Ultra-high-sensitivity immunoassay for assaying β amyloid and tau protein in human plasma for diagnosing Alzheimer’s disease: Development and comprehensive study

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Background: In clinics, Alzheimer’s disease is identified by neuropsychological tests and neuroimaging. Such diagnosis takes time or costs. An immunoassay for detecting plasma biomarkers is greatly demanded. However, the known biomarkers like Aβ1-40, Aβ1-42, or tau protein in blood are rare. The assay methods to detect these plasma biomarkers must be very sensitive. In this work, the ultra-high-sensitivity immunomagnetic reduction using magnetic nanoparticles are utilized to assay these plasma biomarkers. The results are compared with those of neuropsychological tests and neuroimaging.

Methods: In combination of antibody-functionalized magnetic nanoparticles with immunomagnetic reduction technology, human plasma Aβ1-40, Aβ1-42 and tau protein are assayed. The subjects are categorized to normal controls (NC, n = 109), mild-cognition-impairment (MCI) group (n = 24), and Alzheimer’s-disease (AD) group (n = 62) according to NIA-AA guideline recruited in Taiwan. The neuroimaging includes MRI and PiB-PET. Besides, 16 normal controls and 16 AD patients were enrolled in Arizona.

Results: The plasma Aβ1-40, Aβ1-42, or tau protein was assayed as 1-100 pg/ml. The ratio of plasma Aβ1-42 to Aβ1-40 was found to be a promising parameter to differentiate NC from patients of MCI and AD, showing the sensitivity and the specificity higher than 90%. Furthermore, the plasma amyloid ratio is highly and positively correlated to the results of PiB-PET, with the correlation coefficient of 0.52. The product of plasma Aβ1-42 and tau protein acts a suitable parameter for differentiating MCI and early-stage AD, showing the sensitivity and the specificity higher than 80%. The concentration of plasma tau protein significantly increases from NC to MCI, and to early-stage AD. The atrophy of hippocampus is correspondingly observed by MRI. The common cut-off value in terms of the product of plasma Aβ1-42 and tau protein for discriminating AD patients including MCI due to AD from normal controls is obtained.

Conclusion: In-vitro assay of plasma Aβ1-40, Aβ1-42 and tau protein using antibody-functionalized magnetic nanoparticles and immunomagnetic reduction technology might be a practical way for diagnosing MCI and AD.