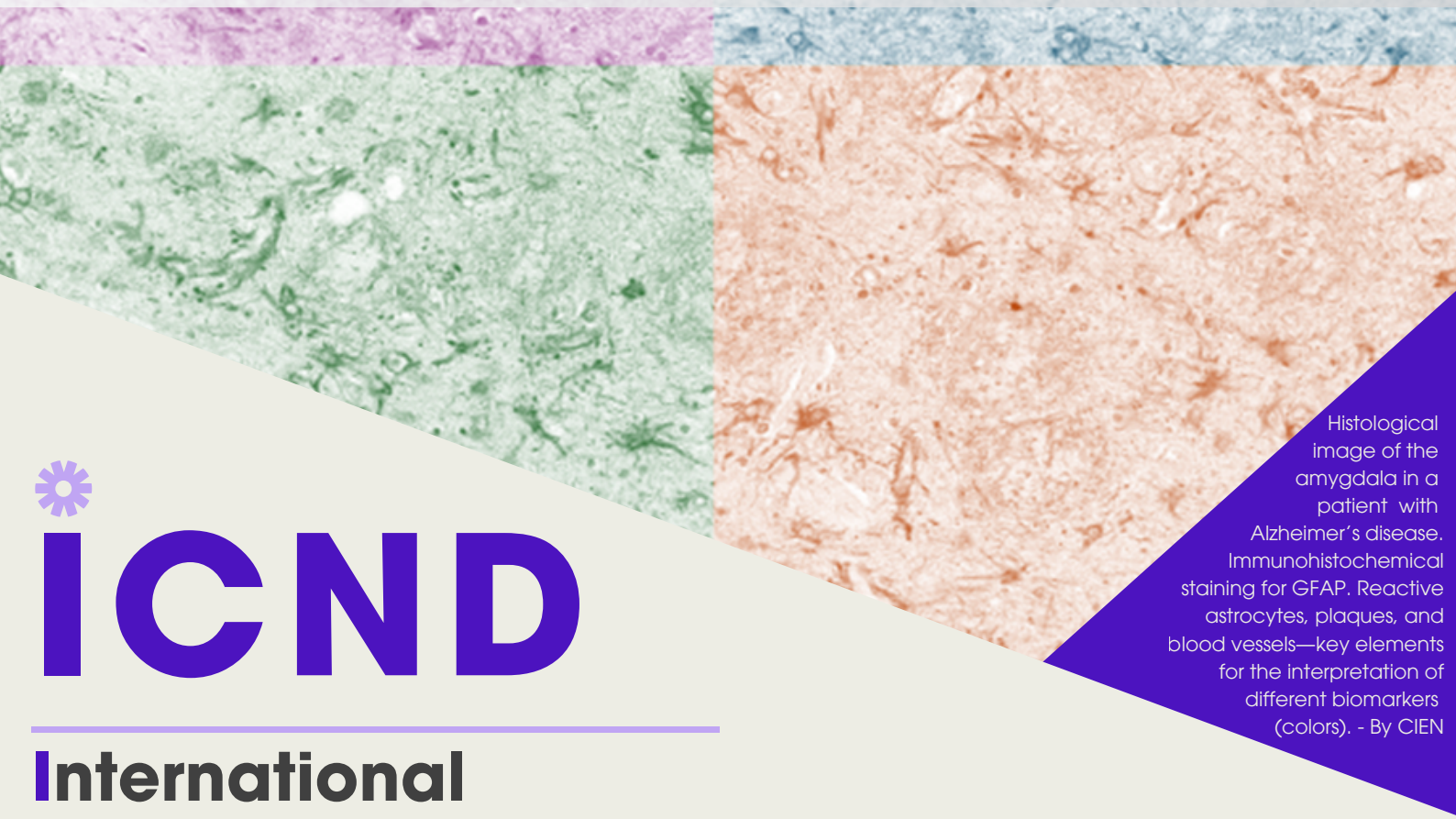
BOOK OF ABSTRACTS – 2026



Histological image of the amygdala in a patient with Alzheimer's disease. Immunohistochemical staining for GFAP. Reactive astrocytes, plaques, and blood vessels—key elements for the interpretation of different biomarkers (colors). - By CIEN

ICND

International Congress on Neurodegenerative Diseases

Biomarker-based research into neurodegenerative diseases: a new era

21-23 · SEPTEMBER · 2026

SEVILLE · SPAIN

www.ciiien.org

FUNDACIÓN REINA SOFÍA

GOBIERNO DE ESPAÑA · MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES

Instituto de Salud Carlos III

cien Fundación Centro de Investigación Enfermedades Neurológicas

NO8DO AYUNTAMIENTO DE SEVILLA

IBiS INSTITUTODEBIOMEDICINADESEVILLA

SPONSORS

Diamond Sponsor:

Lilly

Quanterix
Discovery Fueled by Ultra-Sensitivity

SIEMENS Healthineers

Platinum Sponsor:

ESTEVE

Bronze Sponsor:

Eisai

FUJIREBIO

LANTHEUS

Olink

INDEX

INDEX

SELECTED POSTER PRESENTATION & EVALUATION

The 10 pre-selected posters will be presented orally before the evaluation committee, according to the assigned dates and times.

Monday 21

16:00 - 16:30 h **Lunch & Posters**

Presentation Schedule	Title	Poster Nr.
16:00 - 16:04	Human IL-34 Deficiency Primes Microglia Toward Alzheimer's Disease-Associated States	40
16:05 - 16:09	Assessment of lncRNAs as Potential Biomarkers for Phenoconversion to Parkinson's Disease in G2019S LRRK2 Mutation Carriers	39
16:10 - 16:14	Mitochondrial DNA in blood serum as a biomarker of Lewy Body Diseases	31
16:15 - 16:19	Effect of glycation on synaptic vesicles and their interactions with α-synuclein: a potential molecular link between diabetes and neurodegeneration	17
16:20 - 16:24	Natural history and predictive factors of cerebral microbleed accumulation in cognitively unimpaired older adults	49

Tuesday 22

15:15 - 15:45 h **Lunch & Posters**

Presentation Schedule	Title	Poster Nr.
15:15 - 15:19	Targeting a Disease-Associated MicroRNA Attenuates Cognitive Deficits and Alzheimer's Disease Pathology in APP/PS1 Mice	20
15:20 - 15:24	Aged ferritin-enriched microglia exhibit a dystrophic phenotype with ultrastructural signs of metabolic dysfunction in Alzheimer's disease	54
15:25 - 15:29	Clinical implementation of plasma p-tau217 (Elecsys): post-validation performance of a dual-cutoff approach	30
15:30 - 15:34	Gamma-frequency transcranial Alternating Current Stimulation (Gamma-tACS) as potential treatment for Alzheimer disease: A preclinical study	44
15:35 - 15:39	ADAM10-regulatory microRNAs identify Alzheimer's disease and the additional metabolic burden of type 2 diabetes	29

POSTER HIGHLIGHTS SESSION

The 10 selected posters will be presented orally during the Poster Highlights Session at the assigned times.

Wednesday 23

15:00 - 16:00 h **Poster Highlights Session**

Presentation Schedule	Title	Poster Nr.
15:00 - 15:04	Longitudinal progression of brain hypometabolism patterns in autopsy-confirmed AD and LATE	45
15:05 - 15:09	Short-latency afferent inhibition tracks cholinergic basal forebrain integrity and cognitive decline in Parkinson's disease	36
15:10 - 15:14	Astrocyte reactivity-p-tau217 coupling identifies a high-risk biomarker signature in preclinical Alzheimer's disease	28
15:15 - 15:19	Disrupted Synchrony-Noise Balance as a System-Level Signature of Motor Cortex Instability in Parkinson's Disease	43
15:20 - 15:24	Serial ante-mortem MRI analysis of regional atrophy progression in autopsy-confirmed LATE-NC with hippocampal sclerosis	50
15:25 - 15:29	An NRF2-dependent lipidomic signature associates synaptic loss with TAU pathology in Alzheimer's Disease	2
15:30 - 15:34	Perivascular spaces reflect neuropathological severity of Cerebral Amyloid Angiopathy in Alzheimer's disease	35
15:35 - 15:39	Myeloid cell CD300f R218Q variant enhances phagocytosis and is associated with milder Alzheimer's disease pathology	41
15:40 - 15:44	Multimodal characterization of cognitively declining individuals with normal plasma p-tau217 levels	47
15:45 - 15:49	Dynamic remodeling of SUMO-1ylation across the central nervous system and peripheral compartments during Alzheimer's disease progression	52

BOOK OF ABSTRACTS 2026

POSTER N.º 1

Introduced by: Mariana da Silva Passarini

Title:

ABSCISIC ACID AS A NATURAL IMMUNOMODULATOR AGAINST NEUROINFLAMMATION AND IMMUNE-MEDIATED NEURONAL DAMAGE

First Author: Mariana da Silva Passarini

Authors: Mariana da Silva Passarini[a], Ania Canseco-Rodríguez[a], Ana María Sánchez-Pérez[a]

Filiation: [a]Department of Medicine, Universitat Jaume I, Avda Sos Banyat S/N, Castelló de la Plana 12071, Spain

Abstract:

Neuroinflammation is a common feature of neurodegenerative diseases, where sustained activation of microglia and infiltrating macrophages contributes to neuronal dysfunction and disease progression. Abscisic acid (ABA), a natural phytohormone, has shown beneficial effects in preclinical models of Alzheimer's and Parkinson's disease, including restoration of microglial morphology, reduction of neuroinflammation and improvement of behavioral deficits. However, the cellular mechanisms behind these effects remain unclear. In this work, we investigated how ABA affects different cellular components of the neuroimmune response under inflammatory conditions.

Human HMC3 microglial cells and murine RAW264.7 macrophages were pretreated with ABA prior to lipopolysaccharide (LPS) stimulation. In stimulated HMC3 cells, ABA altered the metabolome secretome, suggesting a shift towards a less inflammatory phenotype. In stimulated RAW264.7 macrophages, ABA preserved cell viability, reduced nitric oxide production and modulated phagocytic activity.

Next, we evaluated ABA potential to protect neurons from inflammatory ambience, to that end differentiated SH-SY5Y neuron-like cells were pretreated with ABA and exposed to stimulated immune cultures conditioned media.We observed that ABA- reduced neuronal oxidative stress and preserved dendritic morphology in differentiated SH-SY5Y cells, indicating a protective action on neuronal cells.

Taken together, our findings indicate that ABA modulates neuroimmune responses and reduce immune-mediated neuronal damage, by independent mechanisms. These results support ABA as a natural immunomodulator and reinforce its potential as a therapeutic molecule for neurodegenerative diseases.

POSTER N.º 2

Introduced by: Ana I Rojo

Title:

AN NRF2-DEPENDENT LIPIDOMIC SIGNATURE ASSOCIATES SYNAPTIC LOSS WITH TAU PATHOLOGY IN ALZHEIMER'S DISEASE

First Author: Daniel Carnicero-Senabre

Authors: Daniel Carnicero-Senabre[abcd], Marta Olazabal-Chias[abcd], Marko Kratochvil[abcd], Maribel Escoll[abcd], Angel J García-Yagüe[abcd], Antonio Cuadrado[abcd], Ana I Rojo[abcd]

Filiation: [a]Instituto de Investigaciones Biomédicas Sols-Morreale (CSIC-UAM), Madrid, España, [b]Departamento de Bioquímica, Facultad de Medicina, Universidad Autónoma de Madrid, Madrid, España, [c]Instituto de Investigación Sanitaria Hospital Universitario La Paz (IdiPAZ), Madrid, España, [d]Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Madrid, España

Abstract:
Synaptic loss is a major contributor to cognitive decline during aging and neurodegenerative diseases such as Alzheimer's disease (AD), where synaptopathy plays a central role in hippocampal dysfunction. In this study, we investigated the role of NRF2, a master regulator of cellular homeostasis, in preserving synaptic integrity in hAPP(V717I)/hTAU(P301L) (AT) mice. In vivo analysis revealed that NRF2 deficiency leads to a significant reduction in vGLUT1 and PSD95 levels, accompanied by a decrease in the number of synaptic contacts. Given the dynamic membrane remodeling that characterizes synapses, we analyzed the lipid composition of synaptosomes from AT-NRF2-KO and AT-NRF2-WT littermates. Our results showed an accumulation of ceramides and ether-linked lipids in AT-NRF2-deficient mice. Notably, untargeted lipidomic analysis identified more than 200 dysregulated lipid species in the plasma of NRF2-deficient animals, enabling the generation of an NRF2-associated lipid signature (NRF2-score). This score was subsequently validated in the AT model, where it robustly reflected NRF2-dependent lipidic alterations and correlated with synaptic dysfunction. Importantly, translational analyses revealed that synaptopathy-associated lipid alterations were mirrored in plasma, including increased levels of ceramides and ether lipids. Furthermore, in a pilot study of plasma samples from AD patients, the NRF2-score enabled stratification of individuals according to their plasma pTAU217 levels measured by SIMOA, discriminating subjects with high versus low TAU pathology burden. These findings demonstrate that NRF2 plays a critical role in maintaining synaptic integrity in AD and identify a lipid-based biomarker signature with potential translational value for patient stratification and disease monitoring. The candidate panel of dysregulated lipids identified here warrant validation in larger clinical cohorts.

BOOK OF ABSTRACTS 2026

POSTER N.º 3

Introduced by: Juan Antonio García León

Title:

ASTROCYTES IN ALZHEIMER´S DISEASE DEVELOP A SENESCENT STATE WHICH IMPACTS THEIR NEURONAL SUPPORT

First Author: Juan Antonio García León

Authors: Juan Antonio García León[a], Laura Caceres Palomo[bc], Laura Trujillo-Estrada[a], Juan Jose Perez-Moreno[d], Elba Lopez-Oliva[a], Alberto Pascual[e], Javier Vitorica[f], Antonia Gutierrez[a]

Filiation: [a]Department of Cell Biology, Genetics and Physiology, Faculty of Sciences. University of Malaga. IBIMA-Plataforma Bionand. CIBERNED. Malaga, Spain. [b]Department of Cell Biology, Genetics and Physiology, Faculty of Sciences. University of Malaga. IBIMA-Plataforma Bionand. CIBERNED. Malaga, Spain. [c]Current address: Achucarro Basque Center for Neuroscience, Leioa, Spain. [d]Department of Cell Biology, Faculty of Biology, University of Seville. IBiS-University Hospital Virgen del Rocio/CSIC/University of Seville. CIBERNED. Seville, Spain. [e]Instituto de Biomedicina de Sevilla (IBiS)-Hospital Universitario Virgen del Rocio, CSIC/Universidad de Sevilla. CIBERNED. Sevilla, 41013, Spain. [f]Department of Biochemistry and Molecular Biology, Faculty of Pharmacy, University of Seville. IBiS-University Hospital Virgen del Rocio/CSIC/University of Seville. CIBERNED. Seville, Spain.

Abstract:

Background:

Alzheimer's disease (AD) is characterized by a complex pathology, not fully resolved yet. This fact, together with the lack of reliable models, has impeded the development of effective therapies. Glial cell dysfunction has been proposed to be involved in AD pathogenesis, but this cannot be properly modeled using the available animal models, so we hypothesized that cells derived from AD patients can serve as a better platform for studying the disease. In this sense, human pluripotent stem cells (hPSC) allow the generation of different types of neural cells, which can be used for disease modeling, identification of new targets and drugs development.

Methods:

We have generated hiPSC-derived astrocytes from AD patients and cognitively unimpaired age-matched individuals and evaluated their metabolism and phenotype employing confocal imaging immunofluorescence, electron microscopy, flow cytometry, RT-qPCR, transcriptomics and functional assays.

Results:

All astrocytes expressed functional markers including aldehyde dehydrogenase 1A1 (ALDH1A1), glutamate transporter GLAST, glial fibrillary acidic protein (GFAP), aquaporin-4 (AQP4) and vimentin. However, astrocytes from AD patients showed increased expression of reactive markers. In addition, these astrocytes showed a senescent phenotype determined by the expression of specific markers and at the transcriptome level. When co-cultured with hiPSC-derived neurons, senescent astrocytes provided poorer neuronal support.

Conclusions:

Our data suggest that astrocytes derived from AD patients present an intrinsic pro-inflammatory and senescent phenotype which compromise their functionality. Elucidating the mechanisms inducing these processes and their functional consequences should help for a better understanding of role that astrocytes play in AD, by direct functioning and also through their interactions with neurons and the other glial cells. This should lead to the identification of potential therapeutic targets for future AD treatments.

Acknowledgments:

This study was supported by Instituto de Salud Carlos III (ISCiii) of Spain, co-financed by FEDER funds from European Union, through grants and PI24/00274 (to AG) and PI24/00308 (to JV); by CIBERNED (to AG and JV); by Junta de Andalucia through grants UMA20-FEDERJA-048 (to JAGL) and PPRO-CTS950-G-2023 (to AG) co-financed by Programa Operativo FEDER.

POSTER N.º 4

Introduced by: Marta Alaiz-Noya

Title:

CHRONIC STEROID SULFATASE INHIBITION NORMALIZES STRIATAL BIOENERGETICS AND IMPROVES COGNITION IN THE R6/1 HUNTINGTON'S DISEASE MODEL

First Author: Marta Alaiz-Noya

Authors: Marta Alaiz-Noya[ab], Elena Rodríguez-Sandoval[b], Juan Antonio Fernández-Cabrera[ab], María Camacho-Cabrera[c], Leopoldo Pérez-Rosendo[c], Sandra Gavalda[a], Ángel Cebolla-Ramírez[a], Alejandro Martín-Montalvo[cd], Daniel Zamanillo[a], Ángel Carrión[b]

Filiation: [a]Olavide Neuron STX (ONESTX). Seville, Spain, [b]Dpt. Physiology, Anatomy and Cellular biology, University of Pablo de Olavide. Seville, Spain, [c]Andalusian Center for Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucia-University of Pablo de Olavide-University of Seville-CSIC, Seville, Spain, [d]Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Madrid, Spain

Abstract:
Huntington's disease (HD) has no curative or disease-modifying treatment; current management is purely symptomatic. Steroid sulfatase (STS) inhibition increases sulfated neurosteroid availability, and these neurosteroids regulate neuronal excitability, calcium homeostasis, and contribute to neuroprotection, making STS a plausible therapeutic target. We evaluated the STS inhibitor LON-21 (STX64/irosustat) in the R6/1 HD mouse model, examining both its behavioral effects and its impact on mitochondrial function in the striatum. Male and female R6/1 mice and wild-type (WT) littermates received LON-21-supplemented diet at two doses for 4 months, after which a behavioral battery assessed cognitive and motor function. Brain STS activity was measured to confirm target engagement, and mutant huntingtin (mHTT) expression and additional disease biomarkers were characterized in the same animals. In a separate cohort treated for 6 weeks, ex vivo mitochondrial bioenergetics — oxygen consumption rate and extracellular acidification rate — were assessed in fresh striatal slices by Seahorse analysis. LON-21 improved cognitive performance in R6/1 mice, most consistently in fear conditioning and, in females, in 24-hour novel object recognition, alongside reduced brain STS activity confirming target engagement. In striatal slices, R6/1 vehicle mice showed altered mitochondrial bioenergetics relative to WT, and LON-21 normalized this profile to WT-like values with no effect in healthy tissue, indicating a state-dependent action. These results support chronic STS inhibition as a disease-modifying strategy for HD, acting on both cognitive and cellular bioenergetic deficits.

BOOK OF ABSTRACTS 2026

POSTER N.º 5

Introduced by: Innas Ouled Chaara

Title:

CSPα/DNAJC5 MAINTAINS NIGROSTRIATAL DOPAMINERGIC TERMINALS

First Author: Innas Ouled Chaara

Authors: Innas Ouled Chaara[ab], Nozha Borjini[ac], Rafael Fernández Chacón[ac]

Filiation: [a]Instituto de Biomedicina de Sevilla (IBiS, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla), Dpto. de Fisiología Médica y Biofísica, Facultad de Medicina, Seville. [bc]Centro Investigación en Red Enfermedades Neurodegenerativas (CIBERNED), Instituto de Salud Carlos III (ISCIII), Spain.

Abstract:

Dopaminergic neurons of the substantia nigra pars compacta (SNc) possess highly elaborate axonal arborizations that generate thousands of synaptic terminals throughout the dorsal striatum. Together with long unmyelinated axons and sustained pacemaker-dependent Ca^{2+} influx, this architecture imposes considerable energetic and proteostatic demands that may contribute to the selective vulnerability of these neurons in Parkinson's disease (PD). Cysteine String Protein α (CSPα; encoded by DNAJC5) is a synaptic vesicle–associated co-chaperone that maintains presynaptic proteostasis by stabilizing SNARE complexes and preventing synaptic degeneration. Although CSPα has been implicated in α-synuclein homeostasis and synaptic maintenance, its role in the integrity of nigrostriatal dopaminergic terminals remains unclear. Here, we investigated the consequences of CSPα deficiency on the nigrostriatal pathway. Global CSPα knockout mice exhibited a significant reduction of tyrosine hydroxylase–positive (TH^+) terminals in the dorsal striatum by postnatal day 30. This pathology was accompanied by microgliosis, astrogliosis, increased microglial CD68 expression, and internalization of TH^+ particles by microglia, consistent with active phagocytic clearance of degenerating dopaminergic terminals. To assess cell-autonomous effects, we generated conditional Dnajc5flox/flox mice expressing Cre recombinase under the Th promoter. Conditional mutants survived to adulthood but displayed impaired motor coordination on the rotarod and a reduction in striatal TH^+ terminals. These alterations were evident at 3 and 6 months of age and persisted in mice aged 12 months. Together, our findings identify CSPα as a critical presynaptic chaperone required for the long-term maintenance of nigrostriatal dopaminergic terminals. Loss of CSPα compromises dopaminergic axon integrity and motor function, highlighting impaired presynaptic proteostasis as a potential mechanism contributing to Parkinsonian neurodegeneration.

