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SUPPLEMENTARY METHODS

Faecal sample collection and 16S rRNA gene sequence

Fecal samples were collected before and after the 6-month intervention. Each fecal sample was snap frozen in liquid nitrogen within minutes of donation and kept at -80 ^oC or briefly stored in -40 ^oC freezers before transport to the laboratory. DNA was extracted from stool sample (200 mg) using QIAamp DNA Stool Mini Kit (Qiagen, Hilden, Germany) following the manufacturer's instructions, with additional homogenized steps in a bead beater (FastPrep, Thermo Electron Corporation, Waltham, MA, USA). The amount of DNA was determined using a NanoDrop ND-1000 spectrophotometer (Nano Drop Technologies, Wilmington, DE, USA). The integrity and size of DNA were measured by electrophoresis on 1.0% agarose gel containing 0.5 mg/mL ethidium bromide. All DNA was stored at -20 ^oC until further analysis.

The V3-V4 hypervariable regions of the bacteria 16S rRNA gene were amplified by PCR with barcode-indexed primers 338F (5'-ACTCCTACGGGAGGCAGCAG-3') and 806R (5'-GGACTACHVGGGTWTCTAAT-3') by thermocycler PCR system (GeneAmp 9700, ABI, USA). The PCR reactions were conducted using the following program: 3 mins of denaturation at 3 mins of denaturation at 95 $^{\circ}$ C, 27 cycles of 30 s at 95 $^{\circ}$ C, 30 s for annealing at 55 $^{\circ}$ C, and 45 s for elongation at 72 $^{\circ}$ C, and a final extension at 72 $^{\circ}$ C for 10 mins. PCR reactions were performed in triplicate 20 µL mixture containing 4 µL of 5 × FastPfu Buffer, 2 µL of 2.5 mM dNTPs, 0.8 µL of each primer (5 µM), 0.4 µL of FastPfu Polymerase and 10 ng of template DNA. The resulted PCR products were extracted from a 2% agarose gel

and further purified using the AxyPrep DNA Gel Extraction Kit (Axygen Biosciences, Union City, CA, USA) and quantified using QuantiFluor[™]-ST (Promega, USA) according to the manufacturer's protocol.

The purified amplicons were pooled in equimolar concentration, and paired-end sequencing was performed using an Illumina Miseq instrument (Illumina, San Diego, California, USA) according to the manufacturer's instructions. Raw sequencing data has been deposited in the NCBI Sequence Read Archive (SRA) database with accession number PRJNA480547.

Overlapping paired-end reads from the original DNA fragments were merged using FLASH (version 1.2.10).¹ Reads were assigned to each sample according to the unique barcode of each sample. To obtain effective reads, raw reads were quality-filtered using QIIME (version 1.17) as follows: (i) The 250 bp reads were truncated at any site receiving an average quality score < 20 over a 10 bp sliding window, with the truncated reads shorter than 50 bp being discarded; (ii) exact barcode was matched, with no mismatch in primers and barcodes, and reads containing ambiguous characters were removed; (iii) only sequence longer than 10 bp that overlapped were assembled according to their overlapped sequences. Reads which could not be assembled were discarded.

The operational taxonomic unit (OTU) were clustered with 97% similarity cutoff using UPARSE Pipeline (<u>http://drive5.com/usearch/manual/uparse_pipeline.html</u>), and chimeric sequences were identified and removed using UCHIME and Silva (SSU123) 16S rRNA

database.^{2 3} Taxonomic ranks were assigned to each sequence using Ribosomal Database Project (RDP) Multiclassifier tool which is available from the RDP website (http://rdp.cme.msu.edu/classifier/), using 70% confidence values as cutoff. In order to calculate alpha diversity, three metrics were applied: Ace and Chao1 estimators (estimating the community richness), and Shannon estimator (estimating the community diversity). Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt), a programme that predicts abundances of gene families based on 16S-based structure of the microbiota was used to investigate the functional profiles in microbial communities.⁴ KEGG biochemical pathways were then identified from the inferred metagenome.

Quantitative analysis of microbial metabolomics

A complete set of 240 feacal samples were available from 120 participants before and after the intervention. All standard compounds were commercially purchased from Sigma-Aldrich (St. Louis, MO, US), Nu-Chek Prep (Elysian, MN, USA) and Santa Cruz (Dallas, TX, USA). Ultrapure water was prepared by the Milli-Q system (Millipore, Billerica, MA). The stock solutions of all reference standards were prepared in HPLC grade methanol or ultrapure water or sodium hydroxide solution with a concentration of either 5 or 1 mg/mL. The three groups of mixed stock solutions were mixed to create stock calibration solutions based on their solubility and chemical properties. Further serial dilutions of the working standard solutions were made to generate 8 calibrators at a wide concentration range covering from 0.008 to 250 µg/mL. A mixture of internal RI markers was prepared by combining equal volumes of 5 mg/mL chloroform stock solutions of 13 normal alkanes with carbon chain lengths of C8, C9, C10, C12, C14, C16, C18, C20, C22, C24, C26, C28, and C30 to monitor the data quality and compensate for matrix effects.

