

## SUPPLEMENTARY FIGURES

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**Supplementary Figure 12.** Identification of Urolithin C-glucuronide and Urolithin C comparing retention times and  $m/z$  measured in urine and faeces, respectively, with retention times and  $m/z$  of authentic standards.

**Supplementary Figure 13.** Identification of Tryptophan betaine comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.

**Supplementary Figure 14.** Identification of Oxindole-3-acetic acid comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.

**Supplementary Figure 15.** Identification of Pipecolic acid betaine comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.

**Supplementary Figure 16.** Identification of Phenyllactic acid comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.

**Supplementary Figure 17.** Identification of 3-methylpyrogallol-sulfate comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.

**Supplementary Figure 18.** Identification of Phenylacetylglutamine comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.

**Supplementary Figure 19.** Identification of P-cresol sulfate comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.

**Supplementary Figure 20.** Identification of Indoxyl sulfate comparing retention time,  $m/z$  and spectrum measured in serum with retention time,  $m/z$  and spectrum of an authentic standard. We noted a shift in retention time (0.3 min) for indoxyl sulfate compared to the original data collected.

**Supplementary Figure 21.** Identification of Phenol sulfate comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.

**Supplementary Figure 22.** Identification of 3-carboxy-4-methyl-5-propanyl-2-furanpropionic acid (CMPF) comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.

**Supplementary Figure 23.** Identification of trimethylamine-N-oxide (TMAO) comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.

**Supplementary Figure 24.** Retention times of bile acid authentic standards.

**Supplementary Figure 25.** Identification of Glycochenodeoxycholic acid sulfate comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.

**Supplementary Figure 26** Diverging bar charts showing Spearman's correlations between MD Index and annotated metabolites from faecal, serum and urine metabolome.

**Supplementary Figure 27** Barcoding plots of the contrasted MSP species between ConD and MedD diets at baseline.

**Supplementary Figure 28** Barcoding plots of the contrasted MSP species between ConD and MedD diets at 4w.

**Supplementary Figure 29** Barcoding plots of the contrasted MSP species between ConD and MedD diets at 8w.

**Supplementary Figure 30** Distinctive metabolic, dietary and microbial signatures between ConD and MedD diets after 4 weeks.

**Supplementary Figure 31** N-integrative supervised analysis of different types of 'omics datasets.

**Supplementary Figure 32** Correlation of microbiome-related metabolites with dietary and clinical variables.

**Supplementary Figure 33** Box plots showing faecal concentrations of several BAs measured throughout the intervention.

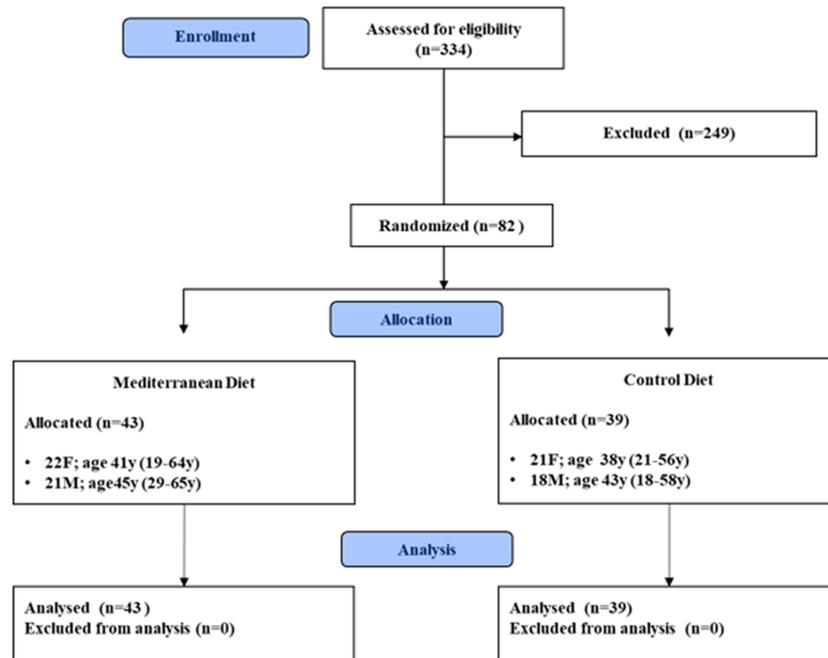
**Supplementary Figure 34** Box plots showing differences in HOMA variation classifying the subjects in HOMA reducers and non-reducers after 4 weeks of intervention.

**Supplementary Figure 35** Box plots showing differences in abundance of Co-Abundance Groups obtained from 16S rRNA gene sequences in subjects classified as HOMA reducers and non-reducers after 4 weeks of intervention.

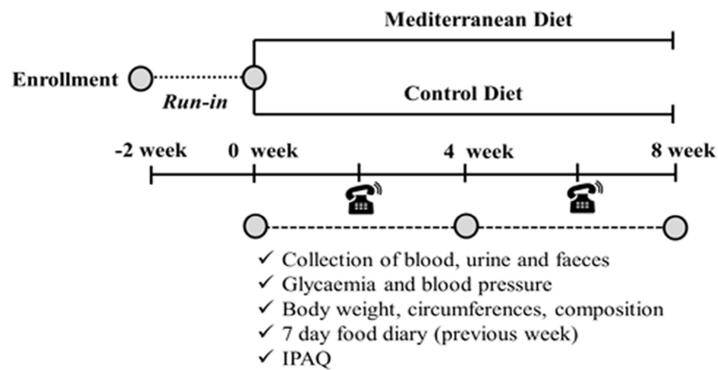
**Supplementary Figure 36** Circular tree showing clustering of the subjects based on *Faecalibacterium prausnitzii* pangenome.

## SUPPLEMENTARY FIGURES

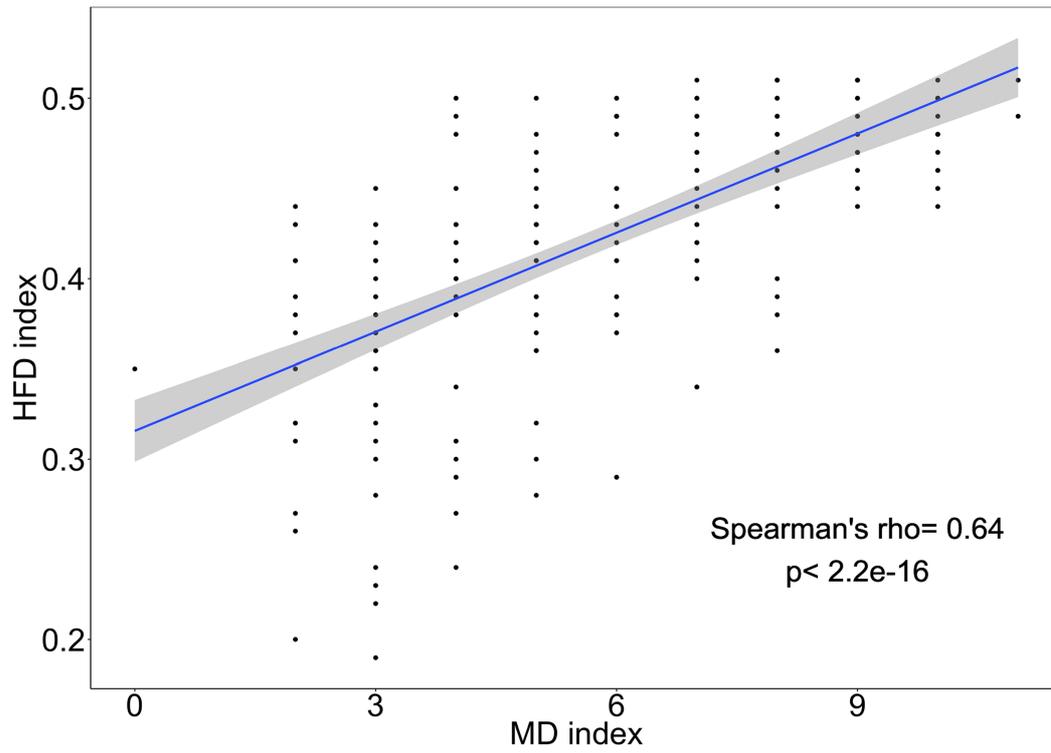
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B

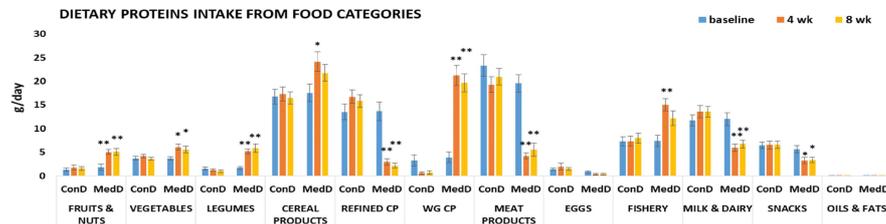


Supplementary Figure 1 (A) Participant flow and (B) study design.

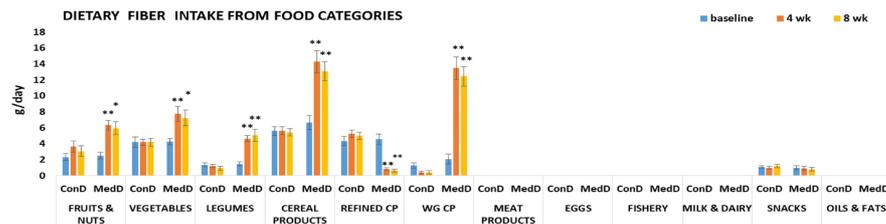


**Supplementary Figure 2** Spearman's rank-order correlation between MD index and Healthy Food Diversity (HFD) index.

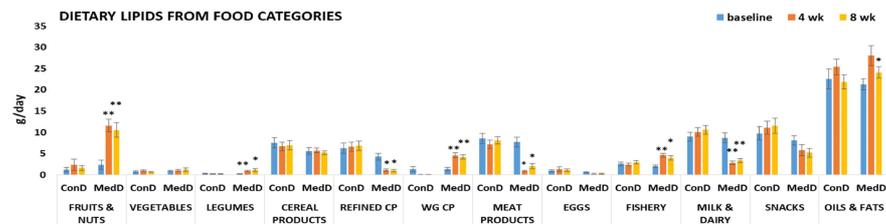
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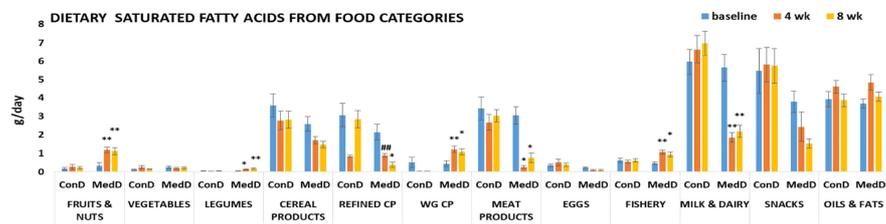
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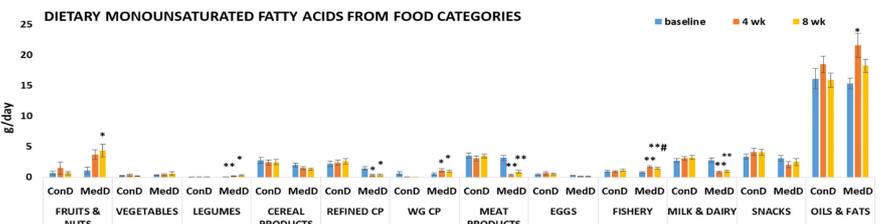
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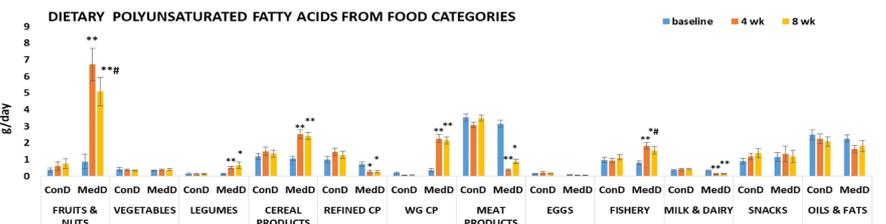
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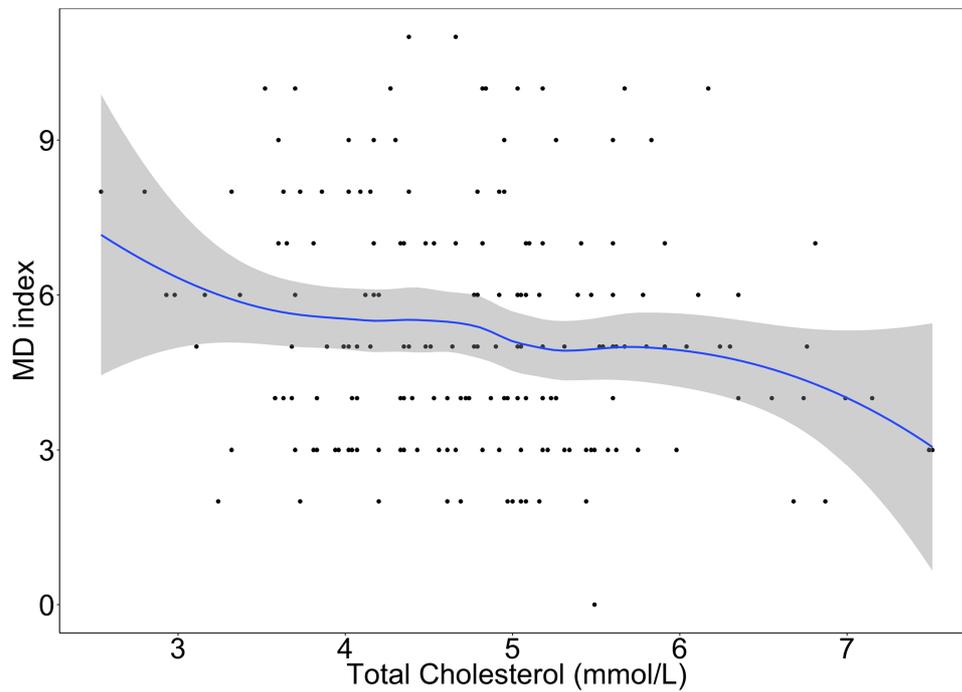
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F