Acknowledgements: We thank Dr. Lin Gao and Dr. José López Barneo for advice and for sharing the TH-Cre mice and Dr. Patricia González-Rodríguez for advice. Supported by Spanish Agencia Estatal de Investigación and Ministerio de Ciencia, Innovación y Universidades (MICIU) and European Regional Development Fund (ERDF), (MICIU/AEI /10.13039/501100011033, FEDER, UE) project PID2022-138957NBI00 and FPI contract PRE2022-000660, the Andalusian Consejería de Salud y Consumo (RH-0064-2021), Plan Propio de Investigación de la Universidad de Sevilla Contrato Acción II.4 PPIT and the Spanish Instituto de Salud Carlos III (ISCIII).

BOOK OF ABSTRACTS 2026

POSTER N.º 6

Introduced by: Nozha Borjini

Title:

EPILEPSY IN A MOUSE MODEL OF CLN4 (KUFS DISEASE)

First Author: Nozha Borjini

Authors: Nozha Borjini[ab], Santiago López-Begines[ab], Rafael Fernández-Chacón[ab]

Filiation: [a]Instituto de Biomedicina de Sevilla (IBiS, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla), Dpto. de Fisiología Médica y Biofísica, Facultad de Medicina, Seville, [b]Centro Investigación en Red Enfermedades Neurodegenerativas (CIBERNED), Instituto de Salud Carlos III (ISCIII), Spain

Abstract:

Autosomal-dominant adult-onset neuronal ceroid lipofuscinosis (CLN4), originally known as Kufs disease, is a rare genetic disorder and a severe form of neuronal ceroid lipofuscinoses (NCL) that affects the nervous system. The neuronal accumulation of autofluorescent material (lipofuscin) and the ultrastructural detection of granular osmiophilic deposits (GRODs) are the major neuropathological hallmarks of the disease. We havereported in our recently published work (López-Begines, Borjini et al., Sci. Adv. 2025), that mutant CSPα mice reproduced these hallmarks and showed peri-microglial lipofuscin with occasional microglial engagement of lipofuscin-positive material. Building on these findings, the present study focused on epileptiform vulnerability by administering a single kainic acid challenge to Thy1-GFP-CSPα-L115R mice and NTC littermates. Mutant mice displayed a pronounced seizure phenotype, including higher seizure frequency, increased total seizure time, and longer individual events, confirmed by event-level raster plots. Post-kainic acid hippocampal analyses revealed increased cFOS expression reflecting heightened neuronal activity, together with elevated lipofuscin-561 signal. Staining for Synaptobrevin-2, a presynaptic vesicle protein, showed treatment-dependent alterations in the CA3 region, suggesting changes in synaptic integrity or presynaptic organization. Additionally, glial panels showed GFAP upregulation in astrocytes and Iba1 labeling in microglia, consistent with reactive gliosis triggered by kainate and potentially amplified in the CSPα-L115R background. These convergent neuronal, synaptic, and glial responses indicate that CSPα-L115R expression heightens activity-dependent seizure susceptibility and modulates downstream cellular stress pathways. All immunostaining results (Synaptobrevin-2, GFAP, Iba1, CSPα, cFOS) represent preliminary data supporting ongoing analyses in this model.

BOOK OF ABSTRACTS 2026

POSTER N.º 7

Introduced by: Francisco Vaquer Jiménez

Title:
IRON CHELATION BY PHYTATE (IP6) AND ITS IMPACT ON THE OXIDATIVE DEGRADATION OF NEUROTRANSMITTERS

First Author: Francisco Vaquer Jiménez

Authors: Francisco Vaquer Jiménez[abc], Miguel Adrover Estelrich[abc], Maria del Pilar Sanchís Cortés[abc], Bartolomé Vilanova Canet[abc]

Filiation: [a]Interdisciplinary Group on Neurodegeneration, Vascular and Metabolic Diseases (INNoVAM), Departament de Química, Universitat de les Illes Balears, Ctra. Valldemossa km 7.5, E-07122 Palma de Mallorca, Spain, [b]Health Research Institute of the Balearic Islands (IdISBa), Ctra. Valldemossa 79, 07010, Palma de Mallorca, Spain, [c]Institut Universitari d'Investigació en Ciències de la Salut (IUNICS), Universitat de les Illes Balears, Ctra. Valldemossa km 7.5, E-07122 Palma de Mallorca, Spain

Abstract:
Altered iron homeostasis and associated oxidative stress are key factors in the pathogenesis of various neurodegenerative diseases, where accumulated free metal catalyses the degradation of essential neurotransmitters. Therefore, we study here the chelating capacity of phytate (IP6) on iron Fe(III) and its protective effect against the oxidative degradation of catechol (dopamine and adrenaline) and non-catechol neurotransmitters (serotonin, histamine, and adenosine). Using UV-Visand NMR spectroscopies we demonstrate that catecholamines are highly prompt to undergo Fe(III)-oxidative degradation. In addition, we prove that IP6 effectively inhibits dopamine and adrenaline degradation by competing for iron coordination. To validate these findings in vivo, a model of 40 rats distributed into four groups supplied with: i) control; ii) phytate; iii) iron; or iv) iron and phytate overload diets was used. We then analyzed the prefrontal cortex, hippocampus, and striatum by LC-MS/MS. Results in brain tissue confirmed that phytate supplementation prevents the decrease in neurotransmitter levels induced by iron excess. In conclusion, IP6 acts as a potent neuroprotective agent capable of mitigating oxidative stress and preserving cellular neurochemical integrity, positioning itself as a promising therapeutic strategy against neurodegeneration associated with pathological iron accumulation.

BOOK OF ABSTRACTS 2026

POSTER N.º 8

Introduced by: Virginio García-Martínez

Title:
PHOSPHO-TAU 217 AND PHOSPHO-TAU 181 OVERPRODUCTION INDUCED BY ACUTE 3-NITROPROPIONIC ACID ADMINISTRATION IN THE RAT CEREBELLUM IS PREVENTED BY KAEMPFEROL ADMINISTRATION

First Author: Virginio García-Martínez

Authors: Virginio García-Martínez[ab], Virginio García-López[abc], Dorinda Marques-da-Silva[de], Carlos Gutiérrez-Merino[b], Carmen López-Sánchez[ab]

Filiation: [a](1) Human Anatomy and Embryology Department, Faculty of Medicine and Health Sciences, University of Extremadura, 06006 Badajoz, Spain, [b](2) Institute of Molecular Pathology Biomarkers, University of Extremadura, 06006 Badajoz, Spain, [c](3) Department of Medical and Surgical Therapeutics, Pharmacology Area, Faculty of Medicine and Health Sciences, University of Extremadura, 06006 Badajoz, Spain, [d](4) School of Technology and Management, Polytechnic Institute of Leiria, Morro do Lena, Alto do Vieiro, 2411-901 Leiria, Portugal, [e](5) LSRE-LCM and ALiCE–Associate Laboratory in Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal

Abstract:
It has been previously demonstrated that 3-nitropropionic acid (NPA) originates neurological alterations in the striatum, hippocampus and vicinal motor and pre-motor cortical areas, and in the cerebellum, coinciding with those found in Huntington's disease. In previous works, we have shown that intraperitoneal administration of kaempferol can efficiently protect against striatum degeneration and against motor neurological dysfunctions induced by NPA. In the present work, we have experimentally evaluated the hypothesis that kaempferol (a natural antioxidant present in vegetables and fruits used in human nutrition) protects both against the amyloid β overproduction and the rise of phospho-Tau 217 and phospho-Tau 181 in the rat cerebellum induced by acute 3-nitropropionic acid administration. For this purpose, we have administered NPA and kaempferol intraperitoneal injections to adult Wistar rats following our protocol described in previous work. Cerebellar slices were used for 2,3,5-triphenyl tetrazolium chloride (TTC) staining, hematoxylin–eosin staining, Nissl staining, Congo Red staining, immunohistochemistry and Western blots. Our results show that intraperitoneal administration of kaempferol protects against the increase in pro-inflammatory cytokines that potentiate the activation of complement C3 protein (a biomarker of A1-type reactive astrocytes generation) and overproduction of neurotoxic amyloid β (Aβ) peptides in the cerebellum in NPA-treated rats. Interestingly, we show that kaempferol also protects against the NPA-induced increase in phospho-tau 217 and phospho-tau 181 in the cerebellum, and our results pointed out that the NPA-induced phospho-tau 217 colocalizes with Aβ(1-42) more closely than phospho-tau 181, both in dentate nucleus and cerebellar cortex. In conclusion, the results of this work show a potent protection of kaempferol against the NPA-induced increase in degeneration biomarkers in the cerebellum.
Funding: This work has been financed in part with research grant from the Junta de Extremadura. The project has been 85% co-financed by the European Union, the European Regional Development Fund, and the Regional Government of Extremadura. Managing Authority: Ministry of Finance.GR24140. (CTS005) to C.L.-S; and LSRE-LCM and ALiCE centers, supported by Fundação para a Ciência e a Tecnologia, I.P./MCTES through Portuguese national funds: UID/50020/2025 (DOI: 10.54499/UID/50020/2025) and LA/P/0045/2020 (DOI:10.54499/LA/P/0045/2020) to D.M.-S.

BOOK OF ABSTRACTS 2026

POSTER N.º 9

Introduced by: Rita Scarcello

Title:

SUMO-DEPENDENT REGULATION OF ATAXIN-7 IN AN IN-VITRO MODEL OF SPINOCEREBELLAR ATAXIA TYPE 7

First Author: Rita Scarcello

Authors: Rita Scarcello[ab], Marco Cimino[b], Rachele Marino[ab], Corinna Giorgi[b], Valentina Tirelli[c], Rita Maccarone[a], Marco Feligioni[bd]

Filiation: [a]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy. [b]EBRI Rita Levi-Montalcini Foundation, Rome, Italy. [c]Core Facilities, Istituto Superiore Di Sanità, Rome, Italy. [d]Casa di Cura Igea - Department of Neurorehabilitation Sciences, Milan, Italy

Abstract:

Spinocerebellar ataxia type 7 is a rare neurodegenerative disease caused by expression of expanded CAG-repeats in Ataxin-7 protein. This mutation promotes formation of nuclear inclusions that sequester variety of cellular proteins, including key components of SUMOylation pathway. While recent studies have started to elucidate SUMO-2/3 role in ATXN7 aggregation, involvement of SUMO-1 has yet to be clarified.

The aim of this study is to investigate the reciprocal interaction between SUMO-1 and ATXN7.

HEK-293T cells were transfected with GFP-tagged ATXN7 constructs carrying either 10 (wild-type) or 113 (mutant) CAG repeats, alone or together with mCherry-SUMO-1 and HA-SUMO-2. Protein localization, interactions, and aggregation were subsequently evaluated by Immunofluorescence (IF), Proximity ligation assay (PLA), Dot blot, and Western blot.

ATXN7-113Q formed significantly more intranuclear inclusions than the wild-type protein, reflecting polyglutamine length–dependent toxicity, as confirmed by soluble/insoluble fractionation. These aggregates preferentially colocalized with SUMO-1, whereas SUMO-2/3 association was reduced. Biochemical assays revealed reduced ubiquitination together with an elevated LC3-II/LC3-I ratio, consistent with altered protein degradation. While individual SUMO-1 or SUMO-2 overexpression had no effect, their combined expression significantly decreased ATXN7-113Q aggregation, suggesting cooperative regulation of proteostasis carried out by SUMOs proteins.

Our results show that mutant ATXN7 leads to the accumulation of insoluble aggregates that sequester SUMO-1, reduced protein ubiquitination, and altered autophagic activity. Importantly, co-expression of SUMO-1 and SUMO-2, but not either paralog alone, attenuated ATXN7-113Q aggregation, supporting a cooperative role for SUMO proteins in maintaining proteostasis and limiting mutant ATXN7 toxicity.

BOOK OF ABSTRACTS 2026

POSTER N.º 10

Introduced by: Rachele Marino

Title:

SUMOYLATION-MEDIATED CONTROL OF TDP-43 LOCALIZATION AND STABILITY: A POTENTIAL MECHANISM IN ALS

First Author: Rachele Marino

Authors: Rachele Marino[ab], Rita Scarcello[ab], Corinna Giorgi[b], Albert Acewicz[c], Tomasz Stępień[c], Rita Maccarone[d], Marco Feligioni[ef]

Filiation: [a]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, 67100 L'Aquila, Italy, [b]European Brain Research Institute - Rita Levi Montalcini Foundation, 00161 Rome Italy. [c]Department of Neuropathology, Institute of Psychiatry and Neurology, Warsaw Poland, [d]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, 67100 L'Aquila, Italy. [e]European Brain Research Institute - Rita Levi Montalcini Foundation, 00161 Rome Italy. [f]Department of Life Science, Health, and Health Professions, Link Campus University, Rome Italy

Abstract:
Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterized by progressive motor neuron degeneration in which toxic cytoplasmic TDP-43 aggregates are the main pathological hallmark in ~97% of cases. During disease progression, TDP-43 undergoes nuclear depletion and cytoplasmic mis-localization, often associated with stress granule (SG) formation. Post-translational modifications (PTMs), particularly SUMOylation, are emerging as key regulators of TDP-43 function, but their role remains unclear. This study investigated the role of SUMO1 and SUMOylation in regulating TDP-43 localization, stability, and aggregation under physiological and oxidative stress conditions. Using SH-SY5Y neuroblastoma cells, oxidative stress induced by sodium arsenite promoted TDP-43 cytoplasmic re-localization, aggregation, and colocalization with SGs, accompanied by reduced SUMO1 expression. Co-immunoprecipitation revealed a SUMO1/TDP-43 interaction under basal conditions that was disrupted upon stress, concomitant with reduced SUMOylation, decreased nuclear TDP-43, and increased cytoplasmic levels. SUMOylation was associated with the soluble, non-aggregated fraction of TDP-43, whereas it was nearly absent in the insoluble fraction. A non-SUMOylable TDP-43 mutant (K136R), a conjugation-deficient SUMO1 variant (□C4), and SUMO1 knockdown (via shRNAs) all promoted TDP-43 aggregation and cytoplasmic mis-localization. Interestingly, global SUMOylation progressively decreased in PBMCs from ALS patients with disease progression. Consistently, post-mortem ALS brain tissue showed reduced neuronal SUMO1 levels in association with TDP-43 aggregates compared with healthy controls. Overall, our findings demonstrate that SUMO1-mediated SUMOylation is a critical regulator of TDP-43 nuclear retention and stability. Its impairment promotes TDP-43 mis-localization and aggregation, supporting a mechanistic role in ALS pathogenesis and highlighting SUMOylation as a potential therapeutic target.

BOOK OF ABSTRACTS 2026

POSTER N.º 11

Introduced by: Asmae Benchohra

Title:

UNMASKING ALZHEIMER'S ASSOCIATED PATHOLOGICAL AGEING IN MICE MODELS THROUGH DIFFERENTIAL BIOINFORMATIC ANALYSIS OF MALDI-MSI DATA

First Author: Asmae Benchohra

Authors: Asmae Benchohra[abcd], Francisco Sancho-Bielsa[ebcd], Lydia Giménez-Llort[fg], Francisco Javier Alcaín[ebcd], Javier Frontiñan Rubio[ebcd], Mario Durán Prado[ebcd]

Filiation: [a]Applied Molecular Studies in Health Sciences Group, Medical School, University of Castilla-La Mancha, Ciudad Real, Spain, [b]Department of Medical Sciences, Medical School, University of Castilla-La Mancha, Ciudad Real, Spain, [c]IB, University of Castilla-La Mancha, Albacete, Spain, [d]IDISCAM, Toledo, Spain. [e]Oxidative Stress and Neurobiology Group, Medical School, University of Castilla-La Mancha, Ciudad Real, Spain, [f]Department of Psychiatry and Forensic Medicine, Faculty of Medicine, Universitat Autònoma de Barcelona, Bellaterra, Spain, [g]Institut of Neurocience, Faculty of Medicine, Universitat Autònoma de Barcelona, Bellaterra, Spain

Abstract:
Distinguishing physiological brain ageing from Alzheimer's-associated pathological ageing remains a major challenge, as age-related molecular alterations often obscure disease-specific changes. Additionally, matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI) generates thousands of peptide-mass tags (PMTs) whose biological identities remain unknown and must be determined to translate data into biomarkers. Here, we present an integrated framework to discriminate between physiological and AD-associated pathological ageing. Starting from 11,001 PMTs from the hippocampus and cortex of female 3xTg-AD mice and age-matched wild-type controls at 6 and 12 months, we implemented a biologically motivated sequential filtering strategy. PMTs significantly differing between genotypes at 6 months were excluded to remove early disease-associated alterations. The remaining PMTs were retained only if they significantly changed between 6 and 12 months in either genotype and discriminated wild-type and AD mice at 12 months, reducing the dataset to 42 candidate PMTs in the hippocampus and 133 in the cortex. Candidate PMTs were assigned to putative proteins by in silico peptide matching, while ambiguous annotations were resolved by complementary prioritisation based on mass accuracy and protein interaction networks. Candidate proteins were ranked by their Disease Effect and classified as high-, moderate-, or low-Disease Effect proteins. Representative high- (DNAH17) and low- (GEN1) Disease Effect proteins were selected for immunofluorescence validation. Immunofluorescence confirmed the predicted downregulation of DNAH17 in the hippocampus and GEN1 in the cortex of 12-month-old AD mice, validating the computational prioritisation. Collectively, this framework systematically allows obtaining PMTs into biologically validated biomarker candidates of Alzheimer's-associated pathological ageing.

BOOK OF ABSTRACTS 2026

POSTER N.º 12

Introduced by: Cynthia Campos Moreno

Title:

CONNECTING THE PERIPHERY WITH THE BRAIN: THE ROLE OF THE VISCERAL ADIPOSE TISSUE IN TAU PATHOLOGY

First Author: Cynthia Campos Moreno

Authors: Cynthia Campos Moreno[a], Miriam Bettinetti Luque[a], Juana Andreo López[a], Mario Morales Cabello[a], Ian Perea Santaella[a], Laura Trujillo Estrada[a], Antonia Gutiérrez Pérez[a], Melissa García Caballero[a], Iván Durán Jiménez[a], Raquel Sánchez Varo[b], David Baglietto Vargas[a]

Filiation: [a]Faculty of Sciences, University of Málaga

Abstract:
Alzheimer's disease (AD) is a complex neurodegenerative disorder, in which multiple cellular and molecular mechanisms are taking place. Recent evidence suggests that metabolic alterations are a determining factor in the pathogenesis of this dementia. Furthermore, diabetes and obesity, two major metabolic diseases, constitute risk factors for AD. Both diseases are associated with an expansion in size and a functional alteration of visceral adipose tissue (VAT). In this study, we hypothesize that VAT dysregulation induced by obesity or diabetes could act as a key mediator of the impact of these metabolic diseases on AD pathogenesis. To investigate our hypothesis, we employed histological staining, immunohistochemical techniques, and biochemical assays to determine changes in the VAT of diabetic/obese mice compared to WT control mice. In addition, we performed adipose tissue transplants from db/db (diabetic and obese) mice and animals maintained on a Western diet into 3xTg-AD and Tau P301S mice, respectively. Our study demonstrates that both 3xTg-AD mice and Tau P301S mice that received fat from obese/diabetic animals, exhibit a significant increase in tau pathology and neuroinflammation. This increase in tau pathology was associated with elevated levels of IL-1β and microglial activation, reflecting the involvement of the immune system. This study highlights the importance of peripheral metabolic alterations and their role in the progression of Alzheimer's disease, and the significant contribution of the active immune response to mediate this effect.
Acknowledgments: This work has been funded by the Ministry of Science and Innovation (PID2019-108911RA-100 and PID2024-161545OB-100), the Alzheimer's Association (project AARG-22-928219), IBIMA Bionand Platform grant INTAR25-11, the University of Malaga's Own Plan B1-2021_32 and PPRO-B2-2026-04, and the Carlos III Health Institute (project PI21/00915 and CIBERNED) co-financed with ERDF funds from the European Union and by the Junta de Andalucía (CTS-950).

