

Figure legend of supplementation

Fig. S1 | Parent-Nebula of serum metabolomics dataset. In Parent-nebula, ‘features’ are mapped as nodes in network graph. The edges illustrated the spectral similarity of adjacent ‘features’. Not all ‘features’ are shown in the Parent-Nebula, as the isolated nodes are removed.

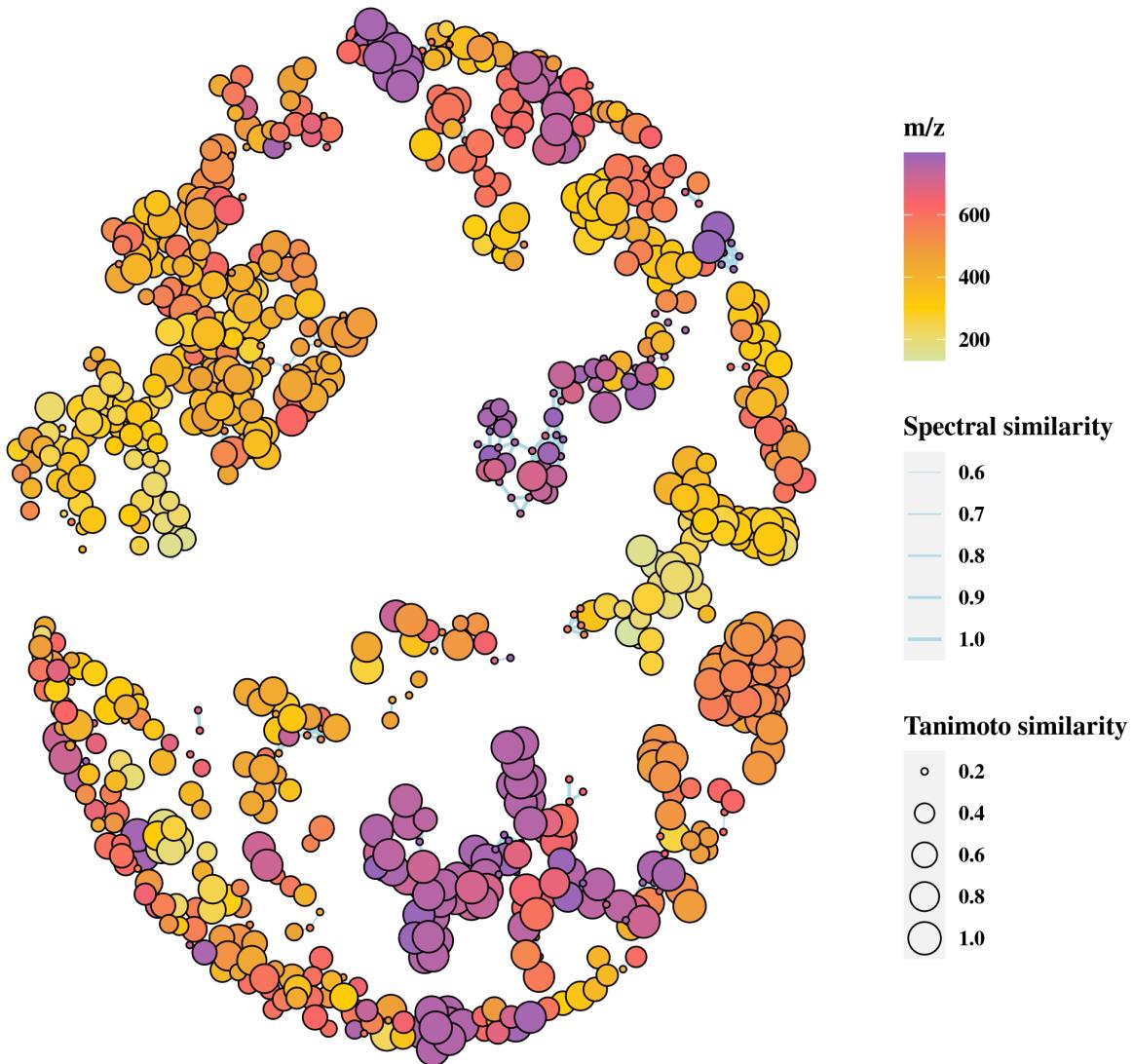


Fig. S1: Parent-Nebula of serum metabolomics dataset.

Fig. S2 | Child-Nebulae of serum metabolomics dataset. The Child-Nebulae are created according to chemical classes in Nebula-Index. The classified ‘features’ of chemical classes are mapped into corresponding Child-Nebulae.

