**Supporting Information**

**2. Methods**

**2.1 Materials and chemicals**

HPLC-grade methanol, acetonitrile, ethanol, acetic acid, ammonium methyl acetate, chloroform and methyl tert-butyl ether were purchased from Merck (Germany). Standard chemicals were bought from BioBioPha/Sigma-Aldrich.

**2.2 UPLC-MS/MS targeted metabolomic detection**

**2.2.1 Methods for extraction of hydrophilic compounds**

The plasma samples were thawed on ice and mixed by 3 volumes of ice-cold methanol, the mixture was then whirled for 3 min and centrifuged with 12,000 rpm at 4 °C for 10 min. Then the supernatant was collected and centrifuged at 12,000 rpm at 4 °C for 5 min. Finally, the supernatant was collected again for LC-MS/MS analysis.

**2.2.2 UPLC conditions of hydrophilic compounds**

The sample extracts were analyzed using an LC-ESI-MS/MS system (UPLC, Shim-pack UFLC SHIMADZU CBM A system, https://www.shimadzu.com/; MS, QTRAP® System, https://sciex.com/). The analytical conditions were as follows: UPLC: column, Waters ACQUITY UPLC HSS T3 C18 (1.8 µm, 2.1 mm\*100 mm); column temperature, 40 °C; flow rate, 0.4 mL/min; injection volume, 5 μL; solvent system, water (0.1% formic acid): acetonitrile (0.1% formic acid); gradient program, 95:5 v/v at 0 min, 10:90 v/v at 11.0 min, 10:90 v/v at 12.0 min, 95:5 v/v at 12.1 min, 95:5 v/v at 14.0 min.

**2.3 UPLC-MS/MS targeted lipidomic detection**

**2.3.1 Methods for extraction of hydrophobic compounds**

The plasma samples were melted on ice, vortexed for 10 s and then centrifuged with 3,000 rpm at 4 °C for 5 min. 50 μL of each sample was taken and homogenized with 1 mL mixture (include methanol, MTBE and internal standard). The mixture was whirled for 2 min, followed by addition of 500 μL water, and whirled again for 1 min. After centrifugation with 12,000 rpm at 4 °C for 10 min, 500 μL supernatant of each sample was taken and concentrated. Next, dissolve the extract with 100 μL mobile phase B, then stored in -80 °C. Finally, take the dissolving solution into the sample bottle for LC-MS/MS analysis.

**2.3.2 UPLC conditions of hydrophobic compounds**

The sample extracts were analyzed using an LC-ESI-MS/MS system (UPLC, Shim-pack UFLC SHIMADZU CBM A system, https://www.shimadzu.com/; MS, QTRAP® System, https://sciex.com/). The analytical conditions were as follows, UPLC: column, Waters ACQUITY UPLC HSS T3 C18 (1.8 µm, 2.1 mm\*100 mm); column temperature, 40 °C; flow rate, 0.4 mL/min; injection volume, 5 μL; solvent system, water (0.04% acetic acid): acetonitrile (0.04% acetic acid); gradient program, 95:5 v/v at 0 min, 5:95 v/v at 11.0 min, 5:95 v/v at 12.0 min, 95:5 v/v at 12.1 min, 95:5 v/v at 14.0 min.

**2.4 ESI-Q TRAP-MS/MS conditions**

LIT and triple quadrupole (QQQ) scans were acquired on a triple quadrupole-linear ion trap mass spectrometer (QTRAP), QTRAP® LC-MS/MS System, equipped with an ESI Turbo Ion-Spray interface, operating in positive and negative ion mode and controlled by Analyst 1.6.3 software (Sciex). The ESI source operation parameters were as follows: source temperature 500 °C; ion spray voltage (IS) 5500 V (positive), -4500 V (negative); ion source gas I (GSI), gas II (GSII) and curtain gas (CUR) were set at 55, 60, and 25.0 psi, respectively; the collision gas (CAD) was high. Instrument tuning and mass calibration were performed with 10 and 100 μmol/L polypropylene glycol solutions in QQQ and LIT modes, respectively. A specific set of MRM transitions were monitored for each period according to the metabolites eluted within this period.

**2.5 Statistical analysis**

The following results were obtained with R 3.5.3. At first, the data of endogenous metabolites in terms of homogeneity and reproducibility was visualized by principal component analysis (PCA). Then, the orthogonal partial least squares discriminant analysis (OPLS-DA) was further applied to remove irrelevant variables. The variable importance in the projection (VIP) values of each metabolite were obtained to measure the contribution of the variable to the model. The validity of OPLS-DA model was judged by R2Y (the interpretability of the model for the categorical variable Y) and Q2 (predictability of the model). The logistic regression analysis was performed to evaluate the diagnostic value of the combined biomarkers model. Model performance was assessed by the receiver operating characteristic curve (ROC) was plotted using R software (Belgium, Version 12.4.2.0). The analysis of metabolic pathways was conducted by the Kyoto Encyclopedia of Genes and Genomes (KEGG) (<https://www.kegg.jp/>) [1]. The enrichment of differential expression metabolites was visualized as bubble chart. The function of metabolites was assigned according to the Human Metabolome Database [2].

1. Kanehisa, M. and S. Goto, *KEGG: kyoto encyclopedia of genes and genomes.* Nucleic Acids Res, 2000. **28**(1): p. 27-30.

2. Wishart, D.S., et al., *HMDB: a knowledgebase for the human metabolome.* Nucleic Acids Res, 2009. **37**(Database issue): p. D603-10.

图表

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Supplementary Figure1 (PD\_vs\_PR)

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Supplementary Figure 2 (PD\_vs\_SD)

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Supplementary Figure 3 (SD\_vs\_PR)