BOOK OF ABSTRACTS 2026

POSTER N.º 13

Introduced by: Desire Humanes-Valera

Title:

STRIATAL ASTROGLIOSIS IN MOUSE MODELS OF TOP-DOWN CORTICOSTRIATAL OVERACTIVITY AND SYNUCLEINOPATHY

First Author: Desire Humanes-Valera

Authors: Desire Humanes-Valera[a], Miryam Moreno-Gomez[b], Adolfo A. García-Galache[c], Jesús Pardo-Valencia[c], Noelia Mercado-García[a], Beatriz Pro-Sánchez[a], Marta Gutiérrez-Fernández[a], Ana Revuelto-González[d], Tiziano Balzano[a], Javier Blesa[e], Claudia Ammann[a], Analía Bortolozzi[f], José A. Obeso[g], Guglielmo Foffani[h]

Filiation: [a]HM CINAC (Centro Integral de Neurociencias Abarca Campal), Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain. Instituto de Investigación Sanitaria HM Hospitales. [b]HM CINAC (Centro Integral de Neurociencias Abarca Campal), Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain.Universidad Autónoma de Madrid, Madrid, Spain.Instituto de Investigación Sanitaria HM Hospitales. [c]HM CINAC (Centro Integral de Neurociencias Abarca Campal), Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain. Universidad Politécnica de Madrid, Madrid, Spain. Instituto de Investigación Sanitaria HM Hospitales. [d]HM CINAC (Centro Integral de Neurociencias Abarca Campal), Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain. Universidad Complutense de Madrid, Madrid, Spain. Instituto de Investigación Sanitaria HM Hospitales. [e]HM CINAC (Centro Integral de Neurociencias Abarca Campal), Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain. CIBERNED, Instituto Carlos III, Madrid, Spain. Instituto de Investigación Sanitaria HM Hospitales. [f]Institut d'Investigacions Biomèdiques de Barcelona, Spain. [g]HM CINAC (Centro Integral de Neurociencias Abarca Campal), Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain. Universidad CEU-San Pablo, Madrid, Spain. CIBERNED, Instituto Carlos III, Madrid, Spain. Instituto de Investigación Sanitaria HM Hospitales. [h]HM CINAC (Centro Integral de Neurociencias Abarca Campal), Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain Reina Sofia Foundation Alzheimer Center, CIEN Foundation, ISCIII, Madrid, Spain. Instituto de Investigación Sanitaria HM Hospitales

Abstract:

The prevailing theory about the pathogenesis of Parkinson's disease postulates a bottom-up propagation of Lewy pathology from the periphery to the central nervous system, reaching sensorimotor cortical areas only at the latest stages of the disease. However, mounting evidence suggests that both pathological and neurophysiological alterations are already evident in the sensorimotor cortex of patients since the earliest prodromal stages. According to our cortical pathogenic theory, these early cortical alterations may add a top-down mechanism to the onset and progression of the disease. Here we developed mouse models of top-down corticostriatal overactivity and synucleinopathy. Specifically, we injected viral vectors in the sensorimotor cortex to chronically increase corticostriatal activity with chemogenetics and to overexpress alpha-synuclein in corticostriatal projections. These corticostriatal manipulations induced a subtle but structured increase in spontaneous motor behavior, with partially dissociable effects on locomotor activity and directional bias, together with robust astrogliosis in the dorsal striatum ipsilateral to the injected cortex, in absence of overt striatal dopaminergic degeneration. This astroglial response was robust across biological and experimental conditions and was spatially localized to the caudal dorsomedial striatum, consistent with the projection field of the targeted sensorimotor cortex. Cortical alterations can thus act as an early top-down corticostriatal stressor, which may be relevant for the pathogenesis of Parkinson's disease and related synucleinopathies.

BOOK OF ABSTRACTS 2026

POSTER N.º 14

Introduced by: Natalia del Rey-Díez

Title:

SINGLE-CELL RESOLUTION ANALYSIS OF SEX DIFFERENCES IN THE HUMAN BRAIN IN ALZHEIMER'S DISEASE

First Author: Natalia del Rey-Díez

Authors: Natalia del Rey-Díez[abc], Cristina Galiana-Roselló[ba], María de la Iglesia-Vayá[a], Francisco García-García[ba]

Filiation: [a]Joint Unit of Biomedical Imaging and Artificial Intelligence FISABIO-CIPF, Foundation for the Promotion of Health and Biomedical Research in the Valencian Region, Valencia, Spain. [b]Computational Biomedicine Laboratory, Principe Felipe Research Center (CIPF), Valencia, Spain. [c]PhD Program in Biotechnology, Universitat Politècnica de València (UPV), Valencia, Spain

Abstract:
Alzheimer's disease (AD), the most common cause of dementia, presents an evident sexual dimorphism in its prevalence, prognosis, and progression. Women are diagnosed with AD more frequently than men and, once diagnosed, decline cognitively at a faster rate. This clinical disparity is well documented, but its cellular and molecular basis in the hippocampus, one of the main brain regions involved in memory impairment in AD, remains poorly understood. Here, we determined which hippocampal cell populations are differentially affected by sex in AD, using single-nucleus transcriptomics to move beyond bulk-tissue observations and identify the cellular origin of sex-aware vulnerability. We assembled a large harmonized single-nucleus RNA sequencing cohort of human hippocampal samples from AD patients and cognitively healthy controls (over one hundred samples), drawn from public repositories. After quality control, processing, and integration of all datasets, we performed a consensus annotation of the major cell types in the hippocampus using various strategies. Next, we calculated the statistical power for each annotated cell type and performed a sex-stratified differential expression analysis for each of them. The integrated atlas allowed us to identify the main neuronal and non-neuronal populations of the human hippocampus, while minimizing batch effects derived from the datasets and preserving the underlying biological structure. The differential analysis revealed transcriptional programs associated with sex and disease status, identifying cell-type-specific molecular alterations that could explain women's greater vulnerability to AD.
Keywords: Alzheimer's disease (AD), single-nucleus RNA sequencing, sex differences

BOOK OF ABSTRACTS 2026

POSTER N.º 15

Introduced by: Elena Rodríguez Sandoval

Title:

DREAM INHIBITION MITIGATES AGE-RELATED NEURODEGENERATION AND ALZHEIMER'S DISEASE PATHOLOGY

First Author: Elena Rodríguez Sandoval

Authors: Elena Rodríguez Sandoval[a], Inés Sánchez Romero[a], Juan Antonio Fernández Cabrera[a], José Manuel Hernández Curiel[a], Francisco Hernández Rasco[b], Cristina Muriana Fernández[a]

Filiation: [a]Universidad Pablo de Olavide, [b]Universidad de Sevilla

Abstract:
Aging causes a widespread decline in cognitive, sensory, and motor functions, increasing vulnerability to neurodegenerative disorders like Alzheimer's disease (AD). The protein DREAM regulates key neuronal processes, including excitability, gene expression, and cellular stress responses. Our laboratory findings link DREAM deficiency to cognitive improvement during aging, along with increased adult neurogenesis compared to age-matched wild-type mice.
To investigate the involvement of DREAM in AD pathology, genetic and pharmacological (repaglinide [RPG]) inactivation of DREAM was applied to two distinct AD models: 1) an acute model induced by intrahippocampal beta-amyloid oligomers, and 2) the classical APP/PS1 transgenic model.
Our findings demonstrate that both genetic and pharmacological blockade of DREAM delays the onset of neurodegeneration in aged mice and Alzheimer's disease models.
These differences in DREAM expression were further validated in human cohorts, including AD patients, age-matched cognitively unimpaired controls, and superagers.
To achieve this, published gene expression datasets from studies utilizing single-cell RNA sequencing and bulk RT-qPCR were compiled and analyzed using R.

BOOK OF ABSTRACTS 2026

POSTER N.º 16

Introduced by: Sergio Bocanegra Mata

Title:

EARLY REGENERATIVE RESPONSE IN THE AXOLOTL STRIATUM (AMBYSTOMA MEXICANUM) AFTER EXCITOTOXIC INJURY INDUCED BY QUINOLINIC ACID

First Author: Sergio Bocanegra Mata

Authors: Sergio Bocanegra Mata[a], Rodrigo Erick Escartín Pérez[b], Felipe Vaca Paniagua[b], Juan Carlos Martínez Lazcano[c]

Filiation: [a]UNAM, INNN, [b]UNAM, [c]INNN

Abstract:

Neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and Huntington's disease are associated with neuroinflammation, excitotoxicity, and progressive neuronal loss. During inflammatory responses in the central nervous system, activation of the tryptophan–kynurenine pathway leads to the production of quinolinic acid (QUIN), an endogenous NMDA receptor agonist capable of inducing excitotoxic neuronal damage. In contrast, the axolotl (Ambystoma mexicanum) exhibits a remarkable capacity for nervous system regeneration, making it a valuable model for studying mechanisms of neural damage and repair.

The aim of this study was to establish and characterize an excitotoxic striatal injury model in A. mexicanum through the administration of QUIN. Molecular docking analyses suggested a potential interaction between QUIN and the NR2B subunit of the NMDA receptor. A stereotaxic surgical procedure was standardized using external anatomical landmarks to generate localized striatal lesions. Behavioral, histological, and molecular assessments were performed 48 hours after injury.

Behavioral analysis revealed alterations in locomotor activity and behavioral organization in QUIN-treated animals compared with intact and vehicle-treated groups. Histological evaluation using Nissl staining demonstrated morphological changes and alterations in cellular density within the injured striatal region. In addition, preliminary Western blot analysis of GAD67 suggested changes in GABAergic neurotransmission following excitotoxic injury. Together, these findings support the successful establishment of a reproducible neurochemical lesion model in the axolotl striatum.

This experimental platform provides a useful approach for investigating the early cellular and molecular responses associated with excitotoxic injury, neurodegeneration, and regeneration in the central nervous system. Ongoing transcriptomic analyses will further contribute to the identification of molecular pathways involved in tissue damage and regenerative processes, providing insights that may be relevant to understanding mechanisms of functional recovery in neurodegenerative disorders.

BOOK OF ABSTRACTS 2026

POSTER N.º 17

Introduced by: Melina Salazar Osorio

Title:

EFFECT OF GLYCATION ON SYNAPTIC VESICLES AND THEIR INTERACTIONS WITH A-SYNUCLEIN: A POTENTIAL MOLECULAR LINK BETWEEN DIABETES AND NEURODEGENERATION

First Author: Melina Salazar Osorio

Authors: Melina Salazar Osorio[a], Rodrigo Casasnovas Perera[a], Laura Mariño Perez[a]

Filiation: [a]Universidad de las Islas Baleares

Abstract:

Type 2 diabetes mellitus (T2DM) is associated with an increased risk of Parkinson's disease (PD), but the molecular mechanisms linking both disorders remain unclear. Glycation by reactive dicarbonyls such as methylglyoxal (MG) may modify synaptic membrane lipids and α-synuclein (αS), potentially impairing vesicle trafficking and neurotransmitter release.

We combined experimental biophysical approaches with all-atom molecular dynamics simulations. Glycation kinetics were monitored by fluorescence spectroscopy using DOPS vesicles as a simplified membrane model, while glycation products were characterized by high-resolution mass spectrometry in neuronal-like POPE:POPS:POPC (5:3:2) vesicles. Simulations examined a neuronal membrane interacting with the N-terminal 37-residue fragment of αS under native, protein-glycated, and protein-plus-membrane-glycated conditions.

DOPS vesicles required a tenfold higher MG concentration than αS (50 versus 5 mM) to reach a comparable apparent glycation rate, suggesting greater susceptibility of αS under the tested conditions. Mass spectrometry identified carboxyethylated POPE and POPS and, notably, methylglyoxal-derived phospholipid dimers connecting two aminophospholipids. To our knowledge, these phospholipid–phospholipid cross-links have not been previously reported and included POPE–POPE and POPS–POPS homodimers and a POPE–POPS heterodimer. Simulations showed that protein glycation alone had a limited effect on αS–membrane association, whereas inclusion of membrane glycation caused markedly stronger disruption and complete αS detachment. These findings identify intermolecular phospholipid cross-linking as a novel outcome of synaptic membrane glycation and suggest that membrane modification may be a major determinant of altered αS–membrane interactions, linking metabolic dysfunction in diabetes to synaptic impairment and neurodegeneration.

BOOK OF ABSTRACTS 2026

POSTER N.º 18

Introduced by: Clara García-Mayor

Title:

MICROGLIA REPLACEMENT TO MODULATE NEUROINFLAMMATION IN ALZHEIMER'S DISEASE

First Author: Clara García-Mayor

Authors: Clara García-Mayor[abc], Julio Viñuales-García[ab], Clara Muñoz-Castro[abc], Nicolás Capelo-Carrasco[abc], Sebastián Jiménez-Muñoz[abc], María Manfredi-Lozano[ab], Vicente Roca-Agujetas[abc], Alberto Pascual[a], Antonia Gutiérrez[dc], Marisa Vizuete[abc], Javier Vitorica[abc]

Filiation: [a]Hospital Universitario Virgen del Rocio/CSIC/University of Seville, Instituto de Biomedicina de Sevilla (IBiS), Seville, Spain. [b]University of Seville, Department of Bioquímica y Biología Molecular, Seville, Spain. [c]Centro de Investigacion Biomedica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain. [d]University of Malaga/Instituto de Investigacion Biomedica de Malaga (IBIMA), Department of Biologia Celular, Genetica y Fisiologia, Malaga, Spain

Abstract:

Microglia are the main primary immune cells of the brain and play important homeostatic functions that seem to be lost in neurodegenerative diseases, including Alzheimer's Disease (AD). In our laboratory, we have observed a microglial degenerative process in the hippocampus of AD patients. Besides, persistent microglial activation has been described in AD transgenic mice, which leads to a chronic neuroinflammatory environment in the brain. In recent years, microglial depletion approaches in mouse models have provided new insights into the role of these cells in physiological and pathological conditions. In this regard, our group has performed a pharmacological microglial depletion treatment with PLX3397, a CSF1R inhibitor, in old APP-mice models of AD. In agreement with other reports, we observed that microglial depletion is followed by a rapid and complete repopulation. Our results showed that these emerging microglia are less activated but appear to fulfil the functions of the resident microglia. Although we didn't see any differences in the plaque burden or the number of dystrophic neurites, we did observe a reduction in the main inflammatory cytokines. Additionally, the behavioural tests performed have shown a tendency towards improvement in the cognitive decline of these AD mice. All in all, this study sheds some light on our understanding of microglia in a disease context and test whether microglial renewal approaches could be a promising therapeutic strategy for neurodegenerative diseases.

BOOK OF ABSTRACTS 2026

POSTER N.º 19

Introduced by: Kamila Drzazga

Title:

PAR-2 RECEPTOR PLAYS PIVOTAL ROLE IN P. GINGIVALIS INFECTION OF CEREBRAL MICROVASCULAR ENDOTHELIUM

First Author: Kamila Drzazga

Authors: Kamila Drzazga[ab], Małgorzata Benedyk-Machaczka[a], Jan Potempa[a]

Filiation: [a]Department of Microbiology, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Kraków, Poland. [b]Doctoral School of Exact and Natural Sciences, Jagiellonian University

Abstract:

In recent years there have been increasing number of studies linking periodontal disease with higher occurrence of Alzheimer's disease and its severity. One of the major pathogens responsible for acute periodontitis and comorbidities is Porphyromonas gingivalis. Those bacteria produce many virulence factors including gingipains – cysteine proteases with specificity to arginine (Rgp) or lysine (Kgp). Although it has been reported that P. gingivalis and its virulence factors can be present in brains of Alzheimer's patients as well as in animal in vivo models, the mechanism behind is still not clear. To access the CNS bacteria have to bypass the blood brain barrier (BBB), which is not only a physical barrier but also molecularly selective and patrolled by immune cells. This work focuses on the role of protease-activated receptor 2 (PAR-2) in initial stages of P. gingivalis infection of murine microvascular endothelium, one of the cell type building the BBB. PAR-2 is a transmembrane, G-protein coupled receptor that releases tethered ligand upon proteolytic activation and is a target for gingipains cleavage. Its activation is permanent until receptor degradation in the cell, which points to promising mechanism behind bacterial infection.

Isolated murine microvascular endothelial cells (WT and Par2ko) were infected with the wild-type W83 strain or its gingipains-null mutant strain ΔKRAB. The results show that gingipains facilitated the adhesion and internalization of P. gingivalis into brain microvascular endothelial cells in a PAR2-dependent manner. Second, gingipain-dependent infection perturbed the transcriptional landscape of tight junction, adhesion molecules and inflammatory factors through PAR2 signalling. Lastly, gingipains affected cells morphology and integrity through tight junctions proteins degradation.

BOOK OF ABSTRACTS 2026

POSTER N.º 20

Introduced by: Miren Ettcheto

Title:

TARGETING A DISEASE-ASSOCIATED MicroRNA ATTENUATES COGNITIVE DEFICITS AND ALZHEIMER'S DISEASE PATHOLOGY IN APP/PS1 MICE

First Author: Mireia Millet-Sigalat

Authors: Mireia Millet-Sigalat[abcd], Leila Driouech[ace], Judit Chamorro-Duran[f], Marina Carrasco[abcg], Ester Verdaguer[bce], Carme Auladell[bce], Antoni Camins[abcg], Jordi Olloquequi[bcd], Miren Ettcheto[abcg].

Filiation: [a]Department of Pharmacology, Toxicology and Therapeutic Chemistry, Faculty of Pharmacy and Food Science, Universitat de Barcelona. Barcelona, Spain. [b]Biomedical Research Networking Center in Neurodegenerative Diseases (CIBERNED), Instituto de Salud Carlos III, Madrid, Spain. [c]Institute of Neuroscience, Universitat de Barcelona, Spain. [d]Department of Biochemistry and Physiology, Faculty of Pharmacy and Food Science, Universitat de Barcelona. Barcelona, Spain. [e]Department of Cellular Biology, Physiology and Immunology, Faculty of Biology, Universitat de Barcelona, Barcelona, Spain. [f]Department of Pharmacology, Toxicology and Therapeutic Chemistry, Faculty of Pharmacy and Food Science, Universitat de Barcelona. Barcelona, Spain. [g]Institut d'Investigació Sanitària Pere Virgili (IISPV), Reus, Spain.

Abstract:

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive decline and memory impairment. It is hallmarked by amyloid plaque deposition and neurofibrillary tangles, while neuroinflammation, synaptic dysfunction and oxidative stress play key roles in its pathophysiology, highlighting its multifactorial nature. Therefore, identifying novel therapeutic targets capable of modulating multiple pathological processes remains a major challenge. Recent studies have reported dysregulated microRNA (miRNA) expression in different tissues of AD patients, identifying miRNAs as promising biomarkers and therapeutic targets. Previous work from our group demonstrated that miR-X is overexpressed in SH-SY5Y cells following β-amyloid exposure. Based on these findings, the present study aimed to evaluate the role of miR-X in AD progression and to assess its therapeutic potential.

Five-month-old male APPswe/PS1dE9 (APP/PS1) mice were treated for 1.5 months with vehicle (CT), anti-miR-X (A-X), or a negative control miRNA inhibitor (CT-miR). Cognitive performance was evaluated through behavioral tests, while molecular and histopathological alterations associated with AD were also analyzed.

Treatment with anti-miR-X improved learning and memory performance in APP/PS1 mice and attenuated neuroinflammation, as demonstrated by reduced microglial and astrocytic reactivity. These beneficials effects were accompanied by increased dendritic spine density in the hippocampus and a reduced β-amyloid plaque burden in both the cortex and hippocampus.

Overall, these findings support a potential role for miR-X in AD development and highlight its therapeutic potential as a novel target to attenuate cognitive deficits and neuropathological hallmarks of the disease.

BOOK OF ABSTRACTS 2026

POSTER N.º 21

Introduced by: Carmen López-Sánchez

Title:

THE ACTIVATION OF COMPLEMENT C3 PROTEIN AND THE GENERATION OF REACTIVE A1 ASTROCYTES THAT MEDIATE RAT BRAIN DEGENERATION, INDUCED BY 3-NITROPROPIONIC ACID, ARE PREVENTED BY KAEMPFEROL ADMINISTRATION

First Author: Carmen López-Sánchez

Authors: Carmen López-Sánchez[ab], Virginio García-López[abc], Carlos Gutiérrez-Merino[b], Virginio García-Martínez[ab]

Filiation: [a]Human Anatomy and Embryology Department, Faculty of Medicine and Health Sciences, University of Extremadura, 06006 Badajoz, Spain. [b]Institute of Molecular Pathology Biomarkers, University of Extremadura, 06006 Badajoz, Spain. [c]Department of Medical and Surgical Therapeutics, Pharmacology Area, Faculty of Medicine and Health Sciences, University of Extremadura, 06006 Badajoz, Spain

Abstract:
The natural antioxidant kaempferol is present in vegetables and fruits used in human nutrition. We have previously shown that intraperitoneal kaempferol administration strongly protects against striatum neurodegeneration induced by intraperitoneal injections of 3-nitropropionic acid (NPA), an animal model of Huntington's disease. Additionally, we have demonstrated that reactive A1 astrocytes generation constitutes an early event in the neurodegeneration induced by NPA intraperitoneal injections. In the present work, we have experimentally evaluated the hypothesis that kaempferol protects both against the activation of complement C3 protein and the generation of reactive A1 astrocytes in rat brain striatum and hippocampus. For that, we have administered NPA and kaempferol intraperitoneal injections to adult Wistar rats following the protocol described by us in previous work. Samples were analyzed by using TTC (2,3,5-triphenyl tetrazolium chloride) staining, Western blotting, immunohistochemistry and TUNEL staining. Our results reveal that kaempferol administration prevents proteolytic activation of complement C3 protein and generation of reactive A1 astrocytes NPA-induced in the striatum and hippocampus. Also, it blocked the NPA-induced increase of NF-κB expression and enhanced secretion of cytokines IL-1α, TNFα, and C1q, which have been linked to the generation of reactive A1 astrocytes. In addition, kaempferol administration prevented the enhanced production of amyloid β peptides in the striatum and hippocampus, a novel finding in NPA-induced brain degeneration found in this work.
Funding: This work has been financed in part with research grant from the Junta de Extremadura. The project has been 85% co-financed by the European Union, the European Regional Development Fund, and the Regional Government of Extremadura. Managing Authority: Ministry of Finance.GR24140. (CTS005) to C.L.-S.

BOOK OF ABSTRACTS 2026

POSTER N.º 22

Introduced by: Jorge Sáez Leyva

Title:

THE α-SECRETASES ADAM10 AND ADAM17 ARE INCREASED IN PLASMA OF COVID-19 PATIENTS

First Author: Jorge Sáez Leyva

Authors: Jorge Sáez Leyva[ab], Juan García-Arriaza[cd], Oscar Moreno-Pérez[efg], Esperanza Merino[egh], María-Salud García-Ayllón[abi], Javier Sáez-Valero[abe]

Filiation: [a]Instituto de Neurociencias de Alicante, Universidad Miguel Hernández-CSIC, San Juan de Alicante, Spain. [b]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), San Juan de Alicante, Spain. [c]Department of Molecular and Cellular Biology, Centro Nacional de Biotecnología (CNB), Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain. [d]Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Madrid, Spain. [e]Instituto de Investigación Sanitaria y Biomédica de Alicante (ISABIAL), Alicante, Spain. [f]Endocrinology and Nutrition Department, Dr. Balmis General University Hospital, Alicante, Spain. [g]Clinical Medicine Department, Universidad Miguel Hernández, Elche, Spain. [h]Infectious Diseases Unit, Dr. Balmis General University Hospital, Alicante, Spain. [i]Unidad de Investigación, Hospital General Universitario de Elche, FISABIO, Elche, Spain.

