The Future of Biomedical Research Lecture Series

Scanning small molecules in the blood, CSF and brain during mild cognitive impairment and progression to Alzheimer’s Disease

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Date: 10/11/2017 - 12:30h
Place: Salón de Actos CIPF

Abstract: Dementia is a devastating illness for both patients and their families, with Alzheimer’s disease (AD) estimated to account for up to 80% of total dementia cases. The ‘World Alzheimer’s report 2015’ estimates that there are approximately 46 million AD patients worldwide. Three of the four treatments for AD (Donepezil, Rivastigmine and Galantamine) are cholinesterase inhibitors that target the pathological reduction of acetylcholine levels, while the fourth treatment Memantine is an NMDA antagonist. Unfortunately these drugs only treat symptoms and are not disease-modifying. Since all clinical trials have failed to find a successful therapy, the effort to find new drug targets has intensified and we are using more “unconventional” untargeted discovery methods. We used metabolomics to study the blood of dementia patients. From these first studies we found that particular lipids were depleted in the circulation. After these initial findings we have used our methods in brain, CSF and blood, some in longitudinal and validation cohorts in order to find drug targets and biomarkers that can help with diagnosis at an earlier stage, before memory loss is irreversible. Metabolic fingerprinting can be useful at many levels, and I will show examples for diagnosis, therapy optimising and repurposing, propose life-style interventions and biomarkers that could be implemented in early-AD clinical trials.