Fig. S3 | Showing \log_2 (Fold change) of groups in Child-Nebulae of serum metabolomics dataset. The \log_2 (Fold change) value of HM versus HS group is shown in Child-Nebulae as gradient color. The nodes with white color indicate ‘features’ with missing quantification value (these ‘features’ were detected

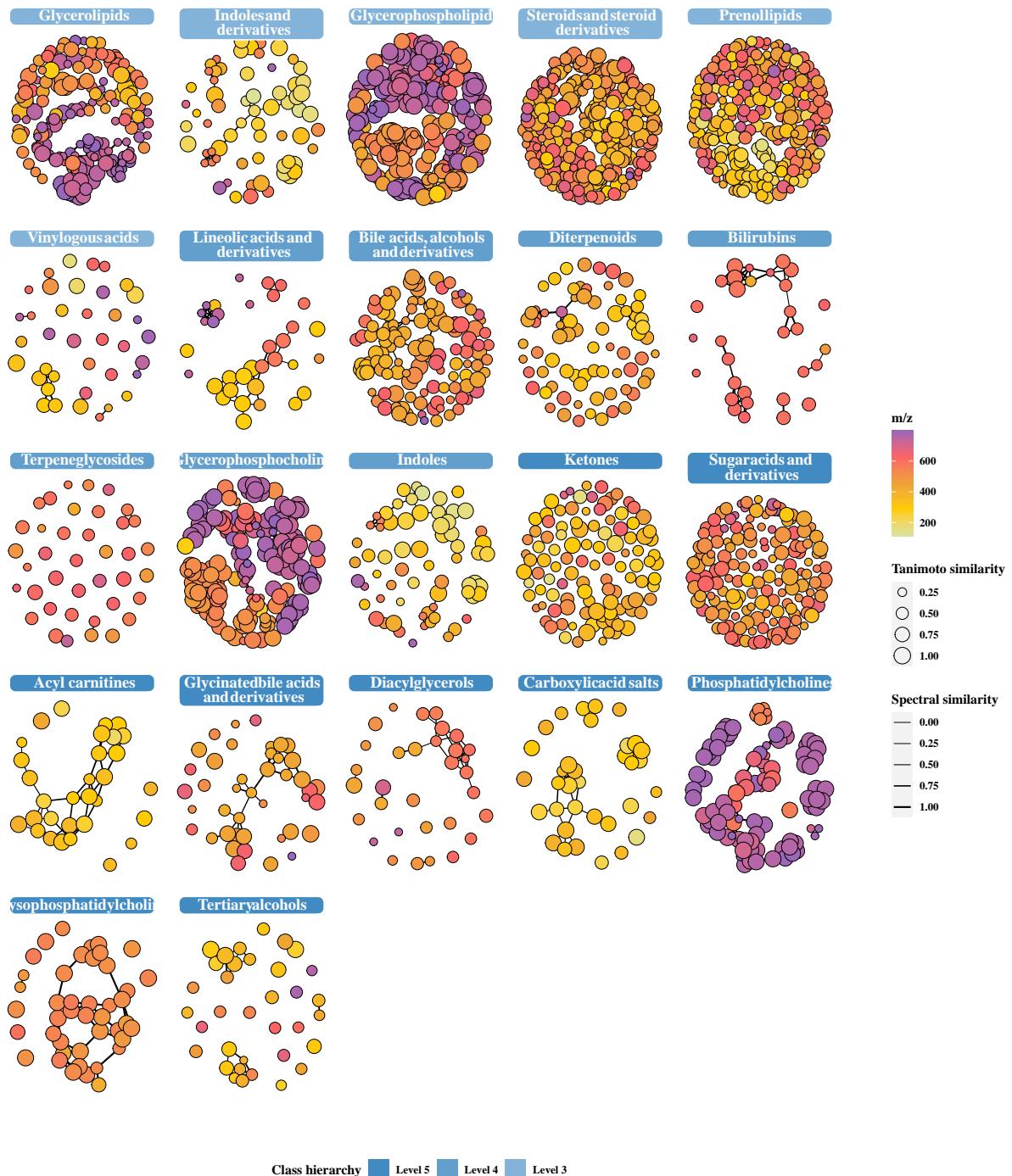


Fig. S2: Child-Nebulae of serum metabolomics dataset.

in our re-analysis, but not in Wozniak et al.)

Fig. S4 | In-depth visualization of Child-Nebulae of ‘Lysophosphatidylcholines’ and ‘Bile acids, alcohols and derivatives’. See Fig. 4 for description.

Fig. S5 | Pathway analysis of ‘Acy carnitines’ (ACs), ‘Lysophosphatidylcholines’ (LPCs), ‘Bile acids, alcohols and derivatives’ (BAs) in serum metabolomics dataset. a) The carnitine system in mitochondria. Abbreviation: CPT1, carnitine-palmitoyltransferase-1; CACT, carnitine-acylcarnitine translocase; CrAT, carnitine acetyltransferase; CPT2, carnitine-palmitoyltransferase-2. b) Enrichment analysis of LPCs in pagerank algorithm with Kyoto Encyclopedia of Genes and Genomes (KEGG) metabolomic pathway. Abbreviation: P A2, phospholipase A2; PC-Sterol O-AT, phosphatidylcholine-sterol O-acyltransferase; LP, lysophospholipase; 1-AGPC O-AT, 1-acylglycerophosphocholine O-acyltransferase; c) Enrichment analysis of BAs in pagerank algorithm with KEGG metabolomic pathway. Abbreviation: GC, beta-glucuronidase; GCS, beta-D-Glucuronoside; GT, glucuronosyltransferase; TCDC 6 -H, taurochenodeoxycholate 6alpha-hydroxylase; TCDC, taurochenodeoxycholate; GCC, Glycocholate; GCCDC, Glycochenodeoxycholate; Conju. BAs syn., ‘Conjugated bile acid biosynthesis, cholate’; BA-CoA, bile acid-CoA:amino acid N-acyltransferase.