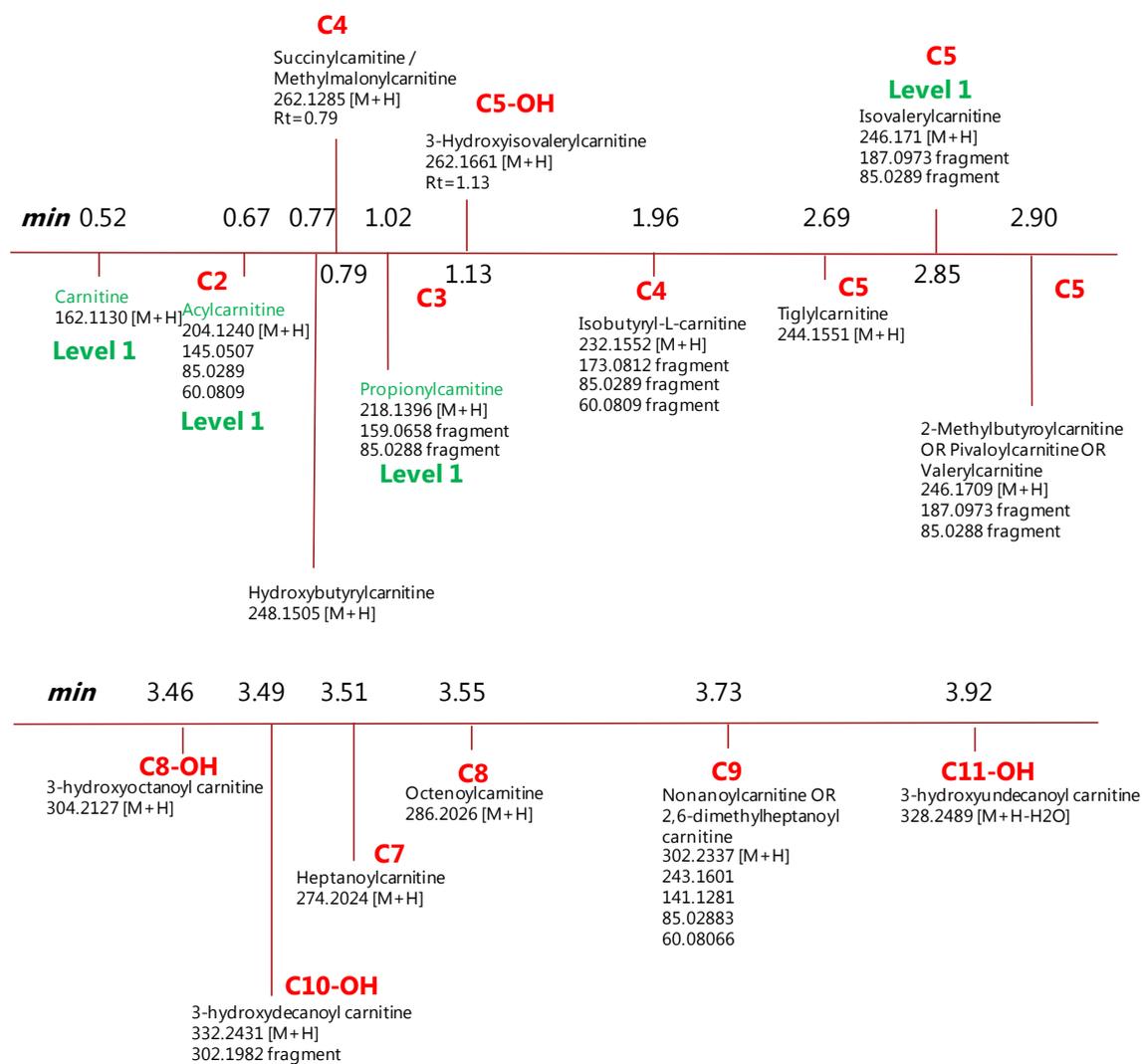


**Supplementary Figure 3** Daily intake (g/day) of (A) proteins, (B) dietary fiber, (C) total lipids, (D) saturated fatty acids, (E) monounsaturated fatty acids and (F) polyunsaturated fatty acids from the food categories (fruits & nuts, vegetables, legumes, cereal products, refined cereal products, wholegrain-based cereal products, meat products, eggs, fishery, milk & dairy products, snacks, oil & fats) recorded by subjects in Control (ConD, n=32) and Mediterranean (MedD, n=30) diet group at baseline (week 0), 4w and 8w. Bars indicate the means±SEM. \* indicates  $p<0.05$  and \*\* indicates  $p<0.001$  for MedD vs ConD at specific time point compared to baseline; # indicates  $p<0.05$  and ## indicates  $p<0.001$  for MedD vs ConD at 8w vs 4w; 2-way ANOVA with repeated measures and Tukey post hoc test.

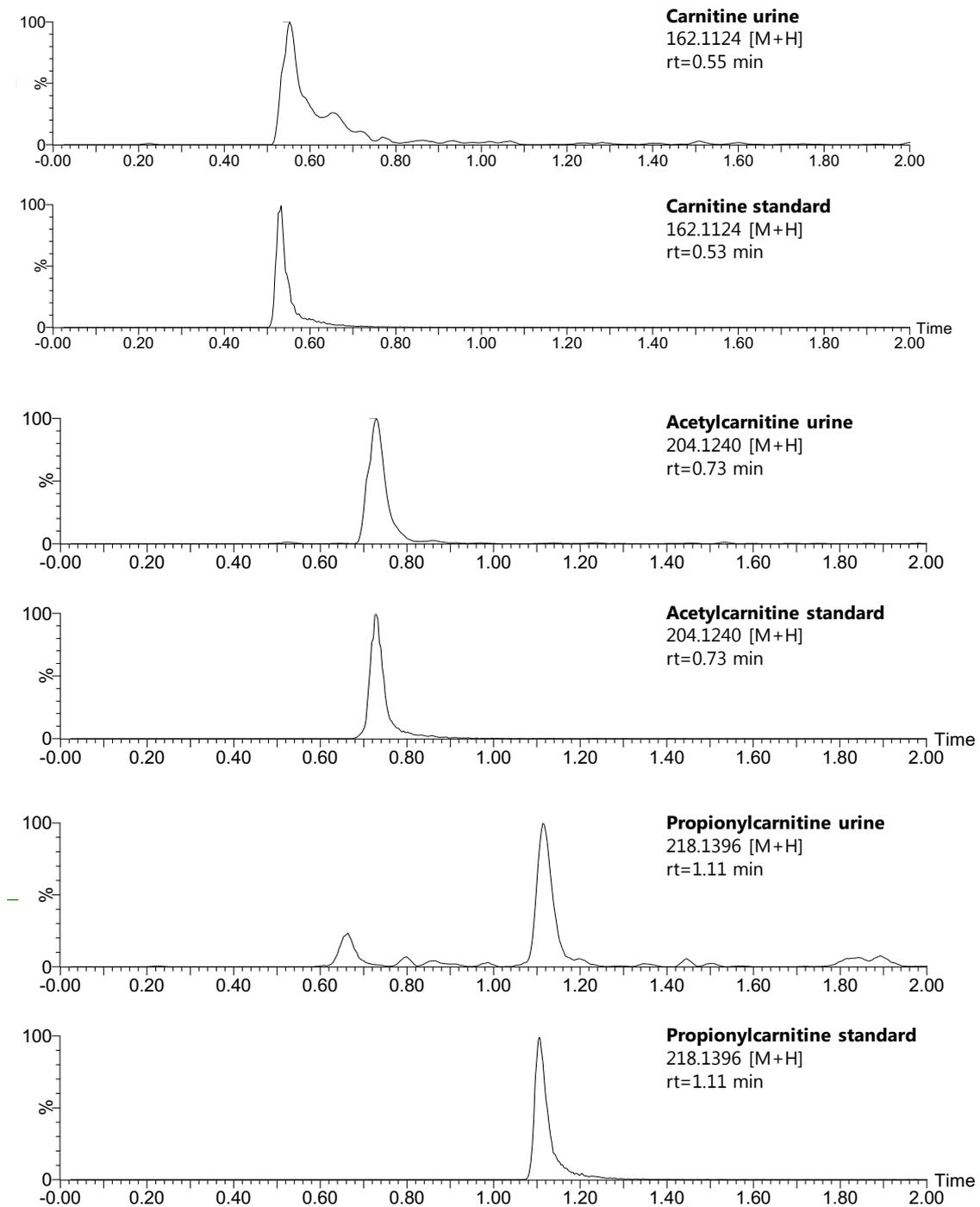


**Supplementary Figure 4** Linear regression analysis used to test if the MD index significantly predicted Total Cholesterol reduction, after adjusting for age, gender, BMI and energy intake. The result of the regression indicated the predictors explained the 28% of the variance (Adjusted R-squared= 0.26, pvalue: 1.206e-11). Total Cholesterol (mmol/L) = 4.38 – 0.08 MD index.

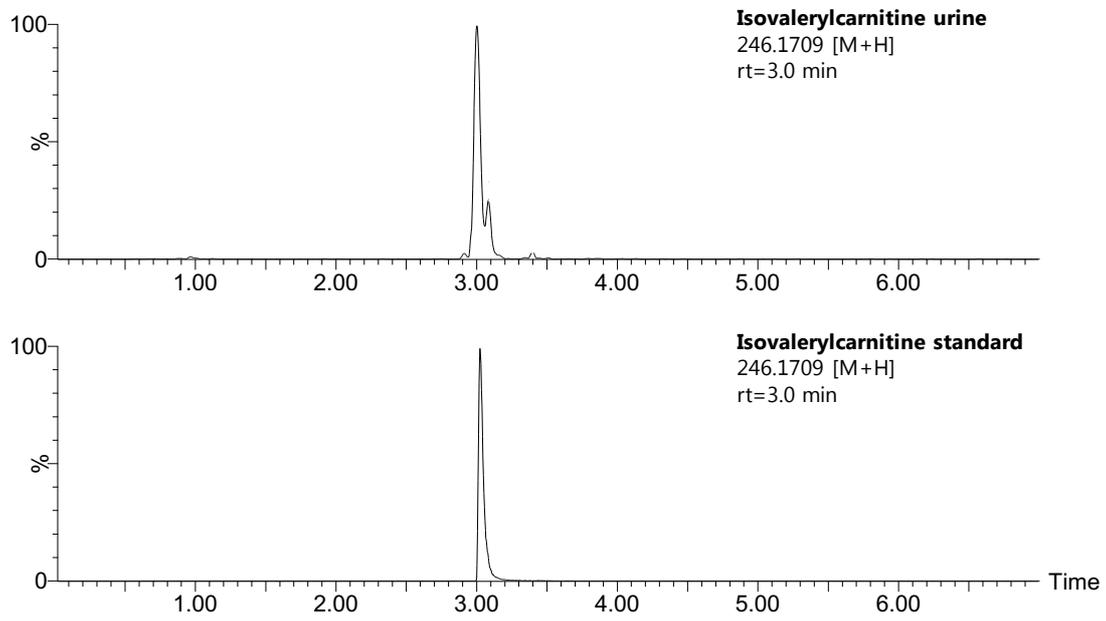
## Acylcarnitines



**Supplementary Figure 5.** Retention times and measured features of acylcarnitines. The acyl chain length is marked with the red letters from C2 to C11. Carnitine, acylcarnitine, propionylcarnitine and isovalerylcarnitine were validated using authentic standards (level 1 identification). The other acylcarnitines were identified at level 3.



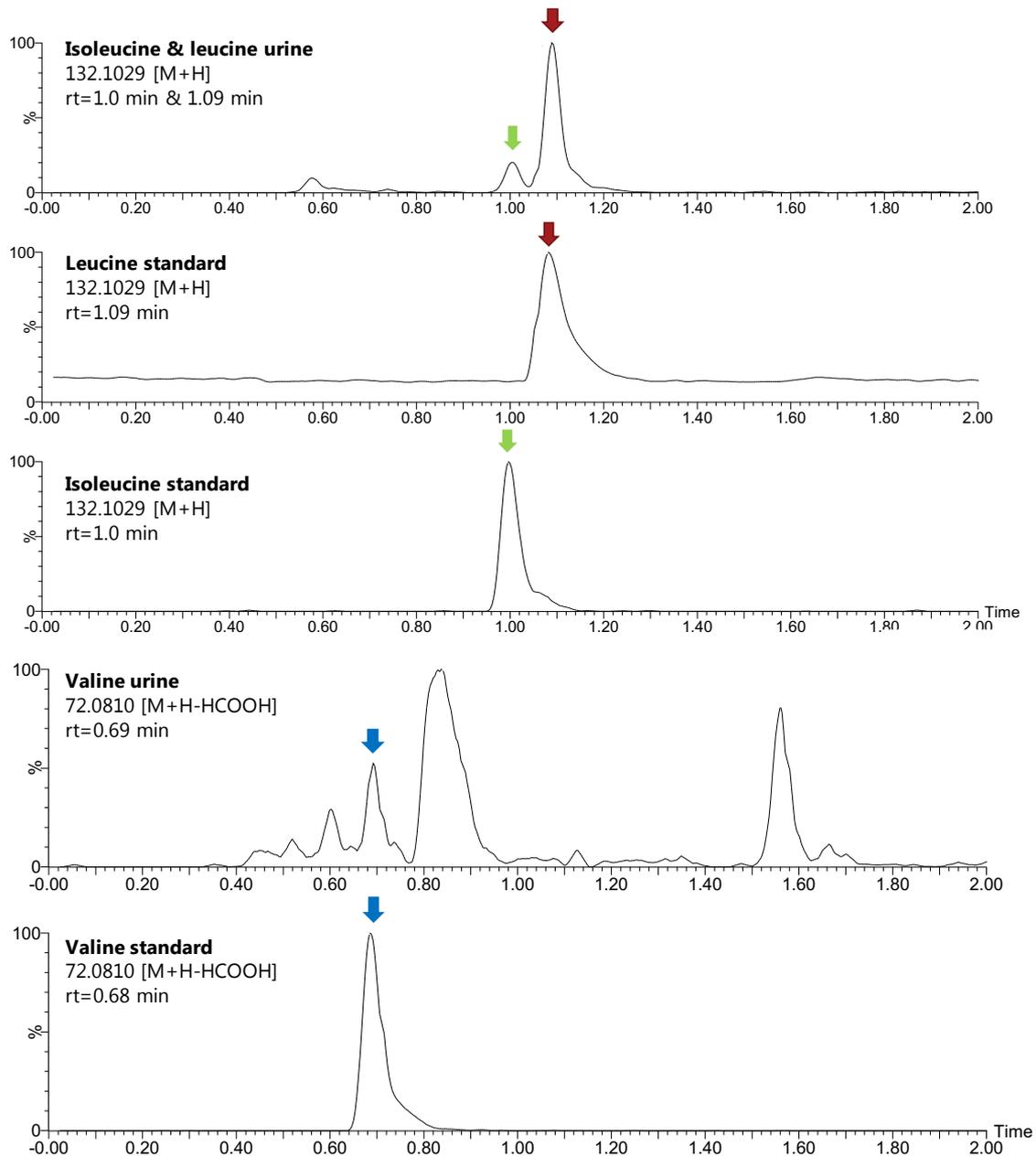
**Supplementary Figure 6.** Identification of acyl carnitines comparing retention time and  $m/z$  measured in urine with retention times and  $m/z$  of authentic standards.



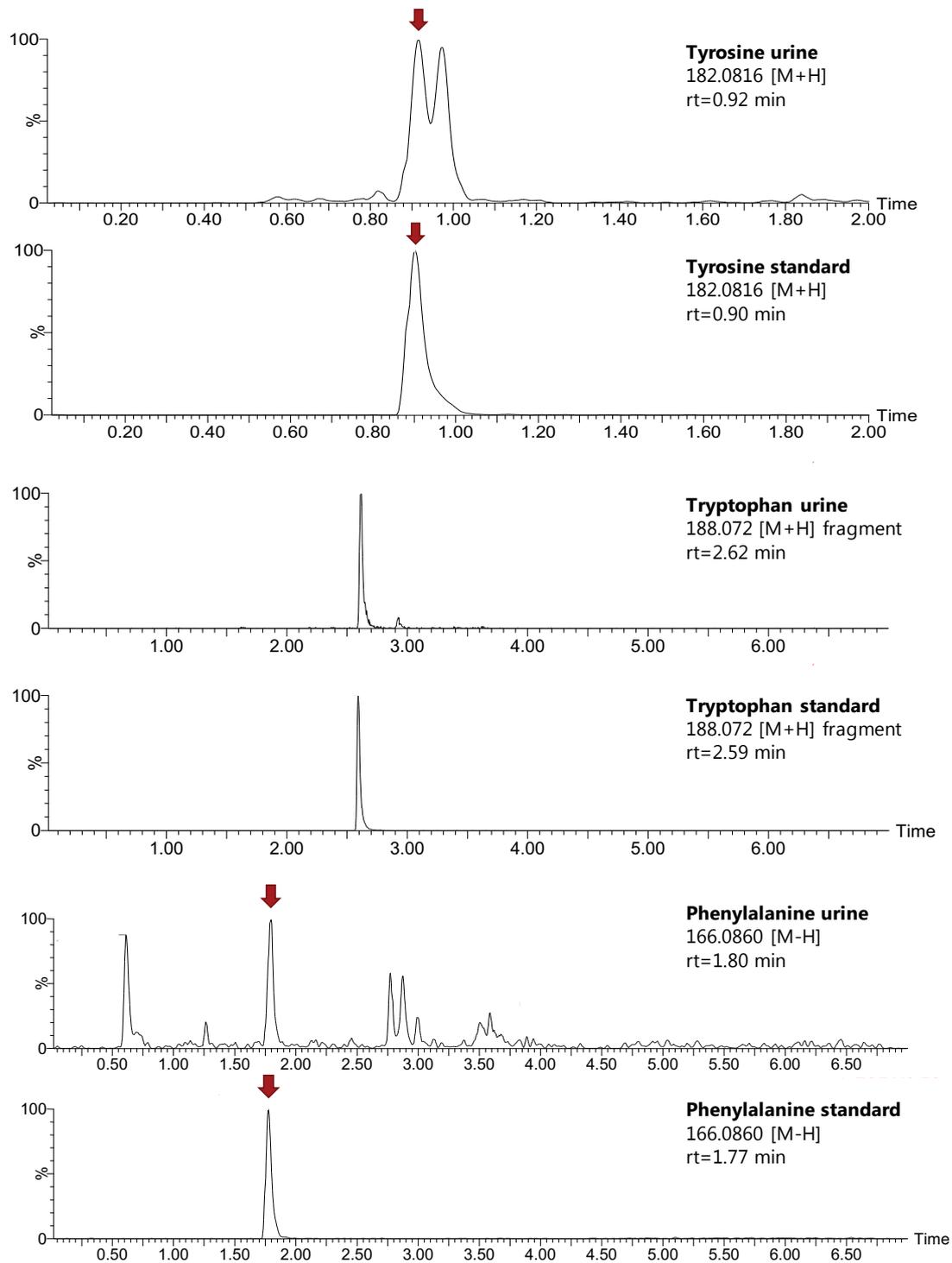
**Supplementary Figure 7.** Identification of isovalerylcarnitine comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.