Abstract:

ADAM10 and ADAM17, members of the membrane-bound disintegrin and metalloproteinase (ADAM) family, act as α-secretases in the non-amyloidogenic processing of the amyloid precursor protein and therefore have a potential role in Alzheimer's disease (AD). Both α-secretases also mediate the processing of angiotensin-converting enzyme 2 (ACE2), the cellular receptor for SARS-CoV-2. During viral entry, TMPRSS2, the spike-priming protease of SARS-CoV-2, may compete with ADAM10 and ADAM17 for ACE2 processing. ACE2 cleavage has been proposed to enhance viral infectivity; however, the relevance of protease activation during acute COVID-19 remains unclear. In this study, we investigated whether the plasma levels of ADAM10, ADAM17, TMPRSS2 and ACE2 are altered in patients with moderate or severe COVID-19 from the first wave of the pandemic. We used electrophoresis and Western blotting to quantify the active forms of these proteases, which coexist in circulation with their inactive species. We also examined their levels in the serum of transgenic K18-hACE2 mice challenged with a lethal dose of SARS-CoV-2. In both COVID-19 patients and infected K18-hACE2 mice, we observed increased levels of ACE2 fragments, together with an overall increase in the levels of all three proteases. However, analysis of the active protease species revealed that only ADAM10 and ADAM17 exhibited increased activation, whereas the increase in TMPRSS2 was not accompanied by a corresponding increase in its active proteolytic fragment. These findings indicate that ADAM10 and ADAM17 are upregulated during COVID-19, suggesting coordinated regulation. In contrast, our recent findings indicate that ADAM10, but not ADAM17, is downregulated during AD pathogenesis.

BOOK OF ABSTRACTS 2026

POSTER N.º 23

Introduced by: Michelle Estefanía Guamán Chulunchana

Title:

BLOOD-BASED BIOMARKERS AS PREDICTORS OF LONGITUDINAL COGNITIVE DECLINE AND HIPPOCAMPAL ATROPHY -THE VALLECAS STUDY:

First Author: Michelle Estefanía Guamán Chulunchana

Authors: Michelle Estefanía Guamán Chulunchana[a], Linda Zhang[b], Francisco Javier López-González[c], Sonia Wagner Reguero[b], Minerva Martinez Castillo[b], Ana Belén Pastor[a], Nekane Moreno[a], Andrea Ruiz-Calvo[a], Cristina Sánchez-Martín[d], Eva Alfayate[d], Marta Molero-Cartón[d], Elizabeth L. Valeriano-Lorenzo[e], Belén Frades-Payo[e], Meritxell Valentí[e], María Ascensión Zea-Sevilla[e], Alexis Moscoso Rial[f], Alfredo Ramirez[g], Pamela Martino-Adami[g], Steffi G. Riedel-Heller[h], Martin Scherer[i] , Andreas Jeromin[j], Miguel Calero[k], Michel J. Grothe[l], Anja Schneider[m], Teodoro Del Ser[e], Aitana Sogorb-Esteve[a], Jesús Silva-Rodríguez[d], Pascual Sánchez-Juan[n]

Filiation: [a]Department of Biomarkers, Biochemistry and Molecular Genetics, CIEN Foundation, Queen Sofia Foundation Alzheimer Center, ISCIII, Madrid, Spain. [b]CIEN Foundation, Queen Sofia Foundation Alzheimer Center, ISCIII, Madrid, Spain. [c]Bioinformatics department, CIEN Foundation, Queen Sofia Foundation Alzheimer Center, ISCIII, Madrid, Spain. [d]Neuroimaging department, CIEN Foundation, Queen Sofia Foundation Alzheimer Center, ISCIII, Madrid, Spain. [e]Clinical evaluation department, CIEN Foundation, Queen Sofia Foundation Alzheimer Center, ISCIII, Madrid, Spain. [f]Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden. [g]University Hospital Cologne, Cologne, Germany. [h]Institute of Social Medicine, Occupational Health and Public Health, University of Leipzig, Leipzig, Germany. [i]Department of Primary Medical Care, Center for Psychosocial Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. [j]Tau Biosciences, Inc, Carlsbad, CA, USA. [k]Chronic Disease Programme (UFIEC), Instituto de Salud Carlos III, Madrid, Spain. [l]Neuroimaging department, CIEN Foundation, Queen Sofia Foundation Alzheimer Center, ISCIII, Madrid, Spain. [m]DZNE, Germany. [n]Scientific Director, CIEN Foundation, Queen Sofia Foundation Alzheimer Center, ISCIII, Madrid, Spain

Abstract:

Early identification of cognitively unimpaired individuals at high risk of Alzheimer's Disease (AD) progression is a priority. While plasma p-tau217 is a leading biomarker, longitudinal comparisons between mass spectrometry metrics for predicting long-term outcomes remain scarce.

Cognitively unimpaired older adults from the Vallecas Cohort (10-year follow-up) were analyzed. Baseline plasma was analyzed using the PrecivityAD test (C2N) for %p-tau217, p-tau217, and Aβ42/40 ratio. Biomarker efficiency was evaluated to predict: i) cognitive decline/hippocampal atrophy, ii) clinical conversion, and iii) accuracy using time-dependent ROC (tAUC) and predictive values (PPV/NPV) at 5 and 10 years.

Linear mixed models showed top decile (D1) %p-tau217 and APS2 individuals exhibited faster mPACC decline and accelerated hippocampal atrophy vs. Q1-Q2 ($p<0.001$). In Cox models, p-tau217 MS (HR=1.88, $p<0.001$) and APS2 (HR=1.95, $p<0.001$) were the strongest conversion predictors. In adjusted models (including MRI and NfL), %p-tau217 remained strongest (HR=1.69, $p<0.001$), followed by APS2 (HR=1.74, $p<0.001$); Aβ42/40 added no significance ($p=0.08$). Time-dependent ROC analysis showed %p-tau217 and APS2 achieved highest discriminatory power at 5 years (tAUC=0.79/0.75), outperforming clinical-only (0.69) and Aβ42/40 (0.66). At 5 years, both demonstrated similar NPV (~94%) for ruling out progression vs. 91% for Aβ42/40. Top decile %p-tau217 yielded 66% PPV at 10 years for conversion, while Aβ42/40 exhibited the lowest PPV (24.4%).

Plasma %p-tau217 and APS2 score are robust predictors of hippocampal atrophy and clinical progression to AD. The high NPV supports their use as reliable rule-out criteria, while the top decile identifies individuals with a >50% conversion rate within 10 years.

BOOK OF ABSTRACTS 2026

POSTER N.º 24

Introduced by: Minerva Martínez-Castillo

Title:

PLASMA INTEGRINS ASSOCIATE WITH LEWY NEUROPATHOLOGY AND SUPPORT A ROLE FOR INTEGRIN-RELATED PATHWAYS

First Author: Minerva Martínez-Castillo

Authors: Minerva Martínez-Castillo[a], Sonia Wagner-Reguero[a], Iván Burgueño-García[a], Ana Belén Pastor[a], Paloma Ruiz-Valderrey[a], María José López-Martínez[a], Laura Saiz-Aúz[a], Pamela Martino-Adami[b], Alfredo Ramirez[bcdef], Alberto Rábano[a], Pascual Sánchez-Juan[a], Aitana Sogorb-Esteve[ag]

Filiation: [a]Reina Sofia Foundation Alzheimer Center, CIEN Foundation, ISCIII, 28031 Madrid, Spain. [b]Division of Neurogenetics and Molecular Psychiatry, Department of Psychiatry and Psychotherapy, Faculty of Medicine and University Hospital Cologne, University of Cologne. Cologne, Germany. [c]German Center for Neurodegenerative Diseases (DZNE). Bonn, Germany. [d]Department of Neurodegenerative Diseases and Geriatric Psychiatry, University Hospital Bonn, Medical Faculty. Bonn, Germany. [e]Department of Psychiatry and Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases. San Antonio, United States of America. [f]Cluster of Excellence Cellular Stress Responses in Aging associated Diseases (CECAD), University of Cologne. Cologne, Germany. [g]UCL Queen Square Institute of Neurology, University College London, WC1N 3BG, London, UK.

Abstract:

Lewy pathology is characterized by α-synuclein aggregation, dopaminergic neurodegeneration, and neuroinflammation. Integrins regulate immune responses and neuronal survival, but their role in Lewy pathology remains unclear. We investigated the association of plasma integrin alpha-M (ITGAM) and integrin alpha-V (ITGAV) with Lewy-related neuropathology and explored the involvement of integrin-related proteins. Individuals from Vallecas Alzheimer Reina Sofía (VARS) cohort underwent post-mortem neuropathological assessment following a clinical diagnosis of dementia. Lewy pathology burden was determined by α-synuclein Braak staging. Substantia nigra (SN) depigmentation and neuronal density were evaluated as measures of nigral degeneration, and regional α-synuclein pathology was assessed in the SN, olfactory bulb (OB), and cingulate cortex (CC). Ante-mortem plasma proteins were quantified using the Olink Explore 3072 platform. Integrin-associated proteins were selected based on Gene Ontology (GO) annotations. Group comparisons were performed using age- and sex-adjusted generalized linear models, and associations were assessed using Pearson's or Spearman's correlation, as appropriate.

Individuals with greater Lewy pathology showed lower SN neuronal density, reduced ITGAM and ITGAV levels. Neuron counts in SN were positively associated with both integrin levels. ITGAV was associated with regional α-synuclein pathology in the SN, OB, and CC. Negative associations were found between integrins and the main neuropathological assessments. Preliminary exploratory analyses of integrin-related proteins further support the involvement of ITGAV within a broader integrin signalling network associated with Lewy pathology. These findings strengthen the association between plasma ITGAV and Lewy-related neuropathology and support integrin signalling as a promising pathway for blood-based biomarker discovery in Lewy body diseases.

POSTER N.º 25

Introduced by: Sonia Wagner-Reguero

Title:

PROTEOMIC PROFILES OF COGNITIVE DECLINE AND RESILIENCE BY %P-TAU217 STATUS

First Author: Sonia Wagner-Reguero

Authors: Sonia Wagner-Reguero[a], Jesús Silva-Rodríguez[ab], Minerva Martínez-Castillo[a], Ana Belén Pastor[a], Tim West[c], Daniel Connell[c], Justine Coppinger[c], Philip Verghese[c], Francisco J. López-González[a], Elizabeth L. Valeriano-Lorenzo[a], Belén Frades[a], Meritxell Valentí[a], Andrea Ruiz-Calvo[a], María Ascensión Zea-Sevilla[a], Mario Ricciardi[a], Amanda Heslegrave[de], Henrik Zetterbergde[fghi], Rachel Mulvaney[de], Teodoro del Ser[a], Michel J. Grothe[ab], Pascual Sánchez-Juan[ab], Aitana Sogorb-Esteve[ad]

Filiation: [a]Reina Sofía Foundation Alzheimer Centre, CIEN Foundation, ISCIII, Madrid, Spain. [b]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain. [c]C2N Diagnostics, St. Louis, Missouri, USA. [d]UCL Queen Square Institute of Neurology, Queen Suqare House, London, WC1N 3BG. [e]Dementia Research Institute, UCL, London, UK. [f]Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden. [g]Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Gothenburg, Sweden. [h]Hong Kong Center for Neurodegenerative Diseases, Hong Kong Science Park, Shatin, Hong Kong. [i]Wisconsin Alzheimer's Disease Research Center, University of Wisconsin School of Medicine and Public Health, University of Wisconsin-Madison, Madison, WI, USA.

Abstract:

Background: Blood-based biomarkers are transforming the early detection of Alzheimer's disease (AD), with plasma pTau217 emerging as one of the most accurate blood biomarkers for identifying AD pathology and predicting cognitive decline. However, individuals with elevated plasma pTau217 may exhibit different cognitive outcomes, suggesting the presence of biological mechanisms underlying cognitive resilience. This study analyses proteomic profiles from the NULISA (Alamar) CNS and Inflammation panels in biologically and clinically defined groups from the longitudinal Vallecas cohort (Madrid, Spain), aiming to identify molecular patterns associated with cognitive progression and potential protective mechanisms against cognitive impairment.

Methods: A total of 171 participants from the Vallecas cohort, a longitudinal community-based study of older adults from Fundación CIEN (Madrid, Spain), were included. Cognitive status was determined by annual clinical and neuropsychological assessments, and baseline plasma %pTau217 was measured by C2N Diagnostics. The %pTau217 cutoffs were defined as follows: High (>7.4%), Elevated (4.2–7.4%), and Low (<2.6%). Based on this stratification, seven groups were defined: cognitively stable with low %pTau217 (controls), cognitively unimpaired participants at final visit of the study (classified as resilient with E/H %pTau217), cognitively impared (non-resilient, with E/H %pTau217), and slow progressors that exhibit delayed cognitive decline compared to non-resilient individuals (with E/H %pTau217). Differential protein expression between groups was assessed using LIMMA linear models adjusted for age and sex.

Results: Tau biomarkers, including BD-pTau217 were the most significant proteins, as expected from group stratification by plasma %pTau217. GFAP was the most consistently increased protein across controls comparisons, suggesting enhanced astrocytic activation. Inflammatory changes were more pronounced in non-resilient individuals; however, these differences did not remain significant after FDR correction.

Conclusion: Overall, these preliminary findings suggest that cognitive resilience is associated with distinct proteomic signatures beyond tau pathology. Although both the CNS and inflammatory protein panels showed differential trends, none of these differences remained significant after FDR correction. However, they may reflect biologically relevant trends that could be better resolved in larger cohorts. Further in-depth studies are needed to better understand the biological mechanisms underlying these proteomic differences and their role in cognitive resilience.

BOOK OF ABSTRACTS 2026

POSTER N.º 26

Introduced by: Ana I Rodríguez-Pérez

Title:

CANDESARTAN INDUCES NEUROPROTECTIVE PROTEOMIC CHANGES IN BRAIN-DERIVED EXTRACELLULAR VESICLES FROM PATIENTS WITH PARKINSON'S DISEASE

First Author: Ana I Rodríguez-Pérez

Authors: Ana I Rodríguez-Pérez[abc], Laura Camacho-Meño [abc], Carmen M. Labandeira[abcd], Cristina Gianzo-Quintela[abc], Susana Belen Bravo[e], Mateo V. Torres[ac], Helena Bejr-Kasem[bfghij], Angela Molina-Crespo[bk], Mercedes Atienza[bk], José L. Lanciego[blm], José L. Cantero[bk], Jaime Kulisevsky[bfgh], José L. Labandeira-García[abc]

Filiation: [a]Research Center for Molecular Medicine and Chronic Diseases (CIMUS), University of Santiago de Compostela, Santiago de Compostela, Spain. [b]Research Health Institute of Santiago (IDIS), Santiago de Compostela, Spain. [c]Networking Research Center on Neurodegenerative Diseases (CIBERNED), Instituto de Salud Carlos III, Madrid, Spain. [d]Neurology Service, University Hospitalof Ourense, Ourense, Spain. [e]Proteomic Unit, Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain. [f]Movement Disorder Unit, Neurology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain. [g]Department of Medicine, Autonomous University of Barcelona, Barcelona, Spain. [h]Sant Pau Biomedical Research Institute (IIB-Sant Pau), Barcelona, Spain. [i]Neurology Department of the University Hospital of Bellvitge, Barcelona, Spain. [j]Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain. [k]Laboratory of Functional Neuroscience, Pablo de Olavide University, Seville, Spain. [l]CNS Gene Therapy Program, Center for Applied Medical Research (CIMA), University of Navarra, Pamplona, Spain. [m] Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, Chevy Chase, MD, USA.

Abstract:

Introduction: Preclinical and epidemiological studies suggest that angiotensin II type 1 receptor blockers (ARBs) protect dopaminergic neurons; however, direct molecular evidence in patients with Parkinson's disease (PD) is lacking. Brain-derived extracellular vesicles (EVs) provide a minimally invasive approach to monitor physiological changes and responses within the central nervous system.

Objective: To investigate the molecular effects of candesartan treatment in patients with PD by characterizing the proteomic cargo of brain-derived EV subpopulations.

Methods: PD patients enrolled in a randomized, double-blind, phase II clinical trial were included. Serum samples were collected before and after six months of candesartan treatment (up to 8 mg/day). Sequential immunocapture was used to isolate neuronal (nEVs), astrocytic (aEVs), oligodendrocytic (oEVs), and microglial/macrophage-derived EVs (m/mEVs). Proteomic profiling was performed using SWATH-MS.

Results: In PD patients treated with the ARB candesartan, we identified a cell-type-specific proteomic reprogramming consistent with neuroprotective mechanisms. A total of 46 differentially expressed proteins were identified in nEVs, 22 in aEVs, 92 in oEVs, and 48 in m/mEVs. These proteins were involved in key pathways related to dopaminergic vulnerability, neuroinflammation, oxidative stress, synaptic integrity, and glial homeostasis.

Conclusions: This study provides preliminary molecular evidence that ARBs activate neuroprotective mechanisms in PD and supports brain-EV proteomics as a minimally invasive approach for therapeutic monitoring, providing a rationale for larger clinical trials evaluating ARB repurposing.

BOOK OF ABSTRACTS 2026

POSTER N.º 27

Introduced by: Sonia Wagner-Reguero

Title:

OPTIMIZATION AND EVALUATION OF RT-QuIC ASSAYS IN SYNUCLEINOPATHIES

First Author: Iván Pérez-Jara

Authors: Iván Pérez-Jara[a], Sonia Wagner-Reguero[a], Sezgi Canaslan[b], Inga Zerr[bc], Ana Belén Pastor[a], Iván Burgueño-García[a], Laura Saiz-Aúz[a], Alberto Rábano[a], Lorena de Mena[d], Yaroslau Compta[def], Pascual Sánchez-Juan[af], Aitana Sogorb-Esteve[ag]

Filiation: [a]Reina Sofía Foundation Alzheimer Centre, CIEN Foundation, ISCIII, Madrid, Spain. [b]Department of Neurology, University Medical Center Göttingen, Robert-Koch-Str. 40, 37075, Göttingen, Germany. [c]German Center for Neurodegenerative Diseases (DZNE), Göttingen, Germany. [d]Parkinson's Disease and Movement Disorders Unit, Neurology Service, Hospital Clinic de Barcelona, FRCB-IDIBAPS, Barcelona, 08036, Spain. [e]Institut de Neurociències (UBNeuro), Universitat de Barcelona, Barcelona, 08035, Spain. [f]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain. [g]UCL Queen Square Institute of Neurology, Queen Suqare House, London, WC1N 3BG.

Abstract:

Synucleinopathies are neurodegenerative disorders characterized neuropathologically by the presence of Lewy bodies, insoluble intracellular deposits formed by the aggregation of misfolded α-synuclein. α-Synuclein is a protein with prion-like properties that can propagate abnormal protein folding under pathological conditions. The diagnosis of Parkinson's disease, dementia with Lewy bodies, and multiple system atrophy remains particularly challenging during the prodromal stages due to the overlap of heterogeneous and often nonspecific clinical manifestations, as well as the lack of reliable biomarkers of protein aggregation. In the search for novel technologies capable of detecting α-synuclein fibrils, seed amplification assays (SAAs), such as the real-time quaking-induced conversion (RT-QuIC) assay, have emerged. These techniques are based on the prion-like behavior of α-synuclein. In this study, the results obtained in our laboratory were compared with those provided by a collaborating center using three different substrates and two distinct protocols. Analysis of cerebrospinal fluid samples with neuropathologically confirmed diagnoses classified as Braak α-synuclein stages 0 or 5–6 (n = 10 and n = 18, respectively) showed that substrate A and protocol 1 provided the best experimental performance, although the results obtained differed from those reported by the collaborating center. The results obtained yielded a sensitivity of 55.5%, a specificity of 70%, and an accuracy of 60%, compared with 100%, 80%, and 92.8%, respectively, for the results provided by the collaborating center. These findings highlight the importance of establishing a standardized protocol, as RT-QuIC is highly sensitive to methodological variations.

BOOK OF ABSTRACTS 2026

POSTER N.º 28

Introduced by: Elizabeth Valeriano-Lorenzo

Title:

ASTROCYTE REACTIVITY-P-TAU217 COUPLING IDENTIFIES A HIGH-RISK BIOMARKER SIGNATURE IN PRECLINICAL ALZHEIMER'S DISEASE

First Author: Elizabeth Valeriano-Lorenzo

Authors: Elizabeth Valeriano-Lorenzo[ab], Sonia Wagner-Reguero[a], Minerva Martínez-Castillo[a], Andrea Ruiz[a], Ana Belén Pastor[a], Iván Burgueño-García[a], Linda Zhang[a], Mario Ricciardi[a], Maria Ascensión Zea Sevilla[a], Meritxell Valentí[a], Belén Frades-Payo[a], Isabel López[a], Francisco López-Gonzáles[a], Teodoro del Ser[a], Alberto Rábano[a], Aitana Sogorb-Esteve[a], Pascual Sánchez-Juan[a]

Filiation: [a]Reina Sofía Foundation Alzheimer Centre, CIEN Foundation, ISCIII, Madrid, Spain. [b]Department of Psychology, Autonomous University of Madrid, Madrid, Spain.

Abstract:

Background: Astrocyte reactivity has been proposed to modulate early tau phosphorylation in preclinical Alzheimer's disease. In this study, we investigated whether the interaction between plasma p tau217 and GFAP delineates distinct trajectories of cognitive decline, neuroaxonal injury, and hippocampal atrophy in cognitively unimpaired older adults. We also examined whether this astroglial-tau relationship differs across neuropathologically defined groups such as ADpredominant, AD+ (mixed pathology), and non-AD, in post mortem brain tissue.