Fig. S6 | Tracing top ‘features’ in Child-Nebulae of herbal medicine dataset According to the rankings of ‘features’ by statistic analysis, the top ‘features’ are marked with different colors in Child-Nebulae.

Fig. S7 | MS/MS spectra of top ‘features’ of herbal medicine dataset. For top ‘features’, the mirrored MS/MS spectra plots illustrated the raw MS/MS spectra (black bar) and the noise filtered MS/MS spectra (red bar) predicted by SIRIUS. The dot above the bar implied a corresponding relation. The top candidate of chemical structure of ‘features’ are mapped into the plot.

Fig. S8 | Extracted ions chromatography (EIC) of top ‘features’ of herbal medicine dataset. The EIC plot illustrates the peak shape of the top ‘features’ (drawn via MCnebula; detected via Automated Data Analysis Pipeline (ADAP) algorithm in MZmine2).

Fig. S9 | Focus on location of top ‘features’ in annotated Child-Nebulae. Fig. S9 a, b and c illustrate local view of the annotated Child-Nebula of ‘Iridoids and derivatives’, ‘Dialkyl ethers’ or ‘Phenylpropanoids and polyketides’, respectively. Fig. S9 d and e show the chemical structure of ‘feature’ (compound) of ID 2110 and ID 854, respectively. Fig. S9 f and g show the mirrored MS/MS spectra (refer to Fig. S7 for description) and extracted ions chromatography (EIC) of the ‘features’.

