Biomarkers in brain-derived exosomes assist the diagnosis of neurodegenerative diseases

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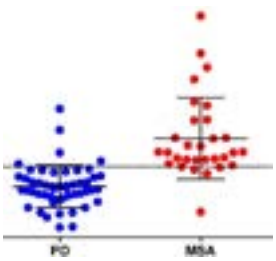
Statement of the Problem: Biomarkers for neurodegenerative diseases are urgently needed. Definite diagnosis for most diseases is possible only postmortem and the rates of misdiagnosis are high. Monitoring progression and treatment effects using clinical criteria is inefficient due to high variability. Current biomarker strategies, such as brain imaging and cerebrospinal fluid analysis have major drawbacks. An attractive alternative is analysis of biomarkers in brain-derived exosomes isolated from the blood.

Methodology & Theoretical Orientation: We examined α-synuclein in neuronal and oligodendroglial exosomes as a diagnostic biomarker for distinguishing between Parkinson's disease (PD) and multiple system atrophy (MSA). α-Synuclein deposition is found as Lewy bodies in PD and glial cytoplasmic inclusions, primarily in oligodendrocytes, in MSA. We compared cohorts of healthy control individuals, patients with PD, and patients with MSA.

Findings: α- Synuclein concentration in both exosome populations were significantly higher in the two diseases than in the controls and in MSA relative to PD. The total α-synuclein levels separated MSA from control with high sensitivity and specificity, whereas the PD group separated only moderately from the other groups. However, the ratio between the α- synuclein levels in the oligodendroglial relative to the neuronal exosomes separated the two disease groups with high sensitivity and specificity. The ratio also correlated significantly with progression of motor symptoms in the PD group.

Conclusion & Significance: Measurement of α-synuclein in brain-derived exosomes offers a minimally invasive means for analyzing biomarkers for PD and MSA, suggesting that in the relatively near future these two diseases could for the first time be diagnosed with high sensitivity and specificity, and their progression could be monitored, using a simple blood test.



Biography

Gal Bitan, PhD, received his PhD in organic chemistry from the Hebrew University of Jerusalem, Israel. Following postdoctoral training at Harvard Medical School and affiliated hospitals, he joined the faculty at UCLA where he is currently a Professor of Neurology. Dr. Bitan's research program focuses on neurodegenerative diseases caused by abnormal protein self-assembly, such as Alzheimer's and Parkinson's diseases. He has made seminal contributions to the study of amyloid-protein oligomers and has been developing novel drug candidates and biomarker measurements for these diseases.