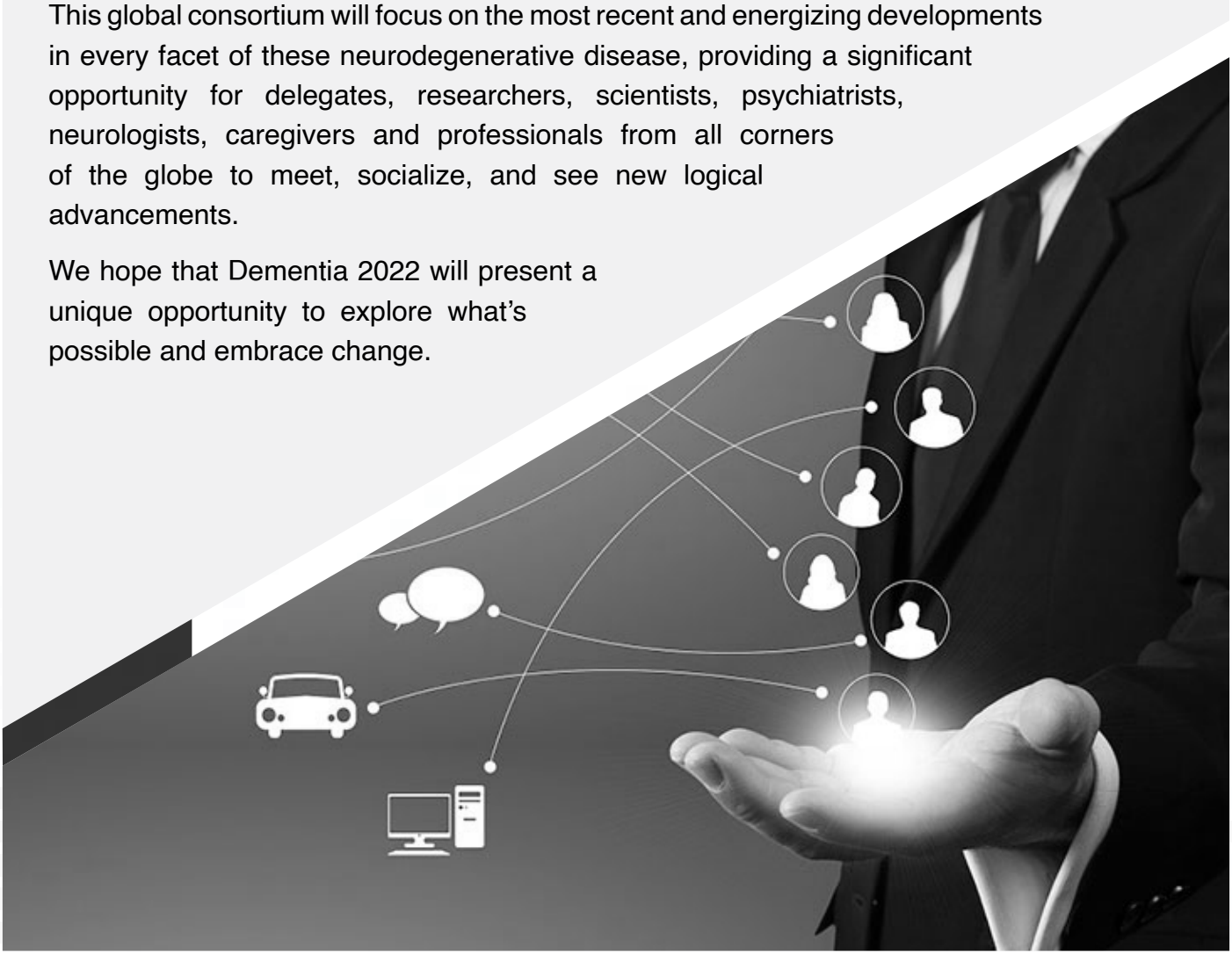
Magnus Group extends immense pleasure and honor to invite you to attend "**International Alzheimer's Disease & Dementia Conference**" (Dementia 2022) during **June 15-16, 2022** which is scheduled in Virtual Format.

This propitious conference is tailored around the theme "*Explicating Advancements to Combat the Silent Epidemic of Dementia and Alzheimer.*"

Dementia affected nearly 50 million people worldwide in 2020. The condition strikes so arbitrarily, and with such little warning that it has earned the moniker "Silent Epidemic." Dementia is expected to double every 20 years, reaching 75 million in 2030 and 131.5 million in 2050. Alzheimer's disease (AD) is by far the most prevalent cause of dementia, accounting for up to 80% of all dementia diagnoses. With the rising prevalence and mortality of Alzheimer's disease, there is a growing sense of urgency in the medical community to develop effective methods for the early detection and successful treatment of this progressive neurodegenerative disease.

This global consortium will focus on the most recent and energizing developments in every facet of these neurodegenerative disease, providing a significant opportunity for delegates, researchers, scientists, psychiatrists, neurologists, caregivers and professionals from all corners of the globe to meet, socialize, and see new logical advancements.

We hope that Dementia 2022 will present a unique opportunity to explore what's possible and embrace change.



KEYNOTE FORUM

DAY 01

INTERNATIONAL ALZHEIMER'S DISEASE & DEMENTIA CONFERENCE

15-16 JUNE

Stoyanova I. I*[1], Klymenko A.[2], Lutz D.[2]

[1]Department of Anatomy and Cell Biology, Research Institute of the Medical University- Varna, Bulgaria

[2]Department of Neuroanatomy and Molecular Brain Research, Ruhr University Bochum, Germany

Can we stimulate neuroplasticity with the cell signaling molecule ghrelin?

The increase in human lifespan during the last century is accompanied by an increased risk for development of age-related disorders including Neurodegenerative diseases (NDD) such as Alzheimer's and Parkinson's disease. These pathologies are characterized by impairment of synaptic activity and plasticity, and loss of neurons in motor, sensory and cognitive systems. The neuropeptide and gastric hormone ghrelin has a very promising therapeutic potential for treatment of NDD with its ability to stimulate the repair and activity of neurons. Therefore, we subjected cultured cerebral and cerebellar cortex neurons, and organotypic cortical slices from rat brains to hypoxia for 6 hours, followed by 24 hours normoxya and treatment with ghrelin. We further quantitatively analyzed immunostainings for ghrelin's receptor (GHSR1), synaptic marker synaptophysin and transcription factor Pax6, a regulator of neural progenitor cell fate. In the cortex, hypoxia down-regulated Pax6 levels, increased GHSR1 expression and its internalization into the nucleus. Additionally, hypoxia drastically reduced the number of synapses. Ghrelin supplementation of the culture medium during the recovery period normalized the expression levels of Pax6 and GHSR1, and significantly elevated synapse density, as compared with the control cultures or with the pre-hypoxic levels. Our findings suggest that ghrelin stimulates neurogenic factors in non-neurogenic brain areas and stimulates synaptic plasticity, both extremely important for protection against neurodegeneration and accompanying dementia.

Audience Takeaway

- Our study provides some new insights about the mechanisms of ghrelin's neuroprotective effect against neuronal damage.
- This information opens avenues for development of new diagnostic and therapeutic approaches to the neurodegenerative diseases manifested with impaired neuronal and synaptic plasticity.
- We hope that our results will have a significant clinical relevance and could be used as a platform for other labs and universities to expand their research or teaching.

Biography

Irina Stoyanova graduated in General Medicine at the Medical Academy, Sofia, Bulgaria and specialized at human anatomy and histology. In 1983 she was appointed as an Assistant Professor and later on, in 2004, as an Associate Professor at the Department of Anatomy, Trakia University, Stara Zagora, Bulgaria. She obtained her PhD in neuroscience in 2002. In 2002-2003 she was a research associate in Neurobiology of Nutrition Laboratory, Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, USA. In 2008-2015 she worked as a postdoc at the University of Twente, Enschede, the Netherlands. In 2011 she was also appointed as an Associate Professor in Human Anatomy and Physiology at the University College Roosevelt, Middelburg, the Netherlands. Since 2015 she is an Associate Professor at the department of Anatomy and cell biology, Medical University, Varna, Bulgaria.

The research interests of Dr. Stoyanova are in the Neurosciences – different aspects of the structural and functional neuromorphology and their clinical implications. She has published widely on these fields. For her achievements she was awarded twice (at International Falk Foundation Symposium of Gastroenterology in Bucharest, Romania, 2000, and at 7th International Symposium on Cytokines and Chemokines (satellite of the 13th World Congress of Gastroenterology), Montreal, Canada, 2005). She is a member of the editorial boards of some international journals - International Journal of Biomedical Sciences (since 2005), Adipobiology (since 2009), Frontiers in Cellular Neuroscience (Since 2021) and Guest Associate editor for Frontiers of Cell and Developmental Biology (2020-2021). She is also a reviewer for other scientific journals.

Mark S. Kindy

Department or Pharmaceutical Sciences, Taneja College of Pharmacy, University of South Florida, USA

Department of Research, James A. Haley VA Hospital, USA

Implications for serum amyloid P in the pathogenesis of Alzheimer's disease

Serum amyloid P component (SAP) is found in all amyloids and studies have suggested that it plays an integral role in the formation, progression, and maintenance of the disease processes. The mouse SAP (mSAP) does not interact with human proteins and since most of the models for Alzheimer's disease (AD), tau pathology, etc. are with human cDNAs/genes, mSAP does not associate with human aggregates and fibrils. SAP regulates inflammation, and inflammatory signaling pathways impair cognitive function in vivo. The biological impact of SAP in AD is not well characterized. Our long-term goal is to determine the mechanisms regulating SAP function, particularly within the setting of AD. The objective of this grant is to characterize the role for SAP in AD. Recent studies from our laboratory and others have provided information for the role of SAP in AD progression: 1) SAP levels are increased in mouse models of inflammation and AD; 2) in humans, SAP is present in the brains of patients with AD and found in the plaques and tangles; 3) SAP stabilizes amyloid fibrils; 4) SAP deficient mice have altered AA amyloid; 5) in human SAP transgenic mice, SAP is associated with A plaques and cerebral amyloid angiopathy (CAA). The central hypothesis is that SAP facilitates AD pathogenesis, via enhancing inflammatory responses, expedites amyloidogenesis (oligomerization), and contributes to disease progression by functioning as a chaperone. This contribution is significant since it will establish that targeting of SAP by therapies have the potential to regulate inflammatory activity through molecular mechanisms. These studies will hopefully provide potential targets for therapeutic intervention in neurological disorders. The proposed research is innovative because we investigate the effect of inflammatory signaling pathways on SAP in neurological diseases, a heretofore-unexamined process.

Audience Takeaway

- Will help understand the implications in AD.
- Provide information on potential targets for therapeutic intervention.
- Will provide a better understanding of the disease process.

Biography

Dr. Kindy studied Biochemistry at Boston University Medical School, and graduated in 1987 with a Ph.D. In his post-doctoral training, he gained significant training and expertise in pathophysiology of disease. As a postdoctoral fellow, he carried out biochemical and molecular and cellular biology studies on c-fos and development. As an Assistant and Associate Professor at the University of Kentucky, he established my research program to investigate the mechanisms of neurodegenerative disorders and development of animal models. For 13 years as an endowed Professor, Professor and Associate Chair for Research at MUSC, and as a Research Career Scientist and then Senior Research Career Scientist in the VA, he consolidated his research program and expanded his studies into the role and mechanisms in disease pathobiology with a focus on neuroinflammation and aging. Since moving the USF and the James A. Haley VAMC in 2015, his research has developed around mechanisms of disease, inflammation and signaling molecules in neurodegeneration.

SPEAKERS

DAY 01

INTERNATIONAL

ALZHEIMER'S DISEASE & DEMENTIA CONFERENCE

15-16 JUNE

Don Kulasiri[1]* and Jingyi Liang[2]

[1]Computational Systems Biology Laboratory, Centre for Advanced Computational Solutions (C-fACS), Lincoln University, New Zealand
[2]Department of Pharmacy, Faculty of Health Sciences, UiT The Arctic University of Norway, Norway

Computational models and biophysics for understanding neuronal dysfunctions in alzheimer's disease

Alzheimer's disease (AD) as the leading cause of dementia affects millions of families across the world. AD causes huge physical social, psychological and financial impacts not only on the patients but also on their families and the whole society. Numerous research has been conducted worldwide on understanding the pathogenesis of AD and seeking a cure for AD.