Method: We included 381 participants (mean age 74.2 ± 3.5 years; 61.2% women) with repeated plasma biomarker assessments, structural MRI, and at least three cognitive evaluations over up to 10 years. Plasma p tau217 was quantified using LC–MS/MS, and GFAP and NfL using SIMOA. Astrocyte reactivity (Ast+ vs. Ast–) was defined using a cutoff based on the Youden index. Participants were classified into four groups according to p tau217 status and astrocyte reactivity. Longitudinal trajectories were modelled using GAMMs for global cognition and hippocampal volume (ICV adjusted), and a GAM for plasma NfL, all including smooth time by group terms and standard covariates. Post mortem analyses used partial correlations adjusted for age at extraction, estimated age at onset, sex, and Thal stage.

Results: Across all outcomes, the Ast+/p tau+ group showed the most adverse profile, with lower baseline cognitive performance and steeper decline (βGroup4=0.41, $p<0.001$), higher baseline NfL levels (non significant slope), and significantly reduced hippocampal volume (βGroup4=–76.1mm³, $p=0.031$) with faster atrophy. In post mortem tissue, only the AD predominant group showed a significant GFAP-p tau217 association (βAD=0.0083, pFDR=0.010).

Conclusions: These findings indicate that elevated p tau217 combined with astrocyte reactivity identifies a biologically vulnerable phenotype characterised by accelerated cognitive decline, pronounced hippocampal atrophy, and stronger GFAP–tau coupling in post mortem tissue.

BOOK OF ABSTRACTS 2026

POSTER N.º 29

Introduced by: Patricia Regina Manzine

Title:

ADAM10-REGULATORY MICRORNAS IDENTIFY ALZHEIMER'S DISEASE AND THE ADDITIONAL METABOLIC BURDEN OF TYPE 2 DIABETES

First Author: Patricia Regina Manzine

Authors: Patricia Regina Manzine[abcde], Suelen Santos Alves[f], Miren Ettcheto[fgh], Amanda Cano[fgi], Maria Aderuza Horst[jk], Maria Isabel Pividori Gurgo[l], Antoni Camins[fgh]

Filiation: [a]Faculty of Nursing, Department of Public Health, Mental Health and Maternal-Child Health, University of Barcelona, Barcelona, Spain. [b]Department of Pharmacology, Toxicology and Therapeutic Chemistry, Faculty of Pharmacy and Food Science, University of Barcelona (UB), Barcelona, Spain. [c]Biomedical Research Networking Center in Neurodegenerative Diseases (CIBERNED), Instituto de Salud Carlos III, Madrid, Spain [d]Institute of Neuroscience (UB), Barcelona, Spain. [e]Marie Skłodowska-Curie Actions (MSCA) - European Commission, Brussels, Belgium. [f]Department of Pharmacology, Toxicology and Therapeutic Chemistry, Faculty of Pharmacy and Food Sciences, University of Barcelona, Barcelona, Spain. [g]Networking Research Center on Neurodegenerative Diseases (CIBERNED), Instituto de Salud Carlos III, Madrid, Spain. [h]Institute of Neurosciences, University of Barcelona, Barcelona, Spain. [i]ACE Alzheimer Center Barcelona, Internacional University of Catalonia, Barcelona, Spain. [j]School of Nutrition, Federal University of Goiás, Goiânia, Brazil. [k]Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, Alberta, Canada. [l]Department of Chemistry, Institute of Biotechnology and Biomedicine Vicent Villar Palasi (IBB), Autonomous University of Barcelona, Barcelona, Spain.

Abstract:

Background: Alzheimer's disease (AD) and type 2 diabetes (T2D) share several pathogenic mechanisms, including impaired amyloid precursor protein (APP) processing, chronic inflammation, and metabolic dysfunction. ADAM10, the principal α-secretase responsible for the non-amyloidogenic cleavage of APP, has emerged as a promising therapeutic target and blood-based biomarker in AD. However, the contribution of ADAM10-regulatory microRNAs (miRNAs) to the molecular interplay between AD and T2D remains poorly understood. Objective: To investigate circulating ADAM10-regulatory miRNAs as potential blood-based biomarkers capable of identifying AD and its association with T2D. Methods: The project was submitted and approved by the bioethics committee. Candidate miRNAs were selected using an integrated bioinformatic approach combining miRTargetLink, miEAA, and miRNet, followed by experimental validation by RT-qPCR in serum samples from participants recruited at the ACE Alzheimer Center Barcelona. Participants were classified according to the AT(N) framework into mild cognitive impairment (MCI; A−T−N−, n = 20), MCI with T2D (n = 13), AD (A+T+N+, n = 20), and AD with T2D (n = 20). Serum miRNA were extracted using the miRNeasy Serum/Plasma Kit and quantified by RT-qPCR, using TaqMan MicroRNA assays. Relative miRNA expression was calculated using the ΔΔCt method with miR-16 as the endogenous control. Results: Among the candidate molecules, miR-92, miR-103, miR-19, and miR-221 were significantly upregulated in AD compared with MCI. Notably, miR-103 and miR-19 exhibited a progressive increase from MCI to AD, reaching their highest expression levels in individuals with concomitant AD and T2D, suggesting sensitivity to both neurodegenerative and metabolic burden. Conclusions: Our findings identify a distinct circulating ADAM10-regulatory miRNA signature associated with AD and further amplified by T2D. These results suggest that dysregulation of ADAM10-related miRNAs contributes to the molecular interface between neurodegeneration and metabolic disease. This miRNA signature represents a promising minimally invasive strategy for patient stratification and supports the development of accessible blood-based biomarkers for precision medicine in AD.

BOOK OF ABSTRACTS 2026

POSTER N.º 30

Introduced by: Ernesto García-Roldán

Title:

CLINICAL IMPLEMENTATION OF PLASMA P-TAU217 (ELECSYS): POST-VALIDATION PERFORMANCE OF A DUAL-CUTOFF APPROACH

First Author: Emilio Franco-Macías

Authors: Ernesto García-Roldán[abc], Laura María Leal Aranda[d], Alba Marta Marín-Cabañas[abc], María Bernal Sánchez-Arjona[abc], Jose Antonio Lojo-Ramírez[e], José Ángel Noval-Padillo[d], Daniel Fatela-Cantillo[d], Emilio Franco-Macías[abc]

Filiation: [a]Memory Unit, Department of Neurology, Virgen del Rocío University Hospital, Seville, Spain. [b]Biomedicine Institute of Seville IBiS, University Hospital Virgen del Rocio, CSIC, University of Seville, Seville, Spain. [c]Andalusia-NEURO-RECA/Roche Alliance in Precision Neurological Medicine, Spain. [d]Clinical Biochemistry Department, Virgen del Rocío University Hospital, Seville, Spain. [e]Nuclear Medicine Department, Virgen del Rocío University Hospital, Seville, Spain.

Abstract:

Background and Objectives:

To evaluate the real-world performance of plasma p-tau217 measured with the Elecsys assay following its clinical implementation, focusing on the dual-cutoff strategy established during the validation study.

Methods:

Consecutive patients evaluated for cognitive complaints with suspected Alzheimer's disease between March and June 2026 underwent plasma p-tau217 measurement using the Elecsys immunoassay on the Cobas platform. Results were classified according to the validated dual-cutoff approach: positive (>0.312 pg/mL), gray zone (0.177–0.312 pg/mL), and negative (<0.177 pg/mL). In the subgroup that additionally underwent amyloid PET, the diagnostic performance of the dual-cutoff strategy was explored.

Results:

A total of 205 patients (mean age 73.5 ± 8.5 years) were included. According to the validated dual-cutoff approach, 103 patients (50.2%) were classified as plasma p-tau217 positive, 67 (32.7%) as negative, and 35 (17.1%) fell within the gray zone. Amyloid PET was available in 11 patients. All four patients with plasma p-tau217 values >0.312 pg/mL (range 0.346–0.605 pg/mL) had positive amyloid PET scans. All five patients with gray-zone values (0.236–0.309 pg/mL) were also amyloid PET positive, whereas both patients with plasma p-tau217 values <0.177 pg/mL had negative amyloid PET scans.

Conclusions:

In this post-validation cohort, the proportion of gray-zone results (17.1%) was substantially lower than that observed during the validation study (27%), supporting the clinical applicability of the dual-cutoff strategy. Preliminary amyloid PET findings suggest that patients with plasma p-tau217 values as low as 0.236 pg/mL within the gray zone may already harbor cerebral amyloid pathology. Additional studies including a larger number of patients with gray-zone values, particularly between 0.177 and 0.236 pg/mL, are warranted before considering refinement of the lower cutoff.

BOOK OF ABSTRACTS 2026

POSTER N.º 31

Introduced by: Margalida Puigròs

Title:

MITOCHONDRIAL DNA IN BLOOD SERUM AS A BIOMARKER OF LEWY BODY DISEASES

First Author: Margalida Puigròs

Authors: Elia Ivars[abcd], Margalida Puigròs[abcd], Burcu Şekerzade[abd], David Adamuz[e], Alex Menéndez[ef], Anna Colell[abc], Katrin Beyer[e], Pau Pastor[ef], Ramon Trullas[abc]

Filiation: [a]Neurobiology Unit, Institut d'Investigacions Biomèdiques de Barcelona, Consejo Superior de Investigaciones Científicas (IIBB-CSIC). [b]Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS). [c]CIBER de Enfermedades Neurodegenerativas (CIBERNED), Instituto de Salud Carlos III. [d]Universitat de Barcelona, Barcelona, Spain. [e]Department of Neuroscience, Research Institute Germans Trias i Pujol, Badalona, Spain. [f]Unit of Neurodegenerative diseases, Department of Neurology, University Hospital Germans Trias I Pujol and the Germans Trias I Pujol Research Institute (IGTP) Badalona, Barcelona, Spain.

Abstract:

Background: Idiopathic REM sleep behavior disorder (IRBD) is a prodromal stage of Lewy Body Diseases (LBD). In previous work, we observed a significant increase in circulating mtDNA (c-mtDNA) copies in serum and CD9-Evs from serum in patients with IRBD who later converted to a LBD. Here, we assessed whether the increased release of cf-mtDNA in serum is also observed in LBD patients and if it is contained in CD9+, CD81+, and CD63+ extracellular vesicles (EVs).

Methods: We used multiplex droplet digital PCR to quantify cf-mtDNA copies and deletion ratio in CSF and serum in a cohort of 114 subjects from the Hospital Germans Trias i Pujol, including 1) 28 patients with prodromal dementia with Lewy Bodies (pDLB), 2) 38 patients diagnosed with LBD, and 3) 48 age-matched controls without clinical neurological symptoms. In addition, we investigated whether CD9-, CD81- and CD63-EVs serum samples contained c-mtDNA.

Findings: Patients with pDLB and LBD exhibited higher c-mtDNA copy number and c-mtDNA deletion ratio in serum than controls. In addition, we found the presence of c-mtDNA in CD9-, CD81- and CD63-Evs in serum. Subjects with pDLB and LBD also showed elevated c-mtDNA copy number and c-mtDNA deletion ratio in serum-derived CD63-EVs but not in CD9-EVs, compared with controls.

Interpretation: These results suggest that mtDNA dysfunction is a biomarker of a primary molecular mechanism in the pathophysiological cascade that precedes the full clinical motor and cognitive manifestations of LBD.

Supported by MJFox Foundation, MJFF-001111; ISCIII EU NextGenerationEU/PRTR, grant PMP22/00100PMP22/00100; and MICIU/AEI/10.13039/- 501100011033, PID2023-153168OB-I00.

BOOK OF ABSTRACTS 2026

POSTER N.º 32

Introduced by: Marta Aramburu-Núñez

Title:

VALIDATION OF A PAPER-BASED LATERAL FLOW TEST FOR MINIMALLY INVASIVE, LOW-VOLUME DETECTION OF PHOSPHORYLATED TAU PROTEIN IN EARLY ALZHEIMER'S DISEASE DIAGNOSIS

First Author: Marta Aramburu-Núñez

Authors: Marta Aramburu-Núñez*[1,2], María Matos Pereira[3], Margarida Ferreira da Cunha[3], Mónica Castro-Mosquera[1], Mariña Rodríguez-Arrizabalaga[1], Manuel Debasa-Mouce[1], Eduardo López Reguera[1], Juan Manuel Pías-Peleteiro[1,2], José Manuel Aldrey[1,2] Daniel Romaus-Sanjurjo[1,2], Alberto Ouro[1,2], Muhammad Raza[3] ,Marco Martins[3], Joao Moura[3], Duarte Mota[3] , Elisabete Fernandes[3#], Tomás Sobrino[1,2#]

Filiation: [1]NeuroAging Laboratory Group, Clinical Neurosciences Research Laboratory, Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain. [2]Centro de Investigación Biomédica en Red en Enfermedades Neurodegenerativas (CIBERNED), Instituto de Salud Carlos III, Madrid, Spain. [3]International Iberian Nanotechnology Laboratory (INL), Braga, Portugal. [#]These authors equally contributed as senior authors.

Abstract:

Phosphorylation of tau at Ser202, Thr205 and Ser208 is a core driver of tau aggregation into neurofibrillary tangles and represents the major tau species detected in the cerebrospinal fluid of Alzheimer's disease patients. A monoclonal antibody directed against these phosphoepitopes has been validated in human post-mortem brain tissue and in transgenic tauopathy mice, where its staining pattern closely matches the AT8 gold-standard antibody and scales with the severity of neurofibrillary pathology across Braak stages (Kemppainen et al., 2025). These findings support mid-domain phosphorylated tau as a robust, clinically meaningful biomarker, providing the immunological rationale for the antibody used in the platform described.

The study proposes a portable, paper-based lateral flow assay (LFA) biosensor for rapid detection of phosphorylated tau, combining gold nanoparticle (AuNP)–streptavidin conjugates for colorimetric signal amplification with the potential integration of magnetic nanoparticles into a microfluidic module for sample preconcentration and purification. The nitrocellulose membrane is functionalized with the pTau antibody (Kemppainen et al., 2025) at the test line and a non-specific antibody at the control line, with a conjugate complex of biotinylated antibodies and AuNPs on the conjugate pad. The assay requires under 120 µL of sample, well below conventional ELISA or Western blot requirements, supporting minimally invasive, decentralized screening.

An image-based reading module quantifies the test-line signal, reducing variability from visual interpretation and enabling quantitative diagnosis. The prototype achieved high analytical sensitivity for synthetic phosphorylated tau in the picogram range, with clear discrimination from a non-phosphorylated control. Validation in real biological matrices CSF, serum/plasma, and tears across Alzheimer's disease stages is now underway.

BOOK OF ABSTRACTS 2026

POSTER N.º 33

Introduced by: Leal-Pérez, Francisco

Title:

CHARACTERIZING THE STRUCTURAL AND BIOPHYSICAL IMPACT OF METHYLGLYOXAL-INDUCED GLYCATION ON ALPHA-SYNUCLEIN AMYLOID FIBRILS

First Author: Leal-Pérez, Francisco

Authors: Leal-Pérez, Francisco[abc], Mariño Pérez, Laura[abc], Adrover Estelrich, Miquel[abc]

Filiation: [a]Universitat de les Illes Balears (UIB), Palma de Mallorca, Spain. [b]Institut d'Investigació Sanitària Illes Balears (IdISBa). [c]Institut Universitari d'Investigació en Ciències de la Salut (IUNICS).

Abstract:
Epidemiological and clinical data point to a mechanistic connection between type 2 diabetes mellitus (T2DM) and neurodegenerative synucleinopathies 1,2. At the molecular level, this link may be mediated by methylglyoxal (MG), a reactive byproduct of glycolysis that promotes non-enzymatic glycation. Although alpha-synuclein (αS) aggregation is well-documented, the biochemical influence of MG on mature amyloid structures remains poorly understood.
Shifting the focus from the aggregation cascade itself, we target the direct impact of MG-induced glycation on pre-formed, wild-type αS amyloid fibrils. Notably, our findings suggest that glycation may structurally reinforce the fibrils compared to their native counterparts, potentially inducing significant morphological remodeling driven by covalent cross-linking.
To evaluate fibrillar stability, we employed a combination of biophysical and molecular imaging techniques to monitor both native and glycated fibrils under thermal and chemical denaturation. NMR and stopped-flow kinetics revealed that while native fibrils disassemble, MG-glycated structures remain intact. This enhanced thermal and chemical stability was validated by CD spectroscopy, TEM and SAXS, further suggesting that MG-induced covalent cross-linking might morphologically reinforce the fibrillar core against disruption.
Characterizing this link is vital due to the clear connection between type 2 diabetes and Parkinson's disease. Understanding how glycation keeps these fibrils stable opens new doors to identify specific biomarkers and develop new treatments based on metabolic regulation.
References
1. Aviles-Olmos I, Dickson J, Kefalopoulou Z, Djamshidian A, Ell P, Soderlund T, Whitton P, Wyse R, Isaacs T, Lees A, Limousin P, Foltynie T. Exenatide and the treatment of patients with Parkinson's disease. J Clin Invest. 2013 Jun;123(6):2730-6.
2. Athauda D, Foltynie T. Insulin resistance and Parkinson's disease: A new target for disease modification. Prog Neurobiol. 2016 Oct-Nov;145-146:98-120.

BOOK OF ABSTRACTS 2026

POSTER N.º 34

Introduced by: Mario López-Manzaneda

Title:

A NOVEL GREEN FLUORESCENCE PROTEIN SPLIT TOOL TO MEASURE MITOCHONDRIAL PROTEIN IMPORT IN LIVE CELLS

First Author: Mario López-Manzaneda

Authors: Mario López-Manzaneda[ab], Rafael Fernández-Chacón[c], Jaime De Juan-Sanz[b]

Filiation: [a]Instituto de Biomedicina de Sevilla (IBiS, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla), Dpto. de Fisiología Médica y Biofísica, Facultad de Medicina and CIBERNED ISCIII, Sevilla, Spain. [b]Institut du Cerveau (ICM) Laboratoire Physiologie Moleculaire de la Bioenergetique Synaptique, Paris, France. [c]Instituto de Biomedicina de Sevilla (IBiS, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla), Dpto. de Fisiología Médica y Biofísica, Facultad de Medicina and CIBERNED ISCIII, Sevilla, Spain.

Abstract:
Mitochondrial biogenesis is heavily dependent on the nuclear genome. From its almost 2000 proteins, 99% of its are nuclear encoded. These proteins are synthesized on cytosolic ribosomes and transferred into the organelle in a process termed as mitochondrial protein import. This process is essential for the correct function of the cells. In fact, there is evidence of alterations in this process in neurodegenerative diseases such as Parkinson's or Alzheimer's diseases. Nevertheless, little is known about the mechanisms that regulate mitochondrial protein import and virtually nothing about how this process adapts to metabolic demands or external challenges in mammalian cells. We have engineered a Green Fluorescence Protein (GFP) Split System that allows for the first time the dynamic study of mitochondrial protein import. This biosensor explores the major import route in charge of transferring two-thirds of all mitochondrial proteins (mitochondrial pre-sequence pathway). Using this tool, we can start to gain unprecedented information about mitochondrial protein import and its regulation with single-cell resolution in health and disease.
Supported by: Ayuda para recualificación del sistema universitario español Modalidad Margarita Salas, Marie Sklodowska-Curie Postdoctoral Fellow of the ARISTOS program and Programa de Formación, Captación, Incorporación y Movilidad de RRHH de I+D+I de la EIDIA Horizonte 2027 to MLM; ERC Starting Grant (ERC-StG-852873), 2019 ATIP-Avenir Grant (CNRS, Inserm) and a Big Brain Theory Grant (ICM) to JdJS and Spanish Agencia Estatal de Investigación and Ministerio de Ciencia, Innovación y Universidades (MICIU) and European Regional Development Fund (ERDF), (MICIU/AEI /10.13039/501100011033, FEDER, UE) project PID2022-138957NBI00 to RFC.

BOOK OF ABSTRACTS 2026

POSTER N.º 35

Introduced by: Mario Ricciardi Serra

Title:

PERIVASCULAR SPACES REFLECT NEUROPATHOLOGICAL SEVERITY OF CEREBRAL AMYLOID ANGIOPATHY IN ALZHEIMER'S DISEASE

First Author: Mario Ricciardi Serra

Authors: Mario Ricciardi Serra[a], Iván Burgueño García[a], Elizabeth Valeriano Lorenzo[a], María Ascensión Zea Sevilla[a], Meritxell Valentí[a], Belén Frades[a], Isabel López Torres[a], Marta Anton Moreno[a], Francisco López González[a], Paloma Ruiz[a], Laura Saiz[a], Alicia Uceda Heras[a], Linda Zhang[a], Eva Alfayate Sáez[a], Marta Molero Cartón[a], María José López Martínez[a], Teodoro Del Ser[a], Michel Grothe[a], Alberto Rábano[a], Pascual Sánchez Juan[a].

Filiation: [a]Reina Sofia Foundation Alzheimer Centre, CIEN Foundation, ISCIII.