## Amino acids

## Isoleucine and leucine

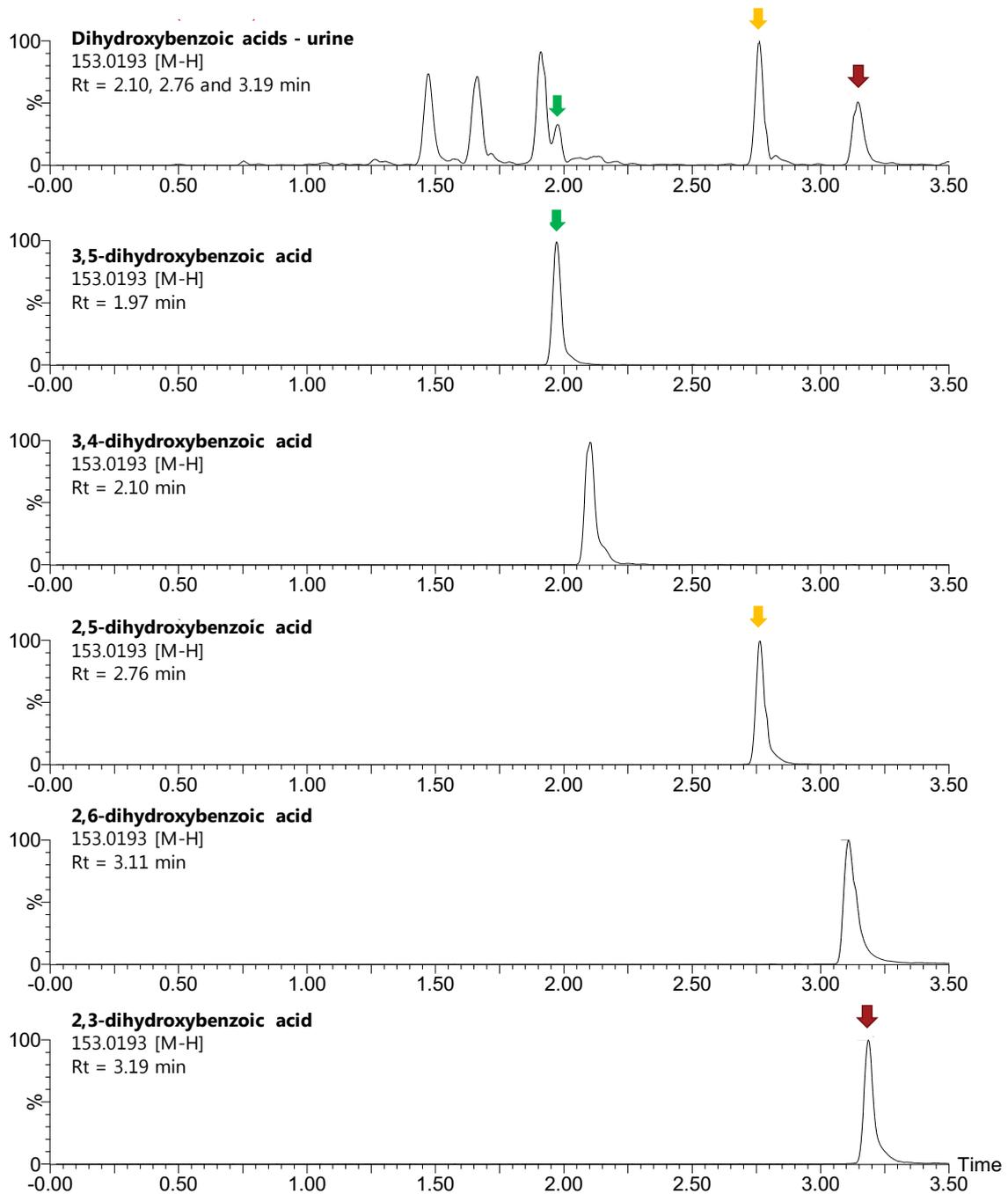


**Supplementary Figure 8.** Identification of branched-chain amino acids comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of authentic standards.

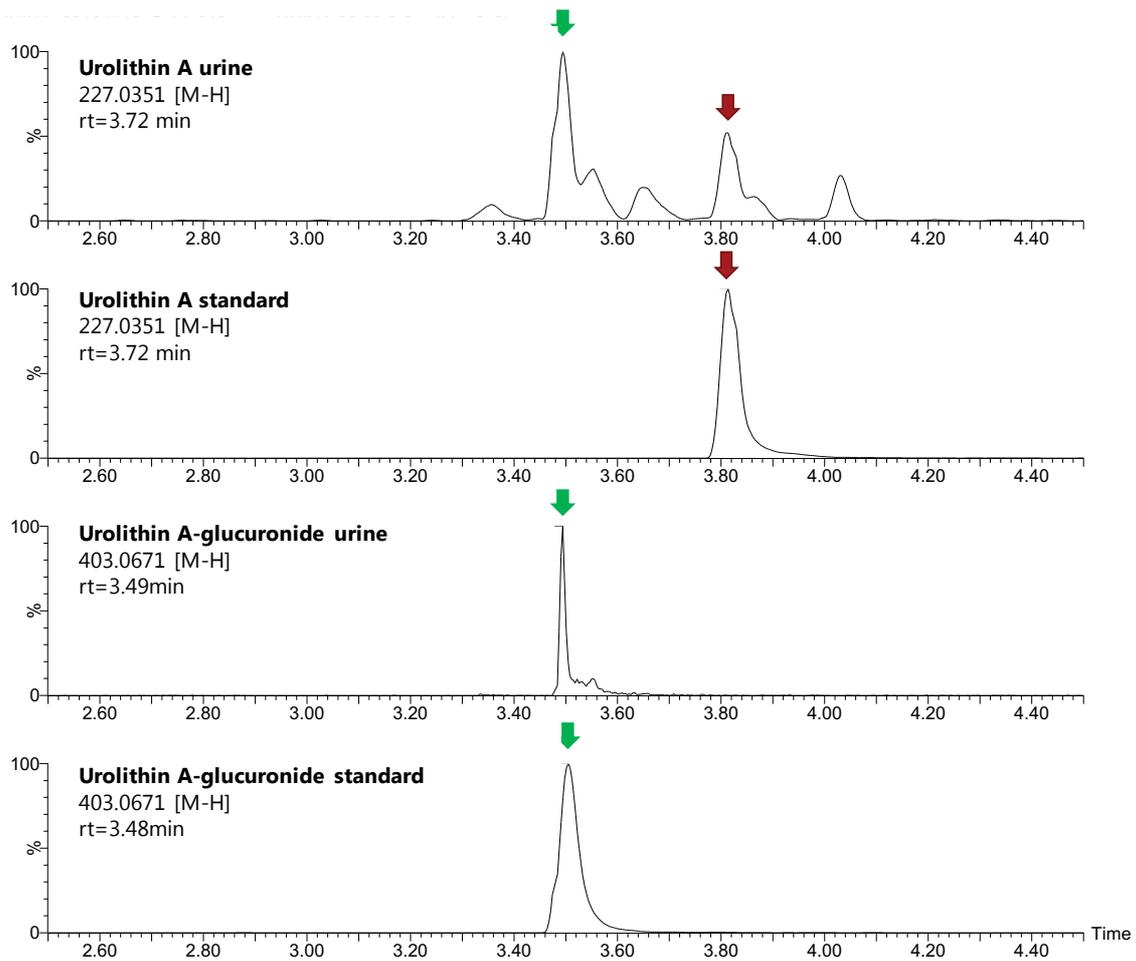


**Supplementary Figure 9.** Identification of aromatic amino acids comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of authentic standards.

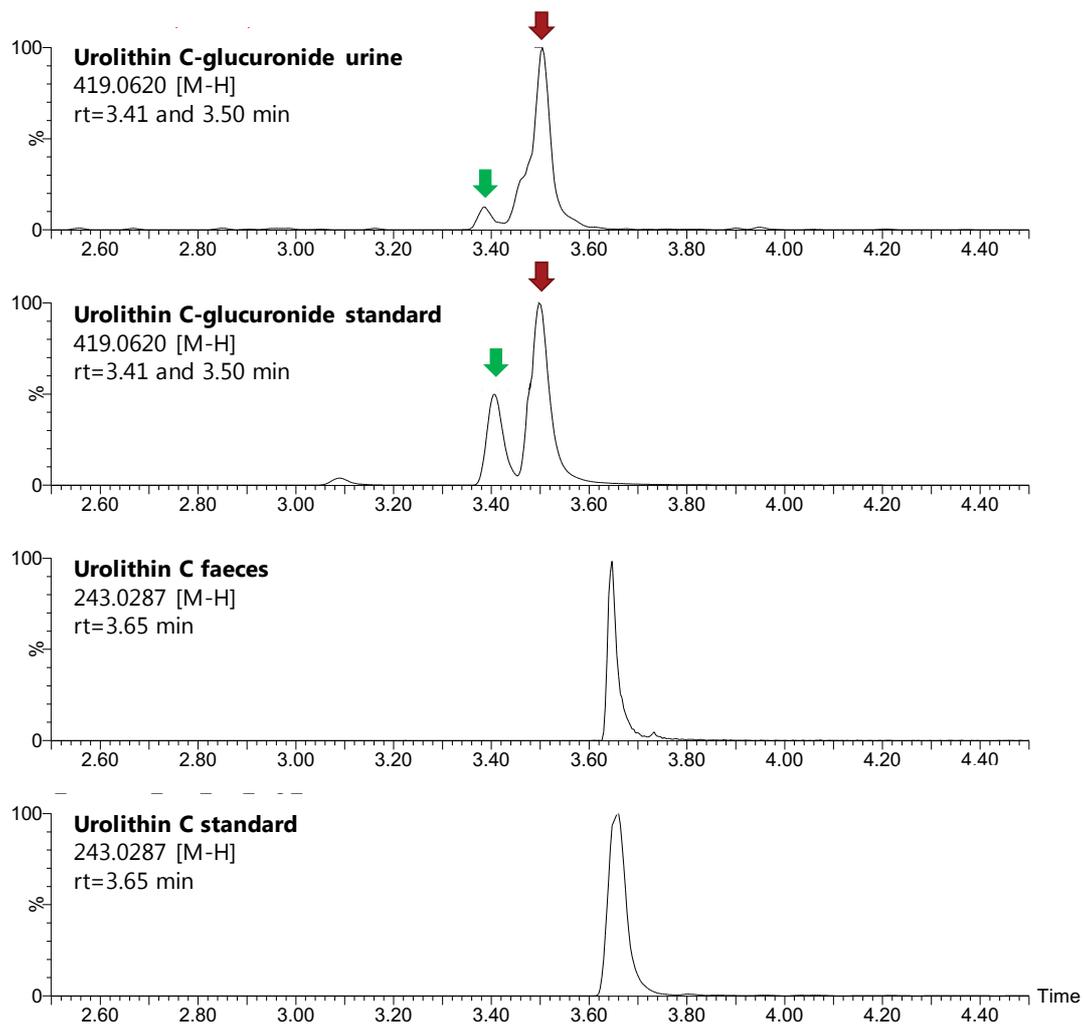
## Plant biomarkers



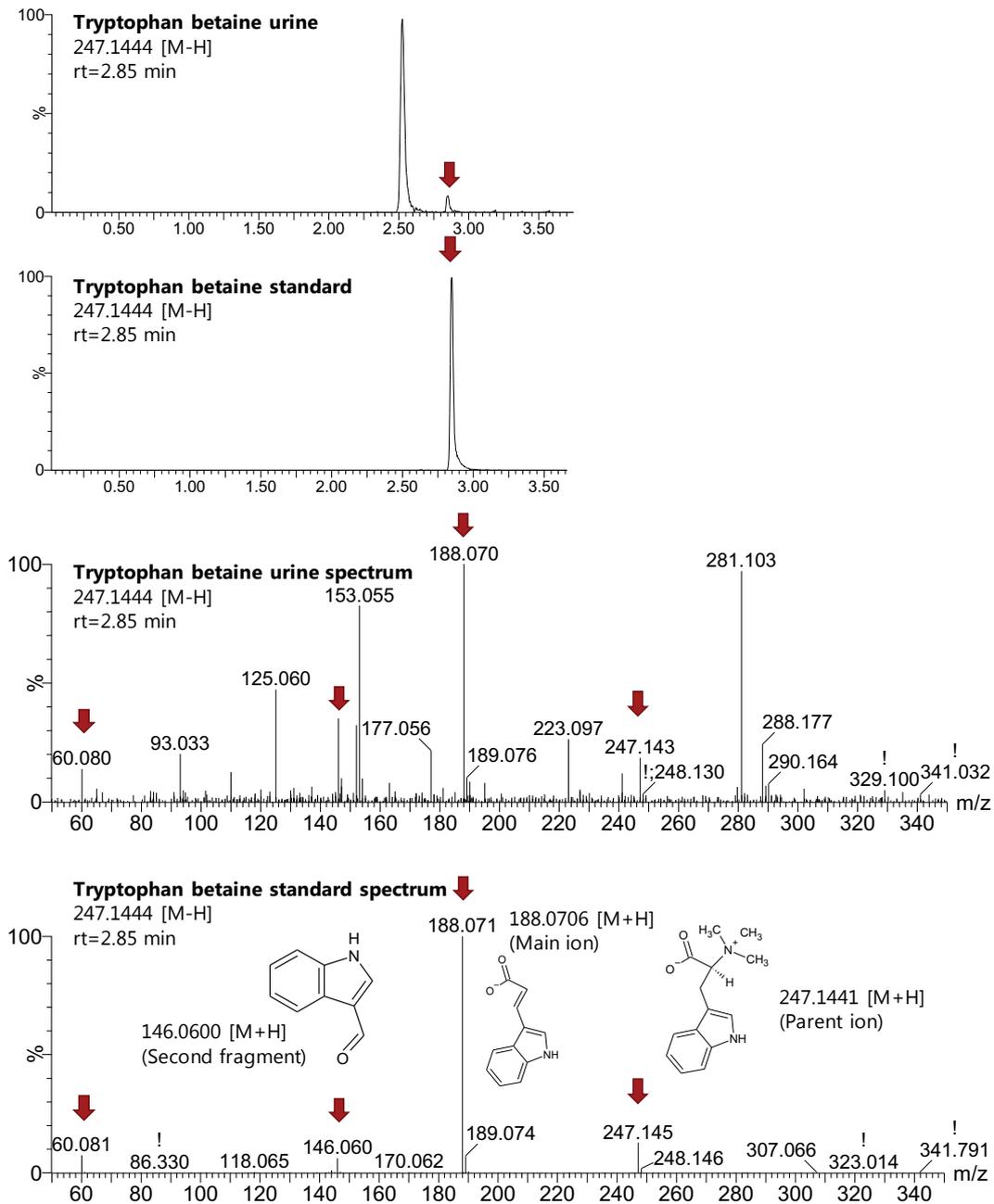
**Supplementary Figure 10.** Identification of dihydroxybenzoic acids comparing retention time and  $m/z$  measured in urine with retention times and  $m/z$  of authentic standards.



