

Thesis Title Antidepressant resistant protein markers in Thai
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ABSTRACT

The depressive disorder has been predicted to be the most burdensome disease in the world in the 21st century. Although, several treatments strategies have been developed for the patients, pharmacotherapy using particular antidepressant is oftenly the first line of treatments. However, an inadequate response following the treatment with antidepressant as well as low remission rates have been reported. To reduce time and increase succeed of the treatment, finding out an indicator for diagnosis and treatment efficacy since early time of treatment is a challenge work for many researchers. In this thesis, protein biomarkers in plasma for the prediction of patient responsiveness to fluoxetine, an antidepressant in the class of serotonin reuptake inhibitors (SSRIs), were identified by two-dimensional gel electrophoresis (2DE) and Matrix Assisted Laser Desorption/ionization Time of Flight Mass Spectrometry (MALDI-TOF MS). The plasma samples were collected from 20 normal and 48 major depressive disorder (MDD) patients, which their responses to the antidepressant were classified into fast response (FR; n = 34), slow response (SR; n = 9) and non-response (NR; n = 5) according to HAM-D score. The separation of the proteins either from whole plasma or after depletion of albumin and IgG was performed in the first dimension by isoelectric focusing (IEF) in IPG strip (7 cm long), and the second dimension of separation was carried out by SDS-PAGE. By comparing %volume (%V) of the protein spots on the gels between MDD and the normals, it showed that the expression levels of α 1-antitrypsin, fibrinogen, haptoglobin, transcription factor, apolipoprotein AI (apo AI), apolipoprotein AII (apo AII), apolipoprotein E (apo E), HDL associated protein and IgG light chain were higher in MDD than in the normal. In addition, while the expression of complement C3 (C3) in MDD was detected, the expression in normal group was very low and could not be detected by 2DE. The differences in the expressions of these proteins except apo AI, apo AII, and C3 were well agree with the previous reports. Higher

expressions of apo AI, apo AII and C3 in MDD observed in this thesis were controversial to the previous reports and need to be validated. The matching and analysis of 2DE spots from the plasma of NR, FR and SR revealed that the expressions of proteins in the inflammatory and immune systems, i.e. α 1-antitrypsin, apo AI, C3, haptoglobin and IgG light chain, in NR were higher than in FR and SR. In contrast, the expressions of transcription factor and Rap 1A were low in NR compared to FR and SR. The results indicated that these proteins in particular Rap 1A would be used as biomarkers in plasma for early prediction of the responsiveness to fluoxetine, which be valuable for the treatment of MDD.