

Biomarker discovery in plasma of diabetic mice based upon metabolite profiling by ultra-performance liquid chromatography with electrospray ionization time-of-flight mass spectrometry

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Biomarker discovery based upon metabolite profiling is now quite common, as same as that in proteome analysis. A reversed-phase liquid chromatography-mass spectrometry (LC-MS) has mainly been used for the extensive analysis of low-molecular mass compounds including metabolites. In a previous research, a couple of biomarker candidates related to hypertension and aging were identified from rat hair analysis. The number of diabetic patients has recently been increasing. Thus, the discovery of new diabetic biomarker(s), led to early detection and/or prevention of Diabetes Mellitus (DM), is strongly required. Based upon the background, the biomarker candidate(s) in diabetic mice were extracted in the present study. The metabolites in plasma of diabetic mice were exhaustively analyzed by ultra-performance liquid chromatography with electrospray ionization time-of-flight mass spectrometry (UPLC-ESI-TOF-MS). The plasma samples were collected from spontaneously diabetic mice (ddY-H) and healthy mice (ddY-L) as the control. The multivariate statistical analyses, such as principal component analysis (PCA) and partial least squares-discrimination analysis (PLS-DA), were adopted to validate the metabolic changes. In addition, another multivariate analysis, the orthogonal partial least-squares analysis (OPLS-DA), was used to monitor the real biological variability and to screen the biomarkers in DM. From the analyses of the group of ddY-H at weeks 5, 9, 13, and 20, we successfully detected various candidates of potential biomarkers in DM, which existed with much higher or lower concentrations as compared with those in ddY-L group. The candidates of potential biomarkers included several biologically important components in Lipid metabolism, Pyrimidine metabolism, Histidine metabolism and so on. The structural elucidation of unknown biomarker candidates is currently proceeding in our laboratory.