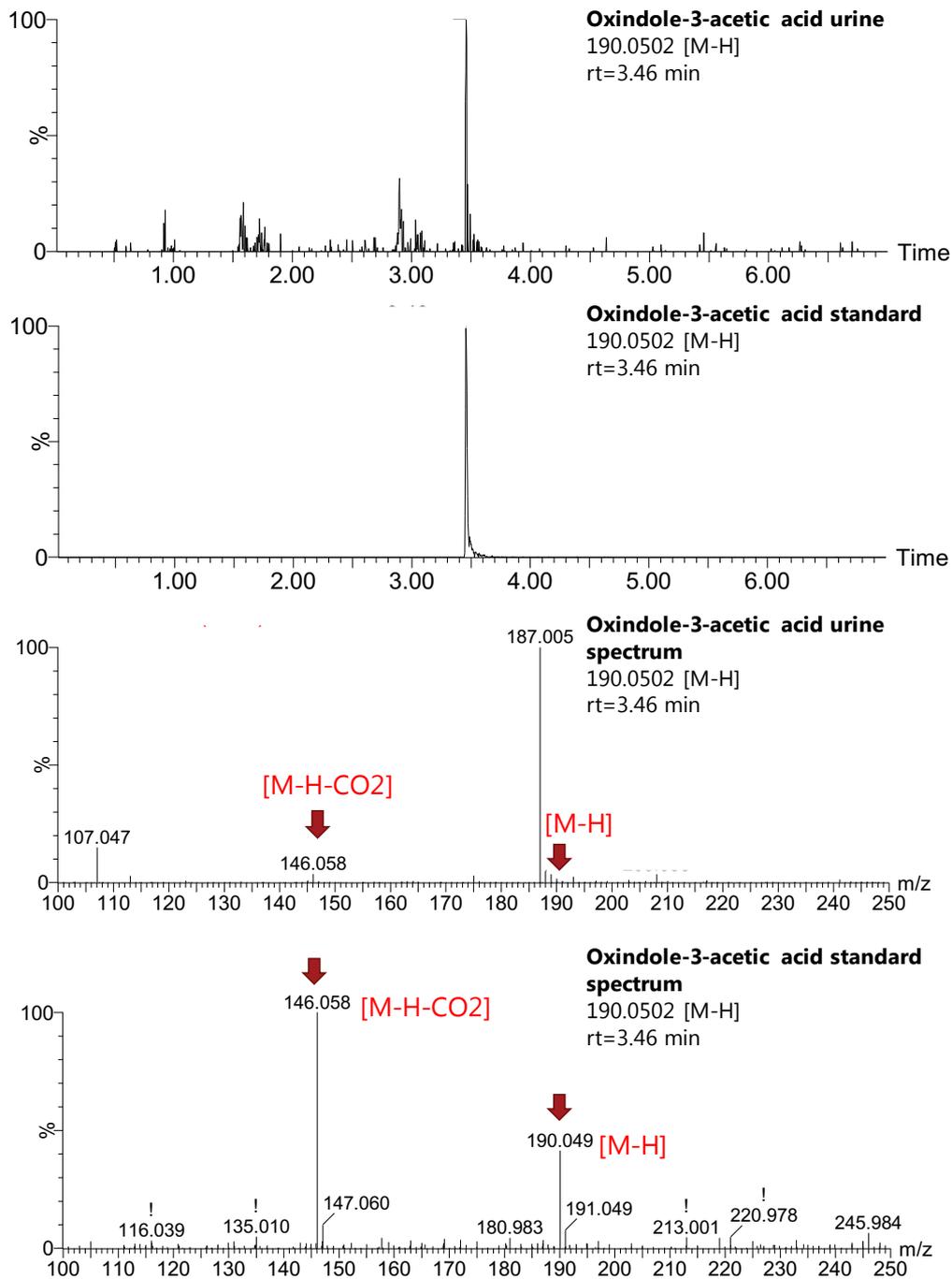
**Supplementary Figure 11.** Identification of Urolithin A and Urolithin A-glucuronide comparing retention times and  $m/z$  measured in urine with retention times and  $m/z$  of authentic standards.



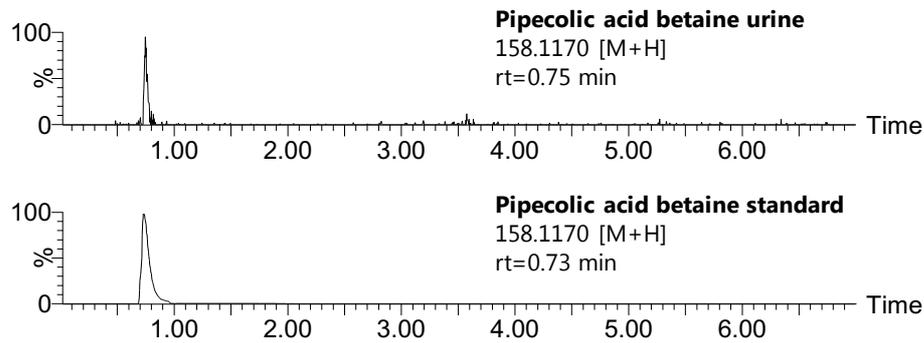
**Supplementary Figure 12.** Identification of Urolithin C-glucuronide and Urolithin C comparing retention times and  $m/z$  measured in urine and faeces, respectively, with retention times and  $m/z$  of authentic standards.



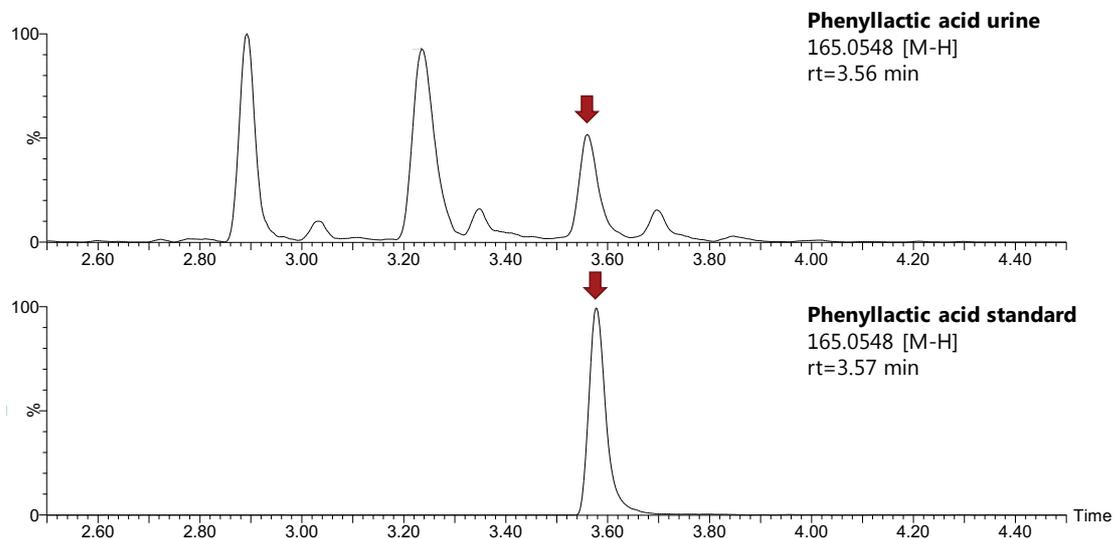
**Supplementary Figure 13.** Identification of Tryptophan betaine comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.



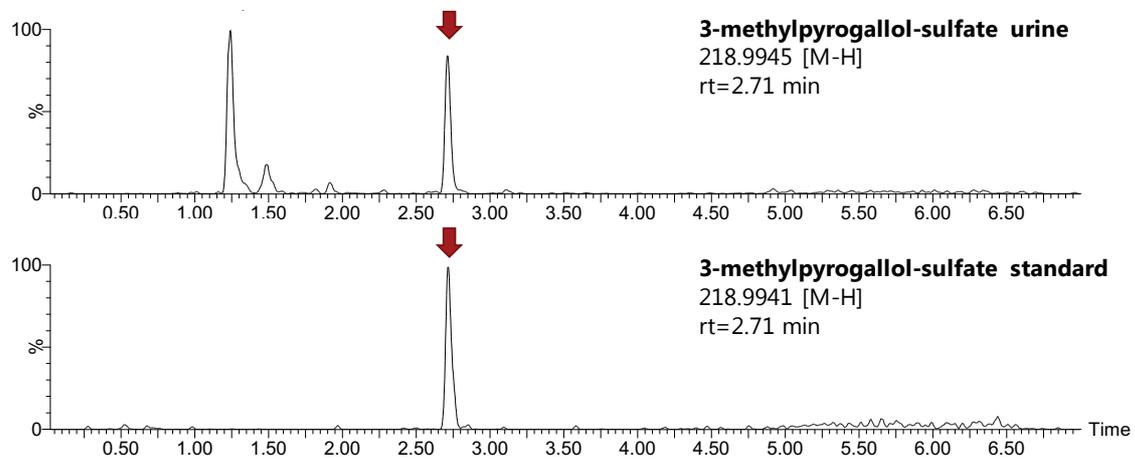
**Supplementary Figure 14.** Identification of Oxindole-3-acetic acid comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.



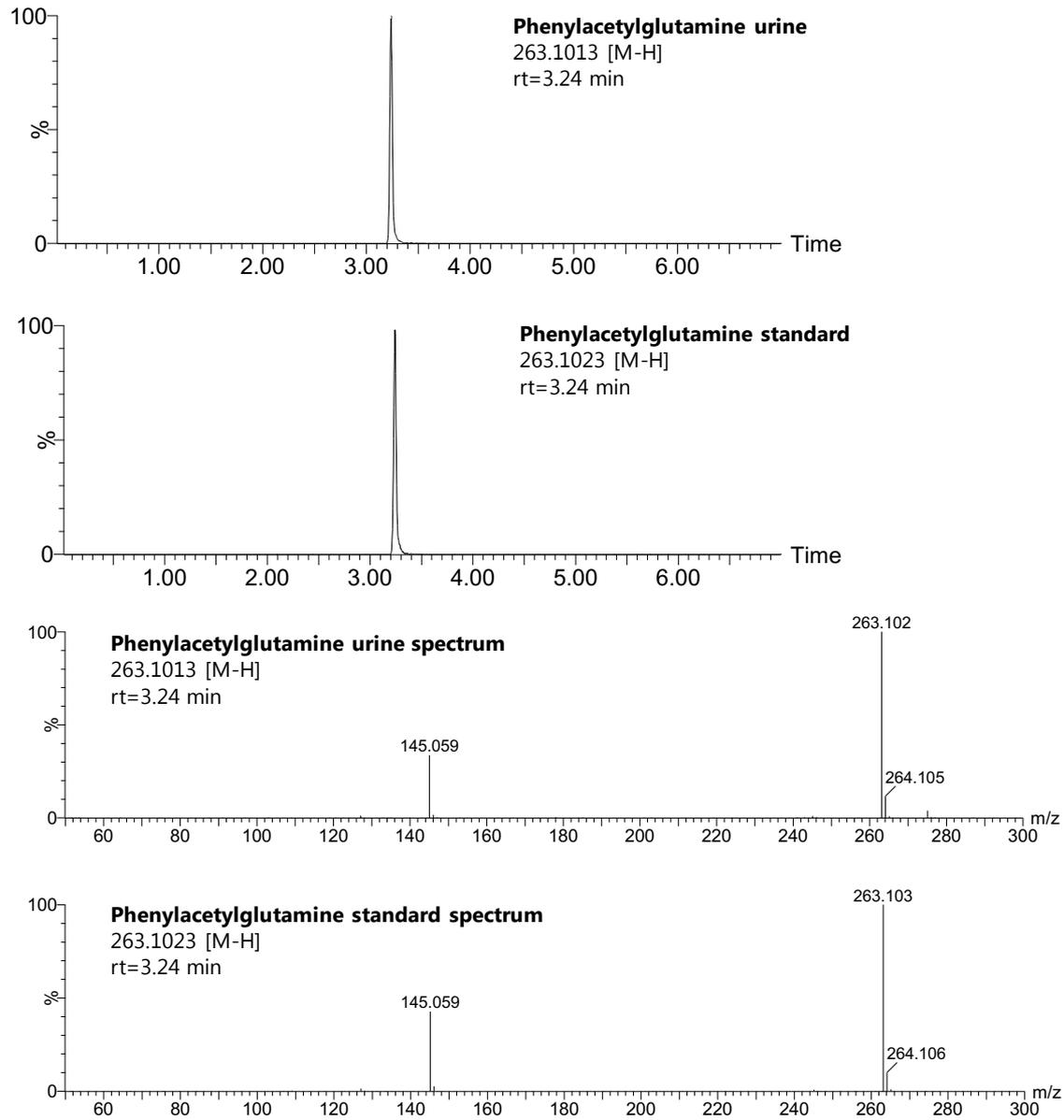
**Supplementary Figure 15.** Identification of Pipecolic acid betaine comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.



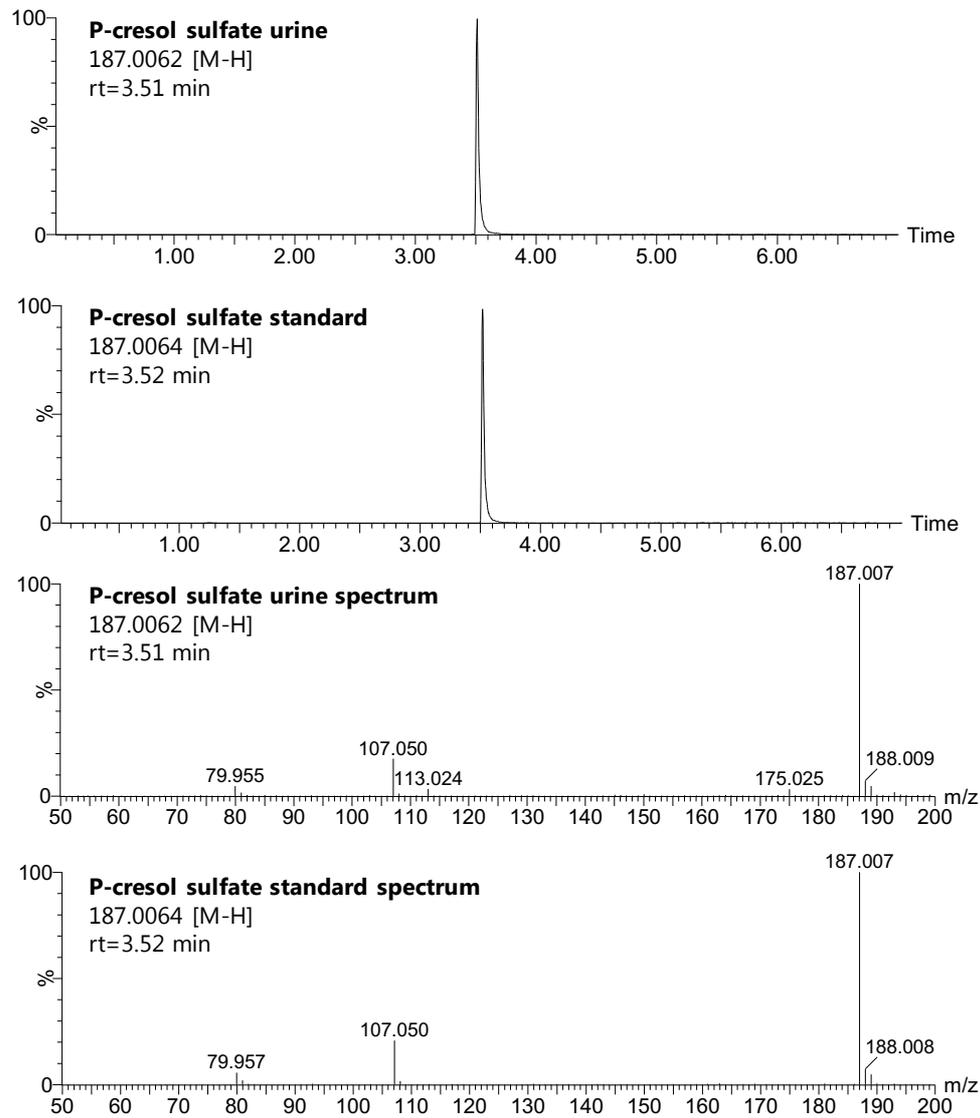
**Supplementary Figure 16.** Identification of Phenylactic acid comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.