Abstract:
Hemorrhagic lesions associated with cerebral amyloid angiopathy (CAA) represent late manifestations of vascular injury. Enlarged perivascular spaces in the centrum semiovale (CSO-EPVS) have emerged as an MRI marker of non-hemorrhagic vascular changes, although clinicopathological evidence supporting this association in Alzheimer's disease (AD) remains limited. We investigated the association between CSO-EPVS burden on MRI and neuropathological CAA severity in individuals with AD, and assessed whether this relationship was independent of AD neuropathological burden and influenced by the APOE ε4 allele.
Fifty-five individuals with neuropathologically confirmed AD from the VARS cohort (82% women; mean age 84.9 ± 7.4 years) with ante-mortem brain MRI (median MRI-to-death interval 1.2 years [IQR 0.52–3.07]) and post-mortem neuropathological assessment were included. CSO-EPVS burden was rated using the Potter scale, and CAA severity was graded according to VCING criteria. Associations were assessed using partial Spearman correlations and ordinal logistic regression adjusted for age, MRI-to-death interval, Braak stage and Thal phase.
Higher CSO-EPVS burden was independently associated with greater neuropathological CAA severity (partial ρ=0.29, p=0.034). Each one-point increase in CSO-EPVS burden was associated with higher CAA severity (OR=1.97, 95% CI 1.06–3.82, p=0.035). This association was stronger when the MRI-to-death interval was ≤2 years (partial ρ=0.47; OR=2.90) and remained significant in participants without hemorrhagic MRI markers (partial ρ=0.61; OR=4.34). APOE ε4 was associated with greater CAA severity, but not with CSO-EPVS burden. CSO-EPVS burden on MRI is an independent biomarker of neuropathological CAA severity in AD, even in the absence of hemorrhagic MRI markers.

POSTER N.º 36

Introduced by: Juan Francisco Martín-Rodríguez

Title:

SHORT-LATENCY AFFERENT INHIBITION TRACKS CHOLINERGIC BASAL FOREBRAIN INTEGRITY AND COGNITIVE DECLINE IN PARKINSON'S DISEASE

First Author: Juan Francisco Martín-Rodríguez

Authors: Juan Francisco Martín-Rodríguez[abc], Pablo Franco-Rosado[abc], Cristina Perez-Calvo[abd], Elena Iglesias-Camacho[abd], Manuela San-Eufrasio[abc], Ana María Castellano-Guerrero[ab], Francisco J. Gómez-Campos[ab], Patricia Díaz-Galván[ab], Brenda Villarreal-Garza[ae], Miguel Ángel Labrador-Espinosa[af], Jesús Silva-Rodríguez[abg], Antonio Cristobal Luque Ambrosiani[ab], Elena Ojeda-Lepe[ab], Laura Muñoz-Delgado[ab], Daniel Macías-García[ab], Astrid Adarmes-Gómez[ab], Silvia Jesús[ab], Fátima Carrillo[abd], Enrique Claudio-Fernandez[h], Florinda Roldan Lora[h], Michel J. Grothe[abg], Pablo Mir[abd]

Filiation: [a]Unidad de Trastornos del Movimiento, Servicio de Neurología, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, 41013 Seville, Spain. [b]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas, Instituto de Salud Carlos III, 28029 Madrid, Spain. [c]Departamento de Psicología Experimental, Universidad de Sevilla, 41018 Seville, Spain. [d]Departamento de Medicina, Facultad de Medicina, Universidad de Sevilla, 41009 Seville, Spain. [e]Otolaryngology Department, Virgen Macarena University Hospital, 41009 Seville, Spain. [f]University of Gothenburg, Department of Psychiatry and Neurochemistry, 431 39 Mölndal, Sweden. [g]Reina Sofía Alzheimer Center, CIEN Foundation, ISCIII, 28031 Madrid, Spain. [h]Unidad de Radiodiagnóstico, Hospital Universitario Virgen del Rocío, 41013 Seville, Spain.

Abstract:

Objective: To characterise the association between short-latency afferent inhibition (SAI), cholinergic basal forebrain (cBF) atrophy and cognitive performance in Parkinson's disease (PD).

Background: Cognitive impairment in PD is associated with cholinergic degeneration. SAI is a neurophysiological marker of cholinergic circuit integrity; however, its anatomical substrate and relationship to domain-specific cognitive decline remain incompletely characterised.

Methods: We enrolled 119 PD patients spanning the cognitive continuum and 32 healthy controls. SAI was assessed with transcranial magnetic stimulation. MRI provided anterior and posterior cBF volumes and substantia nigra pars compacta free-water as a dopaminergic reference. Cognitive status was assessed with the Parkinson's Disease Cognitive Rating Scale. Bootstrap mediation analysis, adjusted for age, education, sex, disease duration, UPDRS-III, LEDD and total grey matter volume, decomposed the SAI–cognition association into components shared with and independent of cBF volume.

Results: SAI was reduced in patients versus controls. Within PD, SAI was significantly associated with PD-CRS total ($\beta = -0.19$, $p = 0.013$) and posterior-cortical scores ($\beta = -0.42$, $p < 0.001$), but not fronto-subcortical scores. Mediation analysis identified a significant indirect path from SAI to global cognition through posterior cBF (indirect $\beta = -0.071$ [−0.158, −0.013]; 42% of total), with the residual direct path non-significant. A significant indirect path was also observed for posterior-cortical score (15% of total). No association was found between SAI and SNc free-water, and cBF associations strengthened after grey matter adjustment, supporting cholinergic specificity.

Conclusions: These findings position SAI as a candidate functional marker of cholinergic circuit integrity linked to basal forebrain structural status and cognitive decline in PD, pending longitudinal validation.

BOOK OF ABSTRACTS 2026

POSTER N.º 37

Introduced by: Mª Ascensión Zea Sevilla

Title:

MADRID-FRONTOTEMPORAL DEMENTIA. CREATION OF FTD STUDY COHORT FOR THE VALIDATION OF CUTTING-EDGE MARKERS

First Author: Mª Ascensión Zea Sevilla

Authors: Mª Ascensión Zea Sevilla[a], Consorcio Madrid-DFT, Alberto Villarejo[b], Sara Llamas[b], Mariana Muñoz[b], Marta González[b], Victor Blanco[b], David Perez[b], Antonio Sánchez Soblechero[c], Javier Olazarán[c], Ángel Berbel[d], Teresa Lapeña[d], Carlos Serra Smith[e], Ángel Martín Montes[f], Elisa Alonso[f], Maria Teresa Carreras[g], Alba Viera[g], Pablo Lorenzo Barreto [g], Guillermo García Ribas[h], Itziar Palmi[i], Cristina Fernández[j], Carmen Terrón[k], Lucia Valeriano Lorenzo[a], Belén Frades Payo[a], Isabel López[a], Mario Ricciardi[a], Meritxell Valenti[a], Minerva Martínez Castillo[a], Ana Belén Pastor[a], Sonia Wagner Reguero[a], Aitana Sogorb Esteve[a], Francisco J. López González [a], Teodoro Del Ser[a], Pascual Sánchez Juan[a]

Filiation: [a]Reina Sofia Foundation Alzheimer Centre-CIEN Foundation-ISCIII, 28031 Madrid, Spain. [b]Hospital Universitario 12 de Octubre. [c]Hospital Universitario Gregorio Marañón. [d]Hospital Universitario de la Cruz Roja San José y Santa Adela. [e]Hospital Universitario Príncipe de Asturias Alcalá de Henares. [f]Hospital Universitario La Paz. [g]Hospital Universitario La Princesa. [h]Hospital Universitario Ramón y Cajal. [i]Hospital Universitario Infanta Sofía. San Sebastian de los Reyes. [j]Hospital Universitario La Moraleja. [k]Hospital Universitario Ntra. Señora del Rosario.

Abstract:

Introduction

Frontotemporal dementia (FTD) is the third most common cause of neurodegenerative dementia and the diagnostic is a challenge in the absence of neuropathological confirmation. Identifying clinical and biological markers or specific diagnostic techniques is essential to improve the diagnostic accuracy and the differential diagnosis with other neurodegenerative processes.

Materials and methods

The Madrid-DFT Consortium—a multicenter study involving 21 memory clinics—collects clinical, neuropsychological, biomarker, and neuroimaging (3T) data from patients with clinical criteria of behavioral variant FTD (bvFTD) or primary progressive aphasia (PPA). A subgroup of patients with a behavioral presentation suggestive of bvFTD was analyzed, stratified into two groups based on positive or negative Alzheimer's disease (AD) biomarkers (p-tau181 and the p-tau181/Aβ42 ratio). Cognitive, behavioral, and mood comparisons between groups were performed using Wilcoxon tests with Benjamini-Hochberg correction.

Results

Forty-four patients (age 73 ± 8.1; 38.6% female) presenting predominantly with behavioral disturbances were included and classified according to the presence or absence of AD biomarkers: (1) bvFTD-AD+ (p-tau181+ and p-tau181/Aβ42 ratio+; 36.4%) and (2) bvFTD-AD- (p-tau181- and/or p-tau181/Aβ42 ratio-63.3%). The bvFTD-AD- group showed significantly better performance on tasks of immediate verbal memory (p-value = 0.049) and immediate logical memory (p-value = 0.029) compared to the bvFTD-AD+ group. Furthermore, a trend—albeit not statistically significant—was observed toward better performance in attentional span and graphic-visual information processing speed, as well as greater behavioral disturbances in areas such as appetite/eating and inhibition/disinhibition, in the bvFTD-EA- group. There were no significant differences in the Frontal Assessment Battery (FAB) scores or in cognitive flexibility.

Conclusions

These results reinforce the need to integrate clinical and biological markers. The well-phenotyped cohort we are establishing will enable the validation of sensitive indicators and facilitate progress toward a more precise diagnosis through precision medicine.

BOOK OF ABSTRACTS 2026

POSTER N.º 38

Introduced by: María Isabel Tamayo Lopera

Title:

CARE-BASED DIDACTIC MODEL OF ATTENTION AND ITS RELATIONSHIP WITH PSYCHOLOGICAL, PSYCHIATRIC, AND BEHAVIORAL SYMPTOMS IN PATIENTS WITH NEURODEGENERATIVE DISEASES AND SEQUELAE OF NEUROLOGICAL DISEASES: AN INSTITUTIONAL CASE STUDY AT CENTRO RELOJ DE ARENA, MEDELLÍN, COLOMBIA, 2024–2026

First Author: María Isabel Tamayo Lopera

Authors: María Isabel Tamayo Lopera[a], Manuela Hernández Álvarez[b], Luisa Fernanda Castro Marin[b], Leonardo Echeverry Bedoya[b]

Filiation: [a]Centro Reloj De Arena Sas, [b]Centro Reloj De Arena.

Abstract:
Care Pedagogy and Its Relationship with Psychological, Psychiatric, and Behavioral Symptoms in Patients with Neurodegenerative Diseases and Sequelae of Neurological Conditions: An Institutional Case Study at Reloj de Arena, Medellín, 2024–2026. Ninety percent of patients with neurodegenerative diseases exhibit psychological, psychiatric, and behavioral symptoms (PPBS), and medication alone is insufficient. This study explores care pedagogy, a non-pharmacological model combining cognitive, physical, and social stimulation, as well as recreational activities and emotional support.
Institutional case studies reveal improvements, including reduced anxiety, aggression, and agitation, along with better sleep and increased social participation.
The findings support the use of care pedagogy to stabilize symptoms.

BOOK OF ABSTRACTS 2026

POSTER N.º 39

Introduced by: Isabel Espadas

Title:

ASSESSMENT OF LNCRNAS AS POTENTIAL BIOMARKERS FOR PHENOCONVERSION TO PARKINSON'S DISEASE IN G2019S LRRK2 MUTATION CARRIERS

First Author: Isabel Espadas

Authors: Isabel Espadas[a], Fermin Guisado-Sanchez[a], Carmen Conde-Naranjo[a], Laura Morón-Marquez[a], Alfonso Rodriguez-Gil[a], Javier Villadiego[a], Juan Jose Toledo Aral[a]

Filiation: [a]Instituto de Biomedicina de Sevilla IBIS (Universidad de Sevilla, HUVR, Junta de Andalucía, CSIC), Sevilla, Spain.

Abstract:
Parkinson's disease (PD) diagnosis relies on clinical motor symptoms that manifest only after significant dopaminergic neuron loss, highlighting an urgent need for early, minimally invasive biomarkers. Non-coding RNAs, such as long non-coding RNAs (lncRNAs), are critical regulators of neuronal homeostasis and promising biomarker candidates due to their presence and stability in peripheral fluids. This study utilizes a translational framework to evaluate whether early pathological alterations in PD are linked to specific transcriptional changes in lncRNAs. We analyzed peripheral blood RNA-seq data from the PPMI cohort, including 68 LRRK2 G2019S mutation carriers with PD, 42 prodromal individuals, and 110 healthy controls. Differential expression analysis was performed using DESeq2. To validate the central relevance of peripheral findings, we cross-referenced these datasets with human brain single-cell RNA-seq (scRNA-seq) data of PD patients and controls. Peripheral transcriptomic profiling revealed distinctive lncRNA alterations associated with the LRRK2 mutation and disease progression. Cross-referencing with human brain scRNA-seq confirmed the significant dysregulation of several lncRNAs in vulnerable dopaminergic neurons of PD patients that were also found in peripheral blood. Notably, the lncRNA PXN-AS1 exhibited a massive upregulation restricted exclusively to these cells, suggesting localized compensatory or pathological mechanisms. In conclusion, our findings suggest a potential correlation between peripheral non-coding RNA alterations and central neurodegenerative processes. The specific dysregulation of PXN-AS1 across both peripheral blood and vulnerable midbrain neurons highlights its potential as a reliable, accessible biomarker for early, disease-modifying therapeutic interventions in PD.

BOOK OF ABSTRACTS 2026

POSTER N.º 40

Introduced by: Rocío Ruiz

Title:

HUMAN IL-34 DEFICIENCY PRIMES MICROGLIA TOWARD ALZHEIMER'S DISEASE-ASSOCIATED STATES

First Author: Rocío Ruiz

Authors: Rocío Ruiz[ab], Francisco Hernández-Rasco[ab], Itziar de Rojas[cd], Raquel Puerta[ce], Clara Garcia-Mayor[abf], Ana María Espinosa-Oliva[ab], Juan García-Revilla[ab], Paula Bayon[c], Alberto Rivera-Ramos[ab], Farah Real Oualit[ab], Sebastián Jiménez[abf], Maria Eugenia Saez[g], Rocío M. de Pablos[ab], Feiyang Zhao[h], Claudia Olive[c], Pilar Sanz[c], Xavier Montalbán[ci], Sergi Valero[cf], Amanda Cano[cf], María Victoria Fernández[c], Anne Marie Wells[hjk], Jose Enrique Cavazos[hjk], Sudha Seshadri[hjk], Merce Boada[cf], Santos Mañes[l], Michael T. Heneka[d], Francisco Javier Vitorica[abf], Alfredo Ramirez[hmnop], José Luis Venero[ab], Agustín Ruiz[cfhjq]

Filiation: [a]Instituto de Biomedicina de Sevilla, IBIS/Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Sevilla, Spain. [b]Departamento de Bioquímica y Biología Molecular, Facultad de Farmacia, Universidad de Sevilla, Sevilla, Spain. [c]Research Center and Memory Clinic. Ace Alzheimer Center Barcelona- Universitat Internacional de Catalunya, Barcelona, Spain. [d]Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Esch-sur-Alzette, Luxembourg. [e]Doctorate in Biotechnology, Facultat de Farmàcia i Ciències de l'Alimentació, Universitat de Barcelona, Avda. Diagonal 643, 08028, Barcelona, Spain. [f]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain. [g]CAEBi, Centro Andaluz de Estudios Bioinformáticos, Sevilla, Spain. [h]Glenn Biggs Institute for Alzheimer's & Neurodegenerative Diseases, University of Texas at San Antonio, San Antonio, TX, USA. [i]Department of Neurology, Multiple Sclerosis Centre of Catalonia (Cemcat), Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain. [j]South Texas Alzheimer's Disease Research Center, San Antonio, TX, USA. [k]Department of Neurology. Long School of Medicine, University of Texas at San Antonio, San Antonio, Texas, USA. [l]Department of Immunology and Oncology, Centro Nacional de Biotecnología/Consejo Superior de Investigaciones Científicas, Madrid, Spain. [m]Division of Neurogenetics and Molecular Psychiatry, Department of Psychiatry and Psychotherapy, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany. [n]Department of Old Age Psychiatry and Cognitive Disorders, University Hospital Bonn, Bonn, Germany. [o]Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), University of Cologne, Cologne, Germany. [p]Department of Psychiatry. Long School of Medicine, University of Texas at San Antonio, San Antonio, Texas, USA. [q]Department of Microbiology, Immunology and Molecular Genetics. Long School of Medicine, University of Texas at San Antonio, San Antonio, Texas, USA.

Abstract:

Genome-wide association studies have identified the common IL-34-Y213X nonsense variant as a genetic risk factor for late-onset Alzheimer's disease (AD), yet its biological consequences remain largely unknown. Here, we combined human genetics, cerebrospinal fluid (CSF) and serum proteomics, transcriptomics, phenome-wide association analyses, and preclinical models to define the impact of genetically determined IL-34 deficiency. IL-34-Y213X was identified as a common dose-dependent loss-of-function allele, reducing IL-34 concentrations by up to 2.5 standard deviations in CSF and serum. IL-34 deficiency profoundly reshaped CSF proteomic networks, with downregulation of pathways involved in axon guidance and microglial support, together with upregulation of inflammatory and extracellular matrix signatures, and was associated with multiple neurological, inflammatory, and metabolic traits. Transcriptomic profiling of purified microglia from healthy IL-34 knockout mice revealed that IL-34 deficiency alone

was sufficient to induce a robust pro-inflammatory and disease-associated microglial (DAM) program, enriched for inflammatory pathways and Alzheimer's disease risk genes, including APOE, CLU, and CASS4. In APP/PS1 mice, IL-34 deficiency selectively depleted homeostatic gray-matter microglia, disrupted microglial tiling, and impaired plaque encapsulation, leading to altered amyloid plaque structure and increased neuritic damage. Importantly, these findings were recapitulated in postmortem temporal cortex from AD patients homozygous for IL-34-Y213X, who exhibited markedly reduced cortical microglial density and increased spatial dispersion, consistent with disruption of microglial network organization. Together, our findings define IL-34 deficiency as a common genetically determined condition that reprograms microglial identity, compromises microglial resilience, and exacerbates AD pathology, highlighting IL-34 signaling as a promising therapeutic target for neurodegenerative disease.

BOOK OF ABSTRACTS 2026

POSTER N.º 41

Introduced by: Hugo Peluffo

Title:

MYELOID CELL CD300F R218Q VARIANT ENHANCES PHAGOCYTOSIS AND IS ASSOCIATED WITH MILDER ALZHEIMER'S DISEASE PATHOLOGY

First Author: Lihong Song

Authors: Lihong Song[abc], Gabriele Ghisleni[d], Fabio Andrés Cawen[ac], Itziar de Rojas[efg], Anna López-Carrasco[h], Natalia Rego[i], Raquel Puerta[fj], Anna Antonell[kglm], Adrià Tort-Merino[kglm], Laura Montrreal[f], Frances Evans[e], Beibei Xu[ac], Aran Murphy[h], Mariam Shahdel[h], Pamira Kadreeva[h], Albert Lladó[kglm], Raquel Sánchez-Valle[kglm], Merce Boada[fg] , Amanda Cano[fg], Agustín Ruiz[fgn], Alzheimer's Disease Neuroimaging Initiative (ADNI)[o], Michael T. Heneka[p], Margarita Martín[abq], Hugo Peluffo[akr]

Filiation: [a]Biochemistry and Molecular Biology Unit, Biomedicine Department, Faculty of Medicine, University of Barcelona, Barcelona, Spain. [b]Multidisciplinary and translational research in inflammation and immunoallergy (METRI²A), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain. [c]Institut de Neurociències, Universitat de Barcelona, Barcelona, Spain. [d]Catholic University of Pelotas, Pelotas, Rio Grande do Sul, Brazil. [e]Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Esch-sur-Alzette, Luxembourg. [f]Ace Alzheimer Center Barcelona, Universitat Internacional de Catalunya, Barcelona, Spain. [g]CIBERNED, Network Center for Biomedical Research in Neurodegenerative Diseases, National Institute of Health Carlos III, Madrid, Spain. [h]Biochemistry and Molecular Biology Unit, Biomedicine Department, Faculty of Medicine, University of Barcelona, Barcelona, Spain. [i]Institut Pasteur de Montevideo, Uruguay. [j]Doctorate in Biotechnology, Facultat de Farmàcia i Ciències de l'Alimentació, Universitat de Barcelona, Barcelona, Spain. [k]Institut de Neurociències, Universitat de Barcelona, Barcelona, Spain. [l]Alzheimer's disease and other cognitive disorders Group, Hospital Clínic de Barcelona. [m]FRCB-IDIBAPS, Barcelona, Spain. [n]Biggs Institute for Alzheimer's and Neurodegenerative Diseases, University of Texas Health Science Center, San Antonio, Texas, USA. [o]Alzheimer's Disease Neuroimaging Initiative (ADNI). [p]Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg. [q]REI - RICOR, Instituto de Salud Carlos III, Madrid, Spain. [r]Institut Pasteur de Montevideo.

Abstract:
Many Alzheimer's disease (AD) risk genes are immune receptors or members of the endo-phagocytic system expressed by microglia and macrophages. CD300f is a lipid-binding immune receptor with an important role in phagocytosis and inflammation that shares many ligands with the AD risk gene TREM2. Aging is the main risk factor for AD, and CD300f is important for healthy mice aging, including the maintenance of cognitive abilities. We here show a disease modifying role for myeloid cell CD300f in AD by describing a gain-of-function variant in CD300f cytoplasmic tail that is associated with reduced clinical severity. The R218Q variant (C/T, rs2034310) is associated with better CDR-SB and MMSE clinical scores and healthier biomarker profile including decreased total CSF Tau levels and increased hippocampal glucose metabolism. The R218Q substitution is functionally relevant, modifying intracellular signaling and enhancing the half-life of CD300f, the phagocytic capability and its anti-inflammatory capacity. The CSF and serum levels of soluble CD300f correlates with the levels of p-Tau, disease progression and other immune receptors and inflammatory mediators such as TREM2. Soluble CD300f has been shown to be neurotoxic and interfere with synaptic pruning, and the R218Q variant induces a reduction of the levels of soluble CD300f in both CSF and serum. In vitro activation of CD300f show that it can regulate the expression of several AD risk genes. Taken together, these data implicate CD300f and its R218Q variant in the regulation of the progression of AD and may constitute promising targets for the design of neuroprotective strategies.

