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Biochemical detection of misfolded amyloid-beta oligomers for sensitive diagnosis of Alzheimer's disease

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Alzheimer's Disease (AD), the most common form of dementia, is a progressive neurological disorder affecting more than 5 million people in US. Unfortunately, there is not effective treatment or accurate pre-clinical diagnosis for AD. The neuropathological hallmarks of AD are neuronal loss, synaptic alteration and brain accumulation of misfolded protein aggregates. Compelling evidence suggest that the misfolding and aggregation of amyloid-beta peptide (Aβ), is the triggering factor of AD pathology. The clinical diagnosis of AD is made at late stages of the disease and includes clinical, neuropsychological and imaging methods. At this time however, validated diagnostic markers for early diagnosis of the disease are not available. The goal of this study was to develop an early and sensitive method for biochemical diagnosis of AD based on specific detection of misfolded Aβ oligomers, which have been shown to play a central role in AD pathogenesis. Our experimental approach was to exploit the functional property of Aβ oligomers to accelerate the polymerization of monomeric Aβ as a way to measure their presence in biological fluids. Using this approach we were able to detect as little as 3 femto-moles of Aβ oligomers. Most importantly, using cerebrospinal fluid we were able to distinguish AD patients from control individuals not affected by neurodegenerative diseases and patients affected by a variety of other neurodegenerative disorders with overall sensitivity of 93% and specificity of 85%. These findings provide the basis to develop a highly sensitive and specific biochemical test for AD diagnosis with the potential for pre-symptomatic detection of the disease. This achievement would be a major milestone in the field, because it will have a direct impact on the development of novel therapeutic approaches and on giving existing therapies the highest possibility to produce benefit to the patients.

Biography

Dr Soto is Professor of Neurology and Director of Mitchell Center for Alzheimer's disease and related Brain Disorders at the University of Texas Medical School in Houston. He received his PhD in biochemistry and molecular biology from the University of Chile in 1993. Between 1995 and 1998 he was Assistant Professor at the New York University School of Medicine. Between 1999 and 2003, Dr Soto was Senior Scientist, Chairman of the Department of Molecular Neurobiology and Executive Scientific Advisor at Serono International in Switzerland. Between 2003 and 2008, he was Professor of Neurology at the University of Texas Medical Branch in Galveston. Dr Soto has received numerous awards and has been invited speaker to many International scientific meetings worldwide. He has been awarded many grants from NIH, and private foundations for a total funding of over 30 million dollars. Dr Soto's has published over 130 peer-review publications which have been extensively highlighted in the scientific literature and lay media with several hundreds of articles published in newspapers, magazines, TV and radio worldwide about his work.

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