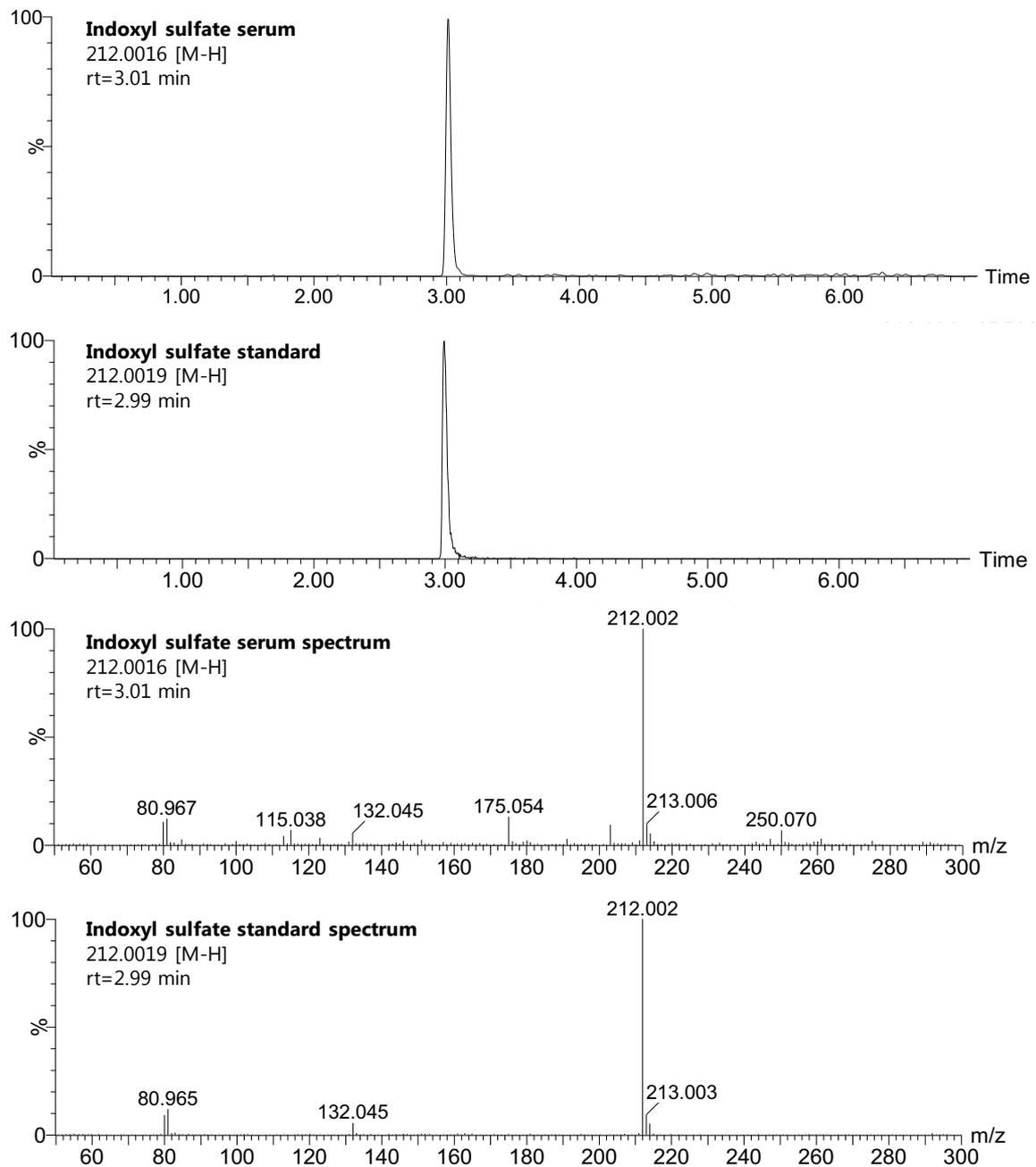
**Supplementary Figure 17.** Identification of 3-methylpyrogallol-sulfate comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.

**Proteolytic degradation products**

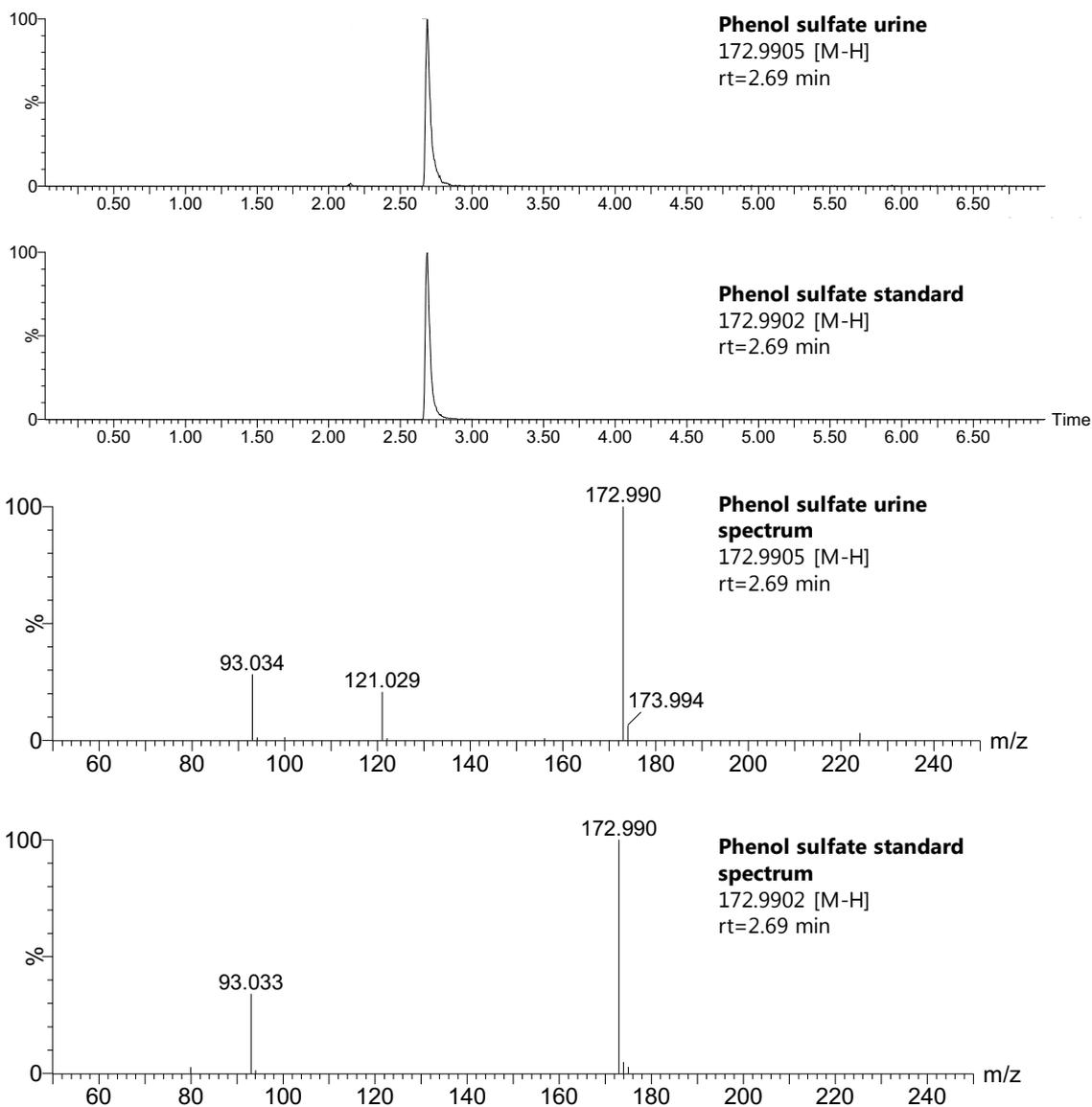
**Supplementary Figure 18.** Identification of Phenylacetylglutamine comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.



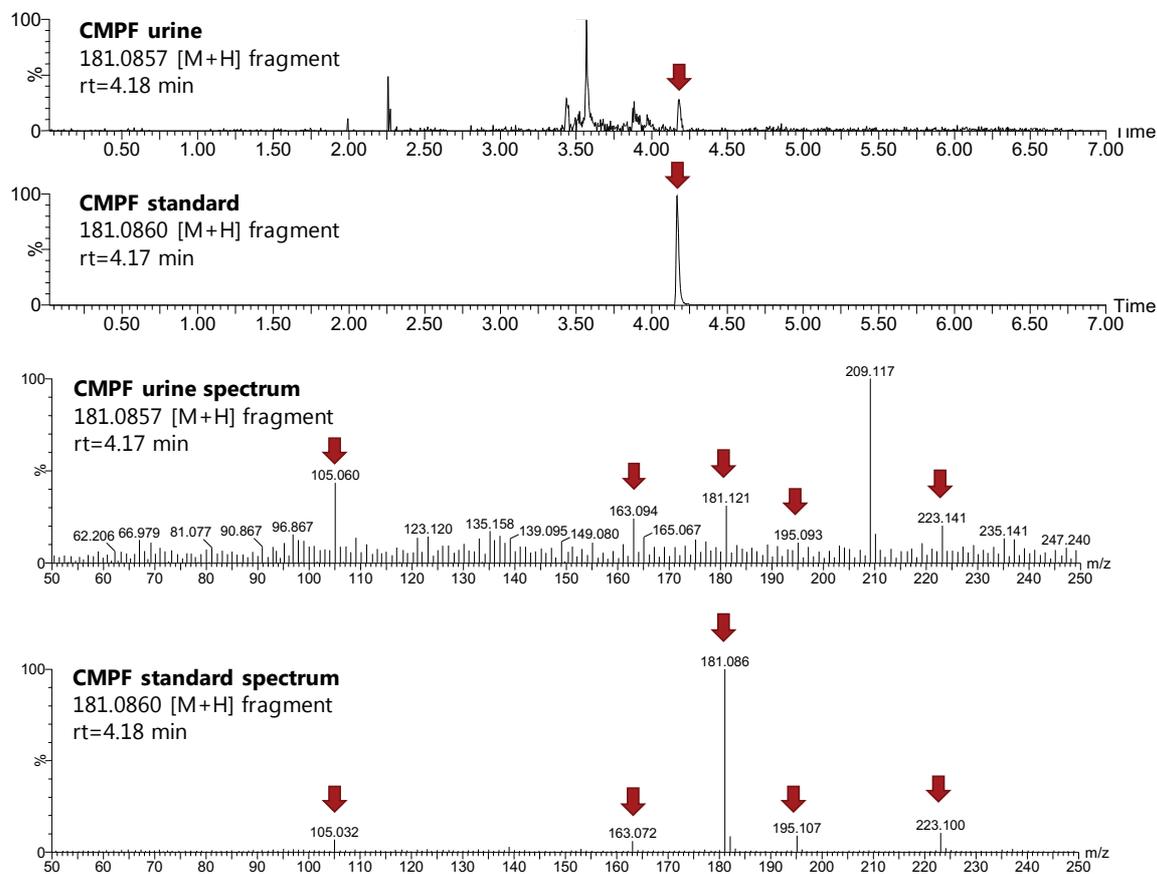
**Supplementary Figure 19.** Identification of P-cresol sulfate comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.



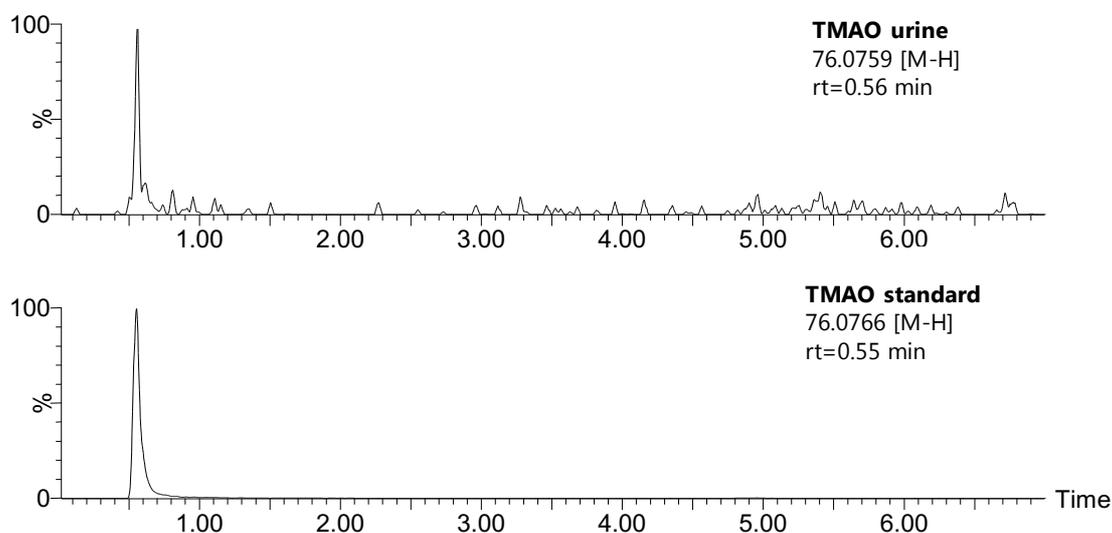
**Supplementary Figure 20.** Identification of Indoxyl sulfate comparing retention time,  $m/z$  and spectrum measured in serum with retention time,  $m/z$  and spectrum of an authentic standard. We noted a shift in retention time (0.3 min) for indoxyl sulfate compared to the original data collected.



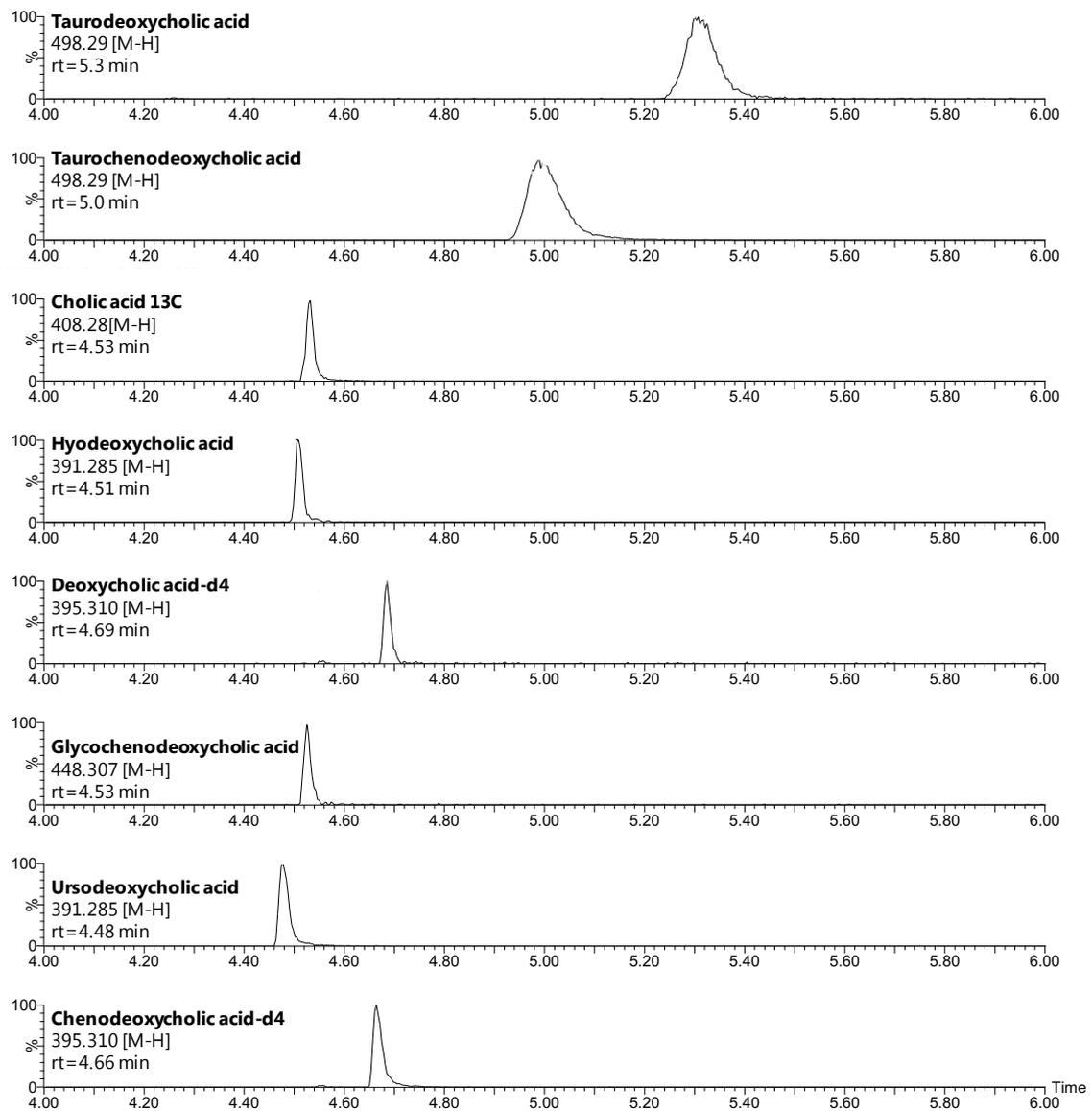
**Supplementary Figure 21.** Identification of Phenol sulfate comparing retention time,  $m/z$  and spectrum measured in urine with retention time,  $m/z$  and spectrum of an authentic standard.

