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A Plasma-based Biomarker Panel Identifies Preclinical Alzheimer's Disease (S38.001)

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Abstract

OBJECTIVE: Identify and validate a blood-based biomarker of preclinical Alzheimer's disease (AD) using lipidomics. **BACKGROUND:** The lack of an easy to obtain and accurate biomarker of preclinical Alzheimer's disease limits our ability to detect the earliest stages of the disease where the neurologic substrate may be most receptive to intervention. **DESIGN/METHODS:** We collected yearly cognitive data and blood samples from 525 community-dwelling older adults for up to five years. During the study, 28 individuals phenoconverted from cognitively normal to either amnestic Mild Cognitive Impairment (aMCI) or AD. We performed untargeted, then targeted metabolomic analyses using mass-spectrometry (MS)-based methods on the banked plasma samples from these subjects, 74 with stable normal cognitive performance, and 75 who presented with incident aMCI/AD in discovery and blinded validation phases. A classifier model was developed and receiver operating characteristic (ROC) analyses for group classification were performed. **RESULTS:** Our metabolomics analyses identified ten lipid species including eight phospholipids and two acylcarnitines whose plasma levels were significantly altered in the cognitively normal individuals destined to phenoconvert to aMCI/AD in the next 2-3 years compared to those who remained cognitively normal with a ROC area under the curve (AUC) of 0.96. In the blinded validation phase, the biomarker panel classified the groups with a ROC AUC of 0.92. Sensitivity and specificity of the biomarker panel in the validation cohort was 90%. **CONCLUSIONS:** In a cognitively well-defined cohort of community-dwelling seniors, we discovered and validated a set of ten plasma lipids that primarily reflect cell membrane integrity, and was over 90% accurate in predicting phenoconversion from cognitively normal to either aMCI or AD within a 2-3 year timeframe. This biomarker panel may be sensitive to the synaptic loss and early neurodegeneration that defines the preclinical stage of AD. With further clinical confirmation this lipidomic biomarker panel may allow us to detect preclinical AD more readily and provide opportunities for earlier and more successful therapies. **Study Supported by: NIH R01AG030753**

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