Computational modelling based on biophysics has been successfully applied to neuroscience. It provides a strong foundation for applying the modelling approach to AD research. Computational modelling offers great opportunities on investigating the underlying mechanisms of the disease and its progression, from molecular/cellular level to system level. Using conceptual models, hypotheses on AD can be investigated individually or comprehensively through well-designed computational experiments. With the development of technology, a great number of simulation software or platforms, either for general or biological/neuronal-specific purposes, are wildly available, which largely advance the modelling research on AD.

In this presentation, we discuss how the computational modelling approach can help scientists understand the dysregulation in AD, with examples of context-driven biophysics and computational modelling approaches related to AD. We focus on modelling studies on the inter-and intra-neuronal signalling pathways that are involved in the degeneration of AD, particularly on the dysfunction of the signal transduction at the synapse as well as the axon.

We briefly discuss neuron and its environment as complex dynamic systems; initiation of action potential and its relevance to AD; role of calcium in AD, related pathways, and hypotheses; and biophysics of Aβ and computational modelling.

Audience Takeaway

- How computer models can be used to understand AD.
- Develop ways of therapeutic interventions for AD.
- New ideas for different research directions.

Biography

Professor Don Kulasiri obtained his PhD specialising in Bioengineering and Computation from Virginia Tech, Blacksburg, USA. He had been a visiting professor to Stanford University, Princeton University, USA, and has been visiting Wolfson Centre for Mathematical Biology, Mathematical Institute, University of Oxford, UK, regularly since 2008. He is the Professor in Computational Modeling and Systems Biology, a Personal Chair, at Lincoln University, Christchurch, New Zealand since 1999. He has published over 175 publications including 6 research monographs and 1 edited book. His current research interests include systems biology; stochastic modelling; bio-engineering; complex interactive dynamics and thermodynamics in small scale systems.
Dr. Jingyi Liang obtained her PhD in Computational Systems Biology at Lincoln University, New Zealand. She has been involved in research in C-fACS since 2011. She joined the Computational Pharmacology Group at the University of Tromsø, Norway in 2018. Her research interest is mathematical modelling in pathology and pharmacology.

Yung-Feng Liao*, Bo-Jeng Wang, Po-Fan Wu, and Yun-Wen Chen

Laboratory of Molecular Neurobiology, Institute of Cellular and Organismic Biology, Academia Sinica, Taipei, Taiwan

Novel pharmacological targets of Alzheimer's disease

Alzheimer's disease (AD) is characterized by a chronic decline in cognitive function and is pathologically typified by cerebral deposition of amyloid-β peptide (Aβ). The production of Aβ is mediated by sequential proteolysis of amyloid precursor protein (APP) by β- and γ-secretase, which has been regarded as the amyloidogenic pathway of AD pathogenesis. An RNA interference-based screen has led us to identify an ErbB2-centered signaling network that preferentially govern the proteostasis of APP-C99, a direct substrate of γ-secretase. Down-regulation of ErbB2 by CL-387,785 decreases the levels of C99 and secreted Aβ in cellular, zebrafish, and mouse models of AD, through the activation of autophagy. Oral administration of CL-387,785 for 3 wk significantly improves the cognitive functions of APP/PS1 transgenic mice, establishing ErbB2 as a novel therapeutic target for AD. A previous report documents the significant correlation between lipid metabolism and incipient AD by using microarray correlation analyses. We thus attempt to determine the mechanism through which alterations in lipid compositions of biomembranes might contribute to the pathogenesis of AD. Given that the level of phosphatidylinositol-4,5- bisphosphate [PI(4,5)P2] in the membrane has been implicated to modulate Aβ production, we then investigate whether PIP5K type Iα (PIP5K1A) can affect Aβ production by modulating the PIP2 content of the membrane. Our data show that overexpression of PIP5K1A results in significant enhancement of non-amyloidogenic APP processing, leading to a marked decrease in secreted Aβ and a concomitant redistribution of APP from endosomal compartments to the cell surface. These results suggest that PIP5K1A may be a valuable therapeutic target for AD through its effect on promoting non-amyloidogenic processing of APP.

Audience Takeaway

- ErbB2 and PIP5K1A are identified as novel pharmacological targets of AD.
- ErbB2-specific inhibitors could be derived from the molecular structure of CL-387,785.
- There is no PIP5K1A inhibitor available. How to generate chemical inhibitors that can modulate PIP2 content of cellular membranes could potentially contribute to a breakthrough in terms of expanding the therapeutic approaches for AD.

Biography

Dr. Yung-Feng Liao studied Biochemistry at the National Yang-Ming Medical College, Taipei, Taiwan, and graduated as MS in 1987. After working as a research assistant at the Graduate Institute of Biological Chemistry, National Taiwan University, Taipei, Taiwan, Dr. Liao then joined the research group of Prof. Kelley Moremen at the Department of Biochemistry and Molecular Biology, University of Georgia, Athens, GA, USA, and obtained his PhD degree in 1998. After completing postdoctoral fellowship supervised by Dr. Livingston Van De Water at the Massachusetts General Hospital and Dr. Michael Wolfe at the Brighm and Women's Hospital, Harvard Medical School, Boston, MA, USA, he obtained the faculty position at the Institute of Cellular and Organismic Biology, Academia Sinica, Taipei, Taiwan in 2002. Since then, Dr. Liao has been the principal investigator of the Laboratory of Molecular Neurobiology in the Institute of Cellular and Organismic Biology (ICOB), Academia Sinica, a premier research institution in Taiwan. Currently, Dr. Liao holds the rank of Research Fellow at the ICOB. He has published more than 60 papers in reputed journals and has been serving either as an editorial board member or as a peer reviewer of prestigious journals.

Ravi Samuel
The Psychotherapy Clinic, India

Cognitive and psychological vulnerability in developing dementia - A comparative study of paid institutional, Free institutional and residential care!

The prevalence of Dementia is on the rise due to increasing longevity. In addition, co-morbid medical conditions and depression lead to the onset of cognitive impairment - the prevalence of medical ailments like diabetes mellitus, hypertension, and depression are high among the elderly. Over and above this, the place of Residence determines the nutrition, exercise, social activities and cognitively stimulating environment. This presentation is about a survey research study to ascertain the living conditions, psycho-social status, cognitive impairment and physical disability. The instruments used for the analysis were Mini-Mental Status Examination for Cognitive Impairment, WHODAS for physical and cognitive disability, and an interview schedule to ascertain the psychological status and social support from family and friends. In Paid Homes, 74 per cent were males, in Free Homes, 23 per cent were females. In PR, 26 per cent were females. The mean age in POAH was 72.41, with an SD of 5.6. In FOAH mean age was 69.91 with an SD of 6.2, and in PR, the mean age was 66.46 with an SD of 4.4. Cognitive impairment and physical disability were highest in Free Homes, followed by those in their Residence and then in Paid Homes. Education, structured activities, and social support were higher in Paid Homes, lesser in Residence, and very poor in Free Homes. Statical tests of association showed significant differences among the different residential settings. The presentation will discuss further findings of this study.

Audience Takeaway

- The different living circumstances in various living facilities for elders and their effect on elders' cognition.
- The cognitive and disability profile of elders in different living facilities.
- Social support, health service utilisation, and living conditions can make them vulnerable to depression. In addition, a cognitively non-stimulating environment, and other medical ailments, increase the vulnerability to Dementia.
- Can we predict the trajectory of cognitive and health profiles given the medical and psycho-social factors?
- Can we create algorithms which predict the medical trajectory – to plan for care and finance?
- To plan policies and programmes for the elderly living in different residential facilities.
- To perform further research on the Old Age Homes.
- To form evidence-based policies for families and Institutions to provide good quality care to prevent cognitive impairment.
- To develop cognitively stimulating activities for Old Age Homes.

Biography

Dr. Ravi Samuel is a PhD in Social Work, India, specialising in Cognitive Behaviour Therapy and Cognitive Rehabilitation since 1991. He did his post-graduate training at National Hospital, Queen Square, London, as Paul Hamlyn Fellow from 1998-1999. Dr Ravi Samuel has presented papers in seven World Alzheimer's Congresses. He has published few papers on Cognition in Dementia, Disability among the aged, Cognitive Rehabilitation and Mortality among Dementia patients in National and International Journals. He has also written a chapter for a book on Care of the Caregivers of Patients with Dementia.

Shubhangi Pingle*, K Ravibabu, Geethu Mathew, Rajani G. Tumane, Avinash Gaikwad, Raju

Regional Occupational Health Centre (Southern), NIOH, INDIA

Lead toxicity associated protein and its role in alzheimers disease & dementia in industrial workers

The interaction between proteomic profiling and Alzheimer's disease, Dementia in industrial workers was not explored in occupational settings. Therefore, the present study, aimed to assess the proteomic profiling with among workers exposed to Pb with contemplation of varied blood lead levels and duration of exposure. The study on the serum markers with reference to lead toxicity is limited in human beings. The obtained protein markers can be correlated with the exposure pattern and can have a broad range of potential applications. They may be used for clinical diagnostic or prognostic purposes like Alzheimer's disease and Dementia. The novel mechanistic links between lead exposure and protein expression can be evaluated. The earlier studies were conducted on common effect of heavy metals and does not covered about specific lead toxicity on proteomic profile. This is different pursuit in which the interaction between Alzheimer's disease, Dementia and proteomic profiling will be explored in occupational settings.

Assessment of proteomic profiling in occupational lead exposures settings will identify the functional classification and protein – protein interactions. It also highlights the interaction between Alzheimer's disease, Dementia and proteomic profiling among lead exposed workers.

Audience Takeaway

- The study on the serum markers with reference to lead toxicity is limited to human beings. The obtained protein markers can be correlated with the exposure pattern and can have a broad range of potential applications. They may be used for clinical diagnostic or prognostic purposes. The novel mechanistic links between lead exposure and protein expression can be evaluated. he earlier studies were conducted on the common effects of heavy metals and do not cover specific lead toxicity on proteomic profile. This is a different pursuit in which the interaction between proteomic profiling and Alzheimer's disease, Dementia in industrial workers will be explored in occupational settings.

Biography

Dr. Shubhangi Pingle graduated, post-graduated and obtained her doctorate from RTM Nagpur University. She is Scientist D, ROHC, NIOH Banglore, ICMR, India. She Published 110 research papers in National and International journals. She acquired 15 years of research experience in proteomics, Diagnostic Biomarkers, Development of ELISA and Animal cell culture biology. She has three Indian Patent granted and 6 submitted. She completed projects cost around ~US$ 3 million. She implemented many areas first time in the diagnostic field of research by her differing approach. She has expertise in preventive measures of occupational health diseases used for beneficiation of industry workers.

Anand K. Tiwari

Department or Biotechnology & Bioengineering, Institute of Advanced Research, India

Mitochondria and alzheimer's disease : Participation of miro protein

Alzheimer's disease (AD) is a neurodegenerative disease, characterized by loss of memory and cognitive impairment due to the accumulation amyloid beta 42 ($A\beta_{42}$) plaque and neurofibrillary tangles (NFT) due the hyperphosphorylated Tau protein in the parts of brain. Due a significant increase in AD patent number world-wide (~50 million people worldwide), it has been considered as one of the most challenging problems that need immediate concern. Several lines of evidences suggested that mitochondria play a crucial role in the onset of several neurodegenerative diseases including AD. It has been also shown that abnormality with mitochondrial function is the first step of development of AD and related pathologies. Miro, a Rho GTPases and mitochondrial outer membrane protein forms a major protein complex with Milton, and mediates mitochondrial axonal transport. In AD, an abnormal mitochondrial function and altered axonal transport has been reported but the possible link between Miro and AD associate genes (Appl, $A\beta_{42}$ and Tau) is not well understood. Herein, using Drosophila melanogaster, an invertebrate model, we have demonstrated the possible genetic interaction between Miro and Appl, $A\beta_{42}$ and Tau gene in Drosophila.

