## NMR Spectroscopic Approach Reveals Metabolic Diversity of Human Blood Plasma Associated with Protein-Drug Interaction

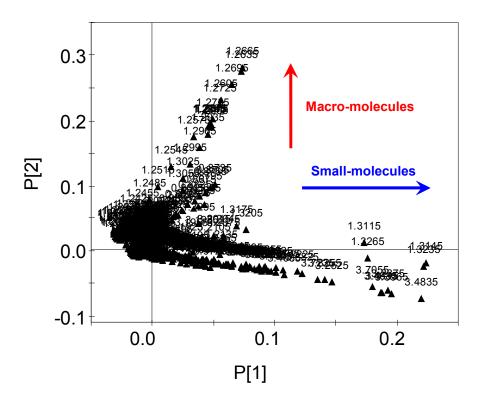
Yuanyuan Du,<sup>†</sup> Wenxian Lan,<sup>‡</sup> Zhusheng Ji,<sup>†</sup> Xu Zhang,<sup>†</sup> Bin Jiang,<sup>†</sup> Xin Zhou,<sup>†</sup> Conggang Li,<sup>†</sup> and Maili Liu\*<sup>†</sup>

<sup>†</sup>Wuhan Center for Magnetic Resonance, State Key Laboratory of Magnetic Resonance and Atomic and Molecular Physics, Wuhan Institute of Physics and Mathematics, Chinese Academy of Sciences, Wuhan, 430071, P. R. China

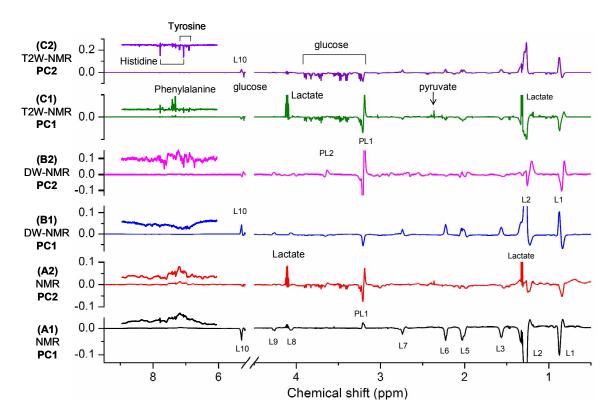
<sup>‡</sup>Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, P. R. China

## **Relative contents measurements**

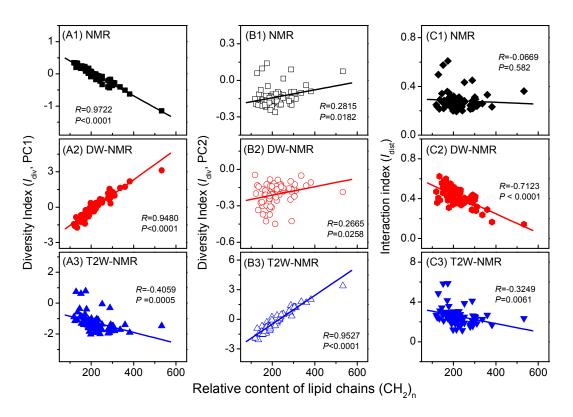
The relative contents of total lipids and the other metabolites were measured by the integration from the peaks of lipid chains  $(CH_2)_n$  at  $\delta 1.37 \sim \delta 1.20$  (L2), choline head group  $-N^+(CH_3)_3$  at  $\delta 3.25 \sim \delta 3.12$  (PL1), and fatty acyl group  $-CH_2CO$  at  $\delta 2.25 \sim \delta 2.20$  (L6) from the DW-NMR spectra, and the peaks of lactate at  $\delta 4.12 \sim \delta 4.10$  (-CH) and pyruvate at  $\delta 2.36 \sim \delta 2.35$  (-CH<sub>3</sub>) from the T2W-NMR spectra, respectively. In all cases, the same relaxation times ( $T_1 \& T_2$ ) and the same diffusion coefficients were assumed for each of the compounds in all samples.



**Figure S1.** Scattered PCA loadings plot derived from NMR, DW-NMR and T2W-NMR datasets of the intact plasma samples without IBP showing the separation mainly caused by content differences of the macro-molecules and small-molecules. The corresponding scores plot is given in the Figure 2(A).



**Figure S2.** Linear PCA loadings plots (PC1 & PC2) based on the NMR (A1 & A2), DW-NMR (B1 & B2) and T2W-NMR (C1 & C2) datasets of the blood plasma samples without and with ibuprofen. The major components contributing to the separation of PCA scores plot (Figure 2B-2D) were labeled.



**Figure S3.** Plots of the diversity indexes defined by PC1 (A1-A3) and PC2 (B1-B3), and the interaction index (C1-C3) as function of the relative content of lipid chains  $(CH_2)_n$ , based on PCA of NMR (A1, B1, C1), DW-NMR (A2, B2,C2) and T2W-NMR (A3, B3, C3) datasets. Linear fittings (line symbols) and the fitting parameters (R, P) were also given.