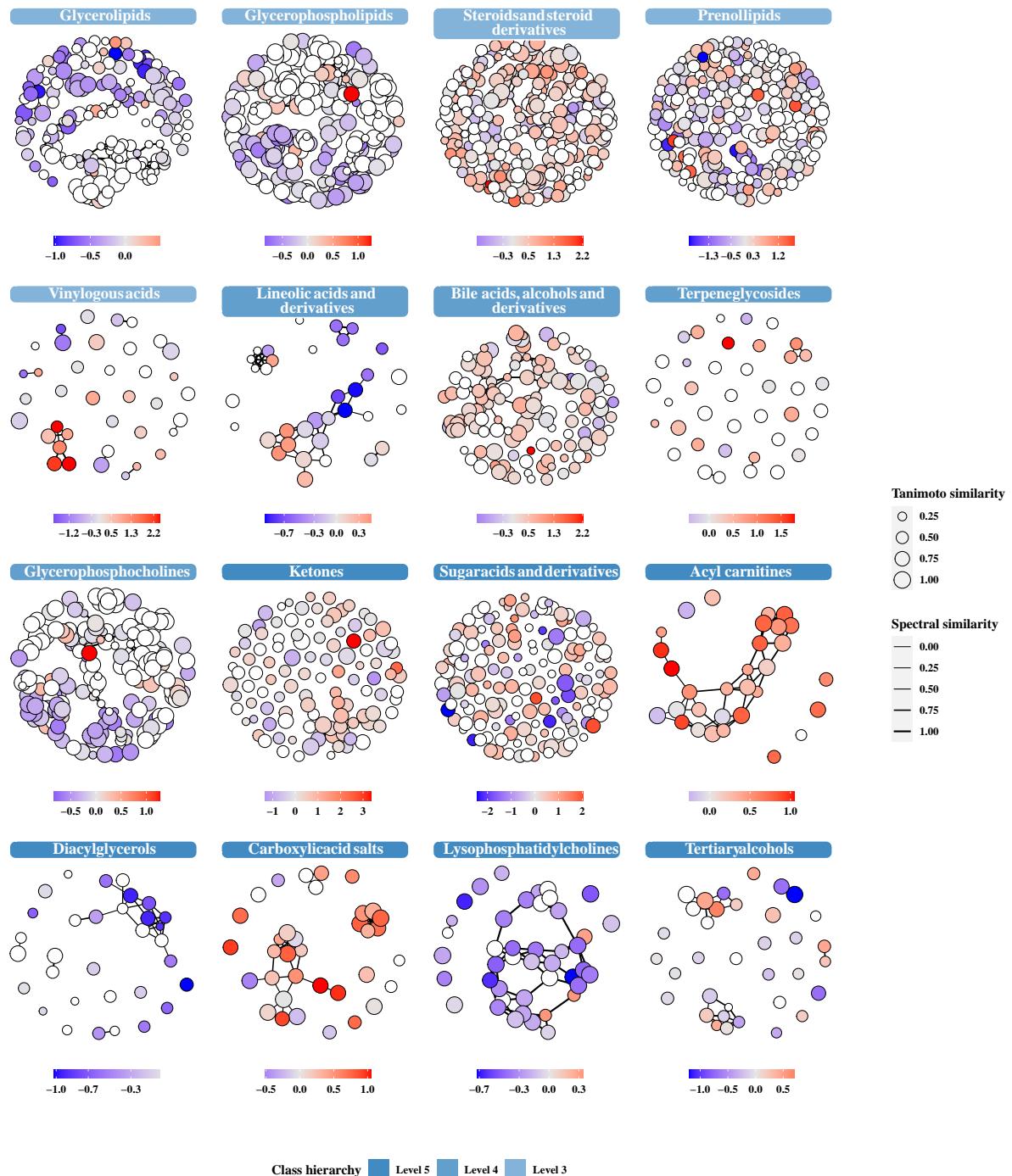


Fig. S3: Showing $\log_2(\text{Fold change})$ of groups in Child-Nebulae of serum metabolomics dataset.

