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Proteomic Analysis of Post-mortem and Ante-mortem Cerebrospinal Fluid for the Diagnosis of Alzheimer's Disease

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Project description
Unless truly effective therapies are developed, Alzheimer's disease (AD) will likely become the greatest public health crisis in the United States within the next 2-3 decades. Both to aid in the development of these disease-modifying therapies and to identify individuals who are at high risk for AD or in the earliest clinical stages as targets for therapeutic trials, reliable and valid biological markers will be essential. AD pathology begins 10-20 years before cognitive symptoms. Even the earliest clinical symptoms of AD are accompanied by, and likely due to, neuronal/synaptic dysfunction and/or cell death. Thus, it is critical to identify individuals with “preclinical” and very early stage AD, prior to marked clinical symptoms and neuronal loss, so new therapies will have the greatest clinical impact. In order to accomplish this goal, it is likely that a battery of biomarkers is needed, rather than a single individual marker. Cerebrospinal fluid (CSF) from subjects with dementia of the Alzheimer type (DAT) that has been evaluated by Alzheimer Disease Center (ADC) clinicians represents an excellent resource to identify antecedent biomarkers of AD as well as possible markers of disease progression. However, the definitive diagnosis of AD still depends on autopsy confirmation of the neuropathological lesions of AD. CSF collected post-mortem from AD patients who have comprehensive neuropathological evaluations represents an important and complementary resource to correlate changes in the CSF proteome with AD pathological findings. We hypothesize that specific CSF proteins have potential as antecedent biomarkers for AD and will provide clinically useful standards for: A) identifying the presence of AD at the very earliest clinical stage of dementia; B) predicting the presence of AD histopathology in cognitively normal elderly subjects and thereby forecasting their risk for developing future dementia, C) accurately revealing the presence of AD versus non-AD pathology in demented subjects, and D) monitoring disease progression in subjects with AD dementia. The data obtained may provide insights into molecular pathogenic mechanisms of disease and suggest possible therapeutic strategies.

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