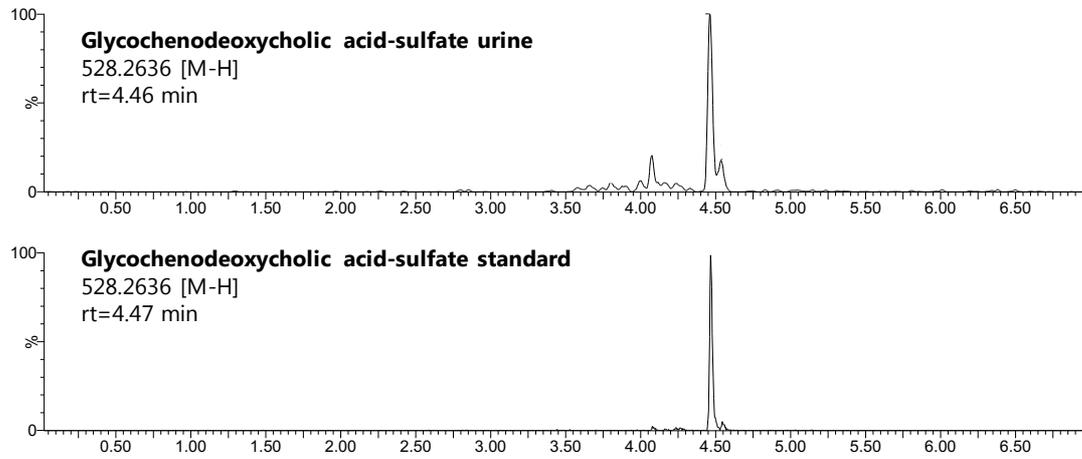
**Biomarkers of fish**

**Supplementary Figure 22.** Identification of 3-carboxy-4-methyl-5-propanyl-2-furanpropionic acid (CMPF) comparing retention time, *m/z* and spectrum measured in urine with retention time, *m/z* and spectrum of an authentic standard.

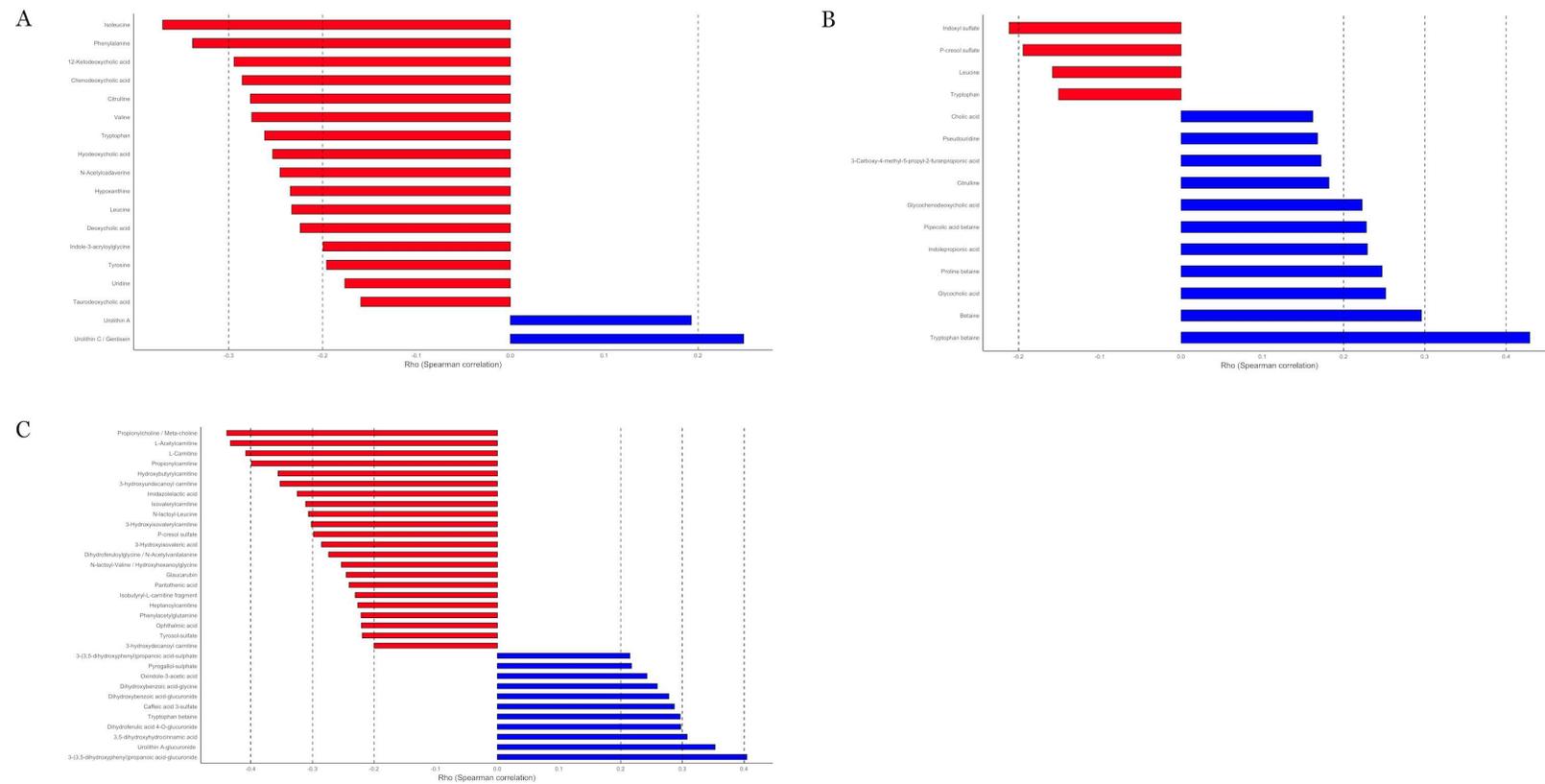


**Supplementary Figure 23.** Identification of trimethylamine-N-oxide (TMAO) comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.

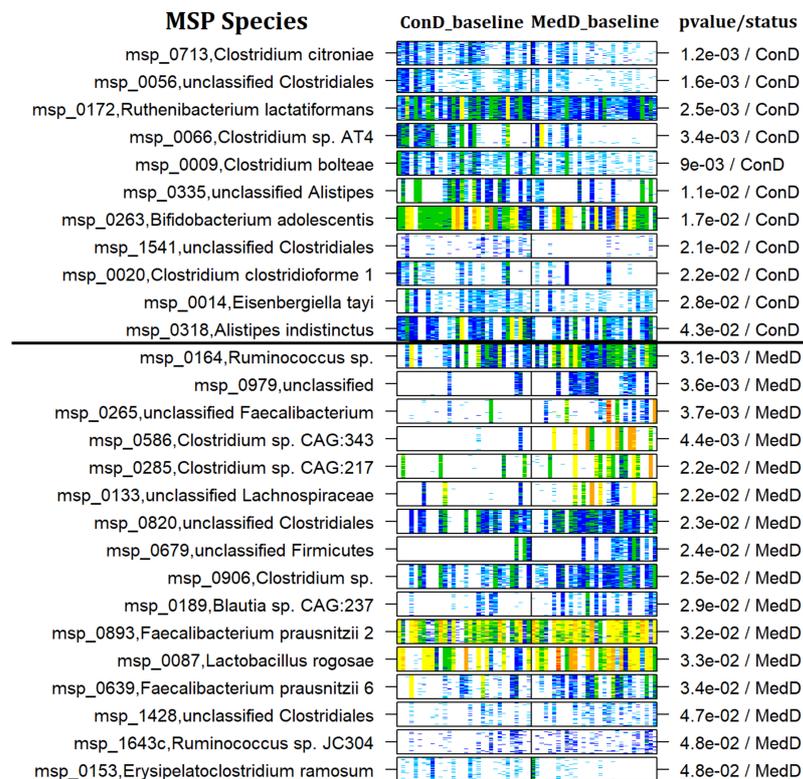
**Bile acids****Supplementary Figure 24.** Retention times of bile acid authentic standards.



**Supplementary Figure 25.** Identification of Glycochenodeoxycholic acid sulfate comparing retention time and  $m/z$  measured in urine with retention time and  $m/z$  of an authentic standard.



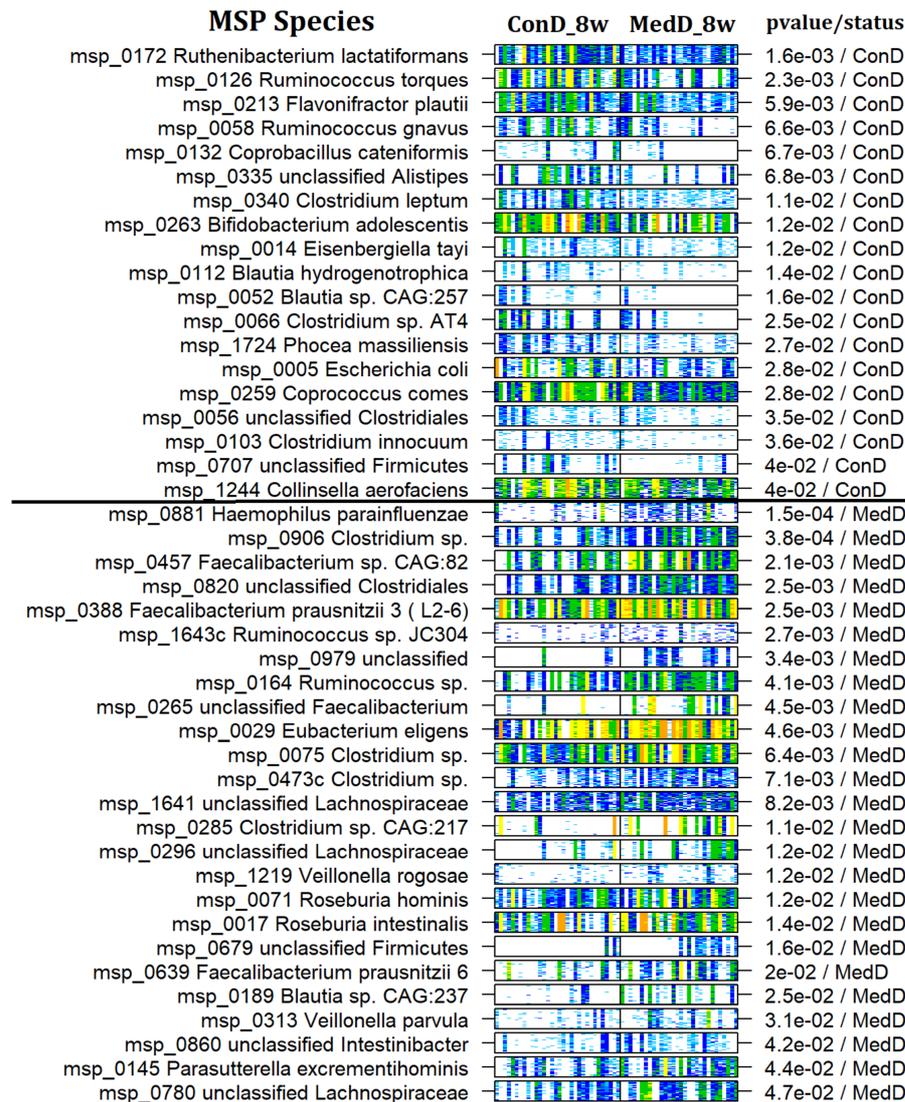
**Supplementary Figure 26** Diverging bar charts showing Spearman's correlations between MD Index and annotated metabolites from (A) faecal, (B) serum and (C) urine metabolome. Red and blue horizontal bars indicate negative and positive correlations, respectively. Spearman's rho coefficients are displayed on the x-axis. (FDR<0.05).



**Supplementary Figure 27** Barcoding plots of the contrasted MSP species between ConD and MedD diets at baseline. Contrasted MSP species were computed using unpaired Wilcoxon rank sum tests on the MSP matrix filtered with a 20% occurrence threshold across samples. Contrasted MSP were organized in rows by blocks of their 50 marker genes and ranked by enrichment status (ConD or MedD) and by pvalues. Within each block, barcoding plots (heatmaps) of the frequency abundances of the marker genes were represented (white, absent; light blue to red, low to high abundance). Individuals were represented in columns by diet-time groups and ordered by their MSP richness at baseline.