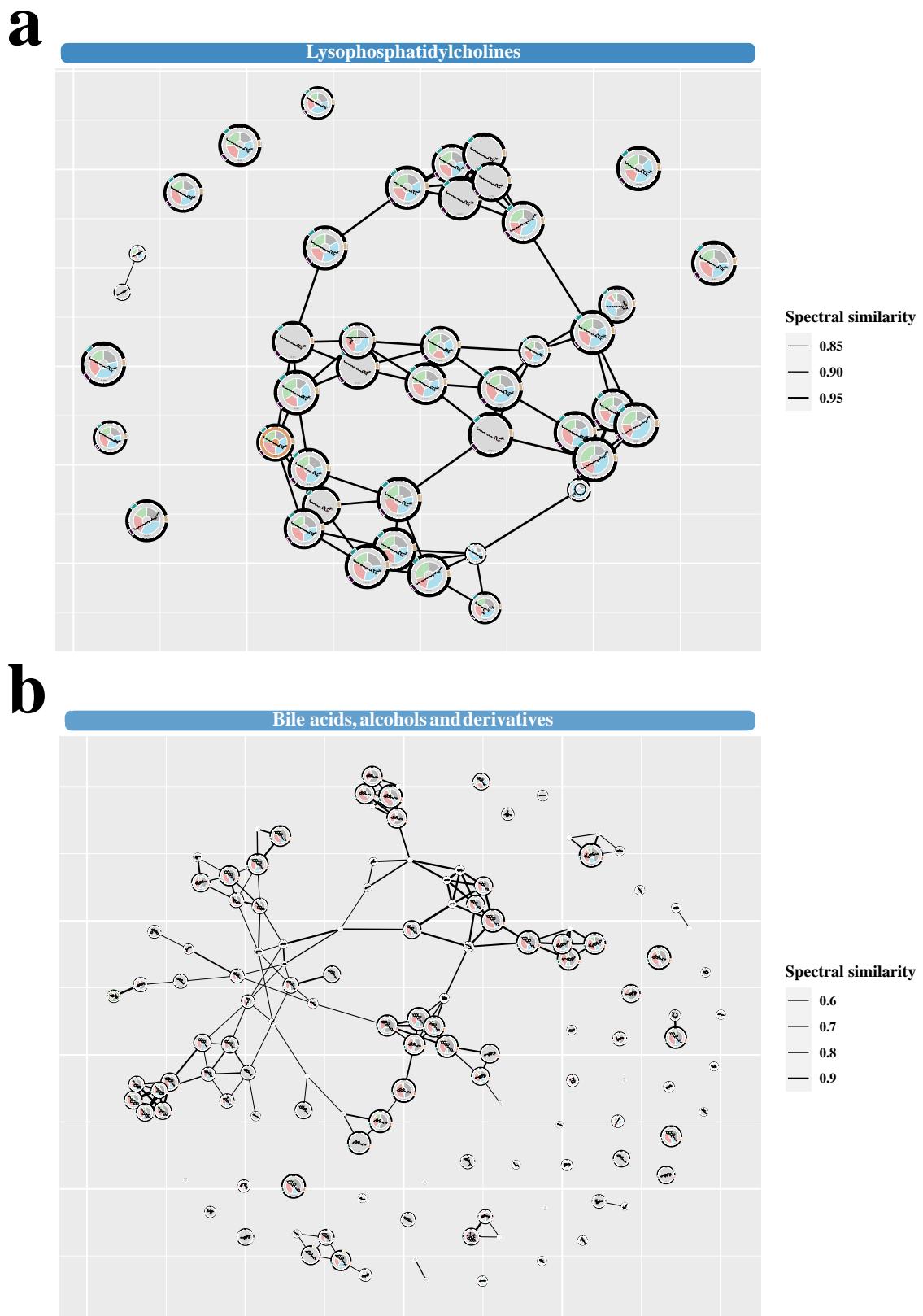


Fig. S4: In-depth visualization of Child-Nebulae of ‘Lysophosphatidylcholines’ and ‘Bile acids, alcohols and derivatives’.