Two hundred and forty human fecal water samples were prepared as follows: Samples were thawed on ice-bath to diminish sample degradation. Approximately 50 mg of stool sample was homogenized with 300 µL of NaOH (1M) solution using a homogenizer (BB24, Next Advance, Inc., Averill Park, NY, USA) and centrifuged at 13,500 rpm and 4 °C for 20 mins (Microfuge 20R, Beckman Coulter, Inc., Indianapolis, IN, USA). Each 200 µL of supernatant was transferred into an autosampler via (Agilent Technologies, Foster City, CA, USA), and the residue was further exacted with 200 µL of cold methanol. After the second step of homogenization and centrifugation, each 167 µL of supernatant was combined with the first supernatant in the autosampler vial. The sample derivation protocols with MCF were based on the method described by MCF were based on the method described by Vilas-boas et al, with some minor modifications. The fecal extracts in the autosampler vial was capped and submitted for automated sample derivation with a robotic multipurpose sample MPS2 with dual heads (Gerstel, Muehlheim, Germany). Briefly, each 20 µL of MCF was added to the mixture and the sample was vortexed vigorously for exact 30 s. Another 20 µL of MCF was added for the second time derivatization. Subsequently, 400 µL of chloroform (385 µg/mL for each) was added, and samples were shaken for 10 s followed by an addition of 400 µL of sodium bicarbonate solution (50 mM) and additional shaking for 10 s. Samples were then centrifuged at 2000 rcf for 10 min at 4 °C in order to clearly visualize the double meniscus.

The bottom chloroform phase was transferred to GC vials containing 100 mg of anhydrous sodium sulfate.

A gas chromatography coupled to time-of-flight mass spectrometry (GC-TOF/MS) system (Agilent 6890N gas chromatography coupled with a LECO Pegasus HT time-of-flight mass spectrometer) operated in electron ionization mode was used to quantitate the microbial metabolites. The instrument variables were set according to Zhao et al[5]. Raw data from GC/TOF-MS analysis was exported to ChromaTOF software (v4.50, Leco Co., CA, USA) for automatically baseline correction, smoothing, noise reduction, deconvolution, library searching, and area calculation. Individual compound identification was performed by comparing both MS similarity and Kovats retention index distance with reference standards utilizing a similarity score cutoff of more than 70%.

References:

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Nutrients	Lower-fat diet	Moderate-fat diet	Higher-fat diet
Energy (male), kcal	2094	2096	2103
Energy (female), kcal	1697	1698	1704
Carbohydrate, % TE	66	55	46
Fat, % TE	20	31	40
SFA, % TE	4	6	7
MUFA, % TE	5	7	9
PUFA, %% TE	11	18	24
Protein, % TE	14	14	14
Dietary fiber†, g	14	13	14
Cholesterol, mg	289	289	289

Supplementary Table 1 Characteristics of the three intervention diets*.

*Values were calculated using Nutrition System of Traditional Chinese Medicine Combining with Western Medicine, version 11.0 (Medical College, Qingdao University, Shandong, China). The nutrition system includes Chinese food composition data, permitting calculation of nutrients intake from menus.

[†] The dietary fiber was kept constant according to the baseline fiber intake level (around 14 g/d), in order to avoid introducing new variations.

TE, total energy; SFA, saturated fatty acid; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

Supplementary Table 2 Median Fold Changes in Individual Ge
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	Le	ower-fat d	iet	Mod	lerate-fat	diet	Hi	gher-fat d	iet
	Median fold change	р	p_FDR	Median fold change	р	p_FDR	Median fold change	р	p_FDR
Bacteroides	0.90	0.13	0.42	0.92	0.04	0.49	1.77	< 0.001	< 0.001
Alistipes	0.70	0.63	0.96	1.66	0.69	0.97	2.19	< 0.001	0.04
Faecalibacterium	1.14	< 0.001	0.04	1.15	0.97	0.97	0.61	0.01	0.04
Blautia	1.64	< 0.001	0.01	0.97	0.81	0.97	0.84	0.06	0.24
Lachnoclostridium	1.22	0.05	0.25	0.87	0.21	0.92	0.82	0.05	0.2
[Eubacterium]_hallii_group	1.04	0.99	0.99	1.02	0.65	0.97	0.98	0.11	0.36
Pseudobutyrivibrio	0.82	0.79	0.97	0.74	0.26	0.92	0.88	0.10	0.36
Dorea	1.36	0.16	0.43	0.86	0.29	0.92	0.81	0.20	0.53
Lachnospiraceae_unclassified	1.22	0.07	0.27	1.01	0.95	0.97	0.85	0.22	0.53
Anaerostipes	1.06	0.87	0.99	1.01	0.28	0.92	1.17	0.40	0.80
Megamonas	1.00	0.38	0.78	1.00	0.83	0.97	1.00	0.37	0.80
Prevotella	3.00	0.39	0.78	0.50	0.97	0.97	1.00	0.47	0.82
Bifidobacterium	1.54	0.53	0.92	1.79	0.90	0.97	1.00	0.54	0.83
Romboutsia	0.76	0.54	0.92	1.00	0.78	0.97	0.81	0.56	0.83
Escherichia-Shigella	1.37	0.75	0.97	2.09	0.53	0.97	2.07	0.65	0.89
[Eubacterium]_coprostanoligenes_group	1.08	0.98	0.99	1.25	0.25	0.92	1.26	0.83	0.95
Dialister	0.48	0.04	0.25	0.60	0.35	0.94	2.56	0.91	0.95
Roseburia	0.98	0.67	0.96	0.76	0.83	0.97	0.92	0.75	0.95
Ruminococcus	1.67	0.69	0.96	0.85	0.01	0.15	0.70	0.95	0.95
Streptococcus	0.89	0.23	0.56	0.83	0.43	0.95	0.82	0.87	0.95
Subdoligranulum	1.29	0.07	0.27	0.80	0.88	0.97	0.95	0.83	0.95
Other	0.96	0.97	0.99	1.19	0.39	0.94	0.97	0.48	0.82

