CHAPTER 5

Conclusion

In summary, significantly elevated $A\beta_{42}$ and clusterin levels were observed in Alzheimer's disease and mild cognitive impairment subjects compared to cognitive normal subjects. On the other hand, serum $A\beta_{40}$ and serum p97 levels in Alzheimer's disease and mild cognitive impairment were not significantly different compared to cognitive normal subjects. Receiver operating characteristic curve analyses revealed that only clusterin could be used for diagnosing patients with cognitive impairment at cut-off points of 80.23 ng/ml with 84% sensitivity, 75% specificity and good accuracy of diagnosis. Indeed, although these markers cannot be used as diagnostic tests for Alzheimer's disease, our results demonstrated an association between serum $A\beta_{42}$ and serum clusterin concentrations in patients with Alzheimer's disease. Sample size, sampling or timing of the sample collection in relation to the clinical period or stage of disease progression should be considered in future studies to improve sensitivity, specificity and accuracy of clinical diagnosis of Alzheimer's disease among individuals and may also help identify individuals with mild cognitive impairment. Additionally, our study is a small cross sectional study. Further longitudinal and larger studies may benefit to provide more information concerning the relationship between plasma levels of Aβ and clusterin and the risk to develop Alzheimer's disease.

In a proteomic study, we found a total of 22 proteins of interest, within p*I* ranges of 5-7 and a MW range of 25-63 kDa expressed in serum of Alzheimer's disease and mild cognitive impairment subjects. Of these, nine proteins related to apolipoprotein E, clusterin, alpha-1-antitrysin, complement C4, transthyretin, serum amyloid P-component, haptoglobin alpha 2-chain, vitamin D-binding protein, and fibrinogen γ chain in the SWISS-2DPAGE database and have been reported to be possible biomarkers of Alzheimer's disease and mild cognitive impairment. We identified 13 new proteins that should be given further study in regard to details of mechanism

pathogenesis and function in Alzheimer's disease. In sum, clusterin appears to be a promising candidate for diagnosis of cognitive impairment. However, confirming protein identification by mass spectrometry should be considered in the future for efficient biomarker discovery in Alzheimer's disease.