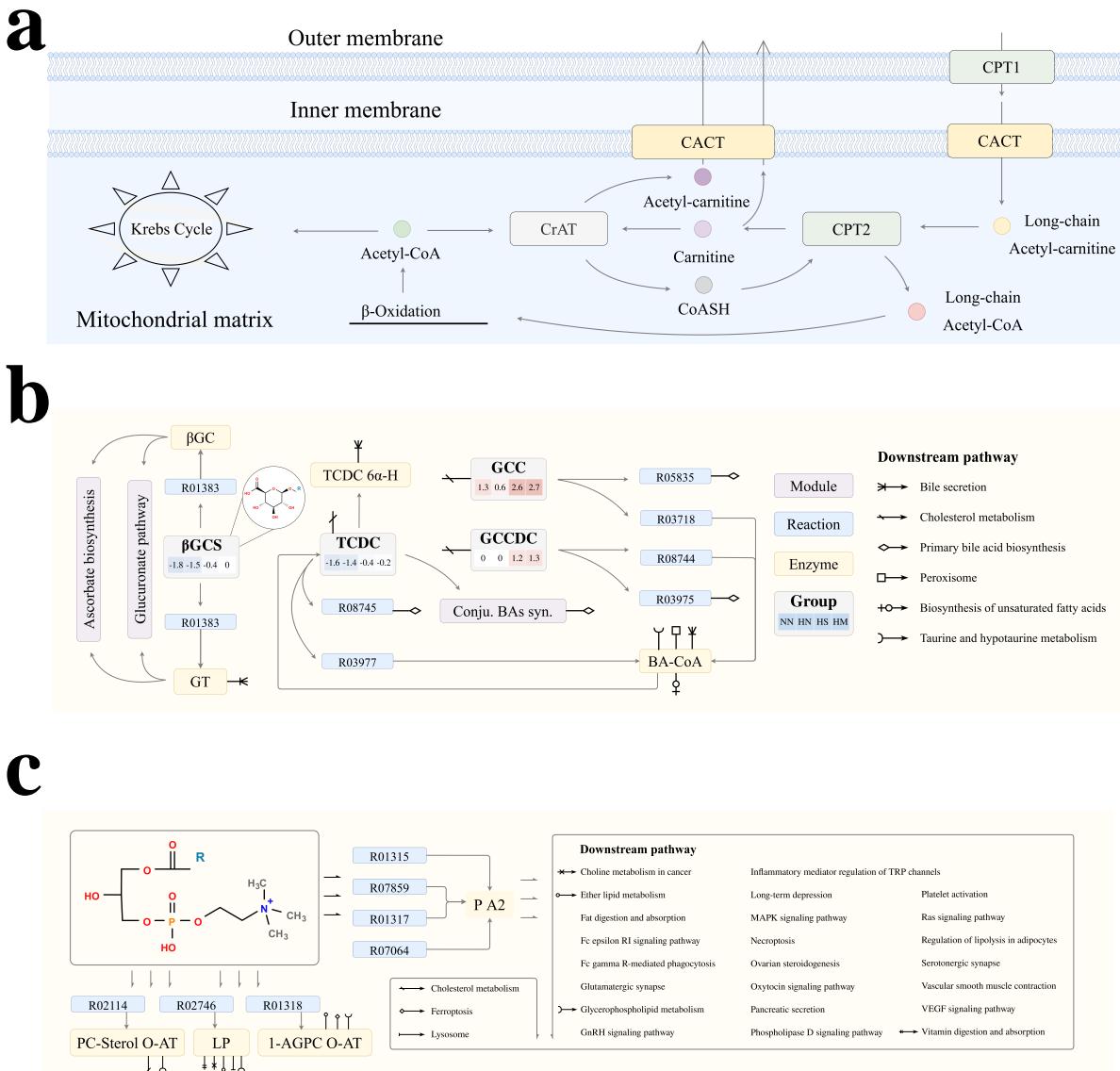


Fig. S5: Pathway analysis of ‘Acyl carnitines’ (ACs), ‘Lysophosphatidylcholines’ (LPCs), ‘Bile acids, alcohols and derivatives’ (BAs) in serum metabolomics dataset.