	Lower-f	at diet		Moderate	fat diet		Higher-	fat diet	
	Median fold change	р	p_FDR	Median fold change	р	p_FDR	Median fold change	р	p_FDR
ko00603: Glycosphingolipid biosynthesis - globo series	0.98	0.63	0.78	1.08	0.14	0.95	1.13	< 0.001	< 0.001
ko00540: Lipopolysaccharide biosynthesis	0.75	< 0.001	0.08	0.97	0.91	0.96	1.25	< 0.001	< 0.001
ko04142: Lysosome	1.08	0.56	0.72	1.10	0.24	0.95	1.32	< 0.001	< 0.001
ko00130: Ubiquinone and other terpenoid-quinone biosynthesis	0.84	0.02	0.14	0.89	0.80	0.95	1.20	< 0.001	< 0.001
ko00140: Steroid hormone biosynthesis	1.09	0.56	0.72	1.00	0.27	0.95	1.33	< 0.001	< 0.001
ko00908: Zeatin biosynthesis	0.99	0.78	0.87	1.00	0.32	0.95	1.07	< 0.001	< 0.001
ko00511: Other glycan degradation	1.03	0.14	0.39	1.08	0.42	0.95	1.08	< 0.001	0.001
ko00564: Glycerophospholipid metabolism	1.01	0.24	0.48	1.00	0.49	0.95	0.97	< 0.001	0.002
ko00627: Aminobenzoate degradation	0.96	0.05	0.23	0.99	0.67	0.95	1.07	< 0.001	0.004
ko00300: Lysine biosynthesis	1.02	0.004	0.08	1.01	0.85	0.96	0.98	< 0.001	0.005
ko04122: Sulfur relay system	1.03	0.28	0.51	1.01	0.27	0.95	0.94	< 0.001	0.005
ko04940: Type I diabetes mellitus	1.00	0.10	0.34	1.00	0.37	0.95	1.03	< 0.001	0.005
ko04141: Protein processing in endoplasmic reticulum	0.93	0.21	0.46	1.02	0.77	0.95	1.08	< 0.001	0.007
ko00020: Citrate cycle (TCA cycle)	0.97	0.27	0.51	0.99	0.80	0.95	1.07	< 0.001	0.007
ko01055: Biosynthesis of vancomycin group antibiotics	0.99	0.44	0.64	1.02	0.23	0.95	1.06	< 0.001	0.01
ko00910: Nitrogen metabolism	1.01	0.34	0.55	1.00	0.34	0.95	1.02	0.001	0.01
ko00720: Carbon fixation pathways in prokaryotes	1.00	0.83	0.90	0.99	0.43	0.95	1.02	0.002	0.01
ko04621: NOD-like receptor signaling pathway	1.00	0.22	0.46	1.00	0.54	0.95	1.03	0.001	0.01
ko00750: Vitamin B6 metabolism	0.97	0.003	0.08	0.99	0.46	0.95	1.02	0.002	0.01
ko03030: DNA replication	0.99	0.07	0.28	0.99	0.62	0.95	1.02	0.002	0.02
ko00510: N-Glycan biosynthesis	1.03	0.44	0.64	0.94	0.91	0.96	1.17	0.003	0.02
ko02010: ABC transporters	1.05	0.28	0.51	1.00	0.40	0.95	0.96	0.005	0.03
ko00520: Amino sugar and nucleotide sugar metabolism	1.00	0.39	0.60	1.00	0.93	0.96	1.01	0.006	0.04
ko00561: Glycerolipid metabolism	1.01	0.29	0.51	0.97	0.06	0.95	0.93	0.006	0.04
ko03430: Mismatch repair	0.99	0.02	0.14	1.00	0.65	0.95	1.02	0.006	0.04

Supplementary Table 3 Median Fold Changes in Predicted Biochemical Pathways.

ko00290: Valine, leucine and isoleucine biosynthesis	1.01	0.03	0.15	1.02	0.58	0.95	0.98	0.007	0.04
ko00250: Alanine, aspartate and glutamate metabolism	1.00	0.003	0.08	1.01	0.18	0.95	1.01	0.008	0.05
ko00590: Arachidonic acid metabolism	0.94	0.02	0.14	0.86	0.92	0.96	1.30	0.009	0.05
ko00600: Sphingolipid metabolism	1.02	0.19	0.45	1.05	0.59	0.95	1.05	0.009	0.05
ko05215: Prostate cancer	1.00	0.40	0.61	1.00	0.68	0.95	1.03	0.01	0.06
ko01051: Biosynthesis of ansamycins	0.97	0.57	0.72	0.96	0.16	0.95	0.97	0.01	0.06
ko00281: Geraniol degradation	0.86	0.02	0.14	0.92	0.80	0.95	1.37	0.01	0.06
ko00730: Thiamine metabolism	1.01	0.14	0.39	1.01	0.41	0.95	0.97	0.01	0.06
ko00360: Phenylalanine metabolism	0.99	0.28	0.51	0.99	0.44	0.95	1.02	0.01	0.06
ko03013: RNA transport	1.01	0.79	0.88	0.99	0.53	0.95	0.98	0.01	0.07
ko00072: Synthesis and degradation of ketone bodies	0.90	0.34	0.55	1.05	0.54	0.95	0.81	0.02	0.07
ko00623: Toluene degradation	1.04	0.95	0.99	1.03	0.90	0.96	1.15	0.02	0.07
ko00642: Ethylbenzene degradation	0.89	0.05	0.23	1.03	1.00	1.00	1.14	0.02	0.08
ko00860: Porphyrin and chlorophyll metabolism	1.00	0.44	0.64	1.02	0.86	0.96	0.97	0.02	0.08
ko00790: Folate biosynthesis	1.00	0.72	0.82	1.00	0.54	0.95	1.03	0.02	0.08
ko00311: Penicillin and cephalosporin biosynthesis	1.04	0.34	0.55	1.04	0.77	0.95	1.20	0.02	0.08
ko03018: RNA degradation	1.00	0.75	0.85	0.99	0.70	0.95	1.03	0.02	0.08
ko00190: Oxidative phosphorylation	1.00	0.02	0.14	1.01	0.86	0.96	1.03	0.02	0.08
ko00523: Polyketide sugar unit biosynthesis	1.01	0.02	0.14	1.02	0.38	0.95	1.02	0.02	0.08
ko04146: Peroxisome	1.01	0.44	0.64	1.01	0.46	0.95	1.03	0.03	0.10
ko00983: Drug metabolism - other enzymes	1.00	0.68	0.80	1.01	0.08	0.95	1.04	0.03	0.10
ko00670: One carbon pool by folate	0.98	0.26	0.49	1.01	0.23	0.95	1.02	0.03	0.11
ko04920: Adipocytokine signaling pathway	0.97	0.46	0.65	1.05	0.39	0.95	1.05	0.04	0.11
ko04612: Antigen processing and presentation	0.99	0.49	0.66	0.99	0.64	0.95	1.02	0.04	0.11
ko04724: Glutamatergic synapse	1.02	0.002	0.08	1.03	0.06	0.95	1.00	0.04	0.11
ko00480: Glutathione metabolism	0.95	0.002	0.08	0.96	0.92	0.96	1.06	0.04	0.11
ko00260: Glycine, serine and threonine metabolism	1.00	0.44	0.64	1.00	0.20	0.95	1.01	0.04	0.11
ko00010: Glycolysis / Gluconeogenesis	1.00	0.84	0.90	1.00	0.35	0.95	0.98	0.04	0.11