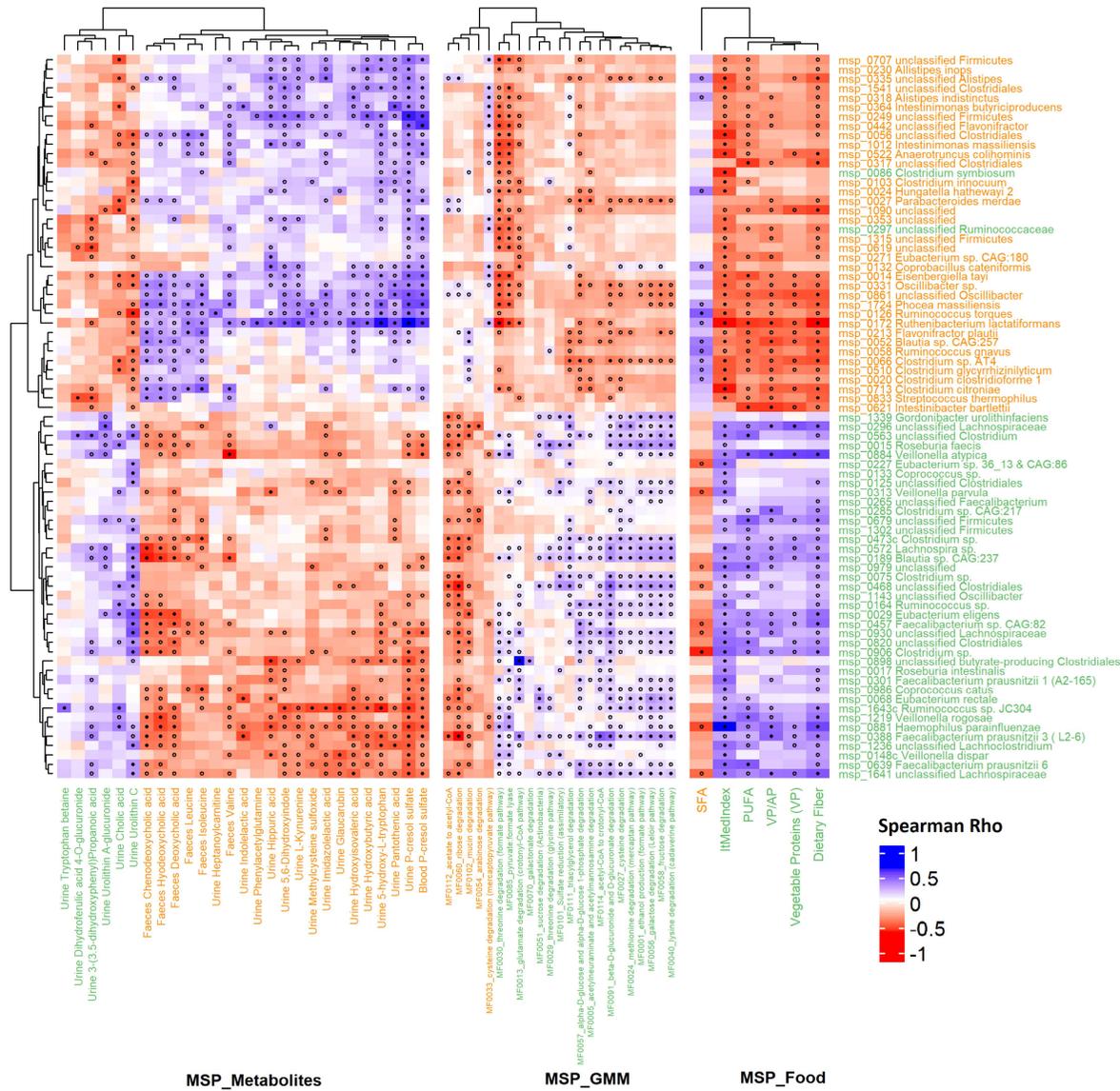
MSP Species	ConD_4w	MedD_4w	pvalue/status
msp_0172 <i>Ruthenibacterium lactatiformans</i>			1.6e-04 / ConD
msp_0066 <i>Clostridium</i> sp. AT4			4.8e-03 / ConD
msp_0024 <i>Hungatella hathewayi</i> 2			5.6e-03 / ConD
msp_0249 unclassified Firmicutes			6.7e-03 / ConD
msp_0335 unclassified Alistipes			6.8e-03 / ConD
msp_0619 unclassified			8.9e-03 / ConD
msp_0058 <i>Ruminococcus gnavus</i>			9.4e-03 / ConD
msp_0707 unclassified Firmicutes			1.1e-02 / ConD
msp_0713 <i>Clostridium citroniae</i>			1.1e-02 / ConD
msp_0056 unclassified Clostridiales			1.3e-02 / ConD
msp_0052 <i>Blautia</i> sp. CAG:257			1.4e-02 / ConD
msp_0317 unclassified Clostridiales			1.4e-02 / ConD
msp_0331 <i>Oscillibacter</i> sp.			1.4e-02 / ConD
msp_0271 <i>Eubacterium</i> sp. CAG:180			1.4e-02 / ConD
msp_0126 <i>Ruminococcus torques</i>			1.5e-02 / ConD
msp_0621 <i>Intestinibacter bartlettii</i>			1.6e-02 / ConD
msp_0027 <i>Parabacteroides merdae</i>			1.6e-02 / ConD
msp_1090 unclassified			1.6e-02 / ConD
msp_0132 <i>Coprobacillus cateniformis</i>			1.7e-02 / ConD
msp_0318 <i>Alistipes indistinctus</i>			1.9e-02 / ConD
msp_0014 <i>Eisenbergiella tayi</i>			1.9e-02 / ConD
msp_0510 <i>Clostridium glycyrrhizinylicum</i>			2.2e-02 / ConD
msp_1315 unclassified Firmicutes			2.7e-02 / ConD
msp_0364 <i>Intestinimonas butyriciproducens</i>			2.7e-02 / ConD
msp_0442 unclassified Flavonifractor			2.8e-02 / ConD
msp_0861 unclassified Oscillibacter			3.2e-02 / ConD
msp_0230 <i>Allistipes inops</i>			3.2e-02 / ConD
msp_1012 <i>Intestinimonas massiliensis</i>			3.3e-02 / ConD
msp_0833 <i>Streptococcus thermophilus</i>			3.3e-02 / ConD
msp_0522 <i>Anaerotruncus colihominis</i>			3.4e-02 / ConD
msp_0103 <i>Clostridium innocuum</i>			3.4e-02 / ConD
msp_0020 <i>Clostridium clostridioforme</i> 1			3.6e-02 / ConD
msp_0353 unclassified			4.2e-02 / ConD
msp_1541 unclassified Clostridiales			4.2e-02 / ConD
msp_1724 <i>Phoceia massiliensis</i>			4.4e-02 / ConD
msp_0213 Flavonifractor plautii			4.5e-02 / ConD
msp_0881 <i>Haemophilus parainfluenzae</i>			9.1e-06 / MedD
msp_0388 <i>Faecalibacterium prausnitzii</i> 3 (L2-6)			9.8e-05 / MedD
msp_0884 <i>Veillonella atypica</i>			2.3e-04 / MedD
msp_1641 unclassified Lachnospiraceae			3.7e-04 / MedD
msp_1643c <i>Ruminococcus</i> sp. JC304			5.2e-04 / MedD
msp_0979 unclassified			1.6e-03 / MedD
msp_0906 <i>Clostridium</i> sp.			1.9e-03 / MedD
msp_0285 <i>Clostridium</i> sp. CAG:217			2.1e-03 / MedD
msp_0164 <i>Ruminococcus</i> sp.			2.4e-03 / MedD
msp_0313 <i>Veillonella parvula</i>			2.6e-03 / MedD
msp_0930 unclassified Lachnospiraceae			2.9e-03 / MedD
msp_1219 <i>Veillonella rogosae</i>			3e-03 / MedD
msp_0189 <i>Blautia</i> sp. CAG:237			3.7e-03 / MedD
msp_0265 unclassified Faecalibacterium			3.7e-03 / MedD
msp_0148c <i>Veillonella dispar</i>			5.8e-03 / MedD
msp_0457 <i>Faecalibacterium</i> sp. CAG:82			5.8e-03 / MedD
msp_0296 unclassified Lachnospiraceae			6.6e-03 / MedD
msp_0898 unclassified Firmicutes			6.7e-03 / MedD
msp_0468 unclassified Clostridiales			7.9e-03 / MedD
msp_0029 <i>Eubacterium eligens</i>			9.3e-03 / MedD
msp_0639 <i>Faecalibacterium prausnitzii</i> 6			9.4e-03 / MedD
msp_1236 unclassified Lachnospiraceae			1.1e-02 / MedD
msp_0301 <i>Faecalibacterium prausnitzii</i> 1 (A2-165)			1.1e-02 / MedD
msp_0075 <i>Clostridium</i> sp.			1.1e-02 / MedD
msp_0820 unclassified Clostridiales			1.4e-02 / MedD
msp_0473c <i>Clostridium</i> sp.			2.3e-02 / MedD
msp_0297 unclassified Ruminococcaceae			2.3e-02 / MedD
msp_0679 unclassified Firmicutes			2.4e-02 / MedD
msp_0572 <i>Lachnospira</i> sp.			2.5e-02 / MedD
msp_0015 <i>Roseburia faecis</i>			2.6e-02 / MedD
msp_0068 <i>Eubacterium rectale</i>			2.6e-02 / MedD
msp_0017 <i>Roseburia intestinalis</i>			2.6e-02 / MedD
msp_0563 unclassified Clostridium			3.2e-02 / MedD
msp_0125 unclassified Clostridiales			3.7e-02 / MedD
msp_1302 unclassified Firmicutes			3.9e-02 / MedD
msp_0986 <i>Coprococcus catus</i>			3.9e-02 / MedD
msp_0086 <i>Clostridium symbiosum</i>			4e-02 / MedD
msp_1143 unclassified Oscillibacter			4.1e-02 / MedD
msp_1339 <i>Gordonibacter urolithinifaciens</i>			4.2e-02 / MedD
msp_0227 <i>Eubacterium</i> sp. 36_13 & CAG:86			4.3e-02 / MedD
msp_0133 <i>Coprococcus</i> sp.			4.9e-02 / MedD

**Supplementary Figure 28** Barcoding plots of the contrasted MSP species between ConD and MedD diets at 4w. Contrasted MSP species were computed using unpaired Wilcoxon rank sum tests on the MSP matrix filtered with a 20% occurrence threshold across samples. Contrasted MSP were organized in rows by blocks of their 50 marker genes and ranked by enrichment status (ConD or MedD) and by pvalues. Within each block, barcoding plots (heatmaps) of the frequency abundances of the marker genes were represented (white, absent; light blue to red, low to high abundance). Individuals were represented in columns by diet-time groups and ordered by their MSP richness at baseline.

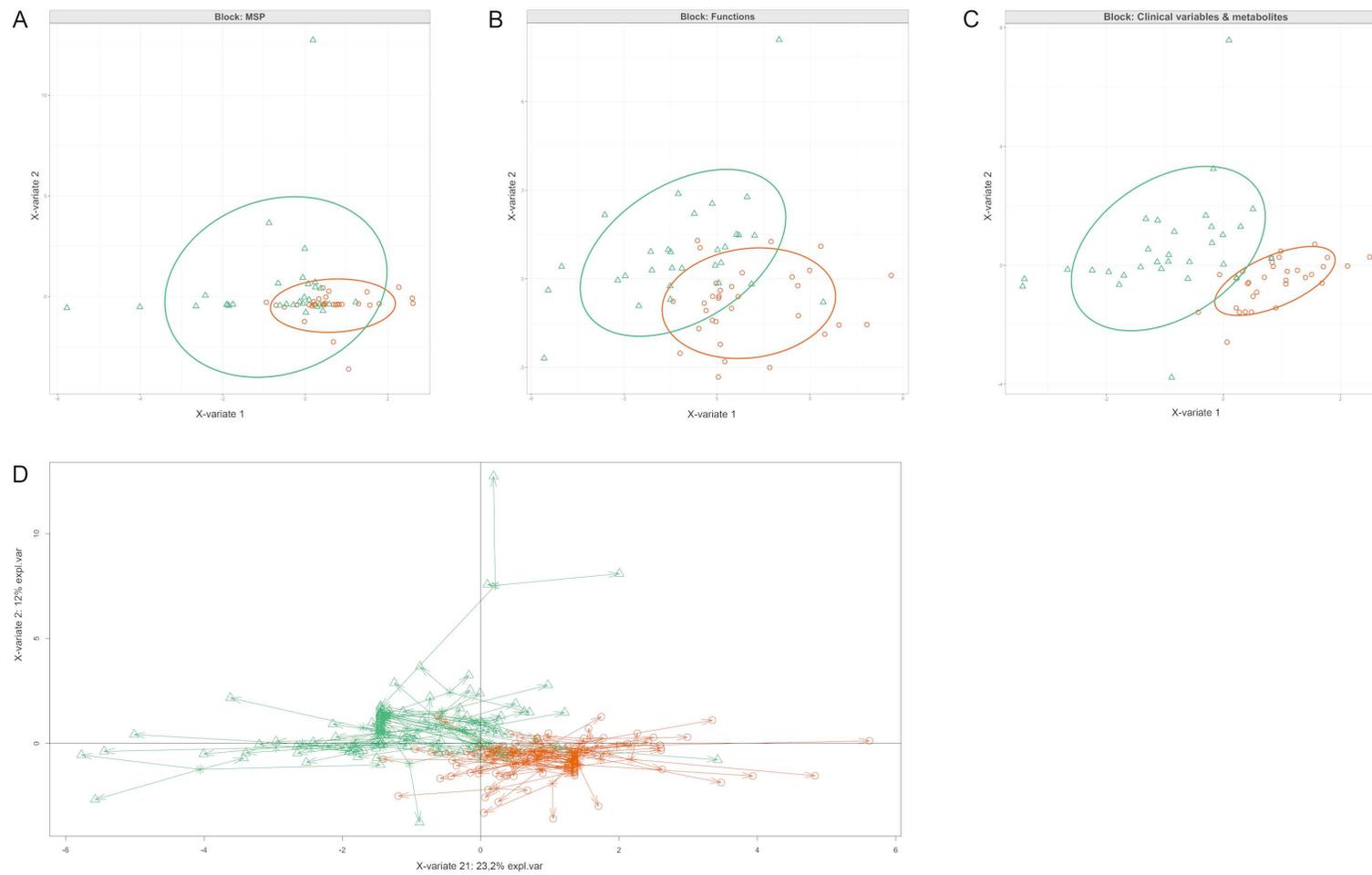


**Supplementary Figure 29** Barcoding plots of the contrasted MSP species between ConD and MedD diets at 8w. Contrastd MSP species were computed using unpaired Wilcoxon rank sum tests on the MSP matrix filtered with a 20% occurrence threshold across samples. Contrastd MSP were organized in rows by blocks of their 50 marker genes and ranked by enrichment status (ConD or MedD) and by pvalues. Within each block, barcoding plots (heatmaps) of the frequency abundances of the marker genes were represented (white, absent; light blue to red, low to high abundance). Individuals were represented in columns by diet-time groups and ordered by their MSP richness at baseline.



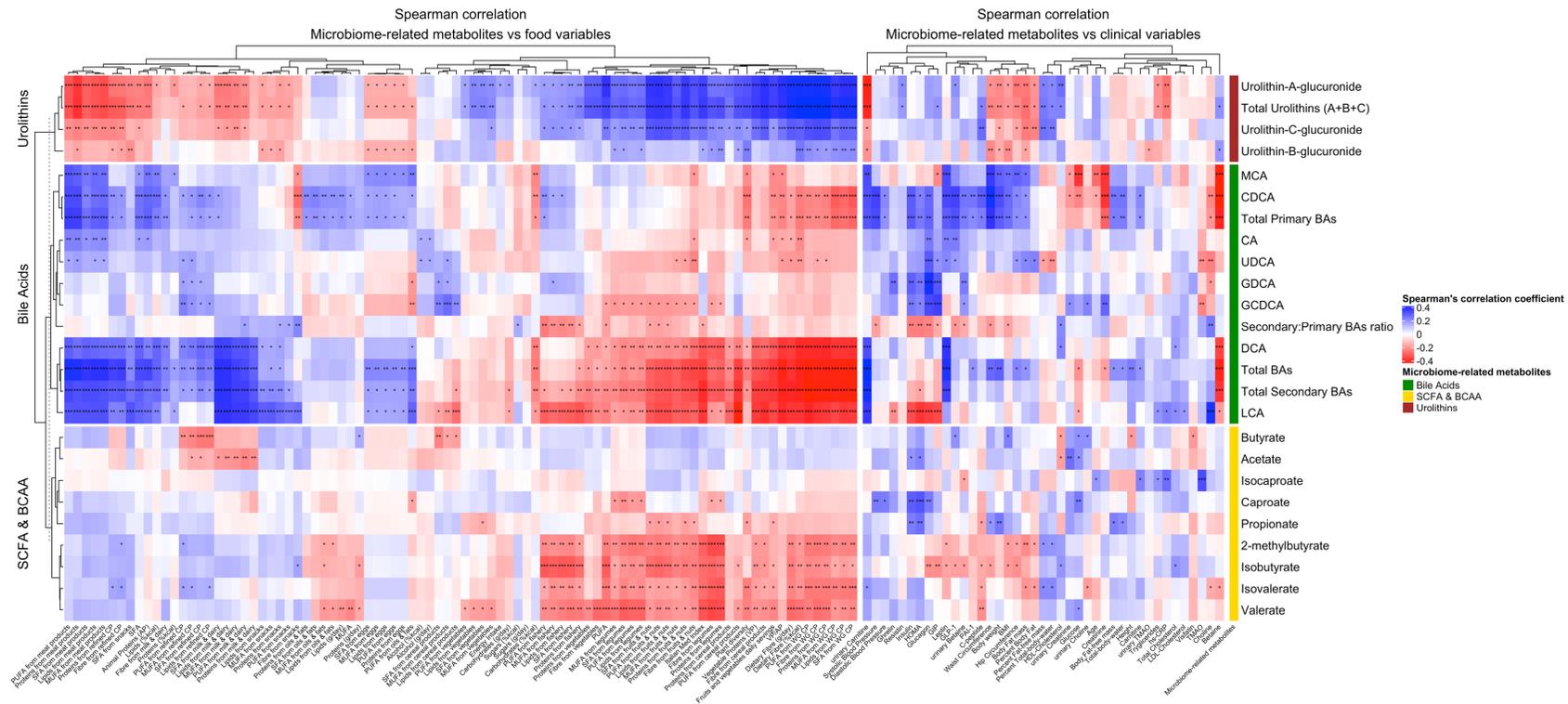


**Supplementary Figure 30** Distinctive metabolites, dietary and microbial signatures between ConD and MedD diets at 4 weeks. Spearman correlations of contrasted MSP species with metabolites, GMM modules and nutrients at 4w. Rows, complete list of contrasted MSP at 4w between ConD and MedD diets ( $p \leq 0.05$ ); Columns; contrasted annotated metabolites, contrasted GMM functional modules and nutrients data. Coloured-text referred to enrichment status (orange; ConD, green; MedD). Adjustments were performed using the Benjamini-Hochberg procedure and Spearman rho values were filtered by keeping correlations with at least one  $FDR \leq 0.05$ . Solid dot,  $FDR \leq 0.05$ ; Open dot,  $FDR \leq 0.2$ .