Audience Takeaway

- They will understand about the molecular details of AD and key players regulating the AD.
- For a teacher, the talk will be helpful to understand the mitochondrial role in AD progression and use of invertebrate model organism for AD research.

Biography

Prof. Anand K. Tiwari, Professor at Institute of Advanced Research, India has expertise (more than 20years) in working with Drosophila model for Alzheimer's disease (AD). His research work in the area improves understanding of Alzheimer's disease and its interacting partners. His recent work will help in designing the therapeutic target for AD and related pathologies. He completed his PhD in 2008 from Banaras Hindu University Varanasi.

Ivanov, S. M.*[1], Atanasova, M.[2], Dimitrov[2], I., Doytchiova, I.[2]

[1]Redesign Science, 180 Varick St, USA

[2]Department of Chemistry, Faculty of Pharmacy, Medical University of Sofia, Bulgaria

Cellular polyamines condense hyperphosphorylated tau triggering alzheimer's disease

Many gaps in our understanding of Alzheimer's disease (AD) remain despite intense research efforts. Perhaps the most prominent gap is the mechanism of tau condensation and fibrillization. One viewpoint is that positively charged tau is condensed by cytosolic polyanions. However, this hypothesis is likely based on an overestimation of the abundance and stability of cytosolic polyanions and an underestimation of crucial intracellular constituents – the cationic polyamines. Here, we propose an alternative mechanism grounded in cellular biology. We describe extensive molecular dynamics simulations and analysis on physiologically relevant model systems, which suggest that it is not positively charged, unmodified tau that is condensed by cytosolic polyanions but negatively charged, hyperphosphorylated tau that is condensed by cytosolic polycations. Our work has broad implications for Alzheimer's research and drug development and the broader field of tauopathies in general, potentially paving the way to future etiologic therapies.

Audience Takeaway

- The talk is primarily intended for researchers in the field of neurodegenerative disorders.
- It focuses on aspects of cellular biology which are currently underappreciated and understudied in Alzheimer's research.
- The presentation lays out a mechanism for tau condensation and fibrillization in AD.
- From the proposed condensation mechanism, the work derives a possible etiologic mechanism and points the research community to molecular targets that warrant investigation.

Biography

Stefan Ivanov graduated with a Master's in Pharmacy from the Medical University of Sofia in 2011. Between 2013 and 2017 he completed a split-site PhD in computational chemistry at the University of Manchester, UK and the Bioinformatics Institute at the Agency for Science, Technology , and Research (A*STAR), Singapore, focusing on protein-protein and protein-ligand interactions. He then pursued postdoctoral work in South Korea, his native Bulgaria, and the US, further extending his experience in modeling proteins, nucleic acids, lipids, and small drug-like molecules before finally moving on to drug discovery in industry at Redesign Science.

Leila Hosseini*, Saeed Sadigh-Eteghad, Javad Mahmoudi

Neurosciences Research Center, Tabriz University of Medical Sciences, Iran

Neuroprotective mechanisms of nicotinamide adenine dinucleotide and related precursors in alzheimer's disease

In the current aging society, the number of patients suffering from Alzheimer's disease (AD) is rapidly increasing, and without therapeutic breakthroughs is estimated to reach 80 million by 2040. As an irreversible chronic neurodegenerative disease, AD is characterized by progressive cognitive deficits, memory loss, and personality changes taking place with advancing age. Synaptic dysfunction, and especially the degeneration of cholinergic neurons, also leads to cognitive impairment and deficits in memory and learning and in emotional resilience. Oxidative stress, apoptosis, inflammation, autophagy, and mitochondrial dysfunction have also been widely shown to be involved in the progress of the disease. Thus, it seems that novel multi-targeted treatments are needed to prevent or slow disease progressive. Nicotinamide adenine dinucleotide (NAD+) is a crucial cofactor involved in a wide spectrum of biological functions including oxidative phosphorylation, mitochondrial function and bioenergetics, cell proliferation, and calcium homeostasis. Also, NAD+ is essential for appropriate function and survival in the central nervous system. Sudies showed that NAD+ precursors appeared to be an effective anti-AD strategy for preventing neuropathological and behavioral symptoms induced by AD in preclinical trials. Such favorable effects are possibly modulated by reducing central Aβ and tau levels and improving brain bioenergetics, inflammation, and oxidative stress regulation.

Biography

Dr. Leila Hosseini received her PhD in physiology from Tabriz University of Medical Sciences, Iran in 2019. Currently working as postdoctoral researcher in Neurosciences Research Center(NSRC), Tabriz University of Medical Sciences, Iran. Published 22 national and international publications. The goal is to develop therapeutic interventions to restore CNS function and improve quality of life of individuals with neurodegenerative diseases.

Marina Mirchandani-Duque[1], Miguel A. Barbancho[1], Alexander López-Salas[1], Jose Erik Alvarez- Contino[1], Natalia García-Casares[1], Kjell Fuxe[2], Dasiel O. Borroto-Escuela[1,2,3], Manuel Narváez [1,2]*

[1]Instituto de Investigación Biomédica de Málaga, Facultad de Medicina, Universidad de Málaga, Spain

[2]Department of Neuroscience, Karolinska Institute, Sweden

[3]Department of Biomolecular Science, Section of Physiology, University of Urbino, Italy

Galanin and neuropeptide Y interaction enhances proliferation of granule precursor cells and expression of neuroprotective factors in the rat hippocampus with consequent augmented spatial memory

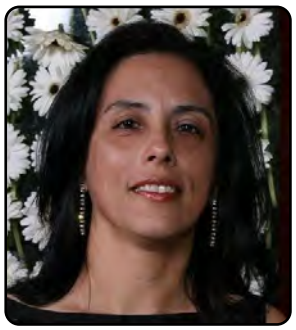
Dysregulation of hippocampal neurogenesis is linked to several neurodegenereative diseases, where boosting hippocampal neurogenesis in these patients emerges as a potential therapeutic approach. Accumulating evidence for Neuropeptide Y (NPY) and galanin (GAL) interaction was shown in various limbic system regions at molecular-, cellular- and behavioral-specific levels. The purpose of the current work was to evaluate the role of NPY and GAL interaction in the neu-rogenic actions on the dorsal hippocampus. We studied the Y1R agonist and GAL effects on: hip-pocampal cell proliferation through the proliferating cell nuclear antigen (PCNA); the expression of neuroprotective and anti-apoptotic factors and the survival of neurons and neurite outgrowth on hippocampal neuronal cells. The functional outcome was evaluated in the object-in-Place task. We demonstrated that the Y1R agonist and GAL and promote cell proliferation and the induction of neuroprotective factors. These effects were mediated by the interaction of NPYY1 (Y1R) and GAL2 (GALR2) receptors, which mediate the increased survival and neurites outgrowth ob-served on neuronal hippocampal cells. These cellular effects are linked to the improved spa-tial-memory effects after the Y1R agonist and GAL coinjection at 24 hours in the object-in-place task. Our results suggest the development of heterobivalent agonist pharmacophores, targeting Y1R-GALR2 heterocomplexes, therefore acting on the neuronal precursor cells of the DG in the dorsal hippocampus for the novel therapy of neurodegenerative cognitive-affecting diseases.

Audience Takeaway

- Understanding Neuropeptide Y and GAL interaction through Y1R-GALR2 heteroreceptor complex.
- How the the Y1R agonist and GAL may promote cell proliferation in the DG of the dorsal hip-pocampus and the induction of neuroprotective factors, such as BDNF and Bcl-2.
- How Y1R-GALR2 heteroreceptor complexes mediate survival and neurites outgrowth on neuronal hippocampal cells.
- How these cellular effects may be linked to spatial-memory effects.
- The development of heterobivalent agonist pharmacophores, targeting Y1R-GALR2 heterocomplexes, therefore acting on the neuronal precursor cells of the DG in the dorsal hippocampus for the novel therapy of neurodegenerative cognitive-affecting diseases.

Biography

Manuel Narváez cursed Medicine and surgery degree in 2005, with the best academic record of his promotion, in 2006 I obtained a competitive pre-doctoral excellence scholarship from the Andalusian board. The research activity developed allowed him to carry out 5 months visits during 2009 and 2010 at the Karolinska Institute in Stockholm to obtain the European mention. In 2012 I obtained the European PhD thesis with cum laude qualification, the extraordinary PhD award from the faculty of medicine, thesis prize from medical college of Malaga (2012) and the prize from college of pharmacists of Malaga (2013). Up to 6 postdoctoral visits to the Karolinska Institute in Stockholm collaborating on multiple research projects establishing collaborative links with the Swedish research group, during the years 2012-2021, total more than 1 year. The research results have been published successively in congresses of international and national relevance. In addition, innovative articles have been published, including in the first quartile of impact index in its category and with quality indices, including high cite numbers. Our team has performed multidisciplinary research and worked in a highly integrative manner at different systems levels, we have contributed to the GPCR receptor-receptor interactions field focus in CNS diseases, such as depression, Parkinson, addiction drugs and Alzheimer.



Rafaella Carvalho Rossato and Cristina Pacheco-Soares*

Laboratório de Dinâmica de Compartimentos Celulares, Universidade do Vale do Paraiba, Brazil

Photobiomodulation and taurine in human neuroblastoma : In vitro study of alzheimer's disease

The limited repair capacity of the central nervous system (CNS) is a viable challenge. Alzheimer's disease (AD) is a progressive and highly prevalent neurodegenerative disease that affects people worldwide. The complete inclusion of the CNS is not yet possible by means and is sought by means, including drug alternatives and LED irradiations to make neural tissue. In this work, we proposed establishing and standardizing an in vitro model of the use of hydrogen peroxide (H2O2) in a human neuroblastoma cell line (SH-SY5Y). Thus, the study explores the effects of taurine in conjunction with LED under oxidative stress to evaluate the neuroprotective effect and the ability of cellular restoration after oxidative stress. Recent research indicates that LED has excellent potential to be included in the treatment of AD, resulting in both therapies (LED and taurine supplementation), which may be promising. This work evaluated LED at wavelength at 660 nm and taurine as a pre-treatment and treatment model in oxidatively stressed cells, evaluating mitochondrial activity by the MTT colorimetric test (quantitative) and labeling of live cell mitochondria by fluorescence using MitoTracker Orange (qualitative). Cell viability was also evaluated by testing the blue cell structures by motive and cellular trypan (qualitative and quantitative). When performing as statistics and set as images, LED in standalone can present neuroprotective effects only in the pre-treatment, or analyzed, when the cell is exposed to LED and taurine and subsequently stressed with H2O2. Comparing the action of the two pre-treatments in contact with the cell and also in contact with cell + H2O2, it can be observed that LED has a more significant cell proliferative effect compared to taurine.

Keywords: Alzheimer's Disease; Neuroprotection; Oxidative stress

Audience Takeaway

- With the presentation of our research, we intend to bring information about the applicability of photobiomodulation associated with drugs.
- Raise awareness of the benefits of photobiomodulation to the central nervous system (CNS).
- Provide subsidies for other works to be carried out associating photobiomodulation with cerebral revascularization, optimizing mitochondrial activity, potentiation of intracellular signaling, among others.

Biography

Dr. Cristina Pacheco-Soares is bachelor and degree in Biological Sciences (1988) from the State University of Londrina, UEL. Master's in microbiology(1992) from the State University of Londrina, UEL. Doctor in Biosciences and Biotechnology(1998) from the State University of Norte Fluminense Darcy Ribeiro, UENF. She is a professor/researcher at the University of Vale do Paraiba (UNIVAP), coordinating the Dynamic Group of Cellular Compartments. She develops research in Photodynamic Therapy (PDT) and Low-Intensity Laser Therapy (LTBI), evaluating the cytotoxic and genotoxic effects of photodynamic mechanisms in tumor cells. She develops research with an in vitro model of Alzheimer's disease, evaluating drug delivery and antioxidant action associated with phototherapy.