ko04914: Progesterone-mediated oocyte maturation	0.99	0.49	0.66	0.99	0.64	0.95	1.02	0.04	0.11
ko05133: Pertussis	0.79	0.17	0.39	1.07	0.59	0.95	1.42	0.04	0.11
ko00471: D-Glutamine and D-glutamate metabolism	0.99	0.13	0.39	1.01	0.22	0.95	1.01	0.04	0.12
ko05200: Pathways in cancer	0.99	0.62	0.77	0.99	0.68	0.95	1.02	0.04	0.12
ko00950: Isoquinoline alkaloid biosynthesis	0.98	0.34	0.55	0.97	0.62	0.95	1.04	0.05	0.13
ko00785: Lipoic acid metabolism	0.87	0.45	0.64	1.01	0.88	0.96	1.19	0.05	0.13
ko00330: Arginine and proline metabolism	1.01	0.003	0.08	1.01	0.46	0.95	0.99	0.05	0.13
ko00030: Pentose phosphate pathway	1.00	0.81	0.90	1.00	0.07	0.95	0.98	0.05	0.13
ko04964: Proximal tubule bicarbonate reclamation	0.99	0.28	0.51	1.00	0.93	0.96	1.23	0.06	0.14
ko04626: Plant-pathogen interaction	1.01	0.68	0.80	0.98	0.83	0.95	0.98	0.06	0.15
ko04112: Cell cycle - Caulobacter	1.01	0.70	0.82	1.01	0.41	0.95	1.01	0.07	0.17
ko04011: MAPK signaling pathway - yeast	1.05	0.39	0.60	1.07	0.51	0.95	1.06	0.07	0.17
ko03060: Protein export	0.99	0.19	0.43	0.99	0.99	0.99	1.01	0.07	0.17
ko02020: Two-component system	1.01	0.53	0.71	0.99	0.78	0.95	0.97	0.07	0.17
ko00633: Nitrotoluene degradation	1.09	0.01	0.14	0.95	0.26	0.95	0.94	0.08	0.19
ko00400: Phenylalanine, tyrosine and tryptophan biosynthesis	1.01	0.56	0.72	1.01	0.70	0.95	0.99	0.08	0.19
ko00562: Inositol phosphate metabolism	0.99	0.67	0.80	1.00	0.97	0.98	1.01	0.10	0.21
ko00430: Taurine and hypotaurine metabolism	1.05	0.16	0.39	1.01	0.59	0.95	1.02	0.10	0.21
ko00780: Biotin metabolism	0.98	0.82	0.90	1.00	0.62	0.95	1.02	0.10	0.22
ko00660: C5-Branched dibasic acid metabolism	1.01	0.16	0.39	1.01	0.71	0.95	0.98	0.10	0.22
ko00071: Fatty acid metabolism	1.01	0.83	0.90	0.99	0.72	0.95	0.96	0.10	0.22
ko05016: Huntington's disease	0.98	0.12	0.36	0.93	0.44	0.95	1.02	0.10	0.22
ko00622: Xylene degradation	0.96	0.66	0.80	0.97	0.19	0.95	0.91	0.12	0.25
ko00410: beta-Alanine metabolism	1.00	0.96	0.99	0.98	0.77	0.95	1.02	0.13	0.26
ko00521: Streptomycin biosynthesis	1.01	0.21	0.46	0.99	0.42	0.95	1.02	0.13	0.26
ko05146: Amoebiasis	1.23	0.01	0.14	1.13	0.92	0.96	1.11	0.15	0.30
ko00195: Photosynthesis	1.03	0.11	0.36	1.01	0.07	0.95	0.96	0.16	0.31
ko00240: Pyrimidine metabolism	1.00	0.16	0.39	1.00	0.43	0.95	1.00	0.17	0.32

