ALZHEIMER DISEASE

DNA damage provides novel and powerful biomarkers of Alzheimer disease

Markers of DNA damage can be used to accurately distinguish individuals with Alzheimer disease (AD) from patients with non-AD dementia and people without dementia, according to recent findings. The study, led by Lenhard Rudolph, Hans Kestler and Christine von Arnim, suggests that chitinase enzyme activity in the cerebrospinal fluid (CSF) has greater power as a biomarker of AD than tau and amyloid- β (A β)—the current ‘gold-standard’ biomarkers of disease.

Damage to DNA occurs as part of the normal ageing process, but there is evidence that the brains of patients with AD are particularly susceptible to accumulation of DNA damage. In 2008, Rudolph and his colleagues identified four markers of DNA damage in mice, including elevated levels of chitinase enzyme activity and stathmin protein. “We were interested to see whether these markers were upregulated in patients with AD,” he explains.

The researchers assessed CSF and serum from 94 patients with AD, 41 individuals with non-AD dementia, and 40 people without dementia. Compared with CSF from individuals with no dementia, CSF from patients with AD had higher levels of both chitinase activity and stathmin protein.

“Chitinase enzyme activity in the CSF was the most powerful single marker to distinguish patients with AD from control individuals,” says Kestler. “This marker had a higher diagnostic power than the standard CSF markers for AD—tau and A β .”

Combination of markers—particularly stathmin and chitinase activity or tau and chitinase activity—enhanced the sensitivity and specificity of AD diagnosis and resulted in increased discrimination of this disease from non-AD dementias.

With regard to future studies, von Arnim says “I think it would be interesting to analyse whether the new biomarkers could predict the risk of AD development or the prognosis of disease progression.” If

Combination of the markers tau and chitinase activity enables estimation of decision regions to discriminate between AD (red) and no dementia (blue). Regions were estimated using a naive Bayes classifier on data from individuals with AD (circles) or no dementia (triangles). Image courtesy of L. Lausser and H. A. Kestler.

this is the case, she hopes that the markers could be used in clinical trials to assess the efficacy of novel therapies for AD.

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