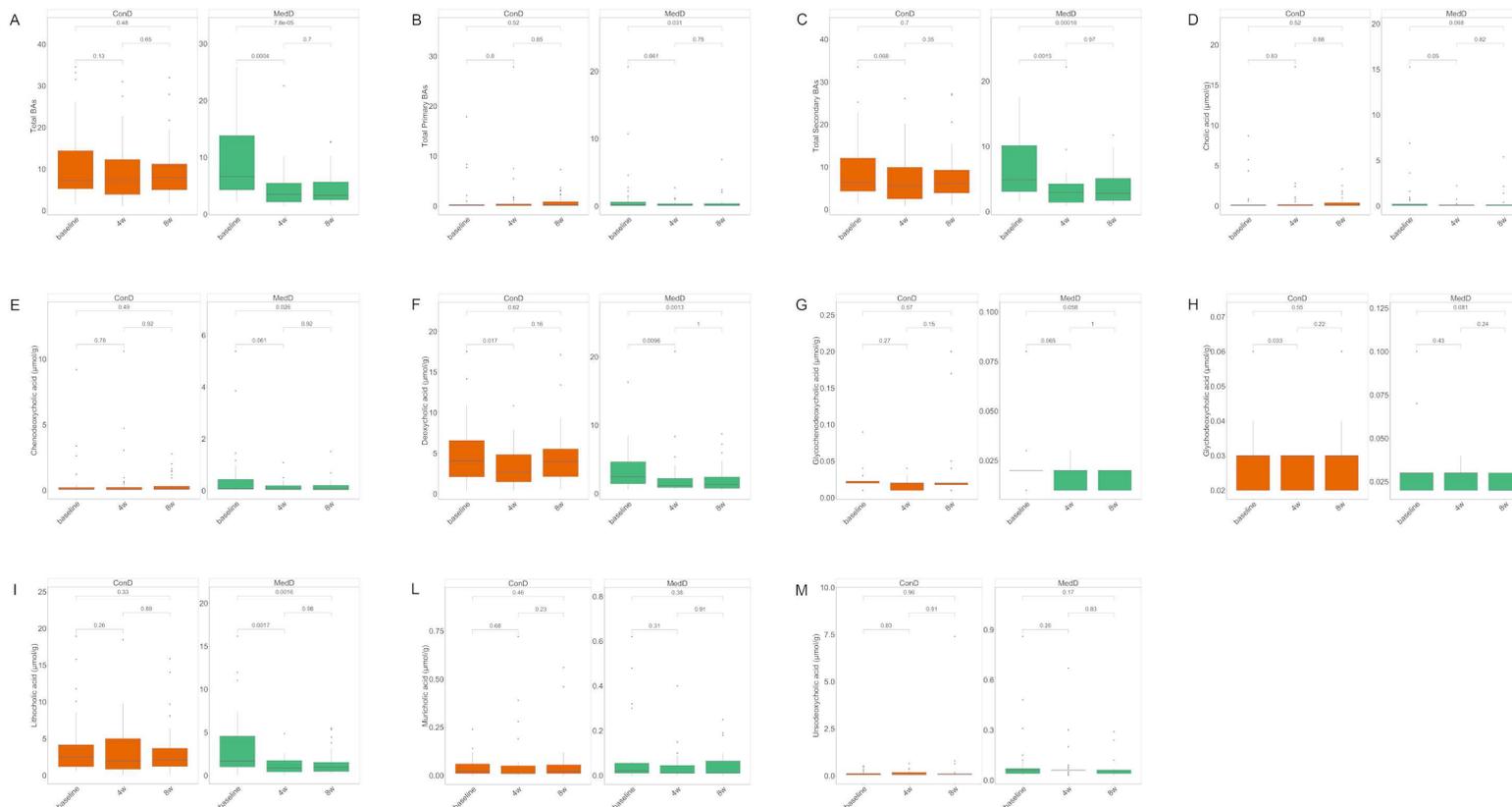


**Supplementary Figure 31** N-integrative supervised analysis of different types of 'omics datasets. The DIABLO model for the discrimination of ConD and MedD groups is displayed as sample plot per single 'omic level. (A) Overall microbiota composition, (B) gut metabolic modules, (C)

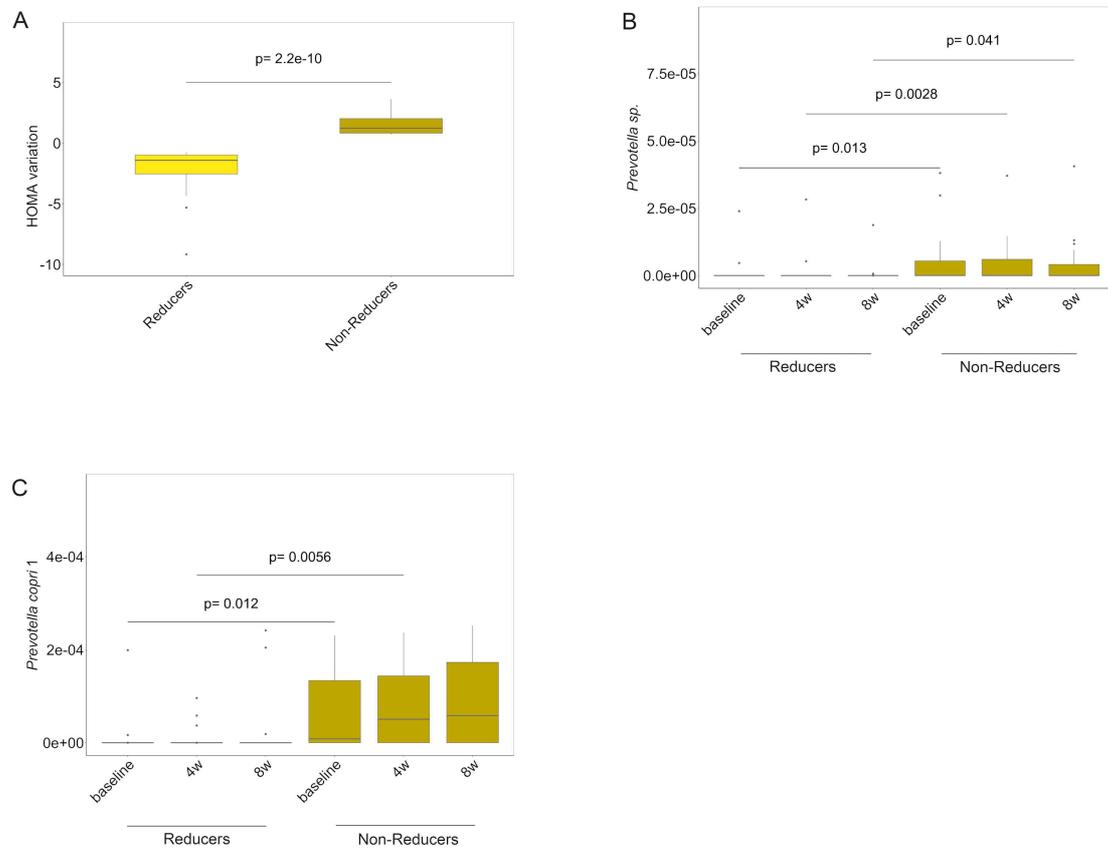
clinical variables and metabolome single-omic levels are reported along with (D) co-inertia analysis quantifying the co-variability between the three multi-omics datasets. Shapes represent the projected coordinates of each subject. The centroid for a given sample between all 'omics datasets is indicated by the start of the arrow and the location of the same sample in each dataset by the tips of the arrows. The length of the arrow is proportional to the divergence between data from different blocks. The percentage of total explained variance describing the separation of the groups on the first two components are displayed on the x and y axis, respectively. Green triangles, MedD subjects. Orange circles, ConD subjects. The integration of meta-omics products was associated with an increase in classification accuracies in discriminating between the ConD and MedD groups with respect to the cases in which a single data type was used. The AUC increased to 0.92 (from 0.88) when using metabolomics data only and to 0.90 (from 0.87) when comparing the ConD and MedD groups at 4 weeks and 8 weeks, respectively.



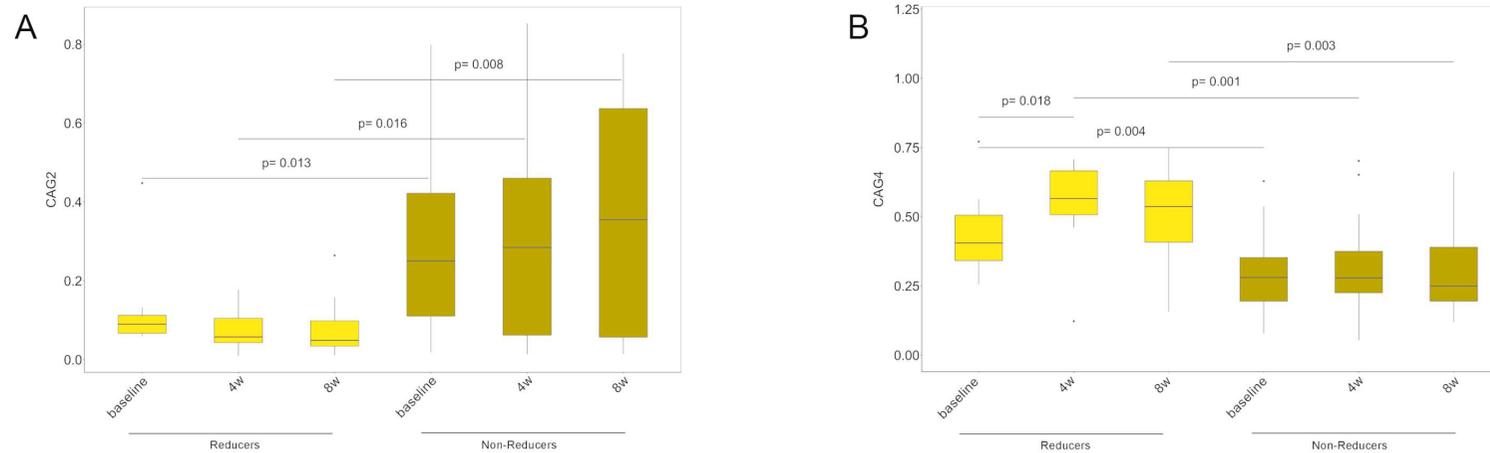
**Supplementary Figure 32 Correlation of microbiome-related metabolites with dietary and clinical variables.** Heatmap showing hierarchical Ward-linkage clustering of microbiome-related metabolites based on Spearman's correlation with dietary variables and clinical parameters. The colour scale represents the scaled version of Spearman's rho coefficients, with red indicating negative and blue indicating positive correlations. BAs, bile acids; CDCA, Chenodeoxycholic acid; MCA, Muricholic acid; DCA, Deoxycholic acid; GCDCA, Glycochenodeoxycholic acid; GDCA, Glychodeoxycholic acid; LCA, Lithocholic acid; UDCA, Ursodeoxycholic acid; SCFA, short-chain fatty acids; BCAA, branched-chain amino acids. TMAO, trimethylamine oxide; GLP-1, glucagon-like peptide-1; GIP, glucose-dependent insulinotropic peptide. VP/AP, Vegetable Protein/Animal Protein; PUFA, polyunsaturated fatty acid; MUFA, monounsaturated fatty acids; SFA, saturated fatty acids; WG, whole grain; CP, cereal products. Adjustments were performed using the the Benjamini-Hochberg procedure and Spearman rho values were filtered by keeping correlations with at least one  $FDR \leq 0.05$ . (\* $FDR < 0.05$ , \*\* $FDR < 0.01$  and \*\*\* $FDR < 0.001$ ).



**Supplementary Figure 33** Box plots showing faecal concentrations of several BAs measured throughout the intervention. (A) Total BAs, (B) Total primary BAs, (C) Total secondary BAs, (D) Cholic acid, (E) Chenodeoxycholic acid, (F) Deoxycholic acid, (G) Glychenodeoxycholic acid, (H) Glychodeoxycholic acid, (I) Lithocholic acid and, (L) Muricholic acid, (M) Ursodeoxycholic acid. Orange indicates ConD while green colour refers to MedD subjects, respectively. P values indicate paired Wilcoxon rank-sum tests within each group. Baseline, 0 weeks; 4w, 4 weeks; 8w, 8 weeks of intervention.



**Supplementary Figure 34** Box plots showing differences in (A) HOMA variation classifying the subjects in HOMA reducers (Yellow) and non-reducers (Dark gold) after 4 weeks of intervention. Differences in levels of (B) *Prevotella* sp. and (C) *Prevotella copri* 1 in HOMA reducers and non-reducers. Statistical differences between groups were determined using unpaired Wilcoxon rank-sum tests. Baseline, 0 weeks; 4w, 4 weeks; 8w, 8 weeks of intervention.

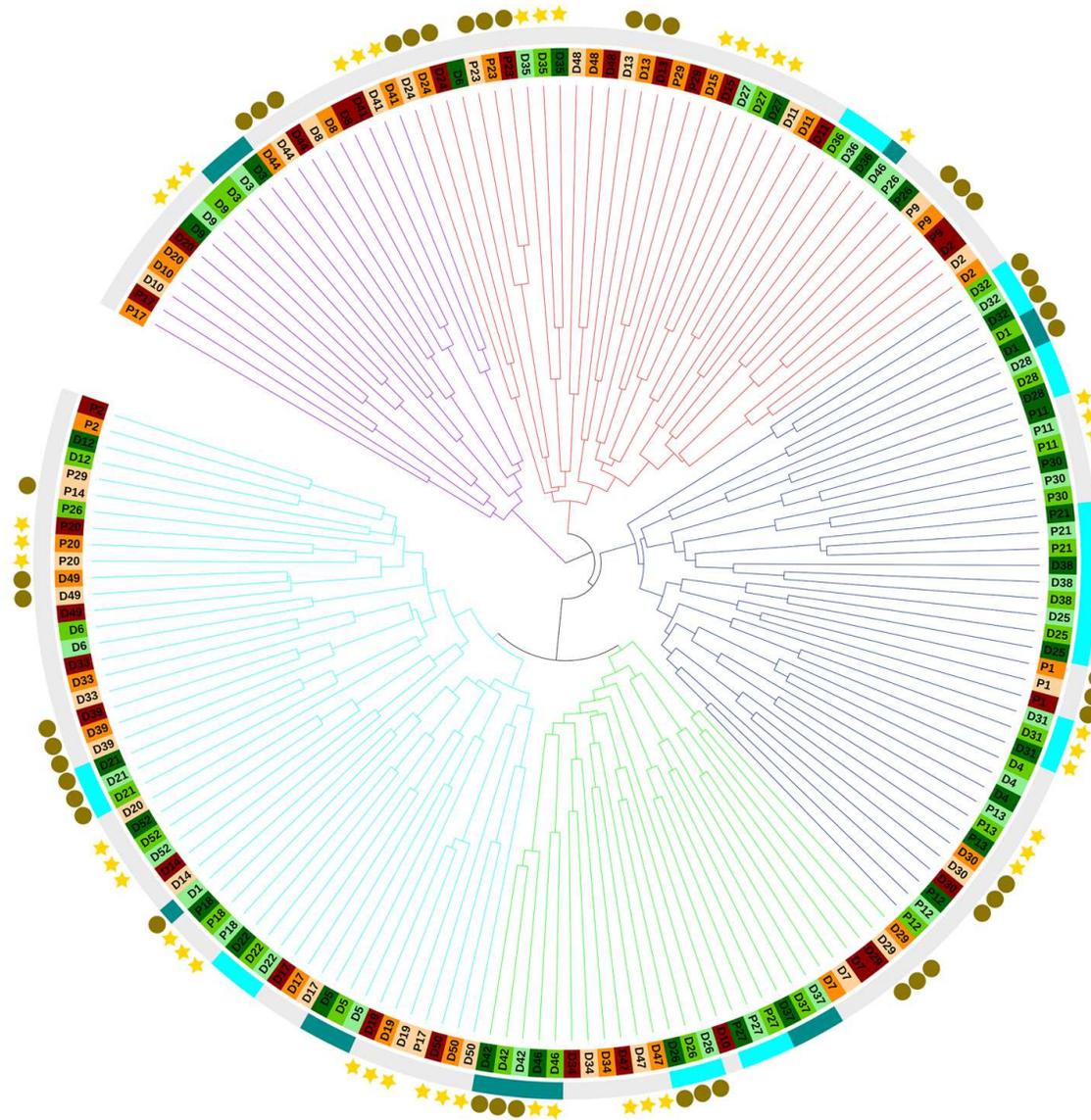


**Supplementary Figure 35** Box plots showing differences in abundance of Co-Abundance Groups (CAGs) obtained from 16S rRNA gene sequences in subjects classified as HOMA reducers (Yellow) and non-reducers (Dark gold) after 4 weeks of intervention. Statistical differences between groups were determined using unpaired Wilcoxon rank-sum tests. Baseline, 0 weeks; 4w, 4 weeks; 8w, 8 weeks of intervention. Only (A) CAG2 and (B) CAG4 are reported, since no significant variation was found for the others.

- Diet**
- ConD\_baseline
  - ConD\_4w
  - ConD\_8w
  - MedD\_baseline
  - MedD\_4w
  - MedD\_8w

- Fibre intake**
- Highest intake
  - Lowest intake

- HOMA reduction**
- Non-reducers
  - Reducers



**Supplementary Figure 36** Circular tree showing clustering of the subjects based on *Faecalibacterium prausnitzii* pangenome. Subjects are coloured according to dietary treatment and time-points. Coloured ring indicates the quartile of highest (green) versus lowest (cyan) increase of dietary fibre intake. Subjects not falling in the highest or lowest quartile were coloured in grey. Yellow stars or dark gold dots indicate HOMA reducers and non-reducers

