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Combination of mass spectrometry-ELISA platforms for Alzheimer blood biomarkers

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Two pathological hallmarks of Alzheimer's disease (AD) are Tau-containing neurofibrillary tangles and amyloid β protein (Aβ)-containing neuritic plaques. Due to the heterogeneity and multifactorial nature of AD, a single biomarker for diagnosis of AD has not been identified. In this study, we have collected peripheral blood mononuclear cells (PBMC) and plasma from AD patients and cognitive normal subjects. We have converted PBMC to induced pluripotent stem cell (iPSC) lines and we have further differentiated iPSC into human 3D neurons. At autopsy, AD pathology was confirmed in brains of patients from whom we derived blood, iPSC and 3D neurons. Quantitation of Aβ and Tau by ELISA illustrated much higher levels of Aβ and phosphorylated Tau at residues Thr 181 and Thr 231 in brain tissue from superior and inferior frontal cortex area, compared to those from cerebellum region. Liquid chromatography/mass spectrometry was used to analyze plasma, iPSC, 3D neurons and post-mortem brain tissue labelled with isobaric mass tags for relative protein quantification. Our study revealed compartmental segregation as well as association of differentially expressed proteins between AD and control subjects. We found that the levels of Tau and neurofilament light and medium polypeptides were increased in 3D neurons derived from AD patients. Analysis of plasma samples also allows us to separate AD patients from healthy subjects. In conclusion, we present a unique platform to discover proteins linked to AD as candidate biomarkers.

Biography

Weiming Xia received his PhD degree from the University of Texas Medical School at Houston in 1994. He pursued his Post-doctoral training in Dennis Selkoe's laboratory and became Assistant Professor at Harvard Medical School in 1999. Currently he is working as an Acting Associate Director of Research at GRECC, Bedford VA Hospital affiliated with Boston University School of Medicine. He has published over 110 original research articles and edited a book. His research focuses on the molecular mechanisms responsible for Alzheimer pathogenesis and biomarkers, and on exploration of therapeutic interventions.

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