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PZP: A novel biomarker for early Alzheimer's disease?

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Alzheimer's disease (AD) is characterized by a long presymptomatic phase in which damage to the brain is already occurring but clinical symptoms are not yet manifested. Diagnosis of AD is hampered by the lack of reliable biomarkers that predict early disease onset and/or progression in the general population. For use in large scale screening an ideal biomarker (or panel of biomarkers) should be measurable in non-invasively obtained biomaterial, e.g. blood. Here we used a discovery based proteomics approach to identify blood-based biomarkers for early AD in samples derived from the prospective Rotterdam Study cohort. We compared the serum proteome of presymptomatic AD cases with cases that remained cognitively healthy and identified 61 differentially expressed peptides, 9 of which were derived from the pan-protease inhibitor PZP. Absolute quantification using selected reaction monitoring assays confirmed increased levels of PZP in serum of presymptomatic AD cases versus controls. We hypothesized that increased PZP levels are derived from the brain and performed immunohistochemical analysis in post-mortem brain material. Increased PZP immunoreactivity was observed in the AD brain compared to controls and this correlated with Braak stage for disease severity. Further analysis indicated PZP was predominantly expressed in microglia and associated with amyloid plaques in the AD brain. We are currently validating PZP as a biomarker for early AD in additional study cohorts and investigating its role in AD pathophysiology. For the latter we are combining immunohistochemistry, laser capture microdissection and advanced mass spectrometry analysis.

Biography

Diana A T Nijholt obtained her PhD in 2012 from the University of Amsterdam on the unfolded protein response. She is currently working as a post-doctoral fellow in the group of Dr. T.M. Luider (Erasmus Medical Center, Rotterdam) with a primary focus on the discovery and validation of biomarkers for neurodegenerative diseases. She has extensive expertise in the mass spectrometry based analysis of tissue and body fluid samples.

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