ko00650: Butanoate metabolism	1.00	0.08	0.28	1.00	0.53	0.95	1.00	0.18	0.35
ko02030: Bacterial chemotaxis	1.05	0.55	0.72	1.02	0.68	0.95	0.94	0.20	0.37
ko00363: Bisphenol degradation	1.01	0.16	0.39	1.00	0.22	0.95	0.99	0.21	0.38
ko00621: Dioxin degradation	0.96	0.90	0.94	0.95	0.24	0.95	0.91	0.21	0.38
ko00624: Polycyclic aromatic hydrocarbon degradation	1.00	0.14	0.39	1.01	0.01	0.95	0.99	0.21	0.38
ko00230: Purine metabolism	1.00	0.13	0.39	0.99	0.80	0.95	1.01	0.21	0.38
ko00830: Retinol metabolism	0.96	0.84	0.90	0.96	0.61	0.95	1.07	0.21	0.38
ko02060: Phosphotransferase system (PTS)	0.97	0.98	0.99	1.03	0.14	0.95	0.94	0.23	0.41
ko00460: Cyanoamino acid metabolism	1.00	0.21	0.46	1.05	0.14	0.95	1.03	0.25	0.43
ko00524: Butirosin and neomycin biosynthesis	0.98	0.85	0.90	1.00	0.43	0.95	0.96	0.27	0.47
ko00960: Tropane, piperidine and pyridine alkaloid biosynthesis	0.98	0.02	0.14	1.02	0.22	0.95	1.00	0.28	0.47
ko00630: Glyoxylate and dicarboxylate metabolism	1.02	0.06	0.23	1.00	0.85	0.96	0.99	0.29	0.48
ko00625: Chloroalkane and chloroalkene degradation	1.07	0.16	0.39	1.01	0.45	0.95	0.98	0.30	0.49
ko00500: Starch and sucrose metabolism	1.02	0.12	0.38	1.00	0.62	0.95	0.99	0.30	0.50
ko00760: Nicotinate and nicotinamide metabolism	0.97	0.05	0.23	1.01	0.77	0.95	0.99	0.32	0.52
ko00051: Fructose and mannose metabolism	1.00	0.16	0.39	1.01	0.19	0.95	1.00	0.33	0.52
ko05010: Alzheimer's disease	1.00	0.09	0.31	1.01	0.26	0.95	1.00	0.34	0.54
ko01040: Biosynthesis of unsaturated fatty acids	1.00	0.37	0.58	0.98	0.77	0.95	0.99	0.34	0.54
ko03320: PPAR signaling pathway	1.00	0.22	0.46	1.00	0.48	0.95	0.99	0.35	0.55
ko03010: Ribosome	1.00	0.25	0.49	1.00	0.16	0.95	1.01	0.35	0.55
ko02040: Flagellar assembly	0.89	0.11	0.36	0.99	0.65	0.95	1.00	0.37	0.57
ko00903: Limonene and pinene degradation	0.98	0.005	0.08	0.93	0.13	0.95	1.04	0.39	0.60
ko00362: Benzoate degradation	1.01	0.10	0.35	1.02	0.69	0.95	0.98	0.42	0.63
ko00626: Naphthalene degradation	0.99	0.77	0.87	0.96	0.27	0.95	1.03	0.42	0.63
ko00312: beta-Lactam resistance	1.11	0.06	0.25	0.99	0.76	0.95	0.96	0.43	0.63
ko00770: Pantothenate and CoA biosynthesis	1.01	0.02	0.14	1.01	0.10	0.95	0.99	0.43	0.63
ko03070: Bacterial secretion system	0.98	0.03	0.17	1.00	0.79	0.95	1.00	0.45	0.66
ko00710: Carbon fixation in photosynthetic organisms	0.99	0.04	0.19	1.00	0.33	0.95	1.00	0.47	0.67
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ko00053: Ascorbate and aldarate metabolism	0.96	0.04	0.21	0.96	0.02	0.95	1.02	0.48	0.68
ko00473: D-Alanine metabolism	1.00	0.01	0.14	1.00	0.54	0.95	1.00	0.49	0.68
ko04910: Insulin signaling pathway	1.01	0.64	0.78	1.01	0.69	0.95	0.98	0.49	0.68
ko00310: Lysine degradation	0.98	0.009	0.14	1.00	0.69	0.95	1.01	0.51	0.70
ko00350: Tyrosine metabolism	0.99	0.54	0.72	1.01	0.77	0.95	1.01	0.51	0.70
ko00791: Atrazine degradation	1.26	0.05	0.23	1.02	0.84	0.96	0.99	0.52	0.71
ko00270: Cysteine and methionine metabolism	1.00	0.25	0.49	1.00	0.45	0.95	0.99	0.57	0.76
ko00340: Histidine metabolism	1.00	0.27	0.51	1.01	0.11	0.95	1.00	0.56	0.76
ko00940: Phenylpropanoid biosynthesis	1.02	0.11	0.36	1.07	0.25	0.95	1.00	0.60	0.79
ko03020: RNA polymerase	1.00	0.23	0.47	1.00	0.50	0.95	1.00	0.60	0.79
ko04070: Phosphatidylinositol signaling system	0.99	0.41	0.62	1.02	0.43	0.95	1.01	0.61	0.80
ko00620: Pyruvate metabolism	1.00	0.39	0.60	1.01	0.20	0.95	1.00	0.63	0.81
ko051111: Vibrio cholerae pathogenic cycle	0.96	0.29	0.51	0.96	0.32	0.95	0.99	0.63	0.81
ko05340: Primary immunodeficiency	0.94	0.34	0.55	0.99	0.74	0.95	1.01	0.68	0.86
ko00450: Selenocompound metabolism	1.00	0.22	0.46	1.00	0.78	0.95	1.00	0.70	0.88
ko00740: Riboflavin metabolism	1.00	0.34	0.55	1.01	0.16	0.95	1.01	0.71	0.88
ko00253: Tetracycline biosynthesis	1.00	0.64	0.78	0.98	0.52	0.95	1.00	0.72	0.88
ko00380: Tryptophan metabolism	0.96	0.25	0.49	0.98	0.87	0.96	1.02	0.72	0.88
ko00280: Valine, leucine and isoleucine degradation	0.96	0.02	0.14	0.99	0.65	0.95	0.99	0.73	0.89
ko05152: Tuberculosis	0.98	1.00	1.00	1.00	0.24	0.95	1.00	0.75	0.91
ko00640: Propanoate metabolism	1.01	0.46	0.65	1.01	0.37	0.95	1.01	0.77	0.91
ko00643: Styrene degradation	1.10	0.39	0.60	1.06	0.97	0.98	1.08	0.76	0.91
ko03410: Base excision repair	0.99	0.47	0.65	1.00	0.57	0.95	1.00	0.80	0.91
ko00680: Methane metabolism	1.03	0.004	0.08	1.00	0.58	0.95	1.01	0.79	0.91
ko03420: Nucleotide excision repair	1.00	0.54	0.72	1.00	0.89	0.96	1.00	0.80	0.91
ko00900: Terpenoid backbone biosynthesis	0.99	0.33	0.55	1.00	0.20	0.95	1.01	0.78	0.91
ko04930: Type II diabetes mellitus	0.99	0.04	0.20	1.00	0.72	0.95	0.99	0.78	0.91
ko05120: Epithelial cell signaling in Helicobacter pylori infection	1.02	0.13	0.39	1.00	0.76	0.95	1.00	0.82	0.92