BOOK OF ABSTRACTS 2026

POSTER N.º 42

Introduced by: Borja Gómez-Cabañes

Title:

SHARED TRANSCRIPTOMIC PROFILES OF MELANOMA BRAIN METASTASES AND NEURODEGENERATIVE DISEASES: ALZHEIMER'S DISEASE, PARKINSON'S DISEASE, AND MULTIPLE SCLEROSIS

First Author: Irene Soler-Sáez

Authors: Irene Soler-Sáez[a], Alcida Karz[b], Marta R. Hidalgo[ac], Borja Gómez-Cabañes[a], Adolfo López-Cerdán[ad], José F. Català-Senent[a], María de la Iglesia-Vayá[d], Eva Hernando[b], Francisco García-García[a]

Filiation: [a]Computational Biomedicine Laboratory, Príncipe Felipe Research Center (CIPF), 46012, Valencia, Spain. [b]Department of Pathology, New York University Grossman School of Medicine, New York, NY 10016, US. [c]Area of Applied Mathematics, Department of Applied Mathematics, Universitat de València, Burjassot, Spain.

Abstract:

Melanoma frequently metastasizes to the brain, potentially facilitated by its neural crest origin, and displays intriguing clinical and molecular links to neurodegenerative disorders. To deepen the understanding of tumor neurobiology, we explored the shared transcriptional profiles between melanoma brain metastases (MBM) and Alzheimer's (AD), Parkinson's (PD), and multiple sclerosis (MS).

Using an in silico R-based approach, we performed differential expression meta-analyses using limma on 3 MBM datasets and 21 neurodegenerative datasets (10 AD, 7 PD, 4 MS). Common dysregulated gene signatures were identified, validated via resampling, and functionally characterized using STRINGdb and clusterProfiler. An open-access web tool was developed (https://bioinfo.cipf.es/metafun-mbm/) to host the interactive data.

All disease combinations shared more genes than expected by random chance. When comparing MBM to non-brain metastases (Scenario 1), we identified a neuronal-like phenotype consisting of 53 dysregulated genes linked to extracellular matrix, neurogenesis, and glycosylation (BGN, ST6GALNAC3). Conversely, comparing MBM to healthy brain controls (Scenario 2) characterized a neurodegenerative tumor profile of 195 genes, predominantly upregulated, involved in PD-associated translation, AD-linked development, and chromatin remodeling. Remarkably, ITGA10 and DNAJC6 emerged as key potential biomarkers significant in both analytical scenarios.

Our findings support the emerging notion that melanoma cells colonize the brain by adopting gene signatures reminiscent of neural cells altered by neurodegeneration. Characterizing these shared central nervous system pathologies uncovers novel MBM pathophysiology and reveals ITGA10 and DNAJC6 as promising biomarkers.

BOOK OF ABSTRACTS 2026

POSTER N.º 43

Introduced by: Chiara Galletti

Title:

DISRUPTED SYNCHRONY-NOISE BALANCE AS A SYSTEM-LEVEL SIGNATURE OF MOTOR CORTEX INSTABILITY IN PARKINSON'S DISEASE

First Author: Chiara Galletti

Authors: Chiara Galletti[abcd], Emmanuelle Wilhelm[ace], Cristina Pagge[ace], Ana McWhinnie[ace], Jaime Caballero-Insaurriaga[ace], Fernando Alonso-Frech[ace], Claudia Ammann[abcf], Guglielmo Foffani[abce]

Filiation: [a]HM CINAC (Centro Integral de Neurociencias Abarca Campal), Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain. [b]Reina Sofia Foundation Alzheimer Center, CIEN Foundation, ISCIII, Madrid, Spain. [c]Instituto de Investigación Sanitaria HM Hospitales, Madrid, Spain. [d]Universidad de Alcalá, Madrid, Spain.

Abstract:
Brain function relies on a dynamic equilibrium between perceptual stability and behavioural flexibility. This equilibrium is often framed at the cellular and synaptic levels as a balance between excitation and inhibition, which is disrupted in Parkinson's disease (PD). However, this view fails to capture system-level dynamics across space and time. Here, we propose the synchrony-noise balance (SynBa) as a governing principle of these dynamics, representing the ratio between coordinated, low-dimensional population fluctuations (synchrony) and independent, high-dimensional fluctuations (noise). We investigated SynBa in the motor cortex of 86 PD patients and 42 healthy controls using multi-muscle TMS-EMG recordings across a battery of TMS protocols, including SICI, ICF, and SICF. SynBa was operationalized as the intra-hemispheric homogeneity of motor-evoked potential amplitude fluctuations across muscles. Our results revealed that homogeneity was lower on the more affected side of PD patients compared to the less affected side and controls across all protocols. This alteration was mechanistically driven by excessive high-dimensional local fluctuations, indicating that increased local variance disrupted the stability of motor networks. Clinically, this disruption correlated with motor symptom severity on the less affected side, where homogeneity was lower in more advanced patients compared to early, levodopa-naïve patients. In contrast, the more affected side showed uniformly reduced homogeneity across disease stages, consistent with a progressive process that reaches early saturation. These findings suggest that PD pathophysiology extends beyond alterations in excitability to a fundamental collapse of synchrony-noise balance, where excessive local noise progressively compromises the system-level stability required for functional motor control.

BOOK OF ABSTRACTS 2026

POSTER N.º 44

Introduced by: Cristina Muriana-Fernández

Title:

GAMMA-FREQUENCY TRANSCRANIAL ALTERNATING CURRENT STIMULATION (GAMMA-TACS) AS POTENTIAL TREATMENT FOR ALZHEIMER DISEASE: A PRECLINICAL STUDY

First Author: Cristina Muriana-Fernández

Authors: Cristina Muriana-Fernández[a], Guillermo Sánchez-Garrido Campos[a], Juan Antonio Fernández Cabrera[a], José Manuel Hernández Curiel [a], Elena Rodríguez Sandoval[a], Javier Márquez- Ruiz[a], Ángel M Carrión[a]

Filiation: [a]Physiology, Anatomy and Cellular Biology Department, Pablo de Olavide University, Avda Rectora Rosario Valpuesta 1, 41089-Seville-Spain.

Abstract:
Transcranial Electrical Stimulation (tES) modulates cortical excitability via weak scalp-applied currents. Among its modalities, 40 Hz gamma transcranial Alternating Current Stimulation (gamma-tACS) is highly relevant for Alzheimer's disease (AD), a currently incurable neurodegenerative disorder characterized by progressive cognitive deficits, aberrant neuronal activity, and disrupted gamma oscillations linked to amyloid-beta (Aβ) and hyperphosphorylated tau (p-Tau) aggregates. Given that AD cases are projected to triple by 2050, non-invasive therapeutic interventions are urgently needed.
Here, we evaluated the therapeutic potential of chronic 40 Hz gamma-tACS in aged (>12-month-old) APP/PS1 mice. The animals received daily stimulation (30 min/day, 5 days/week) for up to four weeks. Neuropixels recordings revealed significantly increased hippocampal low-gamma power post-stimulation, demonstrating preserved network responsiveness to gamma modulation even in advanced stages of pathology. Behaviorally, while gamma-tACS did not alter open-field locomotor activity, it significantly increased latencies in the passive avoidance task, indicating enhanced memory retention. Furthermore, histological analysis showed a robust reduction in Aβ plaque density across both the cortex and hippocampus compared to sham-stimulated controls. Together, these data position tES as a promising non-invasive therapeutic intervention to mitigate AD symptoms.

BOOK OF ABSTRACTS 2026

POSTER N.º 45

Introduced by: Miguel A. Labrador-Espinosa

Title:

LONGITUDINAL PROGRESSION OF BRAIN HYPOMETABOLISM PATTERNS IN AUTOPSY-CONFIRMED AD AND LATE

First Author: Miguel A. Labrador-Espinosa

Authors: Miguel A. Labrador-Espinosa[a], Pascual Sánchez-Juan[a], Jesús Silva-Rodriguez[a], Michel J. Grothe[a]

Filiation: [a]Reina Sofia Alzheimer Centre , CIEN Foundation-ISCIII, 28031 Madrid, Spain.

Abstract:
Background: Limbic-predominant age-related TDP-43 encephalopathy (LATE) can mimic Alzheimer's disease (AD). Imaging-pathological studies suggest that LATE is associated with a temporo-limbic FDG-PET signature distinct from the typical temporo-parietal hypometabolism described in AD, but the temporal evolution of these patterns remains unclear. We investigated longitudinal ante-mortem FDG-PET trajectories in autopsy-confirmed LATE and AD.
Methods: Serial ante-mortem FDG-PET scans acquired over an interval of -11 to 0 years before death were analysed from 30 autopsy-confirmed AD and 10 LATE cases from ADNI (mean: -4.8±2.9 years; median: 3 scans/subject). FDG-PETs were normalized to MNI space, and SUVRs were calculated across 52 Harvard-Oxford regions. Region-wise z-scores quantified hypometabolism relative to healthy elderly controls (n=179). Longitudinal metabolic decline was modelled using linear mixed-effects models, with predicted z-scores estimated every 2 years over the decade before death and referenced to the estimated onset of memory symptoms. We also assessed the inferior-to-medial temporal ratio (IMTr) as a differential marker.
Results: In AD, pronounced hypometabolism (z>1) first emerged in the posterior cingulate cortex and precuneus approximately 6 years before death (5.5±4.5 years after symptom onset), progressively extending to temporal and lateral parietal regions (Fig-1a). By contrast, hypometabolism in LATE first appeared in hippocampal/parahippocampal regions up to 10 years before death, coinciding with symptom onset (0.1±3.3 years), and subsequently involved anterior temporal and frontal regions (Fig-1b). IMTr differed between AD and LATE throughout follow-up, including early stages (t=3.04,p=0.005,Fig-2).
Conclusion: LATE and AD show distinct origins and trajectories of regional hypometabolism, supporting FDG-PET as a tool for differential early diagnosis.

BOOK OF ABSTRACTS 2026

POSTER N.º 46

Introduced by: Jesús Silva Rodríguez

Title:

MEAN DIFFUSIVITY IN MTL GREY MATTER IS MORE SENSITIVE TO PLASMA %PTAU217 LEVELS THAN IN WHITE MATTER IN A COGNITIVELY UNIMPAIRED COHORT

First Author: Jesús Silva Rodríguez

Authors: Jesus Silva Rodriguez[a], Linda Zhang[a], Eva Alfayate[a], Marta Molero-Cartón[a], Sonia Wagner-Reguero[a], Pascual Sanchez-Juan[a], Michel J. Grothe[a]

Filiation: [a]Reina Sofia Alzheimer Centre, CIEN Foundation, ISCIII, Spain.

Abstract:
Background: Plasma p-tau217 has emerged as a reliable early biomarker of Alzheimer's disease (AD) pathology. Grey matter mean diffusivity (gmMD) from diffusion-weighted imaging is thought to reflect early microstructural change preceding detectable structural atrophy and white matter alterations in AD. However, correlates between gmMD and p-tau217 are yet to be studied.
Methods: 924 cognitively unimpaired elderly participants (mean age 74.8, range 69–87; 65% female from the Vallecas Project, a single-centre, 12-year longitudinal cohort with annual follow-ups, with 3T MRI and plasma p-tau217 measurements at baseline were included. %p-tau217, measured by mass spectrometry, was used to stratify participants into four risk groups: Low, Intermediate, Elevated, and High. Diffusion-weighted images were preprocessed using an in-house pipeline. Hippocampal gmMD and hippocampal cingulum white matter MD were extracted and compared between groups, controlling for age, sex, and APOE ε4 carriership.
Results: Sex distribution did not differ between groups, though higher %p-tau217 individuals were significantly older ($p<0.01$). Only the High group showed lower global cognition and memory scores ($p<0.01$). Hippocampal gmMD was significantly higher in Intermediate vs. Low and High vs. Low comparisons, but not Elevated vs. Low. No group differences were observed in hippocampal cingulum MD.
Conclusions: In a large, well-characterised cognitively unimpaired population, hippocampal gmMD changes are already detectable in those with elevated plasma %p-tau217, making it a sensitive indicator of early AD-related neurodegeneration, more so than white matter change.

BOOK OF ABSTRACTS 2026

POSTER N.º 47

Introduced by: Cristina Sánchez-Martín

Title:

MULTIMODAL CHARACTERIZATION OF COGNITIVELY DECLINING INDIVIDUALS WITH NORMAL PLASMA P-TAU217 LEVELS

First Author: Cristina Sánchez-Martín

Authors: Cristina Sánchez-Martín[a], Linda Zhang[a], Marina Fernández-Álvarez[a], Orfeas Vourkas[a], Andrés Jiménez-Pérez[a], Francisco J. López-González[a], Aitana Sogorb-Esteve[a], Sonia Wagner-Reguero[a], Teodoro del Ser[a], Pascual Sánchez-Juan[a], Jesús Silva-Rodríguez[a], Michel J. Grothe[a]

Filiation: [a]Reina Sofia Alzheimer Center, CIEN Foundation, ISCIII, Madrid, Madrid, Spain.

Abstract:
Background: While elevated plasma p-tau217 identifies individuals on a trajectory towards Alzheimer's disease, cognitive decline may also occur in individuals with normal p-tau217 levels, suggesting the involvement of non-AD mechanisms.
Methods: We studied 955 initially cognitively unimpaired (CU) older adults from the Vallecas Project, a longitudinal cohort study including detailed clinical evaluations, blood sampling, and 3T-MRI. Plasma %p-tau217 was measured using mass spectrometry and participants were classified as p-tau217(-) and p-tau217(+) (cut-off: 4.2%). According to clinical conversion to MCI/dementia, participants were further classified as cognitively stable (sCU) or progressive (pCU), and p-tau217(-)pCU were compared to p-tau217(+)pCU and to p-tau217(-)sCU controls. Variables included APOE-ε4 status, cognitive performance, MRI markers of regional atrophy, white matter hyperintensities (WMH), cerebral microbleeds (CMB), and plasma levels of GFAP and NfL. Baseline differences were assessed using ANCOVA and FDR-corrected Wilcoxon tests. Longitudinal analyses employed linear mixed-effects models.
Results: Over a mean follow-up of 5.3 ± 4 years, 55 p-tau217(-) (7.2 %) and 66 p-tau217(+) individuals (33.3%) developed MCI/dementia. APOE-ε4 prevalence was significantly lower in p-tau217(-)pCU compared to p-tau217(+)pCU ($p<0.001$), but groups did not differ in other variables at baseline and exhibited comparable medial temporal lobe (MTL) atrophy (Fig-1a). Longitudinally, both pCU groups showed similar cognitive decline (Fig-2a), but ptau217(-)pCU showed less pronounced atrophy with a distinct temporo-limbic distribution (Fig-1b) and a significantly higher CMB accumulation (Fig-2b).
Conclusions: Cognitively declining individuals with normal plasma p-tau217 are characterized by a distinct temporo-limbic atrophy pattern and increased cerebral microbleed accumulation, suggesting involvement of other MTL-targeting pathologies and cerebrovascular disease.

BOOK OF ABSTRACTS 2026

POSTER N.º 48

Introduced by: Francisco J. López-González

Title:

MULTIMODAL POST-MORTEM MRI STUDY OF CHOLINERGIC SYSTEM DEGENERATION ACROSS NEURODEGENERATIVE DISEASES

First Author: Francisco J. López-González

Authors: Francisco J. López-González[a], Milan Nemy[b], Cene Jerele[bc], Andrés Jiménez-Pérez[a], Alberto Rábano[a], María José López Martínez[a], Pascual Sánchez-Juan[a], Daniel Ferreira[b], Michel J. Grothe[a]

Filiation: [a]Reina Sofia Alzheimer Center, CIEN Foundation, ISCIII, Madrid, Spain. [b]Division of Clinical Geriatrics, Center for Alzheimer Research, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden. [c]University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia.

Abstract:

Background

We propose an imaging-pathologic validation study using multimodal post-mortem MRI to investigate cholinergic system degeneration in autopsy-confirmed dementia cases with underlying AD, Lewy body disease (LBD), mixed AD+LBD pathology, or other neurodegenerative diseases (OD).

Methods

We included 55 brain donors (21 AD, 14 AD+LBD, 8 LBD, 7 OD, and 5 non-demented neurological controls, CTRL) who underwent post-mortem in situ MRI and neuropathological examination. Cholinergic basal forebrain (cBF) volumes were extracted from T1-MRI, mean diffusivity (MD) values for cholinergic fiber pathways (cingulum, external capsule) were extracted from diffusion-weighted MRI; and white matter lesions along cholinergic tracts were also visually rated on FLAIR-MRI using the CHIPS scale. Group differences in cBF volumes, MD, and CHIPS were assessed with Mann-Whitney U tests. Associations of cBF volumes with MD and CHIPS measures of cholinergic pathways were examined using Pearson's correlation.

Results

AD and mixed AD+LBD showed lower cBF volumes and higher MD and CHIPS scores than LBD ($p<0.05$ and $p<0.01$), and mixed AD+LBD also differed from controls ($p<0.05$). Results were similar after adjusting for age differences between the groups. Across all cases, cBF volumes were strongly associated with MD values in cholinergic fiber pathways (cingulum: $r=-0.58$, $p<0.001$; external capsule: $r=-0.60$, $p<0.001$) and CHIPS scores ($r=-0.73$, $p<0.001$).

Conclusions

Post-mortem MRI revealed greater cholinergic system degeneration in pathologically-confirmed AD and mixed AD+LBD than in pure LBD and other neurodegenerative diseases. Multimodal imaging markers of cBF atrophy and cholinergic pathway degeneration are highly intercorrelated and provide complementary tools for comprehensive in-vivo assessment of cholinergic system degeneration.

BOOK OF ABSTRACTS 2026

POSTER N.º 49

Introduced by: Marina Fernández-Álvarez

Title:

NATURAL HISTORY AND PREDICTIVE FACTORS OF CEREBRAL MICROBLEED ACCUMULATION IN COGNITIVELY UNIMPAIRED OLDER ADULTS

First Author: Marina Fernández-Álvarez

Authors: Marina Fernández-Álvarez[a], Jesús Silva-Rodríguez[a], Mario Ricciardi[a], Cristina Sánchez-Martín[a], Linda Zhang[a], Orfeas Vourkas[a], Andrés Jiménez-Pérez[a], Francisco J. López-González[a], Sonia Wagner-Reguero[a], Aitana Sogorb-Esteve[a] ,Teodoro del Ser[a], Pascual Sánchez-Juan[a], Michel J. Grothe[a]

Filiation: [a]Reina Sofia Foundation Alzheimer Centre-CIEN Foundation-ISCIII, 28031 Madrid, Spain.

Abstract:

Background: Cerebral microbleeds (CMBs) are imaging markers of cerebral small vessel disease and linked to novel anti-amyloid therapies, yet their natural history and predictive factors in cognitively unimpaired older adults remain poorly understood.

Methods: We studied 1134 cognitively unimpaired older adults (74.8±3.9 years; 64.2% women) from the Vallecas longitudinal cohort study, including annual cognitive assessments, blood draws, and 3T-MRI acquisitions for up to 10 years (mean: 5.2±4 years; totaling 5810 MRIs). Plasma %ptau217 was measured at baseline using mass spectrometry. CMBs were identified on longitudinal T2*-GRE MRI using neuroradiologic visual ratings and quantified using a complementary automated method. We characterized baseline prevalence, anatomical distribution, and longitudinal changes in CMB burden. Logistic regressions and mixed-effects models tested the predictive value of demographics, vascular risk, %ptau217, APOE-ε4, AD polygenic risk score (PRS), and cognition with incident CMBs and quantitative CMB accumulation, respectively.

Results: Baseline CMB prevalence was 18% (42.1% lobar, 14.4% deep white matter, 43.5% subcortical). Over follow-up, 222/661 individuals (33.6%) developed incident CMBs, predominantly in lobar location. APOE-ε4 (OR=1.91, CI95%=[1.25–2.91], p=0.003) and PRS (OR=0.46, CI95%=[0.28–0.74], p=0.002) were significant predictors of incident CMBs. Quantitative CMB accumulation was associated with APOE-ε4 (IRR=1.09, CI95%=[1.03–1.15], p=0.003), PRS (IRR=0.94, CI95%=[0.89–0.99], p=0.020) and also conversion to MCI (IRR=1.12, CI95%=[1.05–1.19], p<0.001).

Conclusions: CMBs progressively accumulate in more than one-third of cognitively unimpaired older adults and are associated with cognitive decline. APOE-ε4 emerges as the most relevant predictor of CMB accumulation, independent of AD pathologic burden as measured by plasma %ptau217.

BOOK OF ABSTRACTS 2026

POSTER N.º 50

Introduced by: Andrés Jiménez Pérez

Title:

SERIAL ANTE-MORTEM MRI ANALYSIS OF REGIONAL ATROPHY PROGRESSION IN AUTOPSY-CONFIRMED LATE-NC WITH HIPPOCAMPAL SCLEROSIS

First Author: Andrés Jiménez Pérez

Authors: Andrés Jiménez Pérez[a], Linda Zhang[a], Cristina Sánchez-Martín[a], Francisco J. López-González[a], Alberto Rábano [a], Pascual Sánchez-Juan [a], David Wolk[b], Jesús Silva-Rodríguez[a], Michel J. Grothe[a]

Filiation: [a]Reina Sofia Alzheimer Centre, CIEN Foundation, ISCIII, Spain. [b]Department of Neurology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA.

Abstract:

Background:

Limbic-predominant age-related TDP-43 encephalopathy neuropathologic change (LATE-NC) is often comorbid to Alzheimer's disease neuropathologic change (ADNC) and it is linked to hippocampal sclerosis (HS), which contributes to amnestic impairments independently of AD. Previous cross-sectional imaging-pathologic association studies have described a distinct temporo-limbic atrophy pattern associated with HS, but longitudinal studies on the pattern of atrophy progression are lacking.

