DOI: 10.1002/alz.082847

BIOMARKERS

POSTER PRESENTATION

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

BIOMARKERS (NON-NEUROIMAGING)

A structure-based fluid biomarker for the differential diagnosis of early-stage neurodegenerative diseases measured by the immuno-infrared-sensor (iRS)

Martin Schuler[1,2] | Marvin Mann[1,2] | Lennart Carl Langenhoff[1,2] | Brian Budde[1,2] | Léon Beyer[1,2] | Nathalie Woitzik[1,2] | Grischa Gerwert[1,2] | Robin Wanka[2] | Adrian Hoeveler[1,2] | Max-Aylmer Dreier[1,2] | Diana Hubert[1,2] | Sandy Galkowski[1,2] | Jörn Güldenhaupt[1,2] | Carsten Kötting[1,2] | Klaus Bernhard Gerwert[1,2]

[1]Ruhr-University Bochum, Bochum, Germany

[2]Center for Protein Diagnostics (ProDi), Bochum, Germany

Correspondence
MartinSchuler, Ruhr-University Bochum, Bochum Germany.
Email: martin.schuler@ruhr-uni-bochum.de

Abstract

Background: Neurodegenerative diseases like Alzheimer's (AD) and Parkinson's disease (PD) are accompanied by misfolding of the key proteins into beta-sheet enriched structures resulting in high neurotoxicity in early phases. We have developed a diagnostic immuno-infrared-sensor (iRS) that monitors the secondary structure distribution of these key proteins (Abeta for AD, alpha-synuclein for PD) as an early detectable biomarker before the clinical manifestation, which is shown exemplarily for AD.[1]

Method: The iRS combines the secondary-structure-specific infrared spectroscopy in a flow system based attenuated total reflection (ATR) set-up with methods of immuno-detection by surface-immobilized antibodies. The antibodies specifically capture disease-related target proteins (e.g., Abeta) from complex media (cerebrospinal fluid or blood plasma) for measurements. The readout is the amide-I band, which directly reflects the secondary structure distribution of the captured proteins in body fluids and thus, indicates the protein misfolding: The lower the amide-I frequency, the higher the content of misfolded Abeta species in the sample present.[2]

Result: The structure biomarker for Abeta has been validated in multiple independent clinical studies with strong correlation to CSF biomarkers and PET scans.[1,3-5] Especially, very early preclinical AD could be identified in symptom-free individuals before plaque formation, up to 17 years before the diagnosis.[6]

Conclusion: The results demonstrate a highly specific and sensitive immune-assay capable of tracking structural changes of Abeta before clinical manifestation of AD. In addition, alpha-synuclein and TDP-43 misfolding indicate PD and ALS in current discovery studies, providing a tool for differential diagnosis at early stages.

References:

[1]Nabers, A. et al. 2016. Analytical chemistry 88.5: 2755-2762.

[2]Nabers, A. et al. 2016. Journal of biophotonics 9.3: 224-234.
[3]Nabers, A. et al. 2018. EMBO molecular medicine 10.5.
[4]Nabers, A. et al. 2019. Alzheimers Dement. Diagn. Assess. Dis. Monit. 11: 257-263.
[5]Stocker, H., Nabers, A. et al. 2020. Alzheimer's Dement. 16: 283-291.
[6]Beyer, L., et al. 2023. Alzheimer's Dement. 19: 1020-1028