Claudia Colussi*[1], Alessia Bertozzi[1], Marco Rinaudo[2], Lucia Leone[2], Federica Conte[1], Claudio Grassi[2,3]

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Nucleoporin 153 deficiency in adult neural stem cells defines a pathological protein - Network signature and defective neurogenesis in a mouse model of alzheimer's disease

Reduction of adult hippocampal neurogenesis is an early critical event in Alzheimer's disease (AD), leading to progressive memory loss and cognitive decline. The nucleoporin Nup153, besides its role in nuclear transport, has been described as a key regulator of NSC plasticity through gene modulation. Here we investigated the potential role of Nup153 as target to improve neurogenesis in the 3xTg mouse model of AD in vitro and in vivo.

We found that reduced Nup153 levels characterized NSCs from the 3xTg mice (AD-NSCs) and caused inefficient proliferation, migration and differentiation that were restored by Nup153 overexpression in vitro. Lentiviral-mediated Nup153 hippocampal delivery in AD mice led to an increase in the number of BrdU/DCX+, BrdU/NCAM+ and BrdU/NeuN+ cells at 10 days and 1 month respectively. Consistently, LV-Nup153-injected AD mice showed an improvement of cognitive performance in comparison to AD control mice at 1 month after LV-Nup153 injection (MWM test). iPSC-derived brain organoids produced from Control and AD patients were also used to further validate the role of Nup153 in neurogenesis and development. AD organoids produced from AD-iPSC transduced with the LV-Nup153 (AD-ORG-Nup) showed a better maturation at 1 month than control-AD-organoids as well as the presence of ventricle like structures as in healthy control organoids.

A proteomic approach was performed to identify Nup153 interactors in WT- and AD-NSCs potentially implicated in neurogenesis regulation. GO analysis showed that Nup153-bound proteins in WT-NSCs were involved in RNA metabolism (tRNA, mRNA, ncRNA, splicing and transport) and epigenetic mechanisms (DNA methylation, histone modifications). Nup153-bound proteins in AD-NSCs were involved in pathways of neurodegeneration and AD, mitochondrial dysfunction, proteasomal processing, cell cycle and RNA degradation. Our data indicate that Nup153 restoration promotes neurogenesis and cognitive performance. Molecular data suggest that the complex regulatory network orchestrated by Nup153 is based on multiple interactions that are differently regulated in WT and AD-NSCs.

Audience Takeaway

This presentation will provide novel insights in the regulation of adult neurogenesis with a specific focus on:

- Novel epigenetic regulators of neural stem cell function.
- Novel mechanisms of pathogenesis in Alzheimer's disease.
- Modeling of development and neurogenesis through brain organoids.
- Potential therapeutic application to Alzheimer's disease.

Biography

Dr. Colussi received her B.Sc. at the University of Tor Vergata (Rome, Italy) in 1996. She then started her postgraduate training at the Higher Institute of Health studying DNA repair mechanisms in cancers where she was recipient of a fellowship from Italian Association for Cancers. In 2000 she joined the laboratory of Cardiac Regeneration at the New York Medical College (NY) to study the biology of cardiac progenitor cells and in 2003 she completed a Master Degree at the Clinical Pathology Medical School. In 2012 she also completed her PhD in Endocrinology at Catholic University. From 2015 she is Assistant Professor at CNR-IASI performing research focused on the understanding of the key pathological pathways that lead to alteration of synaptic plasticity in AD and neurodegeneration. She has authored 48 papers (h-I 28). She has been serving as external consultant for the Italian Medicine Agency (AIFA) and as member for many International grant advisory committees.

Kesheng Wang*[1], Wei Fang[2], Silas Wang[3], Ying Liu[4], Chun Xu[5]

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Utilizing feature selection to identify proteomic biomarkers for support vector machine learning - Based classification of alzheimer's disease

Background: Proteins play an important role in disease pathways and drug-target discovery. The most widely used biomarkers for Alzheimer's disease (AD) include the apolipoprotein E (APOE) protein, the clinical Cerebrospinal fluid (CSF) protein biomarkers of Aβ plaques (Aβ42), the biomarkers of pathologic tau (total tau-tTau and phosphorylated tau-pTau), and the biomarkers of neurodegeneration injury (such as MRI). There is a critical need to develop machine learning (ML) approaches in translating univariate biomarker findings into clinically useful multivariate decision support systems. This study aimed to perform feature selection of proteomic biomarkers for Support vector machine (SVM) learning-based classification of AD.

Methods: A total of 162 non-Hispanic Whites, including 109 with AD and 53 with cognitive normal functioning (CN), were selected from the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort. 146 proteomic biomarkers were from an ADNI subset of "Biomarkers Consortium Plasma Proteomics Project RBM multiplex data." The Z score was computed for each protein using the mean and standard deviation. An independent samples t-test was used to compare the means in each protein level between AD and CN. Variable cluster analysis using the first principal component (oblique principal component cluster analysis-OPCCA) was used to divide proteomic biomarkers into disjoint clusters. Random forest (RF) was used to test relative predictive importance of biomarkers. The SVM algorithm (linear kernel, radial kernel, and polynomial kernel) was applied to develop a model to predict AD.

Results: The independent t-test revealed that there were significant differences between AD and CN in 44 proteomic biomarkers. The top 9 biomarkers of the 146 analyzed with RF feature importance (BNP, ApoAII, SGOT, A1Micro, ApoE, Calcitonin, Eotaxin3, Vitronectin, and IP10) revealed the optimal model with accuracy of 0.7897 and Kappa of 0.4065, while the top 5 of 44 AD-associated biomarkers (BNP, ApoE, A1Micro, PLGF, and PAPPA) revealed an optimal model with accuracy of 0.8694 and Kappa of 0.6753. Furthermore, the radial kernel model in SVM based on the top 5 of the 44 AD-associated features analyzed had accuracy of 0.8617, Kappa of 0.6658, ROC of 0.8791, sensitivity of 0.7967, and specificity of 0.8461, slightly better than the model produced with the top 9 protein biomarkers selected by RF. After adding 3 clinical CSF biomarkers (Aβ42, tTau and pTau) to the top 5 AD associated biomarkers, the polynomial kernel SVM model provided the optimal model with accuracy of 0.9572, Kappa of 0.9088, ROC of 0.9871, sensitivity of 0.9383, and specificity of 0.9076. Finally, the OPCCA clustered 44 AD-associated biomarkers plus 3 clinical CSF biomarkers into 13 clusters, where tTau and pTau were in one cluster, and Aβ42 with ApoE and ApoAII were in another cluster.

Conclusions: The model using both RF-selected proteomic biomarkers and clinical CSF biomarkers has the potential in predicting AD.

Keywords: Alzheimer's disease; proteomics; biomarkers; machine learning; random forest; support vector machine.

Audience Takeaway

- This study aimed to identify proteomic biomarkers for support vector machine learning-based classification of Alzheimer's disease (AD).
- The audience will understand the application of machine learning techniques in predicting AD and in clinical diagnosis.

- The audience can use these techniques in their research or teaching.
- Feature selection will help improve the efficiency of classification of AD using machine learning.

Biography

Dr. Kesheng Wang is an Associate Professor in Biostatistics at the School of Nursing, West Virginia University. Dr. Wang received his PhD in 2001 from Georg-August-University of Goettingen, Germany. As a postdoctoral fellow, Dr. Wang obtained advanced training in Biostatistics (including Genetic Epidemiology and Statistical Genetics) at the Hospital for Sick Children and University of Toronto, Canada. His research interests focus on theory and application of biostatistics, behavioral epidemiology, and genetic epidemiology/ statistical genetics. Dr. Wang has published more than 150 scientific papers.

Danqing Xiao[1,2]*, Kesheng Wang[3]

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White matter integrity and key structures affected in alzheimer's disease based on diffusion tensor imaging

White matter (WM) degeneration is suggested to predict the early signs of Alzheimer disease (AD). The exact structure regions of brain circuitry involved is not clear. This study aims to examine the associations between WM tract integrity, specifically the specific diffusion tensor imaging (DTI) measures, and AD diagnosis, and denote the key substrate in predicting AD by DTI. This study included four DTI measures, including mean diffusivity (MD), fractional anisotrophy (FA), radial diffusivity (RD) and axial diffusivity (AxD) in 18 main white fiber tract regions measured in 84 non-Hispanic white participants (42 AD patients and 42 controls) from the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset. The multivariable general linear model (GLM) was used to examine the association of AD diagnosis with each DTI measure adjusting for age, gender, and education. The fornix, corpus callosum, anterior corona radiata, and cingulum hippocampus, right uncinate fasciculus, right superior fronto-occipital fasciculus, left inferior fronto-occipital fasciculus, left sagittal striatum, and posterior thalamic radiation showed significant increases in MD, RD and AxD and decreases in FA among AD patients. Females had lower MD values in certain brain regions and elder people had higher MD values in most DTI measures. Variable cluster analysis identified that hippocampus volume (HPV), mini mental state exam (MMSE), cingulate gyrus/hippocampus (CGC and CGH), inferior fronto-occipital fasciculus IFO and uncinate fasciculus (UNC) are highly correlated in one cluster with DTI measures in MD measures, suggesting these WM tracts are highly connected than other regions (such as SFO) among DTI measures in MD. In conclusion, there were significant differences in most DTI measures between AD and controls. Right cingulum gyrus and right uncinate fasciculus, are particularly affected in cognitive test MMSE for dementia in AD patients and could be the biomarker for predicting AD.

Audience Takeaway

- The findings will prompt the clinician to use DTI measure for early detection of the onset of Alzheimer's disease.
- The white matter tracts of focus based on cluster analysis are right cingulate gyrus and the right uncinate fasciculus, likely the regions triggering the conversion to AD from non-symptomatic control or mild cognitive impairment individuals.
- This research helped the view of AD from the connective point of view of the WM connectivity being the source of pathogenesis. Among the WM tracts, right hemisphere is particularly involved in macroscopic structure changes and cognitive functions including short uncinate fasciculus and the long cingulate gyrus.
- Aging is still the main risk factors associated with AD, not gender or education level.

Biography

Dr. Xiao studied Biology at Henan Normal University, China and graduated as BS in 1990. She then studied Biochemistry/Entomology at Chinese Academy of Science, Institute of Zoology, China and graduated as MS in 1993. She then studied Pharmacology at Upstate Medical University, Syracuse, USA and graduated as MS in 1997. She received her PhD of Neuroscience at Boston University, USA in 2003. After 2 year postdoctoral fellowship supervised by Dr. Bertha Madras at Harvard Medical School and 3 years postdoctoral fellowship supervised by Dr. Michale Schwarzschild at Massachussets General Hospital, USA, she obtained the Instructor position of Neurology at MGH. She then studied MRI imaging at MCPHS University, USA and graduated as BS in 2012. She then joined MCPHS and Regis College as a faculty, now Associate Professor. She has published 20 research and review articles in SCI journals.

Xiuli Yang[1,2], Deok Jeong[1,2], Enquan Xu[1,2], Harue Zhang[1,2], Valina L. Dawson[1,2,3,4,5], Hanseok Ko[1,2], Ted M. Dawson[1,2,4,5,6], Mingyao Ying[2,7], Xiaobo Mao*[1,2]

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Pathogenic α-synuclein cell-to-cell transmission mechanism and related therapeutic development

α-Synucleinopathies is characterized with accumulation of misfolded α-synuclein (α-syn), including Parkinson's disease (PD), Dementia with Lewy Bodies (DLB), and Multiple System Atrophy (MSA). Emerging evidence indicates that pathogenesis of α-synucleinopathies may be due to cell-to-cell transmission of prion-like preformed fibrils (PFF) of α-syn. We identified several receptors (Lag3, Aplp1, neurexins) that specifically bind with α-syn fibrils but not α-syn monomer. Lymphocyte-activation gene-3 (Lag3) exhibits the highest binding affinity with α-syn fibrils, and α-syn fibrils binding to Lag3 initiated pathogenic α-syn endocytosis, propagation, transmission, and toxicity. Lack of Lag3 (Lag3-/-) substantially delay α-syn PFF-induced loss of dopamine neurons, as well as biochemical and behavioral deficits in vivo. To determine the neuronal Lag3 and the function in mediating α- synucleinopathies in vivo, we obtained the neuronal Lag3 conditional knockout mice (Lag3n-/-) and found that Lag3n-/- can significantly reduce the behavioral deficits induced by α-syn PFF. Furthermore, we have generated the human dopamine neurons derived from induced pluripotent stem cells (iPSCs) and successfully generated the α-syn PFF model in human neurons. Moreover, we determined the LAG3 expression in human neurons. The LAG3 expression can be up-regulated by progerin, an aging inducer, and the higher LAG3 expression has been confirmed in aged mice compared to young mice. LAG3 inhibitors (anti-LAG3, compound) can inhibit the endocytosis of α-syn PFF and subsequent α-syn pathology propagation and toxicity. The identification of Lag3 that binds α-syn PFF provides a target for developing therapeutics designed to slow the progression of PD and related α-synucleinopathies.

