The study of circulating biomarker panels in early diagnosis of Alzheimer’s disease

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Abstract: Early, reliable and non-invasive diagnosis of Alzheimer disease (AD) is a great challenge, which makes the prognosis and therapeutic interventions quite difficult. We aimed to investigate the expressions of let-7g, miR-197, miR-126 and miR-29a which were screened from 877 microRNAs in 60 serum samples with a microarray platform in prior study in serum of cognitively normal controls (CNC), mild cognitive impairment (MCI), a potential preliminary stage of AD, and AD and identify microRNA panel for predicting and diagnosing AD. Quantitative reverse-transcriptase polymerase chain reaction assay was applied to evaluate the expressions of let-7g, miR-197, miR-126 and miR-29a with two independent cohorts including 202 participants CNC, MCI and AD. Logistic regression model based on microRNA panel was constructed using a training cohort (n=150) and then validated using an independent cohort (n=52). Area under the receiver operating characteristic curve (AUC) was used to evaluate diagnostic accuracy. The expressions of the four microRNAs were significantly decreased in MCI and AD versus CNC, and positively correlated with mini mental state examination (MMSE) score. Then, we identified a microRNA panel with the four microRNAs that demonstrated good diagnostic performance for MCI (AUC=0.788 and 0.815 for training and validation data set, respectively) and AD (AUC=0.769 and 0.823 for training and validation data set, respectively). When combined with MMSE score, the diagnostic performance of the microRNA panel was further improved. These results suggested that the serum
microRNA panel we found has considerable clinical value in diagnosing AD, and the four microRNAs are potential circulating biomarkers.

**Key words:** Alzheimer’s disease; biomarker; microRNA