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Validation of non-amyloid, non-Tau biomarkers for AD

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Project description
Cerebrospinal fluid (CSF) amyloid and Tau biomarkers for Alzheimer’s disease (AD) have significantly enhanced the early detection of AD even when the symptoms are very mild, but their levels remain relatively stable over time despite evidence of disease progression. It would be ideal to have validated biomarkers which provide information on disease stage and rates of progression, and non-amyloid, non-Tau biomarkers can complement established AD biomarkers in a panel that characterizes the disease substrate (AD), severity of neurodegeneration (mild, moderate, severe), and longitudinal decline (rapid vs. slow). Using a panel of 18 CSF analytes independently identified by two separate groups to be associated with AD in two cohorts, a new panel of 12 analytes will undergo technical and biological validation in the current proposal. Each of the three Alzheimer's Disease Centers (ADC) will set up independent assays to technically replicate the previous association with AD, using 120 subjects with normal cognition, very mild dementia/mild cognitive impairment/mild AD, and non-AD disorders to provide biological replication. Validated CSF biomarkers will then be analyzed for their correlation with disease stage and rates of longitudinal cognitive decline, including performance on detailed neuropsychological testing and the Clinical Dementia Rating Sum of Boxes. Successful identification of staging and progression biomarkers for AD will significantly accelerate the clinical drug development process as they can serve as surrogate markers of drug response. Assays for validated biomarkers will also then be set up at each of the three ADCs using standard operating procedures to determine measurement precision, and the standard operating procedures can then be provided to other ADCs and clinical sites to complement the diagnostic panel currently consisting of only amyloid and Tau biomarkers.

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