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Peripheral protein aggregates as biomarkers for neurodegenerative diseases

Teurodegenerative diseases such as Parkinson's disease (PD) and Alzheimer's disease (AD) are characterized by the deposition of misfolded protein aggregates in the central nervous system (CNS). Previous efforts have focused on the development of CNS-proximal clinical biomarkers, including PET neuroimaging and cerebrospinal fluid measures of alpha-synuclein, beta-amyloid and tau. However, these diagnostic techniques are often used in clinical studies on patients with advanced disease state, and are complex, invasive or expensive. Therefore, there remains an urgent need for reliable, inexpensive and minimally invasive peripheral biomarkers. Recent studies have revealed widespread peripheral involvement of PD- and AD-like pathology, often prior to clinical manifestations of the diseases. Indeed, alpha-synuclein and tau deposits have been observed in peripheral tissues in PD and AD, respectively. A formidable challenge is that the levels of these amyloidogenic protein aggregates in peripheral tissues are extremely low and thus only variably detectable using immunological methods. Therefore, highly sensitive analytical platforms are required as the new generation of biomarker assays specific for protein aggregates and amyloid fibrils. The real-time quaking induced conversion (RT-QuIC) has emerged as a robust, rapid and ultrasensitive technology for template-assisted amplification of misfolded protein aggregates in neurodegenerative diseases. Using the RT-QuIC technique, our recent studies have shown that disease-associated protein aggregates are readily detectable in peripheral tissues of patients affected by PD, dementia with Lewy bodies, and AD and other tauopathies. Validation of peripheral protein biomarkers will enable sensitive premortem diagnostic tests for PD, AD, and related disorders, and accelerate clinical trials for disease-modifying therapies.

Biography

Shu G Chen has received his PhD in 1992 from the State University of New York at Buffalo, New York, USA. He is an Associate Professor of Pathology and Neurology at Case Western Reserve University School of Medicine. His research centers on pathogenesis of Parkinson's disease, Alzheimer's disease and other neurodegenerative disorders. He has published more than 80 papers in scientific journals.

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