Audience Takeaway

- The molecular mechanism of pathogenic α-syn cell-to-cell transmission via LAG3.
- LAG3 related therapeutic development against Parkinson's disease and related α-synucleinopathies.
- LAG3 antibody has been approved for cancer therapy, which encourage the application development in neurodegenerative disorders.

Biography

Dr. Mao received his PhD (Physical Chemistry) at the National Center for Nanoscience and Technology, Chinese Academy of Sciences in 2010. He then worked as postdoc in the labs of Profs. Drs. Ted and Valina Dawson at the Institute for Cell Engineering, Department of Neurology, Johns Hopkins School of Medicine (JHSOM) during 2010- 2016. After postdoctoral fellowship, he worked as Assistant Professor in 2017 and became Associate Professor in 2021 at JHSOM. He has published more than 50 research articles in many high-impact journals (*Science, Nature, Nature Medicine, PNAS, Nature Comm, Nano Today*) focusing on pathogenic protein cell-to-cell spreading.

Subramanian Boopathi
Universidad Nacional Autónoma de México, México

Characterization of a new molecules' inhibitor effect on alzheimer's disease amyloid - Beta peptides cascade

Over 50 million people succumbed to Alzheimer's disease (AD) worldwide. Unless scientists predict effective therapeutic strategies, this number will reach 150 million by 2050. AD is characterized by progressive neurodegeneration associated with Amyloid β (Aβ) plaques constituted by the aggregated Aβ peptides, which are produced from the transmembrane Amyloid precursor protein (APP) after being cleaved by β- and γ-secretases. In the case of the healthy brain, Aβ peptides are in monomeric forms soluble in water and are involved in brain development and protect neurons from excitotoxic cell death. In contrast, in the case of AD-affected brain, the peptides aggregate into soluble oligomers and then insoluble fibrils resulting in the formation of plaques, causing neuronal cell death and cognitive impairment such as memory loss, communication difficulties, and personality changes. Since, Aβ oligomers induced toxicity to neurons, in the present talk, I will discuss an overview of the mechanism of AD development, and how our discovery of molecule assists to improve the cognitive ability of AD mice by employing an array of studies of in-silico, in-vitro and in-vivo studies.

Keywords: Alzheimer's Disease, Amyloid peptide, drug, and AD mice

Audience Takeaway

- Audience learns the mechanism of Alzheimer's disease development.
- Audience will be benefitted by gaining knowledge of Alzheimer's disease features and drugs for the treatment of the disease, and why it will affect senior adult populations.
- We characterized new molecules that improve the cognitive ability of AD-affected mice by stopping the killing neurons by Alzheimer's peptide.

Biography

Dr. Subramanian Boopathi obtained a Ph.D. degree in Physics from Bharathiar University in 2016, and he has worked with Professor P. Kolandaivel's mentorship on Alzheimer's disease (AD) research. After that, he completed a three-year postdoctoral: one year (2016–2017) in Prof. Sihyun Ham's group at Sookmyung women's university, South Korea, and two-year (2018–2020) in Prof. Wendy Gonzalez's group at the University of Talca, Chile. Subsequently, he moved to Professor Mai Suan Li's lab at the Institute of Physics Polish Academy Science, Poland, and carried out a scientific work for six months (2018). Now, he is pursuing a third postdoctoral under the supervision of R.G.J at the University of National Autonomous of Mexico. His main field of research focuses on the intriguing feature of Alzheimer's amyloid peptide aggregation in the membrane by computer simulations. He has ten years of research in AD. He has published 18 research articles in SCI journals.

KEYNOTE FORUM

DAY 02

INTERNATIONAL ALZHEIMER'S DISEASE & DEMENTIA CONFERENCE

15-16 JUNE

Mario Allegra*, Ilenia Giardina, Alessandro Massaro, Alessandro Attanzio, Ignazio Restivo and Luisa Tesoriere

Department of Biological, Chemical and Pharmaceutical Sciences and Technologies, University of Palermo, Italy

Brain insulin resistance in alzheimer's disease : Can phytochemicals exert beneficial effects?

Overnutrition and modern diets containing high proportions of saturated fat are amongst the major factors responsible for the development of low-grade, systemic, chronic inflammation, hyperglycaemia and dyslipidaemia. These conditions may eventually lead to Insulin resistance (IR), a reduced ability of an organism to mount a normal and coordinated glucose lowering response via tissue-autonomous and crosstalk-dependent mechanisms. If established, IR predisposes affected and susceptible subjects to a cluster of metabolic disorders such as type II diabetes (T2DM) and cardiovascular diseases. Interestingly enough, recent studies started to recognize IR as a risk factor also for neurodegenerative conditions such as Alzheimer's disease (AD) and other cognitive disorders. Coherently, over 80% of AD patients have T2DM or abnormal serum glucose levels, suggesting that the pathogenic mechanisms of IR and AD might well overlap. IR, indeed, plays a crucial role in the self-feeding cycle between chronic neuroinflammation, mitochondrial dysfunction and oxidative stress responsible for amyloid β-protein deposition and aberrant tau phosphorylation. Moreover, both insulin and amyloid β-protein are metabolized by insulin degrading enzyme and defects in this enzyme can be envisaged as one of the bases for the strong association between T2DM and AD. Furthermore, AD has been demonstrated to be associated with diminished insulin receptors by nearly 80%.

In these scenarios, the molecular interconnections between neuroinflammation and IR could represent a potential therapeutic target to prevent or ameliorate neurodegeneration and cognitive impairment. Along these lines, increasing evidence suggest that improving metabolic impairments could be effective to reduce AD progression and ameliorate cognitive function. Originally considered 'health-promoting' by virtue of their radical-scavenging or direct antioxidant effects on cellular biomolecules, phytochemicals are now believed to effectively modulate the inflammatory response by intercepting reactive species at the level of critical signalling pathways. Coherently, growing evidence shows that certain dietary compounds (i.e., flavonoids, curcuminoids, stilbenes, phenolic acids, carotenoids) could play a beneficial role in neurodegenerative diseases.

This presentation aims to provide an updated vision on the impact of metabolic dysfunctions on AD with a focus on inflammation and IR as risk factors. Moreover, recent evidence on the most promising PhC-based, therapeutic interventions able to counteract AD by ameliorating and contrasting IR will also be presented.

Audience Takeaway

- Audience will get an updated vision of the mechanisms through which IR can be involved in AD development.
- The presentation is intended for scientists and physicians who work in the field of the interconnections between metabolic dysfunctions and neurodegenerative diseases.
- The content of the presentation may be useful to open new perspectives aimed to develop new plant-based, therapeutical tools.

Biography

Prof. Mario Allegra studied Chemistry and Pharmaceutical Technologies at the University of Palermo, Italy and graduated as PharmD in 1997. He then joined the research group of Prof. Perretti at the Department of Biochemical Pharmacology, Queen Mary's University of London. Since 2000 he has been working at the University of Palermo where he received his PhD in Molecular Medicine and now holds a position of Associate Professor of Biochemistry. His research interests cover the role of phytochemicals in oxidative stress-dependent inflammatory conditions. He has published more than 60 research articles in SCI(E) journals, with 4081 citations and an *h*-index of 28.

Jun Hua[1,2]

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Impaired small vessels in neurodegenerative diseases

In the brain, small pial arteries and arterioles with diameters up to 100-150 microns is the primary regulator of local tissue perfusion for the delivery of oxygen and nutrients to meet the metabolic demands from neurons and other cells. Recently, cerebral lymphatic vessels have been identified in the dura mater alongside blood vessels in the brain. These small vessels are believed to be a critical component of the Central nervous system (CNS) as a waste clearance pathway for the Cerebrospinal fluid (CSF) and Interstitial fluid (ISF), which may play a crucial role in many brain diseases. In this talk, I will first describe advanced MRI techniques that we developed for imaging small blood and lymphatic vessels in the brain. I will then discuss the application of these MRI techniques in several brain diseases to study associated neurovascular abnormalities.

Audience Takeaway

- Advanced MRI techniques for imaging small vessels in the brain; Small blood vessel abnormalities in brain diseases; Impaired cerebral lymphatic vessels in brain diseases.
- The techniques are available on mainstream clinical MRI systems that can be shared worldwide.
- Abnormalities in small blood and lymphatic vessels are commonly seen in brain disorders. Noninvasive imaging techniques can provide sensitive and specific information about such abnormalities which can be used as potential biomarkers for tracking disease progression as well as potential treatment targets for the development of novel therapeutic interventions.

Biography

Dr. Hua's research has centered on the development and application of novel MRI technologies for in vivo functional and physiological imaging in the brain. These include the development of human and animal MRI methods to measure functional brain activities, cerebral perfusion and oxygen metabolism at high (3 Tesla) and ultra-high (7 Tesla and above) magnetic fields. He is particularly interested in novel MRI approaches to image small blood and lymphatic vessels in the brain. Collaborating with clinical investigators, these techniques have been applied to detect functional, vascular and metabolic abnormalities in the brain in neurodegenerative diseases.

SPEAKERS

DAY 02

INTERNATIONAL

ALZHEIMER'S DISEASE & DEMENTIA CONFERENCE

15-16 JUNE

Esther Ebenezer

Consultant Psychiatrist and Old Age Psychiatrist Uni KL Royal College of Medicine Perak, Malaysia

Breakthrough in dementia

Alzheimer's dementia is a neurodegenerative disorder that commonly affects the elderly was first described in 1906. Since then over a century researchers and medical professionals have made remarkable advances together with various organisations and fund providers in developing novel drugs and searching for a cure.

Alzheimer's consists of two main pathologies extra-neuronal beta amyloid plaques deposits and intra-neuronal breakdown of individual neuron due to abnormal tau protein. There are other postulates like deposition of magnetic iron oxide, immune mediated process and even Human Herpes virus infection having a part in the pathogenesis of Alzheimer's dementia.

Many developed countries commonly practice the identification biomarkers such as Tau and Beta-amyloid proteins in CSF, identifying high risk gene like APOE4, functional neuroimaging rather than based on mere history. This will aid in making early diagnosis before the destruction of neurons, track the disease progression and monitor treatment effects especially in clinical trials of disease-modifying drugs.

Numerous clinical trial had been conducted to find a cure for Alzheimer's dementia but unfortunately all turned out to be not suitable. Most recently dementia prevention study using antibodies to beta amyloid and tau protein are being carried out but awaiting for the results which will be out in 2 to 5 years' time. There are still many Phase I, Phase II and Phase III studies ongoing and hope to see a breakthrough in the drug therapy for dementia.

Meanwhile it is vital to stay healthy embracing healthy lifestyle with proper diet control, exercising regularly, remain cognitively stimulated and managing the metabolic and vascular risk factors well which had shown positive cognitive outcome.

Audience Takeaway

- The progress that had come through since the terminology Alzheimer's Disease came into place since 1906.
- Developments made in the etiology, diagnosis and treatment evolved, yet adopting healthy life style is vital for everyone.