Methods:

We studied 87 amnestic dementia patients from our brain bank cohort (mean age 88.70±7.5) who underwent serial ante-mortem 3T-MRI acquisitions before death (range 1 to 14 years; median 3 scans/subject) and had detailed neuropathologic evaluation at autopsy that included evaluations of ADNC, LATE-NC, and HS. The CAT toolbox in SPM12 was used to extract gray matter volumes of 52 brain regions using the Harvard-Oxford atlas. Regional z-scores were calculated with reference to a sample of 1032 cognitively normal elderly controls. Linear mixed-effect models were used to estimate regional atrophy trajectories in individuals with LATE-NC+HS (N=40) and typical AD without HS (AD-noHS; N=47). Time of death was used as the temporal anchor and model predictions were generated at pre-defined time points (-10, -6, -2 and 0 years before death) to see the evolution of atrophy in each group.

Results:

LATE-NC+HS and AD-noHS showed similar overall patterns of temporo-parietal atrophy progression (Fig-1). However, in LATE-NC+HS atrophy occurred generally earlier, with significant atrophy in anterior and medial temporal structures as early as 10 years before death and progressed faster over time. Direct comparisons between the two groups revealed more pronounced atrophy in anterior and medial temporal regions at earlier timepoints, which progressed to subcallosal and frontal areas at later time points (Fig.1).

Conclusions:

Longitudinal MRI analysis demonstrates that LATE-NC associated HS has a distinct neurodegeneration trajectory relative to AD-noHS that is characterized by earlier and more pronounced anterior and medial temporal lobe atrophy that progresses to subcallosal and frontal paralimbic cortical areas over time.

BOOK OF ABSTRACTS 2026

POSTER N.º 51

Introduced by: Linda Zhang

Title:

ASYMMETRIC PERFUSION PATTERNS IN EARLY COGNITIVE IMPAIRMENT ASSOCIATED WITH CSF TAU LEVELS AND LATERALISED COGNITIVE DOMAINS

First Author: Linda Zhang

Authors: Linda Zhang[a], Marina Fernandez-Alvarez[a], Cristina Sanchez-Martin[a], Orfeas Vourkas[a], Andres Jimenez-Perez[a], Eva Alfayate[a], Teodoro del Ser[a], Aitana Sogorb-Esteve[a], Isabel Lopez-Torres[a], Oriol Dols-Icardo[b], Agustin Ruiz[c], Pascual Sanchez-Juan[a], Jesus Silva-Rodriguez[a], Michel J. Grothe[a]

Filiation: [a]Reina Sofia Foundation Alzheimer Centre-CIEN Foundation-ISCIII, 28031 Madrid, Spain. [b]Sant Pau Memory Unit, Hospital de la Santa Creu i Sant Pau, Institut de Recerca Sant Pau i Universitat Autònoma de Barcelona, Barcelona, Spain.[c]Ace Alzheimer Center Barcelona – Universitat Internacional de Catalunya, Barcelona, Spain.

Abstract:

Background: Cerebral hypoperfusion has been observed in patients with mild cognitive impairment (MCI) and Alzheimer's disease (AD), although its relation to AD pathology is not well understood. We used multi-post-labelling delay arterial spin labelling (multi-PLD ASL) and CSF AD biomarkers to investigate the relationship between perfusion, AD pathology, and cognition.

Methods: 550 elderly participants (mean age: 70.5 ± 7.6 years, range: 56-93; 67% female) with 3T MRI multi-PLD ASL sequences were selected from the SCAP-AD project. Participants were divided into cognitively unimpaired (Global Deterioration Scale (GDS) 1-2, n=286) and mild impaired (GDS3+, n=264) groups. Preprocessed partial volume-corrected perfusion and arterial transit time (ATT) images were analysed in voxel-wise GLMs, controlling for age and sex. CSF biomarkers (abeta42/40, ptau181, total tau) were analysed in a subset of 141 individuals using a Lumipulse platform with commercially available kits (Fujirebio). Cognitive domain scores were determined using the RBANS neuropsychological battery.

Results: Hypoperfusion was observed in the temporal and anterior cingulate regions in GDS3+ compared to GDS1-2 individuals (dmax=0.32). ATT was slower in GDS3+ individuals in the right temporal lobe only (d=0.28). Asymmetry indices of perfusion and ATT in temporal lobe regions were also calculated. MTL asymmetry was associated with greater CSF ptau181 (p=0.046) and total tau (p=0.043) levels, but not abeta42/40, accounting for age, sex, and GDS score. Perfusion asymmetry in the middle-superior temporal lobe was significantly associated with language (p=0.036) and visuospatial construction (p=0.009) domains.

Conclusions: Cognitively impaired individuals exhibit bilateral temporal lobe hypoperfusion and lateralised ATT delays. Notably, asymmetry in temporal lobe grey matter perfusion appears to be linked to tau rather than amyloid pathology, suggesting that tau may exacerbate perfusion imbalances in early cognitive impairment, with effects on known lateralised cognitive domains.

BOOK OF ABSTRACTS 2026

POSTER N.º 52

Introduced by: Rachele Marino

Title:

DYNAMIC REMODELING OF SUMO-1YLATION ACROSS THE CENTRAL NERVOUS SYSTEM AND PERIPHERAL COMPARTMENTS DURING ALZHEIMER'S DISEASE PROGRESSION

First Author: Rachele Marino

Authors: Rachele Marino[ab], Pamela Cappelletti[c], Rita Scarcello[ab], Ludovica Zaccagnini[b], Kambiz Hassanzadeh[b], Valeria de Turris[d], Marco Cimino[b], Melania Filareti[c], Rita Maccarone[e], Massimo Corbo[f], Annalisa Davin[g], Valentina Medici[g], Tino Emanuele Poloni[g], Marco Feligioni[hc]

Filiation: [a]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, 67100 L'Aquila, Italy. [b]European Brain Research Institute - Rita Levi Montalcini Foundation, 00161 Rome Italy. [c]Casa di Cura Igea - Department of Neurorehabilitation Sciences, Milan, Italy. [d]Center for Life Nano- & Neuro-Science, Fondazione Istituto Italiano di Tecnologia (IIT), 00161 Rome, Italy. [e]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, 67100 L'Aquila, Italy. [f]Need Institute, Foundation for the Cure and Rehabilitation of Neurological Diseases, Milan, Italy. [g]Department of Neurology and Neuropathology, Golgi-Cenci Foundation, Abbiategrasso, 20081 Milano, Italy & Department of Rehabilitation, ASP Golgi-Redaelli, Abbiategrasso, 20081 Milano, Italy. [h] European Brain Research Institute - Rita Levi Montalcini Foundation, 00161 Rome Italy.

Abstract:

Alzheimer's disease (AD) is a progressive neurodegenerative disease characterized mainly by b-amyloid and Tau aggregates. The expression, localization and degradation of both proteins are modulated by different post-translational modifications, including SUMOylation. However, the role of SUMOylation in AD onset and development is poorly known. In this study, we investigated whether SUMO-1ylation undergoes disease stage-dependent changes across brain and peripheral compartments and evaluating SUMO-1 as potential biomarker for AD progression.

SUMO-1 and its conjugating enzyme UBC9 were analysed in human post-mortem brain tissues, peripheral blood mononuclear cells (PBMCs), circulating total (TEV) and neuronal-derived extracellular vesicles (NDEVs) from non-demented subjects, individuals with mild cognitive impairment (MCI), and AD patients. Furthermore, the effects of oxidative stress and okadaic acid on SUMO-1 and UBC9 were analysed in mouse primary cortical neurons.

We identified a progressive redistribution of SUMO-1 and UBC9 from the nucleus to the perinuclear region and cytoplasm along AD stages, accompanied by increased SUMO-1ylation in human frontal cortex. Additionally, SUMO-1 and UBC9 re-localized in the cytoplasm of AD PBMCs, in which SUMO-1 aggregation increased in MCI condition. In TEV, SUMO-1ylation significatively increased in MCI and showed a trend in AD, whereas NDEVs displayed an increase in MCI followed by a significant decrease in AD. In primary cortical neurons, oxidative stress, but not Tau hyperphosphorylation alone, caused abnormal SUMO-1/UBC9 distribution, suggesting oxidative stress as the main cause of SUMO-1ylation impairment. These findings demonstrate dynamic, compartment-specific remodelling of SUMO-1ylation during AD progression and identify extracellular vesicle-associated SUMO-1ylation as promising biomarker of disease progression.

BOOK OF ABSTRACTS 2026

POSTER N.º 53

Introduced by: Javier Sáez-Valero

Title:

MEPRIN-β LEVELS ARE INCREASED IN THE BRAIN AND THE CEREBROSPINAL FLUID OF ALZHEIMER'S DISEASE PATIENTS

First Author: Javier Sáez-Valero

Authors: Sergio Escamilla[abc], Carlos Avilés-Granados[abc], Carmen Márquez-Marco[a], Maximilian Keller[d], Irene Sánchez-Domínguez[ef], Inmaculada Cuchillo-Ibáñez[abc], Fernando Aguado[ef], Henrik Zetterberg[ghijk], Claus U. Pietrzik[d], Javier Sáez-Valero[abc]

Filiation: [a]Instituto de Neurociencias de Alicante, Universidad Miguel Hernández-CSIC, San Juan de Alicante. [b]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), San Juan de Alicante, Spain. [c]Instituto de Investigación Sanitaria y Biomédica de Alicante (ISABIAL), Alicante, Spain. [d]Molecular Neurodegeneration, Institute for Pathobiochemistry, University Medical Center Mainz, Mainz, Germany. [e]Department of Cell Biology, Physiology and Immunology, Faculty of Biology, University of Barcelona, Barcelona, Spain. [f]Institute of Neurosciences, University of Barcelona, Barcelona, Spain. [g]Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden. [h]Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Mölndal, Sweden. [i]UK Dementia Research Institute at UCL, London, UK. [j]Hong Kong Center for Neurodegenerative Diseases, Hong Kong, China. [k] UW Department of Medicine, School of Medicine and Public Health, Madison, Wisconsin, USA.

Abstract:
In this study, we assessed the levels of the alternative β-secretase, meprin-β, in the brain and cerebrospinal fluid (CSF) of subjects suffering Alzheimer's disease (AD). The zymogen and the active proteolytic fragment of meprin-β were characterized by immunoblotting using ectodomain N-terminal and C-terminal antibodies. We examined meprin-β changes in extracts from AD frontal cortex (different Braak stages) compared with controls (non-demented, Braak 0), as well as in CSF samples from AD patients or non-AD controls. CSF meprin-β levels were also determined in 19-month old TgF344-AD and wild-type rats. Brain and CSF from a Mep1b-null mouse served to characterize the specificity of the immunoreactive bands for meprin-β. Human induced pluripotent stem cell (iPSC)-derived neuronal cultures were treated with 2 μM Aβ42 for 24 hours. We found that meprin-β is present in human brain extracts and CSF as several distinct species, attributed to the zymogen and the active fragments. These species were absent in brain and CSF fluid from a Mep1b-null mouse. No fragments of meprin-β were detected in brain extract, either in CSF. Only the mature forms of meprin-β are increased in frontal cortex extracts (from Braak V-VI), but not the zymogen. The MEP1-B mRNA levels are increased in Braaks III-IV and V-VI compared with controls. The meprin-β species are increased in iPSC-derived neuronal cultures treated with Aβ42. Finally, we demonstrated elevated levels of the mature meprin-β in the CSF of AD patients and in TgF344-AD rats. Our data support a role of meprin-β in Alzheimer's pathology.

BOOK OF ABSTRACTS 2026

POSTER N.º 54

Introduced by: Laura Trujillo-Estrada

Title:

AGED FERRITIN-ENRICHED MICROGLIA EXHIBIT A DYSTROPHIC PHENOTYPE WITH ULTRASTRUCTURAL SIGNS OF METABOLIC DYSFUNCTION IN ALZHEIMER'S DISEASE

First Author: Laura Trujillo-Estrada

Authors: Laura Trujillo-Estrada[ab], Elisabeth Sanchez-Mejias[ab], Marina Mejias-Ortega[ab], Vicente Roca-Agujetas[cd], Cristina Nuñez-Diaz[ab], Maria Angeles Arredondo-Alcala[ab], Clara Garcia-Mayor[cd], Clara Muñoz-Castro[cd], Marisa Vizuete[cd], Javier Vitorica[cd], Antonia Gutierrez[ab]

Filiation: [a]Dpto. Biología Celular, Genética y Fisiología, Facultad de Ciencias, Universidad de Málaga. Instituto de Investigación Biomédica de Málaga-IBIMA-Plataforma Bionand, Malaga, Spain. [b]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED). Madrid, Spain. [c]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED). Madrid, Spain. [d]Dpto. Bioquímica & Biología Molecular, Facultad de Farmacia, Universidad de Sevilla, Spain. Instituto de Biomedicina de Sevilla (IBiS)-Hospital Universitario Virgen del Rocío CSIC. Seville, Spain.

Abstract:
Microglia play a critical role in Alzheimer's disease (AD) pathology, as many genetic risk variants for late-onset AD are expressed in these cells. Dysfunctional microglia drive pathological progression through loss of neuroprotective and phagocytic function, however the temporal dynamics and mechanisms underlying microglial dysfunction across AD remains poorly understood. We previously identified a population of dystrophic microglia in the hippocampus of AD patients suggesting that specific pathological mechanisms underlie this dysfunctional transition. Here, we combined confocal immunolabeling, immunogold electron microscopy, image analysis and molecular profiling to characterize the microglial pathology in the hippocampus of aged APP transgenic mice and human postmortem brain samples (Braak 0, II, V–VI). Aged APP microglia accumulated high levels of ferritin, indicative of disrupted iron homeostasis. Ferritin-enriched microglia displayed a dystrophic morphology characterized by spheroidal process swellings and profound mitochondrial abnormalities including the appearance of donut-shaped morphologies, consistent with hypoxia or ROS-induced stress. These pathological microglia preferentially clustered around amyloid plaques and increased in abundance with disease progression. Human AD microglia recapitulated features identified in aged APP microglia. Ultrastructural analysis revelead abundant lipid droplets within ferritin-enriched microglia, suggesting impaired lipid metabolism. Ferritin-enriched microglia included a subpopulation of dark microglia with ultrastructural features of cellular stress. The convergence of ferritin accumulation, mitochondrial abnormalities, lipid dysregulation, and dystrophic morphology supports a ferroptosis-prone metabolically compromised microglial phenotype that emerges with aging and AD progression.
Supported by Instituto de Salud Carlos III PI24/00274(AG), PI24/00308(JV) co-financed with FEDER funds from EU, by Junta de Andalucía PPRO-CTS950-G-2023(AG), US-1262734(JV), and by CIBERNED.

BOOK OF ABSTRACTS 2026

POSTER N.º 55

Introduced by: Iván Burgueño-García

Title:

ANOTHER PERSPECTIVE ON HIPPOCAMPAL SCLEROSIS: LATE AND ASTROGLIOSIS

First Author: Iván Burgueño-García

Authors: Iván Burgueño-García[a], Alicia Uceda-Heras[a], Paloma Ruiz-Valderrey[a], Sandra Lázaro-González[a], Zulema Sanz-Herranz[a], Laura Saiz-Aúz[a], María José López-Martínez[a], Alberto Rábano[a]

Filiation: [a]Reina Sofia Alzheimer Center, CIEN Foundation, ISCIII, Madrid, Spain.

Abstract:

Introduction

LATE-NC is a neurodegenerative pathology characterized by TDP-43(+) inclusions in the medial temporal lobe, frequently occurring in combination with Alzheimer's disease and other dementias. Its close association with hippocampal sclerosis (HS) is a subject of debate. Furthermore, as HS progresses, a proliferation of astrocytes is observed.

Objetives

The objective is to study the relationship between different types of TDP43(+) inclusions and astrogliosis with HS.

Materials and Methods

Complete neuropathological phenotyping was performed on 167 post-mortem brains from the VARS (Vallecas Alzheimer Reina Sofía) clinicopathological cohort, including the classification of LATE-NC and EH pathology. TDP-43(+) inclusions in the amygdala were quantified, and cases were classified according to the presence/absence of 7 different types of TDP-43(+) inclusions. To assess astrogliosis, the percentage of GFAP-stained area was measured at the subiculum-CA1 transition (prosubiculum).

Results

Two patterns are detected in relation to the progression of HS: 1) some types of inclusion (thick neurites, inclusions associated with tangles, inclusions in lamina II) predominate only in the advanced phases of HS, and 2) others (cytoplasmic neuronal inclusions, pre-inclusions) also predominate in the initial phases. The percentage of GFAP-stained area increases with increasing HS stages (Spearman, p-value<0,001) and LATE-NC (Spearman, p-value<0,001).

Conclusions

The different morphological types of TDP-43(+) inclusions appear according to distinct evolutionary patterns in the progression of HS. This fact may contribute to explaining the pathogenic relationship between LATE-NC and HS.

The neuronal loss observed in HS correlates with astrogliosis, adding further evidence for the progression of HS in both early and advanced stages.

BOOK OF ABSTRACTS 2026

POSTER N.º 56

Introduced by: Sara Alberdi-Torres

Title:

DESCRIPTION OF SUBCELLULAR ARCHITECTURE DISTURBANCES ASSOCIATED TO HUNTINGTON'S DISEASE BY IN-TISSUE MULTISCALE 3D ELECTRON MICROSCOPY

First Author: Maria Rosario Fernandez-Fernandez

Authors: Sara Alberdi-Torres[ab], Saul Alcala-Perez[ab], Beatriz Granados-Rodriguez[ab], Jose-Jesus Fernandez[ab], Maria Rosario Fernandez-Fernandez[acd]

Filiation: [a]Centro de Investigación en Nanomateriales y Nanotecnología-Consejo Superior de Investigaciones Científicas (CINN-CSIC/U. Oviedo). El Entrego, Asturias, Spain. [b]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA-FINBA). Oviedo, Spain. [c]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA-FINBA). Oviedo, Spain. [d] Instituto de Biomedicina y Biotecnología de Cantabria-Consejo Superior de Investigaciones Científicas (IBBTEC-CSIC). Santander, Spain.

Abstract:

Huntington's disease (HD) is a genetically inherited dominant neurodegenerative disorder caused by expansion of a CAG repeat sequence in the coding sequence of HTT protein. Patients develop progressive motor dysfunction, cognitive decline, and psychological alterations. There is no effective treatment for the disease and, consequently, the search for efficient therapeutic targets and the identification of reliable biomarkers, to follow disease progression and test the effectiveness of future treatments, are all paramount.

In situ analysis of subcellular architecture and molecular organization of cells and tissues under physiological conditions can be achieved by cryofixation (vitrification) and cryogenic electron microscopy (cryo-EM). Cryo-volume imaging with serial cryo-FIB/SEM (Focused Ion Beam/Scanning Electron Microscopy) operates by cyclically (i) milling a thin layer of the specimen using the FIB, followed by (ii) SEM imaging of the exposed surface. Cryo-volume imaging with cryo-electron tomography (cryo-ET) relies on transmission electron microscopy (TEM) and the volume is computed by combining a series of projection images acquired at different tilted views from a sample thin enough for TEM (typically < 300 nm).

We present here our approach, combining tissue cryofixation, multiscale 3DEM and image processing, applied to understanding disruptions in the subcellular architecture associated to HD neurodegeneration. In-tissue studies of both central and peripheral tissues from animal models and human post-mortem samples have facilitated understanding disruptions in the protein synthesis machinery and the mitochondrial network associated to HD.

BOOK OF ABSTRACTS 2026

POSTER N.º 57

Introduced by: Laura Saiz Aúz

Title:

CIEN TISSUE BANK: THE BUILDING OF A COMPREHENSIVE MULTIDIMENSIONAL CATALOGUE

First Author: Laura Saiz Aúz

Authors: Laura Saiz Aúz [a], Iván Burgueño García[a], Sandra Lázaro[a], Zulema, Sanz[a], Alberto Rábano Gutiérrez[a]

Filiation: [a]Reina Sofia Foundation Alzheimer Centre-CIEN Foundation-ISCIII, 28031 Madrid, Spain.

Abstract:

The CIEN Tissue Bank (CIEN-TB), the biobank of the CIEN Foundation, Carlos III Health Institute, started its activity in 2010 at the Reina Sofía Foundation Alzheimer's Center, that includes a nursing home for patients with dementia. Its brain banking activity comprises an internal program, focused on postmortem brain donations from the Vallecas Alzheimer Reina Sofía (VARS) Cohort, and an external program, aimed at the population of the Madrid Region, principally. Since 2023 the CIEN-TB set up a clinical follow-up program for brain donors registered in the external donation program.

Over 16 years, CIEN-TB has received 952 neurological tissue donations, 197 from its internal program and 755 from the external program. Donations involve postmortem brain tissue, cerebrospinal fluid (CSF), skin, and spinal cord samples in some pathologies. Whenever possible, a postmortem magnetic resonance imaging (MRI) scan is acquired before autopsy. In addition, VARS Cohort participants contribute annual blood samples and MRI during their follow-up at the center.

As part of its transition toward a digital biobank, CIEN-TB initiated in 2022 the scanning of histological slides from the VARS Cohort donated brains, which has been extended to the external program. Furthermore, through the CIEN Biomarker Platform, several multi-omic analyses have been performed on postmortem CSF samples and longitudinal blood samples from VARS participants.

The integration of clinical and longitudinal follow-up data, neuropathological classification, MRI scans, digitized immunostainings, and multi-omic datasets creates a multidimensional, well-classified, coded and accessible catalogue of samples and associated data for research purposes that is presented in this work.

SPONSORS

Meet our sponsors:

Diamond

Platinum

Bronze