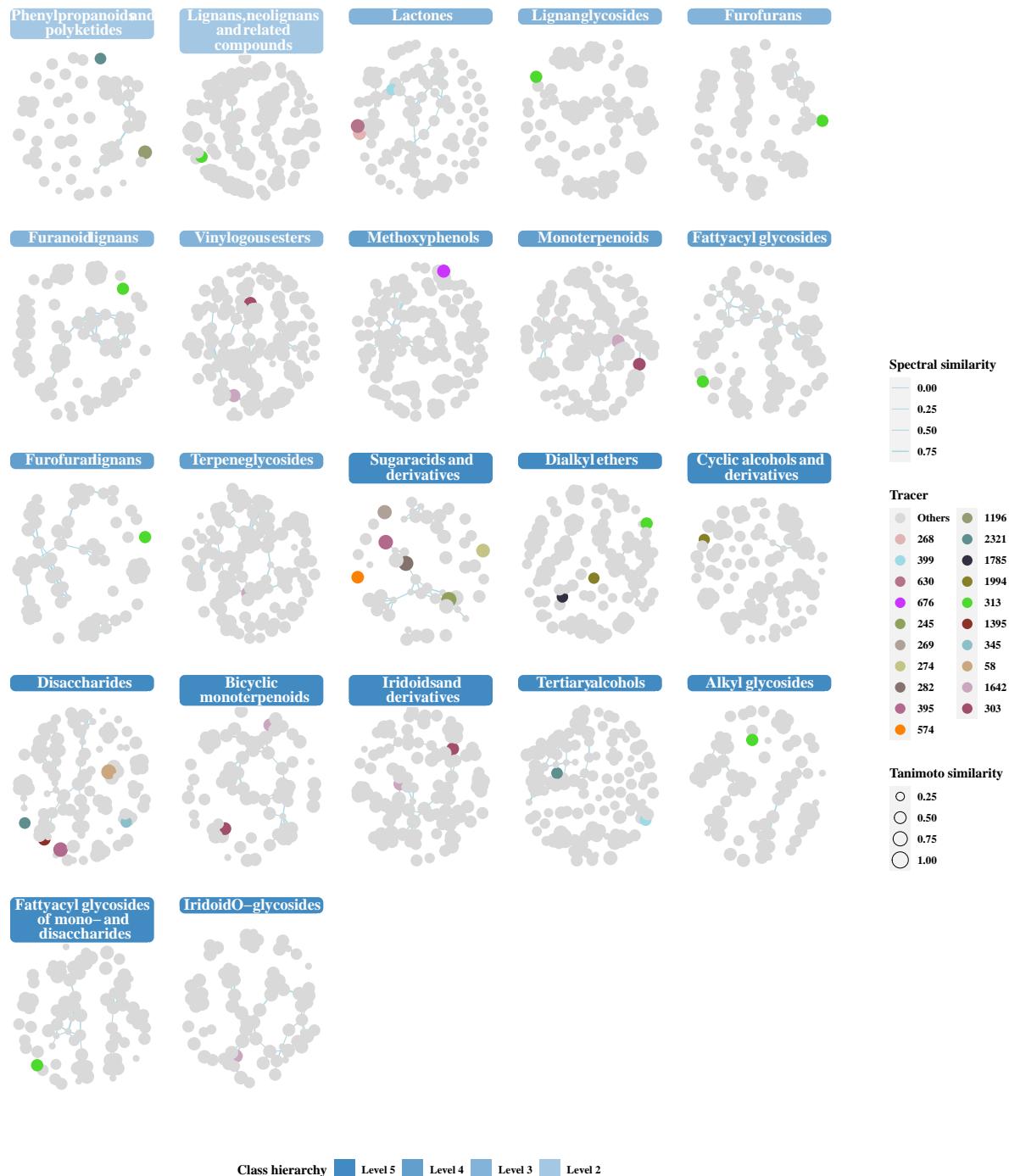


Fig. S6: Tracing top ‘features’ in Child-Nebulae of herbal medicine dataset

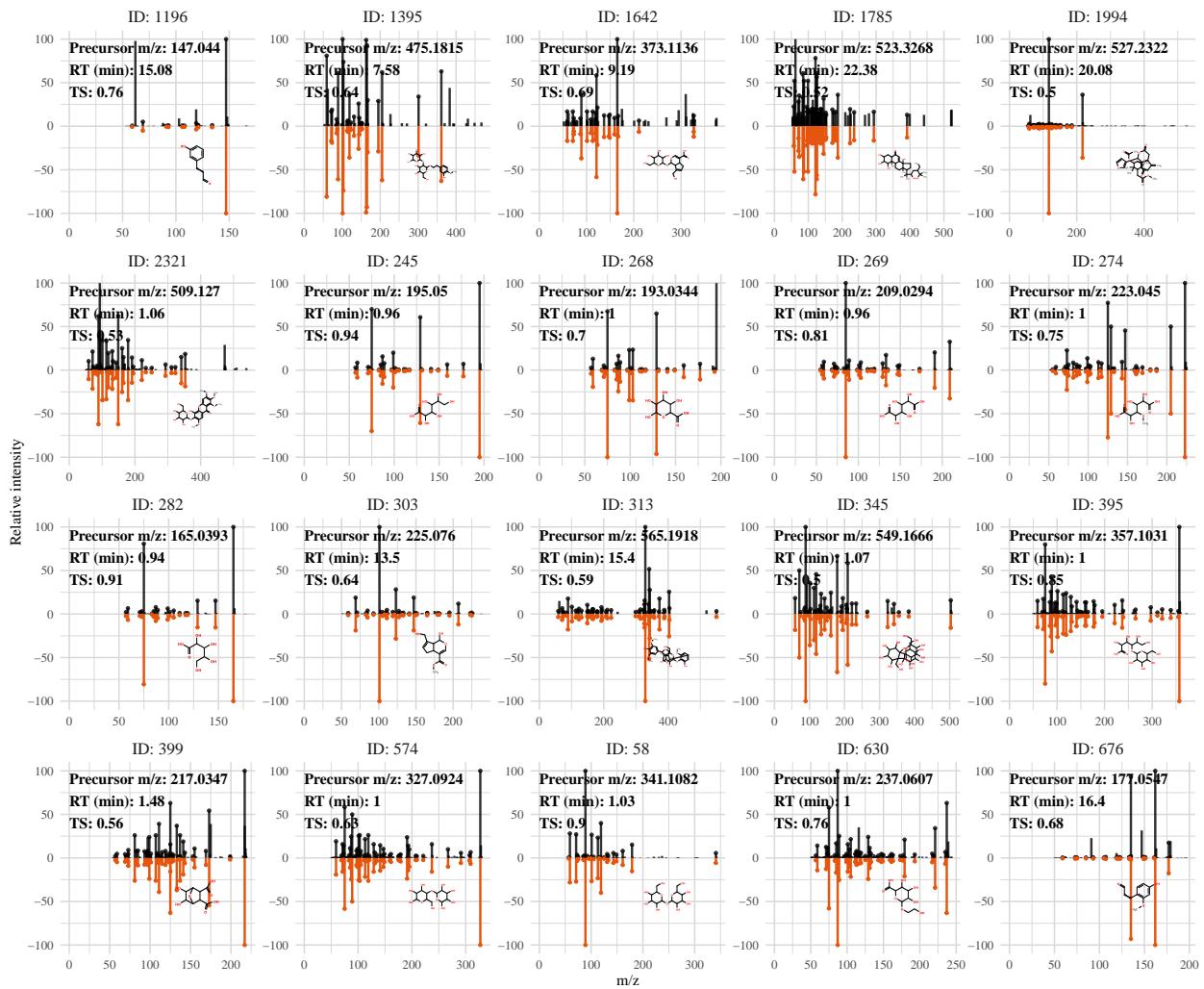


Fig. S7: MS/MS spectra of top ‘features’ of herbal medicine dataset.

