Martin Kleinschmidt, J Mol Biomark Diagn 2016, 7:5(Suppl)
http://dx.doi.org/10.4172/2155-9929.C1.028

Combination of blood-based biomarkers and neuropsychological assessment enables reliable classification of tested subjects by controls, mild cognitive impairment and Alzheimer's disease

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Current treatment of Alzheimer's disease (AD) is initiated at stages where the brain has irrevocably lost numerous neurons. Simple biochemical tests to differentiate normal aging from prodromal or demented stages are needed. Current standards identifying preclinical AD are neuroimaging and cerebrospinal fluid (CSF) analysis, but these methods are more cost-effective and more invasive than blood-based biomarker assays. However; in contrast to the approved methods quantifying the AD biomarker amyloid β (Aβ), Tau and P-Tau in CSF, detection of these biomarkers in blood is much more difficult due to at least 10-fold lower concentrations, but the 100-fold higher overall protein content leading to massive interference in currently used assay systems. Therefore, an assay was developed isolating Aβ by a multivalent capture system which exploits avidity effects by interactions of several anti-Aβ antibodies to multiple epitopes of the Aβ molecule. In our study, all participants were classified by a comprehensive neuropsychological assessment into controls, mild cognitive impairment (MCI) and AD. Blood samples were analyzed for several Aβ species, pro-inflammatory markers, anti-Aβ autoantibodies, and ApoE allele status, respectively. Plasma Aβ(1-42) was significantly decreased in MCI and AD compared to controls and strongly correlates with carrying ApoE ε4 allele. Furthermore, the Aβ(1-42)/Aβ(1-40) ratio is stepwise decreased in controls, MCI and AD, differentiating these groups significantly. Autoantibodies against pyroglutamate-modified Aβ (pGlu-Aβ), but not unmodified Aβ, were significantly decreased in AD compared to MCI and controls. Interestingly, the autoantibodies don't correlate with ApoE ε4, supporting the associated plasma Aβ analysis with additional and independent information.

Biography

Martin Kleinschmidt has received his PhD in 2004 from the Martin-Luther-University Halle-Wittenberg. At the Probiodrug AG, he was responsible for biophysical characterization of interactions by SPR, ITC and X-ray structure analysis. Later, he was the Project Manager for assay development. In 2013, he changed over to Fraunhofer IZI-MWT and is now Head of lab clinical and biophysical analytics. He has published 17 papers in well-known journals and is currently Associate Editor for the *Journal of Alzheimer's Disease*.

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