Metabolomic Analysis of Blood and Urine to identify Alcohol-Dependence Biomarkers

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Introduction: The clinical diagnosis of alcohol-dependence (AD) currently relies on AD assessment questionnairesand biomarkers such as Carbohydrate-DeficientTransferrin (CDT), Gamma Glutamyl Transferase (GGT) and Phosphatidylethanol (PEth). However, both methods of diagnosis lackspecificity and sensitivity. Metabolic fingerprinting using nuclear magnetic resonance spectroscopy (NMR)of plasma may give us a novel andaccurate method for the diagnosis of the disease. Our primary objective was to identify the metabolites/biomarkers that could discriminate between subjects diagnosed asAD, social drinkersnon-dependent and healthy control.

Methods: Blood samples were collected from12 alcohol-dependent subjects, 12 social drinkers and 12 healthy controls. Plasma was separated by centrifugation and analyzed using NMR spectroscopy. Multivariate data analysis including principal component analysis (PCA) and orthogonal partial least squarediscriminantanalysis (OPLS-DA) were used to develop a model to identify the discriminatingmetabolites of AD.

Results: In PCA score plot, one outlier from each group were found and then excluded from the study. The OPLS-DA analysis of the three groupsrevealed a model (R^2= 0.284 and Q^2= 0.16) with 90.91% sensitivity, 81.82% specificity, and 57.58% accuracy. However, this model could not discriminate well the social drinkers and the healthy controls. Further OPLS-DA analysis with the combination of these two groups and comparing with AD showed a model with clear separation between the two groups (R^2= 0.284 and Q^2= 0.348)with sensitivity, specificity and accuracy of 90.91%.

Discussion and Conclusion: Healthy controls and social drinkers groups have more overlapping metabolites but alcohol dependent is clear separated from the two. This method is able to differentiate AD from the social drinkers and healthy controls with good accuracy. Further works with more subjects and metabolites identification is ongoing.

Keywords: Alcohol-Dependence, Metabolomics, Phenotyping, Nuclear Magnetic Resonance, Diagnosis.

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