Molecular Neurodegeneration

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DESCRIPTION

The principal focus of the research group is the application of proteomic and genomic techniques to understand the process of synapse degeneration, an early event in AD and other neurodegenerative diseases. The identification of protein biomarkers and genetic risk factors is meticulously validated in clinical and neuropathological studies using ultrasensitive immunoassays (Simoa) and state-of-the-art technologies including targeted/quantitative mass spectrometry, isolation of synaptosome fractions, RNA sequencing, proximity ligation assays and in vitro massively parallel reporter gene assays.

MAIN LINES OF RESEARCH

- Development of polygenic risk scores based on genetically regulated synapse dysfunction to improve the early detection of individuals at risk for neurodegenerative diseases and psychiatric disorders.
- Development of synaptic biomarkers to improve the diagnosis of neurodegenerative diseases and psychiatric disorders.
- Study of miRNA-mediated synapse dysfunction in neurodegenerative diseases and psychiatric disorders to guide future therapeutic strategies.

SCIENTIFIC CHALLENGES

Our research has a great impact on society because we want to transfer the knowledge and technology of our work to the National Healthcare System. With emerging disease-modifying therapies on the horizon, there is an urgent need for biomarkers that reflect target engagement and therapeutic respon-

se, a gap that could be filled by these promising biomarkers.

- Knowledge and technological transfer. Our goal is to transfer the antibodies and immunoassays validated for synaptic proteins to market. Initially for research use and, in the long term, for approval of in vitro diagnostic assays to incorporate the biomarkers into clinical routine (there are no biofluid markers of synapse loss currently used in clinical routine). In addition, our findings will have an important impact on human health by guiding therapeutic strategies that could prevent or relieve synaptic stresses in AD.
- International funding. One of the strengths of our group is the internationalisation capacity, based on the awarded projects (JPND, Alzheimer Association), the participation in international networks (University of Gothenburg, University of Eastern Finland, University of Amsterdam, University of Pennsylvania, Mayo Clinic, John Hopkins, Oxford University, University of Nottingham among others) and incorporation into international consortium (European Alzheimer DNA Bank). We want to achieve new international grants that support our research in parallel to national funding and collaborations.
- Visibility and scientific dissemination activities. Perform social and health professional talks to transfer our research, as well as participate in different national and international meetings by posters and oral presentations.

ACTIVE GRANTS

- Belbin, Olivia Elizabeth. Prediagnostic early synaptic disturbances in neurodegenerative diseases. JPND2021-650-078. EU JOINT ACTIONS. Alteraciones preclíncas de sinapsis en enfermedades neurodegenerativas. AC21_2/00017. Instituto de Salud Carlos III (ISCIII). Duration: 2022-2024. 154.880,00 €.
- Belbin, Olivia Elizabeth. Estudio traslacional de una predicción de riesgo poligénico y biomarcadores para la detección de la degeneración sináptica en la enfermedad de Alzheimer. PI21/00063. Instituto de Salud Carlos III (ISCIII). Duration: 2022-2024. 111.320,00 €.
- Belbin, Olivia Elizabeth. Role of synaptic miRNA and astrocyte miRNA delivery in Alzheimer's disease. AARG-22-974373. Alzheimer's Association. Duration: 2022-2025. 141.222,50 €.
- Belbin, Olivia Elizabeth. Validación de prototipos de inmunoensayos para la detección y seguimiento de sinaptopatía en biofluidos de pacientes con enfermedades neurodegenerativas y trastornos afectivos. DTS22/00111. Instituto de Salud Carlos III (ISCIII). Duration: 2023-2025. 84.700,00 €.
- Cervantes Gonzalez, Alba. Contratos PFIS 2022. FI22/00241. Instituto de Salud Carlos III (ISCIII). Duration: 2023-2026. 119.567,00 €.

GRANTS AWARDED

- Belbin, Olivia Elizabeth. Grup de Recerca en Demències: Sant Pau. 2021 SGR 00979. Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Duration: 2022-2025. 40.000,00 €.

SCIENTIFIC PRODUCTION

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- Ferrer P, Puertollano D, Querol M, Sánchez É, Valle N, Cervantes A, Nuñez R, Pegueroles J, Dols O, Iulita MF, Aldecoa I, Molina L, Sánchez R, Fortea J, Belbin O, Sirisi S, Lleó A. Amyloid precursor protein ßCTF accumulates in synapses in sporadic and genetic forms of Alzheimer's disease. NEUROPATHOLOGY AND APPLIED NEUROBIOLOGY. 2023; 49(1):e12879. DOI:10.1111/nan.12879. PMID:36702749. IF:5,000 (Q1/2D). Document type: Article.
- Goossens J, González AC, Dewit N, Lidón L, Fortea J, Alcolea D, Lleó A, Belbin O, Vanmechelen E. Evaluation of cerebrospinal fluid levels of synaptic vesicle protein, VAMP-2, across the sporadic Alzheimer's disease continuum. Alzheimers Research & Therapy. 2023; 15(1):186. DOI:10.1186/s13195-023-01336-0. PMID:37898760. IF:9,000 (Q1/1D). Document type: Article.

- Iulita MF, Bejanin A, Vilaplana E, Carmona M, Benejam B, Videla L, Barroeta I, Fernández S, Altuna M, Pegueroles J, Montal V, Valldeneu S, Gimenez S, González S, Torres S, El Bennadi SE, Padilla C, Aranha MR, Estelles T, Illán I, Belbin O, Valle N, Camacho V, Blessing E, Osorio RS, Videla S, Lehmann S, Holland AJ, Zetterberg H, Blennow K, Alcolea D, Clarimón J, Zaman SH, Blesa R, Lleó A, Fortea J. Association of biological sex with clinical outcomes and biomarkers of Alzheimer's disease in adults with Down syndrome. Brain Communications. 2023; 5(2):fcad074. DOI:10.1093/braincomms/fcad074. PMID:37056479. Document type: Article.