Biography

Prof. Dr. Esther Ebenezer is the Professor in Psychiatry at UniKL Royal College of Medicine Perak. She obtained her Master in Psychological medicine from University Malaya and Fellow in Old Age Psychiatry from the University of Western Australia, Perth. She started the '*Memory Clinics'* in University Malaya Medical Centre in 2004 and in Hospital Ipoh during 2006.
Prof. Dr. Esther is the Chairperson of the Dementia Society Perak since 2010 and started the state's first Dementia Daycare Centre. She is well known for her work on dementia and currently working on the *'Ipoh Model of Care for Dementia'*. She is instrumental in building Malaysia's first purpose-built person centred BebeLEC day centre for People with Dementia. Her dream is to build a Dementia Specific Residential Home. She is also an EXCO member of the Alzheimer's disease Foundation Malaysia (ADFM). She had published many articles and invited speaker for many occasions nationwide and in overseas conferences. Prof. Dr. Esther is actively involved as Principal Investigator in many research and clinical trials with new drugs for the treatment of Alzheimer's disease and other psychiatric disorders.

Anthony Pak-Hin Kong

Academic Unit of Human Communication, The University of Hong Kong, Hong Kong

Memory decline in dementia and its impact on spoken spontaneous discourse production

Memory decline and impairments occur predominantly in people with dementia (PWD). Deficits in episodic and verbal short-term memory (vSTM) have been widely reported in PWD. Analysis of spoken spontaneous discourse is becoming more popular in dementia research as well as clinical evaluation of PWD because it considers linguistic deficits with reference to cognitive demands. In particular, episodic memory is responsible for the retrieval of past information, while vSTM is required to store verbal information temporarily to continue the flow of oral discourse. At present, there is limited literature in examining the relationship between memory and discourse production in PWD or speakers with mild cognitive impairment (MCI); none of which has specifically studied Cantonese Chinese-speaking PWD. The current presentation aims to report a recent investigation of how oral discourse production varied as a function of episodic memory and vSTM in native Cantonese-speakers with dementia. Samples of personal narratives and picture description, elicited following the Cantonese AphasiaBank protocol, were included from 104 Cantonese-speaking PWD. The deficits in episodic memory among PWD were evaluated following the protocol in Seixas-Lima et al. (2021). Sub-tasks in Montreal Cognitive Assessment (MOCA) and Oxford Cognitive Screen-Plus were used to assess vSTM impairments. The discourse samples were quantified in terms of global coherence and informativeness. The final results, which echoed Western studies that had shown significant associations between memory and discourse measures, will be presented. Apart from enhancing our understanding of the role memory plays in spoken discourse, this study provided some clinical insights for managing Cantonese-speaking PWD.

Audience Takeaway

- The audience will be able to summarize spoken discourse deficits demonstrated by speakers with dementia.
- In terms of clinical practice, the audience will be able to explain the relationship between memory and spoken discourse.
- In terms of research, the audience will be able to hypothesize factors apart from memory that may impact on spoken discourse production.

Biography

Anthony Pak-Hin Kong is a professor and research scientist specialized in aphasiology at The University of Hong Kong. He is a world-renowned scholar in speech-and-language pathology and is currently Editor-in-Chief of *Cogent Gerontology* (launch in Q4 2022), Section Editor (Linguistics Section) of *PLOS ONE*, and Editorial Board Member of *Perspectives of the American Speech-Language-Hearing Association (ASHA) Special Interest Groups*. His research interests include Chinese aphasiology, discourse production and impairments, development of clinical batteries of language and cognitive disorders, and gesture production and neurogenic communication disorders in multi-lingual speakers.

Esther Ebenezer

Consultant Psychiatrist and Old Age Psychiatrist UniKL Royal College of Medicine Perak, Malaysia

Dementia care model

Malaysia is rapidly ageing with declining number of younger age groups and the young old surpassing the other older groups. As dementia is a age related neuro-degenerative disease of the brain, more and more older people will be inflicted with dementia and this silent epidemic will soon surface out.

Dementia is a progressive disease and People with Dementia (PWD) over the years they will steadily decline in their cognitive function and become much dependent on caregivers. Global Deterioration Scale (GDS) designed by Reisberg et al 1982, is a 7-point rating instrument on staging the magnitude of cognitive decline and functional disability from the point of being normal.

Strategies for dementia care should offer services comprising full range of care covering all the various stages of dementia that is mentioned in the GDS.

Public education and public awareness programs are conducted so that seemingly normal elderly and as well young adults become aware of this dreadful disease so that elderly suspected of dementia get treated at an early stage to improve the quality of life for an extended period of time.

When the disease sets in, at the early stage apart from medication various non-pharmacological measures can be implemented like 'Memory café' for the PWD to be gainfully employed under supervision. This will give them a purpose in life and a sense of wellbeing.

As the disease progresses into a mild to moderate stage dementia specific 'Day Care Centres' are very useful for the PWD to be cognitively, physically as well socially stimulated. Day centres also offer respite for the caregivers who are burnt out with caregiving and offer opportunities for the caregivers to continue working for their livelihood.

During the later stage of the disease where caregiving at home is still possible 'Dementia Home Care' team comprising of doctors and allied health workers can provide required services. When caregiving at home no longer possible then 'Dementia Specific Residential Care' becomes an essential.

Apart from delivering care for PWD, caring and supporting the caregivers who play a vital role in care giving should be upheld with support groups and necessary training programs on how to cope with the disease.

Finally, research niches on various areas of need for dementia care should be carried out not only for academic reasons but also to provide the policy makers evidence-based requirements for dementia care.

Audience Takeaway

- The world population is ageing, and dementia epidemic will become a reality in all parts of the world.
- Adequate services should be implemented to face the demands of dementia care before it becomes apparent.
- Offering services covering all through various stages of dementia will provide a holistic care for PWD.
- I was inspired by the Kumamoto Model of Care for Dementia in Japan, similarly some others would be motivated to carry out similar services.

Biography

Prof. Dr. Esther Ebenezer is the Professor in Psychiatry at UniKL Royal College of Medicine Perak. She obtained her Master in Psychological medicine from University Malaya and Fellow in Old Age Psychiatry from the University of Western Australia, Perth. She started the '*Memory Clinics*' in University Malaya Medical Centre in 2004 and in Hospital Ipoh during 2006. Prof. Dr. Esther is the Chairperson of the Dementia Society Perak since 2010 and started the state's first Dementia Daycare Centre. She is well known for her work on dementia and currently working on the '*Ipoh Model of Care for Dementia*'. She is instrumental in building Malaysia's first purpose-built person centred BebeLEC day centre for People with Dementia. Her dream is to build a Dementia Specific Residential Home. She is also an EXCO member of the Alzheimer's disease Foundation Malaysia (ADFM). She had published many articles and invited speaker for many occasions nationwide and in overseas conferences. Prof. Dr. Esther is actively involved as Principal Investigator in many research and clinical trials with new drugs for the treatment of Alzheimer's disease and other psychiatric disorders.

Rui-Yuan Pan

Beijing Institute of Basic Medical Sciences, China

Microglial energy metabolism disorder in alzheimer's disease

Neuroinflammation is a hallmark of Alzheimer's disease (AD). Microglia are the resident immune cells in the central nerves system (CNS) and function in many aspects of neuroinflammation. The immune functions of microglia such as surveillance and clearance are gradually lost along with aging and the progression of AD. However, what drives such microglial dysfunction is poorly understood. Here, we show how a positive feedback loop in microglia—comprising metabolic, histone lactylation, and transcriptional layers—drives microglial dysfunction and AD pathogenesis, and we demonstrate that inhibiting this vicious cycle in microglia can ameliorate neuroinflammation, Aβ burden and cognitive deficits in AD model mice. Specifically, we found that glycolytic pathway is abnormal activation in Aβ-associated microglia, which resulted in lactate accumulation and elevated histone lactylation (specifically detecting elevated H4K12la marks in microglia). We subsequently found that this lactate-dependent histone modification is enriched at the promoters of glycolytic genes (e.g., *Pkm*). We confirmed that this enrichment activates transcription and thereby increases glycolysis activity, and ultimately demonstrate that a glycolysis/H4K12la/PKM2 positive feedback loop exacerbates microglial dysfunction in AD. Microglia-specific ablation or pharmacologic inhibition of PKM2 attenuated microglial activation, ameliorated neuroinflammation, and improved spatial learning and memory in AD mice. Thus, beyond demonstrating a role for histone lactylation in a neurodegenerative disease and showing how multi-layered regulatory impacts attend altered glucose metabolism in microglia, our study illustrates that disrupting a positive feedback loop may support the development of innovative AD therapies.

Audience Takeaway

- Metabolism disorder is an early causal factor that drives microglial disfunction and neuroinflammation.
- Metabolic-epigenetic crosstalk regulates microglial metabolism disorder in AD.
- AD pathogenesis could be attributed to a system of positive feedback loops, rather than a liner cascade, and targeting the positive feedback loops may support the development of innovative AD therapies.

Biography

Dr. Rui-Yuan Pan studied Biological Science at the Minzu University of China and received his Ph.D. degree in Neuroscience at Institute of Biophysics, Chinese Academy of Sciences, Beijing, China in 2020. Dr. Pan is now training as a postdoctoral researcher in the Brian Science Center, Beijing Institute of Basic Medical Sciences, Beijing, China. His researches focus on the pathogenesis of AD, especially the metabolic regulation of glial functions in neurodegenerative diseases, aiming to identify targets and develop candidate drugs for the diseases. His works have been published in *Cell Metabolism, Science Advances* etc.

Juliet Stromin* and Donne Minne
Department of Psychology, University of Cape Town, South Africa

The relationship between COVID-19 severity and long-term neuropsychological outcomes

In late 2019, the world was introduced to the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) pathogen, a strain of the coronavirus which has caused the respiratory illness termed Covid-19 (coronavirus 2019; Wong, 2021). At the time of writing, there has been a reported six million deaths and approximately 445 million related cases worldwide. Common symptoms include dry cough, fever, fatigue, and shortness of breath (Almeria et al., 2020; Mao et al., 2020).

Similar with that of SARS-CoV, Covid-19 has been shown to bind to the host receptor Angiotensin converting enzyme 2 (ACE2) which is expressed in abundance in the lung on epithelial cells (Yuki et al., 2020). It is posited that Covid-19 attacks and proliferates inside these cells, causing symptoms to emerge (Maiese et al., 2021; Verstrepen et al., 2020; Wong, 2021).

Neurological symptoms have additionally been reported and, among others, include the loss of smell (anosmia) and taste, headaches, dizziness, vomiting, and confusion (Anand et al., 2020; Helms et al., 2020; Herridge et al., 2016; Mao et al., 2020; Mikkelsen et al., 2012; Montalvan et al., 2020; Troyer et al., 2020; Zangbar et al., 2021). These symptoms may be partly attributed to the findings of a recent longitudinal analysis wherein participants received brain scans prior to and post Covid-19 infection (Douaud et al., 2022). These researchers found general brain atrophy following infection.

Related complications have also arisen concerning pneumonia and acute respiratory distress syndrome (ARDS; Verstrepen et al., 2020; Wang et al., 2020; Yuki et al., 2020). Further research suggests that in cases of severe Covid-19, persons may be hospitalised with sepsis, encephalopathy, stroke, epileptic seizures, meningitis, myalgia, organ failure and cerebral hypoxia in which a person experiences oxygen loss to the brain (Almeria et al., 2020; Arentz et al., 2020; Chen, 2021; Djaharuddin et al., 2021; Guan et al., 2020; Li et al., 2020; Rothan & Byrareddy, 2020; Wu et al., 2020; Zhu et al., 2020). Unsurprisingly, there is a high infection-mortality rate with adults with pre-existing co-morbidities at highest risk (Djaharuddin et al., 2021; Nuzzo & Picone, 2020). Common risk factors appear to be hypertension, a history of cardiovascular disease and pulmonary complications (Verstrepen et al., 2020; Wang et al., 2020). It is possible, however, for those to contract the novel illness and remain asymptomatic (Iodice et al., 2021).