ko00040: Pentose and glucuronate interconversions	1.02	0.03	0.17	0.97	0.34	0.95	0.98	0.82	0.92
ko00591: Linoleic acid metabolism	1.02	0.02	0.14	1.00	0.39	0.95	1.02	0.83	0.92
ko00970: Aminoacyl-tRNA biosynthesis	1.00	0.05	0.23	1.00	0.40	0.95	0.99	0.88	0.94
ko04973: Carbohydrate digestion and absorption	0.82	0.08	0.29	0.90	0.47	0.95	1.03	0.86	0.94
ko00982: Drug metabolism - cytochrome P450	1.06	0.97	0.99	0.88	0.59	0.95	1.08	0.88	0.94
ko00061: Fatty acid biosynthesis	1.01	0.86	0.91	1.00	0.56	0.95	1.00	0.88	0.94
ko00401: Novobiocin biosynthesis	0.99	0.21	0.46	1.01	0.22	0.95	0.99	0.89	0.94
ko00440: Phosphonate and phosphinate metabolism	1.02	0.97	0.99	1.00	0.26	0.95	1.00	0.89	0.94
ko03008: Ribosome biogenesis in eukaryotes	0.99	0.05	0.23	1.00	0.55	0.95	1.00	0.88	0.94
ko00121: Secondary bile acid biosynthesis	1.00	0.16	0.39	1.01	0.90	0.96	1.00	0.90	0.94
ko00920: Sulfur metabolism	1.01	0.72	0.82	1.00	0.82	0.95	0.99	0.90	0.94
ko00930: Caprolactam degradation	0.86	0.02	0.14	0.83	0.24	0.95	1.15	0.92	0.95
ko00944: Flavone and flavonol biosynthesis	1.01	0.70	0.82	1.08	0.76	0.95	1.03	0.92	0.95
ko00980: Metabolism of xenobiotics by cytochrome P450	1.06	0.99	1.00	0.88	0.63	0.95	1.06	0.92	0.95
ko00550: Peptidoglycan biosynthesis	1.00	0.62	0.77	1.00	0.34	0.95	1.00	0.94	0.96
ko00120: Primary bile acid biosynthesis	0.99	0.16	0.39	1.01	0.81	0.95	1.01	0.94	0.96
ko00052: Galactose metabolism	0.99	0.06	0.24	1.00	0.38	0.95	1.00	0.97	0.97
ko01053: Biosynthesis of siderophore group nonribosomal peptides	0.91	0.34	0.55	0.96	0.56	0.95	1.01	0.98	0.98
other	0.84	0.02	0.14	0.91	0.49	0.95	1.03	0.79	0.91