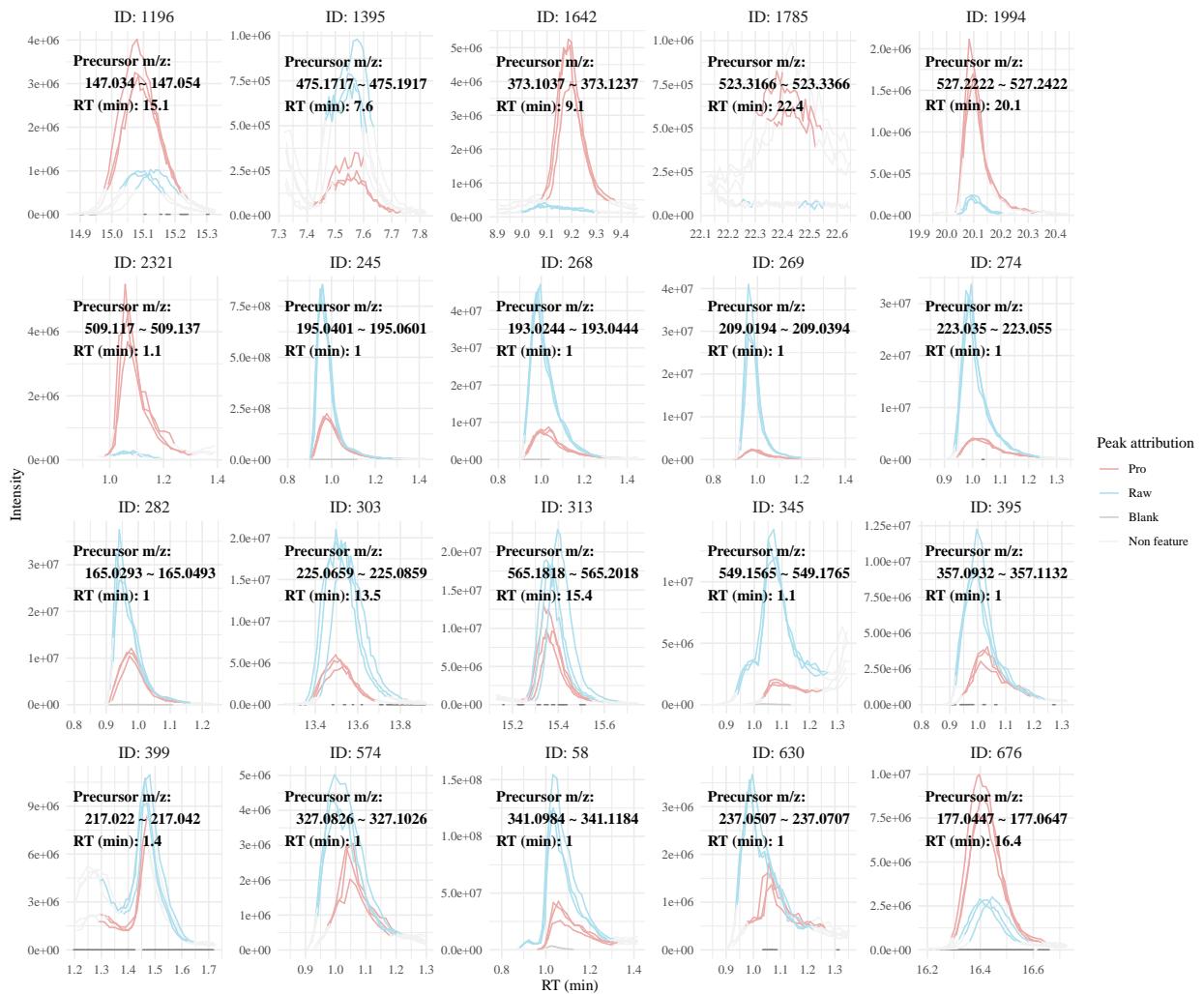


Fig. S8: Extracted ions chromatography (EIC) of top ‘features’ of herbal medicine dataset.

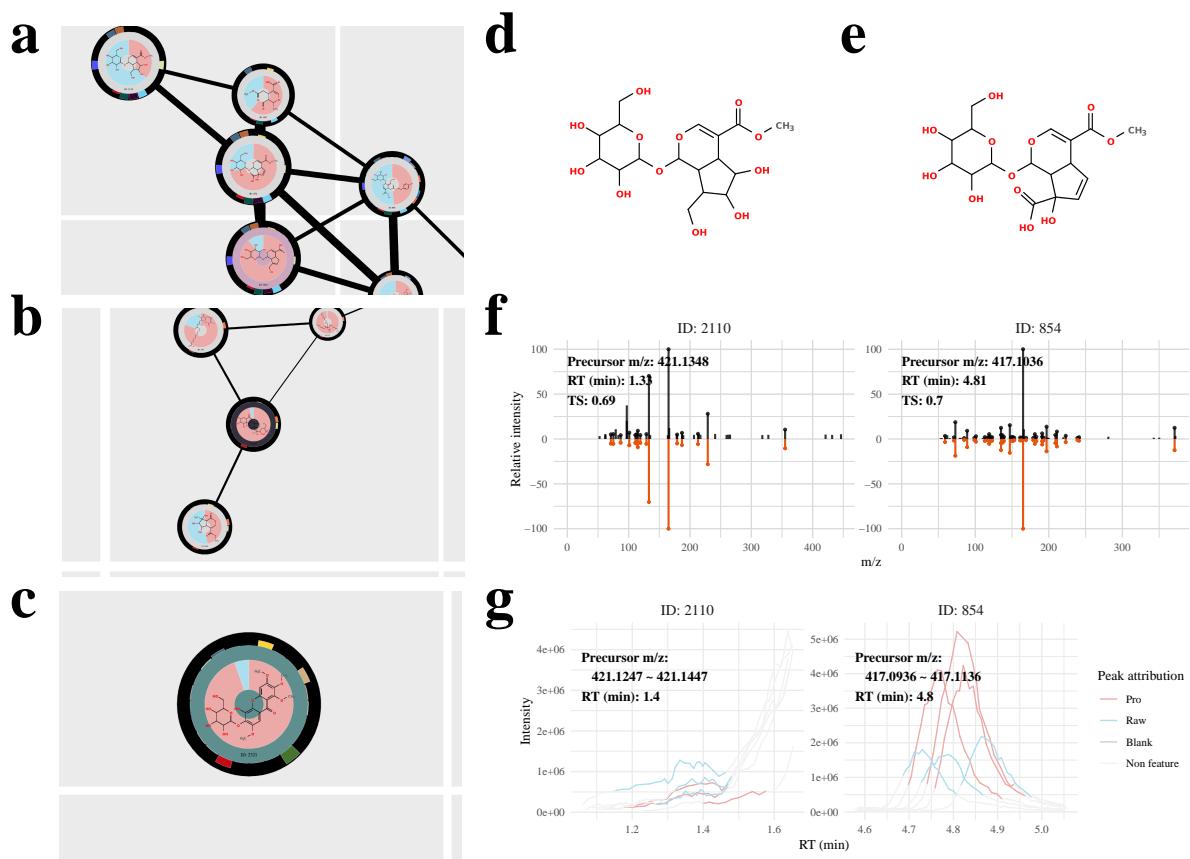


Fig. S9: Focus on location of top ‘features’ in annotated Child-Nebulae.