Furthermore, evidence suggests that the infiltration of Covid-19 can have neuropsychological effects, affecting both cognitive and psychiatric functioning (Almeria et al., 2020; Wildwing & Holt, 2021; Woo et al., 2020). Therefore, a correlational design will be conducted wherein the relationship between Covid-19 illness severity, cognitive functioning and well-being will be investigated. In doing so, the effect of self-awareness of functioning and emotion regulation will additionally be investigated. Data will be analysed using multiple regression analyses and mediation/moderation models. Results are pending.

Audience Takeaway

- Audience will be informed on the current literature surrounding Covid-19 and how infection can lead to neurological symptoms similarly found in those with forms of dementia.
- Audience will learn how Covid-19 may access the brain through multiple pathways, particularly the olfactory pathways.
- Audience will gain a greater understanding of the extent a sample of the South African population experience Covid-19.
- Audience will gain a greater understanding of the longevity of the virus and how it presents long-term.

Biography

Juliet Stromin is a current master's student at the University of Cape Town, specializing in Psychological Research with an interest in later specializing in neuropsychological practice.

J.L. Gomez-Ariza
Department of Chemistry, University of Huelva, Spain
Research Center for Natural Resources, University of Huelva, Spain

Omics methodologies for the study of pollution action on aging and alzheimer

Neurodegenerative diseases associated to aging are one of the most important social, human, family and economic problems of this century, whose etiology, pathology, early symptoms and evolution are not well known. Therefore, the development and application of new methodologies are necessary in order to be able to address the challenge of brain and the central nervous system knowledge.

Long-term exposure to air pollution, noise, and the lack of green spaces has been associated with premature mortality and other detrimental health effects, including premature aging, mental health and neurodegenerative diseases, particularly Alzheimer's disease [Nieuwenhuijsen et al, 2016]. But especially alarming is the evidence that prenatal and postnatal exposure to environmental factors predisposes to the onset of neurodegenerative diseases in adulthood. Neurotoxic metals such as lead, mercury, aluminum, cadmium, and arsenic, as well as some pesticides and metal nanoparticles, have been implicated in AD due to their ability to increase beta-amyloid peptide (Aβ) and phosphorylation of Tau protein (P-Tau), causing the senile / amyloid plaques and neurofibrillary tangles (NFT) characteristic of AD [Quintanilla-Vega et al, 2015].

Considering the metabolic mechanisms involved in the onset and prognosis of neurodegenerative processes induced by our environment. Suitable methodological tools are required for their study. From analytical point of view we can mention the following [Gómez-Ariza et al, 2021]: 1.- Analysis of traces and ultra- traces of metals and metalloids, of an essential nature (Ca, P, S, K, Na, Cl, Mg, Fe, Zn, Mn, Cu, I, Cr, Mo, Se, Co), toxic (Cd, Pb, Al), or neurotoxic (Hg, As), in tissues and biological fluids; 2.- Analysis of traces of chemical species of toxic or essential elements (Speciation): As, Hg, Se; 3.- Methodologies for the identification and analysis of metallo-biomolecules, especially metallo-metabolites and metallo-proteins (Metallomics); 4.- Methodologies for the massive characterization of metabolites altered by pathological processes (Metabolomics).

Audience Takeaway

- Emphasize the importance of the combined use of massive information analytics techniques in the study of such complex problems, such as the influence of our environment and exogenous factors on aging and the onset of Alzheimer's disease.
- The possibility of having methodological tools that allow us to establish possible markers of the aging and neuro degeneration processes, under the influence of the environment, the surroundings and life habits.
- The need to address these studies from a multidisciplinary perspective.

Biography

Jose Luis Gómez-Ariza is full professor of Analytical Chemistry and member of the Research Center for Natural Resources Health and the Environment of the University of Huelva (Spain). Member of the Spanish Society for Analytical Chemistry (SEQA) and the Academy of Sciences, Arts and Letters of Huelva. In 2003 received the Andalusia Research Award and the Huelva Industry Excellence Award. In 2022 has received the Gold Medal of the University of Huelva. He is the author or co-author of over 300 scientific publications (h-index 46), several books and book chapters, as well as over 600 contributions to scientific conferences, he also holds several patents. Over 35 students have received doctorates under his direction.

Irene Luengas-Escuza[1,2], Laura Bayón-Cordero[1,2,3], Sergio Velasco[4], Carlos Matute[1,2,3], Marta Varela[4], M.Victoria Sánchez-Gómez[1,2,3], Izaskun Buendia[2,4]* & Ashwin Woodhoo[4]

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[2]Achucarro Basque Center for Neuroscience, Leioa, Spain

[3]Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Leioa, Spain

[4]Gene Regulatory Control in Disease Laboratory, CIMUS, University of Santiago de Compostela-Instituto de Investigación Sanitaria, Santiago de Compostela, Spain

Neddylation is essential for oligodendrocyte differentiation and myelination process

The myelin sheaths that cover the axons are essential for the conduction of nerve impulses in the nervous system. In this regard, mature oligodendrocytes are the myelinating cells of the central nervous system (CNS). In recent decades, research on the mechanisms involved in myelination has generally focused on transcriptional ones, whereas post-translational ones remain mainly unknown. In this line, neddylation, an ubiquitylation-like pathway that conjugates an ubiquitin-like protein NEDD8 to target proteins, has emerged as a critical regulatory process controlling ubiquitination, protein transcription and signaling transduction. Dysregulation of neddylation has been recently linked to CNS pathological conditions, including epilepsy and multiple sclerosis. On this basis, our aim is to study the role of neddylation in oligodendrocytes and, consequently, in myelination. For this purpose, we used MLN4924 (Pevonedistat), an FDA- and EU-designated Orphan Drug, an inhibitor that acts on NAE, the initiating enzyme in the neddylation cascade. First, we studied its effect during development, by injecting MLN intraperitoneally into rats from postnatal day 7 to 15. In the brain and spinal cord of these rats, there was a significant impairment of the expression of proteins present in the membrane of myelinating oligodendrocytes, such as MBP and MAG. Likewise, in MLN-treated cortical oligodendrocyte cultures, the inhibition of neddylation caused a significant decrease in cell viability and the expression of MBP and MAG, among others. Together, these results indicate that neddylation inhibition compromises both the viability and the level of differentiation and maturation of oligodendrocytes, and may negatively affect the formation and maintenance of myelin sheaths in the CNS. These findings shed light on the post-translational mechanisms involved in myelination and lay the groundwork for future studies on the role of neddylation in degenerative diseases.

Audience Takeaway

- Neddylation is essential for not only neural development but also for glial development.
- Its disruption leads to different neurodenerative diseases.
- Neddylation can be involved in different pathological conditions discussed in the conference.
- It can be pharmacologically and genetically inhibited, affording a good tool for its study.

Biography

Dr. Buendia studied Biology at the Universidad Complutense de Madrid and performed master's studies in "Pharmacological research" at Universidad Autónoma de Madrid in 2011. After she joined the research group of Prof. G. López. In 2015 she received her PhD degree with National award. After two years of postdoctoral contract (Spanish Minsitry), when she performed two international stays in Caen, France, with independent funding's, she spent one more year there. After, she returned to Spain thanks to a postdoctoral contract from the Spanish Ministry (Juan de la Cierva Incorporación) and joined the Gene Regulatory Control in Disease Laboratory, CIMUS, led by Dr. Whoodhoo. She has published more than 35 research articles in SCI journals; she participates in the teaching activities and co-directs a PhD student.

Maria Eugenia Ariza[1,2]*, Irene Mena-Palomo[1], Brandon Cox[1], Britney Martinez[1]

[1]Department of Cancer Biology and Genetics, The Ohio State University Wexner Medical Center, USA

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The herpesviruses protein dutpase induces neuroinflammatory mediators : Implications for neurological diseases associated with infections by these viruses

We have previously reported that the dUTPase protein from human herpesvirus 6A (HHV-6A) and Epstein-Barr virus (EBV) increased the expression and secretion of pro-inflammatory cytokines from hDCs in a TLR2- dependent manner. Because IL-1 and IL-6 can disrupt the blood brain barrier (BBB) and neurocognitive functions and are elevated in patients with Alzheimer disease, we conducted time-course studies to examine whether the HHV-6A dUTPase protein could modulate the expression of genes important in maintaining BBB integrity and/or synaptic plasticity in immortalized human cerebral microvascular endothelial cells, astrocytes, and microglia cells by qRT-PCR. Treatment of human cerebral microvascular endothelial cells with HHV-6A dUTPase protein resulted in a rapid increase in IL-1β (6-fold), IL-6 (11-fold) and TNFα (215-fold) mRNA expression, beginning at 1 h after treatment and reaching maximum induction levels at 4 h (361-fold and 35-fold) for IL-1β and IL-6, respectively, and at 2 h (817.5-fold) for TNFα compared to the control. The increase in IL-1β, IL-6 and TNFα mRNA expression was accompanied by a parallel increase in TLR2 (6-fold) and NFB (11.76-fold) gene expression in these cells. Interestingly, HHV-6A dUTPase induced upregulation of VEGFA (2.4-fold), cyclooxygenase 2 (COX-2)/PTGS2 (12.46-fold) mRNA expression and downregulated the expression of genes important in maintaining BBB integrity (cingulin/CGN and β-catenin/CTNNB1) in human cerebral microvascular endothelial cells. In astrocytes, HHV-6A dUTPase treatment significantly increased IL6 (73-fold), IL-1β (3-fold), TLR2 (6.91-fold), NFB (3.56-fold) and COX2 (3-fold) mRNA expression. In microglial cells the dUTPase proteins from HHV-6A, HSV-1/2 and VZV downregulated (2.5 to 7-fold) the expression of early growth response 1 (Egr-1) gene, a key regulator of synaptic plasticity. In Summary, these studies provide exciting new data suggesting a novel mechanism by which the human herpesvirus dUTPase proteins, including HHV-6, EBV, Human simplex virus (HSV) and Varicella-Zoster virus (VZV) may modulate immune activation and alter BBB integrity as well as the structure/function of neurological synapses resulting in loss of neurocognitive functions and promoting neuronal cell death.

Audience Takeaway

- The etiologies and drivers of AD are poorly understood, and there currently no biomarkers of disease progression. Thus, there is a critical need to identify triggers and drivers of the disease. This presentation will provide exciting new data highlighting previously unexplored mechanisms by which the human herpesvirus dUTPase proteins, including HHV-6, EBV, HSV and VZV may modulate immune activation and alter BBB integrity as well as the structure/function of neurological synapses resulting in loss of neurocognitive functions and promoting neuronal cell death.
- It will raise awareness toward how select herpesvirus dUTPases could be used as a novel target for the development of alternative therapeutic approaches.
- It will also provide a platform for exploring these viral proteins as potential biomarkers and/or aid direct treatment in a subset of AD patients.

Biography

Dr. Ariza received her Bachelor degree in Biochemistry and Molecular Biology at Autonomous University of Madrid, Spain. She then joined Prof. Williams' research group at Ohio State University (USA) where she obtained her PhD degree in Medical Microbiology and Immunology. After a year postdoctoral fellowship with Prof. John Reed at The Burnham Institute she took a position as Team Leader of the anti-infective's group at Biota, Inc, California (USA). Dr. Ariza is currently an Assistant Professor at OSU working on the Immunology/ immunopathology of viral dUTPases as it relates to Alzheimer and ME/CFS. She has over 50 peer-reviewed publications and patents.