	L	ower-fat di	et	Мо	derate-fat	diet	Н	igher-fat d	iet
	Median fold change	р	p_FDR	Median fold change	р	p_FDR	Median fold change	р	p_FDR
Stearic acid	1.14	0.31	0.79	1.24	0.37	0.99	1.23	< 0.001	< 0.001
Butyric acid	1.05	< 0.001	0.005	1.51	0.90	0.99	0.79	< 0.001	0.005
Valeric acid	1.26	0.02	0.27	0.87	0.15	0.99	0.82	< 0.001	0.03
Ethylmethylacetic acid	0.83	0.77	0.90	1.20	0.61	0.99	0.79	0.002	0.04
Indole	0.36	< 0.001	< 0.001	1.22	0.86	0.99	3.07	0.002	0.04
Indoleacetic acid	0.06	0.54	0.86	1.02	0.26	0.99	1.51	0.001	0.04
Arachidonic acid	0.63	0.26	0.72	1.32	0.82	0.99	1.52	0.003	0.04
Palmitic acid	0.45	0.003	0.07	0.58	0.001	0.13	3.34	0.002	0.04
Alpha-Linolenic acid	1.54	0.90	0.96	0.71	0.52	0.99	1.86	0.009	0.11
Oxalic acid	1.01	0.38	0.82	0.71	0.33	0.99	0.79	0.02	0.19
1H-Indole-3-acetamide	1.12	0.99	0.99	0.92	0.94	0.99	1.08	0.07	0.69
Hydroxyphenyllactic acid	0.93	0.70	0.88	1.19	0.69	0.99	1.53	0.08	0.78
L-Asparagine	1.23	0.38	0.82	0.99	0.96	0.99	0.56	0.09	0.78
L-Norleucine	0.68	0.12	0.51	0.83	0.55	0.99	0.85	0.10	0.81
Beta-Alanine	1.09	0.53	0.86	0.99	0.54	0.99	0.72	0.11	0.87
Myristoleic acid	1.83	0.03	0.27	1.59	0.11	0.99	1.41	0.12	0.88
Ornithine	1.15	0.43	0.84	1.31	0.55	0.99	0.73	0.13	0.88
(1)-2-Methylpentanoic acid	2.31	0.02	0.26	1.19	0.68	0.99	1.56	0.45	0.97
2-Hydroxybutyric acid	0.92	0.81	0.92	1.10	0.60	0.99	1.59	0.50	0.97
2-Phenylglycine	2.30	0.05	0.34	0.83	0.74	0.99	0.79	0.82	0.97
3-(3-Hydroxyphenyl)-3-hydroxypropanoic acid	1.92	0.55	0.86	1.05	0.36	0.99	0.42	0.48	0.97
3-Aminoisobutanoic acid	1.07	0.51	0.86	0.97	0.17	0.99	1.05	0.70	0.97
3-Hydroxybutyric acid	0.94	0.72	0.88	0.76	0.18	0.99	0.66	0.82	0.97
3-Hydroxyisovaleric acid	1.17	0.23	0.66	0.76	0.24	0.99	1.35	0.88	0.97
3-Hydroxyphenylacetic acid	1.58	0.006	0.11	1.25	0.05	0.99	0.86	0.40	0.97
3-Indoleacetonitrile	1.25	0.05	0.34	1.09	0.56	0.99	1.15	0.28	0.97
3-Indolepropionic acid	2.55	< 0.001	0.001	1.02	0.31	0.99	1.15	0.89	0.97
3-Methyl-2-oxovaleric acid	1.31	0.96	0.98	0.99	0.74	0.99	1.04	0.47	0.97
3-Methylindole	0.90	0.06	0.34	0.91	0.66	0.99	0.53	0.26	0.97
4-Hydroxybenzoic acid	1.14	0.04	0.28	1.18	0.87	0.99	0.89	0.74	0.97
4-Hydroxyphenylpyruvic acid	1.31	0.16	0.59	1.23	0.81	0.99	1.15	0.85	0.97
4-Methylhexanoic acid	2.25	0.03	0.27	0.64	0.83	0.99	0.64	0.65	0.97
5-Dodecenoic acid	1.03	0.71	0.88	0.91	0.88	0.99	1.26	0.64	0.97
Adipic acid	1.32	0.91	0.96	1.08	0.39	0.99	0.98	0.77	0.97
Arachidic acid	1.34	0.18	0.62	0.90	0.69	0.99	1.18	0.25	0.97
Behenic acid	1.40	0.70	0.88	1.60	0.88	0.99	1.69	0.33	0.97
Capric acid	0.98	0.08	0.46	1.14	0.79	0.99	0.97	0.17	0.97
Caproic acid	1.40	0.84	0.94	0.83	0.92	0.99	1.11	0.81	0.97
Caprylic acid	1.21	0.90	0.96	1.09	0.97	0.99	0.62	0.80	0.97
Cinnamic acid	0.84	0.48	0.86	0.78	0.27	0.99	1.41	0.76	0.97

