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Announcement

Robert Rissman, PhD, is the recipient of the 2024 Alzheimer Award

The *Journal of Alzheimer's Disease* (JAD) is pleased to announce that Robert Rissman, PhD, is the recipient of the 2024 Alzheimer Award. The award is presented by the journal in recognition of Robert Rissman and colleagues' groundbreaking article "Evaluation of Blood-Based Plasma Biomarkers as Potential Markers of Amyloid Burden in Preclinical Alzheimer's Disease" [1]. It is freely available to everyone to read, download, and share. The 2024 award is proudly sponsored by JAD's publisher IOS Press, now part of Sage.

Robert Rissman, PhD, received his Doctorate in Neuroscience from Drexel University School of Medicine in Philadelphia, PA. He is the W.M. Keck Endowed Chair in Medicine and Professor of Physiology and Neuroscience at the University of Southern California (USC). He is Founding Director of the Neuroscience Translational Research Division at USC's Alzheimer's Therapeutic Research Institute in San Diego, CA. His research is predominantly focused on validating plasma biomarkers for Alzheimer's disease and related dementias (ADRD) that can be used to understand disease etiology and as screening tools for clinical trials. His work is also centered on developing and testing novel therapeutics or ADRD in animal and *in vitro* models, particularly from the perspective of informing on and predicting comorbidity. In addition to his basic science translational research, Dr. Rissman is a member of the NACC Biomarker Steering Committee and the Biomarker lead for the Alzheimer's Clinical Trials Consortium (ACTC) and the USC Alzheimer's Disease Research Center (ADRC). He has published over 200 peer-reviewed articles.

Importance of Published Article

The Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) study was a groundbreaking, first of its kind secondary prevention phase 3 trial that sought to test the impact of solanezumab-mediated lowering of monomeric amyloid in 1,169 asymptomatic individuals at risk for progression to Alzheimer's disease (AD). Eligibility was determined by amyloid PET, and participants were determined to be amyloid elevated/positive or non-elevated/negative. Although safe over the time of treatment and having a modest, but significant effect on amyloid PET, solaneuzumab was not found to be efficacious on its primary endpoint, mean change in the Preclinical Alzheimer Cognitive Composite (PACC) score.

Despite the trial's negative results, the data and biomarker resources that came from the trial are invaluable for future research. For example, given the variety of issues surrounding use of amyloid PET or cerebrospinal fluid as screening tools for identifying amyloid positive participants, we assessed how newly developed blood-based biomarkers performed for predicting amyloid PET results in the A4 study.

In our study, we used biobanked plasma from the screening visits of the A4 study to determine whether plasma Aβ40, Aβ42, and Aβ42/Aβ40 levels, as measured by two different IP-MS platforms (MALDI-TOF-MS and LC-MS/MS), can predict brain amyloid PET positivity, in A4 study participants. We also determined the impact of two different plasma processing protocols (2 hours vs. 24 hours) on plasma Aβ40, Aβ42, and Aβ42/Aβ40 levels to predict amyloid PET positivity. Recently published data suggest that lower plasma Aβ42/Aβ40 ratios, as measured using IP-MS, are associated with brain amyloid pathology, accelerated cognitive decline, and increased risk of developing AD dementia. In our study, we found that plasma Aβ42/Aβ40 quantified using either of the available MS methods can predict screening amyloid PET positivity in the A4 study. We also found that blood samples that were collected and processed to plasma within 2 hours after blood draw had increased utility for prediction of amyloid PET status compared to blood samples that were shipped overnight on cold packs and processed to plasma within 24 hours after blood draw.

Overall, our findings demonstrate that plasma screening testing using Aβ42/Aβ40 can be used to identify eligible, cognitively normal individuals for AD prevention trials. Using plasma screening analyses for enrollment in prevention trials can reduce traditional screen-failure rates and save time, funds, and burden on sites and participants.

REFERENCES

[1] Winston CN, Langford O, Levin N, Raman R, Yarasheski K, West T, Abdel-Latif S, Donohue M, Nakamura A, Toba K, Masters CL, Doecke J, Sperling RA, Aisen PS, Rissman RA (2023) Evaluation of blood-based plasma biomarkers as potential markers of amyloid burden in preclinical Alzheimer's disease. *J Alzheimers Dis* **92**, 95-107. doi: 10.3233/JAD-221118.