Jianrong Tang*[1,2], Shuang Hao[1,2], Qi Wang[1,2], Bin Tang[1,2], Zhenyu Wu[1,2]

[1]Department of Pediatrics, Baylor College of Medicine, USA
[2]Jan and Dan Duncan Neurological Research Institute, USA

CDKL5 deficiency augments inhibitory input into the dentate gyrus that can be reversed by deep brain stimulation

Cognitive impairment is a core feature of cyclin-dependent kinase-like 5 (CDKL5) deficiency, a neurodevelopmental disorder characterized by early epileptic seizures, intellectual disability, and autistic behaviors. Although loss of CDKL5 affects a number of molecular pathways, very little has been discovered about the physiological effects of these changes on the neural circuitry. We therefore studied synaptic plasticity and local circuit activity in the dentate gyrus of both *Cdkl5*$^{-/y}$ and *Cdkl5*$^{+/-}$ mutant mice. We found that CDKL5 haploinsufficiency in both male and female mice impairs hippocampus-dependent learning and memory in multiple tasks. *In vivo*, loss of CDKL5 reduced LTP of the perforant path to the dentate gyrus and augmented feedforward inhibition in this pathway; *ex vivo* experiments confirmed that excitatory/inhibitory input into the dentate gyrus is skewed toward inhibition. Injecting the GABAergic antagonist gabazine into the dentate improved contextual fear memory in *Cdkl5*$^{-/y}$ mice. Finally, chronic forniceal deep brain stimulation rescued hippocampal memory deficits, restored synaptic plasticity, and relieved feedforward inhibition in *Cdkl5*$^{+/-}$ mice. These results indicate that CDKL5 is important for maintaining proper dentate excitatory/inhibitory balance, with consequences for hippocampal memory.

Audience Takeaway

- Behavioral testing of learning and memory in mice.
- In vivo synaptic plasticity in freely moving mice.
- In vivo and ex vivo neural circuit analysis in the hippocampus.
- Intracranial drug infusion in mice.
- Deep brain stimulation.

Biography

Dr. Tang earned his Ph.D. in Physiology from East China Normal University in 1997 and did postdoctoral training at University of Hamburg and Max-Planck Institute of Psychiatry. He is currently an Associate Professor at Baylor College of Medicine. The Tang lab studies the neuronal- and circuit-level mechanisms that give rise to higher brain functions (e.g., memory and motor). We recently found that deep brain stimulation in the fimbria-fornix rescues hippocampal memory, synaptic plasticity, adult neurogenesis, abnormal circuit activities, and gene expression in mouse models of intellectual disability disorders. Dr. Tang has published 35 papers in SCI journals including Nature, Neuron.

Chun Xu*[1], Manuel Lee Avila[1], Mario Gil[2], Gladys Maestre[3], Kesheng Wang[4]

[1]Department or Health and Biomedical Science, University of Texas Rio Grande Valley (UTRGV), USA
[2]Department of Psychological Science,UTRGV, USA
[3]Department of Neuroscience, School of Medicine,UTRGV, USA
[4]Department of Family and Community Health, West Virginia University, USA

APOE gene associated with dementia related disorders and neuropsychiatric related phenotypes in the Hispanic/Latino population

Alzheimer's disease (AD), a main cause of dementia is known to have a strong genetic component to its development and is often comorbid with neuropsychiatric conditions. In addition, certain neuropsychiatric disorders are considered as early indicators of AD and present when there are cognitive problems that may lead to AD mainly reported in non-Hispanic/Latino populations. Therefore, we focused on investigating a known AD-related gene, APOE and social-demographic factors in associations with AD and two psychiatric diseases (depression and anxiety) in the U.S. Hispanic/Latino population.

A total of 1,382 subjects were collected from the Texas Alzheimer's Research and Care Consortium (TARCC, N=1,320) and the Initial Study of Longevity and Dementia from the Rio Grande Valley (ISLD-RGV, N=62). Questionnaires for demographics, medical history, and blood/saliva samples were collected. We genotyped the APOE gene. From the three APOE alleles, ε3 (90%), ε4 (21%), and ε2 (6%), APOE-ε4 showed significant association with AD ($p<0.0001$) in the Hispanic population. In addition, APOE ε4 allele was o associated with anxiety ($p<0.0001$), while APOE-ε3 showed an association with depression ($p=0.002$). In conclusion, we provide additional evidence in which APOE-ε4 increased the risk for AD in Hispanics. For the first time, APOE-ε4 and ε3 alleles show increased risks for anxiety and depression in Hispanics, respectively. Further research is warranted to confirm the current findings.

Future directions: in addition to genetic factors, poor lifestyle and cultural values have also been suggested to increase risk for cognitive impairment, like AD, which is our ongoing study.

Audience Takeaway

- The purpose of this study is to explore if Alzheimer's disease (AD) related APOE gene and certain social-demographic factors have associations with AD and two psychiatric diseases (depression and anxiety) in the US Hispanic/Latino population.
- The audience, for an example, for lay population, will be able to learn basic knowledge on AD related APOE gene involved in AD and psychiatric disorders. They may apply this knowledge in their daily life, and/or if they apply for jobs like genetic counseling or medical assistant.
- For faculty, they will advance the knowledge on how known AD associated gene involved in cognitive decline, AD or certain psychiatric diseases in their research and teaching. Specifically for clinic faculty, they can use the knowledge in their clinical practice such as to check if patients or family members carry AD-associated APOE e4 allele.
- For graduate or undergraduate students, they will learn knowledge how genetics and non-genetic factors involved in disease development.

Biography

Dr. Chun Xu received her MD, MSc from Harbin Medical School, and received her PhD degree from Karolinska Institute at Stockholm, Sweden. At present, she is an Associate Professor at the University of Texas Rio Grande Valley.
Dr. Xu is an educator, research scientist and is responsible for education, translational research on biomarker identification for human complex traits (e.g., neuropsychiatric disorders, neurodevelopmental disorders, autoimmune diseases, cancer, and treatment responses. Recently, she applied cutting-edge technologies for meaningful biomarker discovery for diseases and treatment responses. Aabove key findings have been published and presented at national/international conferences. She published over 70 peer-reviewed papers

POSTERS

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15-16 JUNE

Elias mazrooei rad
Khavaran Higher Education Institute, Iran

Nonlinear features of EEG and MRI for the diagnosis of mild alzheimer's disease

Alzheimer's disease is a progressive degenerative disease commonly seen in the elderly. Symptoms of this disease include memory loss, judgment and important behavioral changes in the person. The main purpose and motivation of this study was to design and present a model for the diagnosis of mild Alzheimer's disease. Due to the nature of this disease and its various stages, it is not possible to provide an optimal cognition system without proper knowledge and study. Alzheimer's disease with loss of neuronal synapses in some areas of the brain, necrosis of brain cells in different areas of the nervous system, the formation of spherical protein structures called aging plaques outside neurons in some areas of the brain, and fibrous protein structures called coils. A spiral is identified in the cell body of neurons. The disease is rapidly increasing and effective and definitive treatment depends on early detection of the disease. According to the characteristics of ERP signals, EEG and MRI images and how this disease is related to different features in brain signals and images, this disease can be diagnosed in the early stages with proper processing. In this project, brain subjects and MRI images of 40 subjects were recorded. According to the memory test, the subjects were divided into 3 groups: 19 healthy people, 10 mild patients and 9 severe patients, and the dementia test was performed separately from dementia. First, processes in the field of time and frequency and extraction of various nonlinear features such as Lyapunov view, then correlation and entropy according to the nonlinear and chaotic nature of brain signals and extraction of MRI features such as temporal lobe atrophy, white matter volume and Gray, cerebrospinal fluid and asymmetry have been performed and then the optimal features have been extracted by methods of analysis of variance, genetic algorithm and principal component analysis. Finally, Elman, SVM, and LDA classifiers have been used, and in a combined mode, two CNN classifiers and a perceptron network have been used to combine brain signals and MRI images. Been paid. The important point is that among the three channels Pz, Cz, Fz and among the four modes of closed eye, open eye, reminder and stimulation, the accuracy of Pz channel results and excitation mode is more compared to other channels and modes. Using the Pz channel characteristics and combining with the MRI image features, the accuracy of the LDA classifier performance was about 65.3% in the reminder mode and 67.4% in the excitation mode, while the accuracy of the Pz channel results was supported by the RBF core vector vector machine. In the reminder state it is 76.3% and in the stimulation state 78%, and in the Elman neural network the resolution of separation was 95.9% in the reminder state and 98.8% in the stimulation state. And in the severely ill group it is 97.5%. The use of a combination of brain signal features and MRI images reduced the accuracy of the LDA and SVM results in the three groups and increased the accuracy of Elman neural network result.

Keywords: Alzheimer's disease, EEG, MRI, Nonlinear features, Elman neural network, Deep neural network

Biography

Elias mazrooei is PhD in biomedical Engineering and a researcher in the field of Alzheimer's disease diagnosis by a combination of brain signal methods and medical images to help physicians and patients with deep learning processing methods. He is currently a faculty member and research director at the Khavaran Institute of Higher Education.

Maria Tsamou*[1], Donatella Carpi[2], Francesca Pistollato[2], Erwin L. Roggen[1]

[1]ToxGenSolutions (TGS), The Netherlands

[2]European Commission, Joint Research Centre (JRC), Italy

Search for candidate mirnas implicated in putative Adverse Outcome Pathway (AOP) relevant to sporadic alzheimer's disease

Sporadic (late-onset) Alzheimer's disease (sAD) is a progressive neurodegenerative age-related disease, caused by interaction of genetic and environmental factors, leading to brain damage accompanied by memory loss and cognitive impairment. Up till now, animal-based approaches developed to elucidate the AD-related pathophysiological mechanisms, failed to translate into effective therapeutic treatments or tools for diagnosis. In addition, existing research on AD development is mainly focused on the genetic (familial) type of AD with the most extensively studied AD-related mechanism being, amyloidopathy and tauopathy. The initiating events, needed for detection of early AD pathogenesis, remain elusive. Subsequently, the diagnosis of sAD at early stage is currently poor and inaccurate.

During the last decades, microRNAs (miRNAs) have attracted much attention due to their fundamental role in the modulation of numerous biological processes. Several human miRNAs have been implicated in neurotoxicity and AD development. Systematic literature searches revealed processes shared by neurotoxic compounds and sAD, suggesting that established novel approach methods (NAMs) developed for toxicity testing may provide insight in the early processes of sAD development.

The existing human and animal data, as well as NAMs data were structured using the adverse outcome pathways (AOPs) concept. While developed for toxicology, the AOP concept was proven to be a useful tool for collecting complex biological knowledge on diseases. Proposed AOPs for AD pathogenesis may improve the understanding of the potential chain of events, triggered by molecular initiating events and linked to adverse outcomes. A Tau-driven AOP toward memory loss has been proposed, providing a biologically plausible mechanistic approach by which possible sequential key events are described to be associated with AD pathogenesis. Chemical neurotoxicants have been also suggested as plugs-in for the AOP for memory loss. In addition, the identification of miRNAs functioning these suggested sequential events leading to memory loss may support the discovery of predictive biomarkers commonly dysregulated in both neurotoxicity and AD. Taken together, the existing data of miRNAs may provide an effective approach to understand the mechanisms underlying the AD development, even at early AD stage.

Audience Takeaway

- A proposed Tau-driven AOP for memory loss.
- Environmental induced neurotoxicity and sporadic AD may share common dysregulated processes.
- Creating miR-target interaction networks related to pathological processes involved in sporadic AD initiation and progression, and environmental chemical-induced neurotoxicity, may support the understanding of the mechanisms underlying sAD initiation and early progression.

Biography

Dr. Tsamou studied Food Science and Technology (BSc) at the Agricultural University of Athens, Greece, and Food Safety-Toxicology (MSc) at the Wageningen University, Netherlands. She worked for 3 years as junior researcher at Toxicogenomics, Maastricht University, Netherlands. She then joined the research group of Prof. Nawrot at the Centre for Environmental Sciences (CMK), Environmental Epidemiology, at Hasselt University, in Belgium, where she received her PhD degree. Since 2019 she has been working as scientific researcher at ToxGenSolutions, based in Maastricht, Netherlands. Throughout these years, she has published her research work to scientific journals.

Participants List

UPCOMING CONFERENCES

6th Edition of International Conference on

Neurology and Brain Disorders

October 24-26, 2022 | Orlando, Florida, USA

https://neurologycongress.com/

2nd International

Alzheimer's Disease & Dementia Conference

June 22-24, 2023 | Rome, Italy

https://alzheimers.magnusconferences.com

7th Edition of International Conference on

Neurology and Neurological Disorders

June 22-24, 2023 | Rome, Italy

https://neurology.magnusconferences.com

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