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cis-Aconitic acid	1.68	0.65	0.88	6.36	0.35	0.99	2.23	0.72	0.97
Citraconic acid	1.84	0.12	0.51	0.92	0.25	0.99	1.85	0.41	0.97
Citramalic acid	1.59	0.02	0.25	1.60	0.23	0.99	1.17	0.71	0.97
D-2-Hydroxyglutaric acid	1.29	0.90	0.96	1.16	0.74	0.99	0.89	0.36	0.97
Docosahexaenoic acid	1.07	0.22	0.66	1.11	0.55	0.99	1.70	0.33	0.97
Docosapentaenoic acid n6	2.61	0.19	0.63	0.92	0.54	0.99	2.00	0.26	0.97
Docosatrienoic acid	1.03	0.77	0.90	1.36	0.92	0.99	1.68	0.52	0.97
Dodecanoic acid	1.06	0.86	0.95	1.00	0.87	0.99	0.76	0.27	0.97
Eicosenoic acid	1.00	0.67	0.88	1.40	0.92	0.99	1.51	0.59	0.97
Erucic acid	1.53	0.75	0.90	2.38	0.90	0.99	1.32	0.62	0.97
Fumaric acid	1.75	0.43	0.84	1.17	0.51	0.99	1.20	0.89	0.97
Gamma-Aminobutyric acid	0.91	0.81	0.92	1.53	0.02	0.88	0.96	0.54	0.97
Glutaric acid	0.68	0.55	0.86	1.14	0.48	0.99	0.79	0.19	0.97
Glutathione	1.65	0.71	0.88	1.30	0.09	0.99	0.80	0.28	0.97
Glyceric acid	0.97	0.34	0.81	1.17	0.40	0.99	1.00	0.87	0.97
Glycine	1.20	0.94	0.97	1.20	0.23	0.99	1.40	0.69	0.97
Glycolic acid	3.78	0.12	0.51	2.02	0.46	0.99	1.99	0.88	0.97
Heptadecanoic acid	1.45	0.66	0.88	0.97	0.95	0.99	1.94	0.21	0.97
Heptanoic acid	1.00	0.85	0.95	1.04	0.38	0.99	0.81	0.69	0.97
Homocysteine	1.49	0.58	0.86	3.86	0.004	0.25	4.32	0.86	0.97
Hydrocinnamic acid	1.73	0.55	0.86	1.41	0.28	0.99	1.01	0.81	0.97
Hydroxypropionic acid	1.27	0.63	0.88	0.73	0.31	0.99	1.61	0.47	0.97
Itaconic acid	3.09	0.04	0.28	0.27	0.09	0.99	2.26	0.35	0.97
Dopamine	1181.48	0.03	0.28	1184.89	0.46	0.99	1473.52	0.71	0.97
L-Alanine	1.20	0.94	0.97	1.20	0.23	0.99	1.40	0.69	0.97
L-Aspartic acid	1.25	0.36	0.82	1.27	0.38	0.99	1.62	0.55	0.97
L-Glutamic acid	1.15	0.23	0.66	1.21	0.48	0.99	0.98	0.61	0.97
L-Histidine	1.26	0.14	0.55	1.15	0.73	0.99	1.08	0.56	0.97
L-Homoserine	0.68	0.26	0.72	0.92	0.48	0.99	0.93	0.48	0.97
Linoleic acid	1.54	0.92	0.96	0.96	0.35	0.99	1.34	0.39	0.97
L-Isoleucine	1.32	0.57	0.86	0.94	0.90	0.99	1.43	0.25	0.97
L-Leucine	1.26	0.17	0.59	1.27	0.50	0.99	1.29	0.68	0.97
L-Lysine	1.16	0.48	0.86	1.08	0.58	0.99	1.01	0.85	0.97
L-Methionine	1.30	0.55	0.86	1.25	0.86	0.99	1.08	0.80	0.97
L-Phenylalanine	1.25	0.12	0.51	1.24	0.26	0.99	1.21	0.72	0.97
L-Proline	1.16	0.59	0.86	1.05	0.58	0.99	0.88	0.47	0.97
L-Serine	1.34	0.37	0.82	1.17	0.38	0.99	1.22	0.81	0.97
L-Tryptophan	1.19	0.64	0.88	1.07	0.33	0.99	0.89	0.44	0.97
L-Valine	1.02	0.72	0.88	1.39	0.40	0.99	1.03	0.61	0.97
Malonic acid	1.27	0.35	0.82	0.74	0.89	0.99	0.98	0.89	0.97
Methylsuccinic acid	1.73	0.14	0.56	0.82	0.62	0.99	1.17	0.66	0.97
Myristic acid	1.38	0.69	0.88	1.07	0.93	0.99	1.15	0.79	0.97
N-acetyltryptophan	1.14	0.66	0.88	1.09	0.35	0.99	0.84	0.55	0.97
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Norvaline	1.39	0.57	0.86	0.68	0.58	0.99	0.41	0.17	0.97	
Oxoadipic acid	1.27	0.33	0.81	1.35	0.44	0.99	0.82	0.25	0.97	
Oxoglutaric acid	1.33	0.31	0.79	1.13	0.66	0.99	1.47	0.47	0.97	
Palmitoleic acid	1.23	0.20	0.64	0.71	0.35	0.99	1.26	0.31	0.97	
p-Cresol	0.38	< 0.001	< 0.001	1.33	0.99	1.00	0.36	0.40	0.97	
Pelargonic acid	1.15	0.44	0.84	0.81	0.49	0.99	0.92	0.20	0.97	
Phenylacetic acid	0.83	0.59	0.86	1.26	0.55	0.99	0.70	0.41	0.97	
Phenylethylamine	1.19	0.11	0.51	1.04	0.22	0.99	1.17	0.39	0.97	
Phenyllactic acid	1.12	0.50	0.86	1.06	0.91	0.99	0.97	0.71	0.97	
p-Hydroxyphenylacetic acid	1.23	0.05	0.34	1.12	0.54	0.99	1.13	0.28	0.97	
Pimelic acid	0.98	0.98	0.99	0.98	0.85	0.99	0.90	0.69	0.97	
Propionic acid	1.81	0.20	0.64	1.29	0.97	0.99	1.01	0.18	0.97	
Purine	1.05	0.16	0.59	1.09	0.65	0.99	1.05	0.69	0.97	
Nervonic acid	599.77	0.40	0.82	151.36	0.12	0.99	19.56	0.60	0.97	
Putrescine	2.95	0.02	0.27	1.40	0.31	0.99	1.32	0.29	0.97	
Pyroglutamic acid	1.10	0.29	0.77	0.96	0.81	0.99	0.82	0.86	0.97	
Suberic acid	1.06	0.68	0.88	1.02	0.76	0.99	1.07	0.46	0.97	
Succinic acid	1.80	0.53	0.86	0.83	0.54	0.99	1.09	0.69	0.97	
Tartaric acid	2.94	0.08	0.46	0.12	1.00	1.00	1.51	0.16	0.97	
Tetracosanoic acid	0.94	0.64	0.88	1.01	0.89	0.99	1.24	0.51	0.97	
Vanillic acid	0.89	0.65	0.88	1.18	0.97	0.99	1.41	0.37	0.97	
Malic acid	1.51	0.88	0.96	1.13	0.26	0.99	1.07	0.90	0.97	
Nonadecanoic acid	1.72	0.40	0.82	0.73	0.08	0.99	1.10	0.91	0.97	
Citric acid	1.05	0.73	0.88	1.07	0.06	0.99	0.97	0.92	0.97	
L-Tyrosine	1.39	0.40	0.82	1.13	0.48	0.99	1.36	0.93	0.97	
Pentadecanoic acid	0.90	0.44	0.84	1.50	0.91	0.99	0.84	0.94	0.98	
L-Alpha-aminobutyric acid	1.93	0.12	0.51	1.30	0.45	0.99	1.60	0.95	0.98	
8,11,14-Eicosatrienoic acid	0.88	0.53	0.86	0.97	0.66	0.99	1.03	0.96	0.98	
4-Hydroxycinnamic acid	1.08	0.34	0.81	1.09	0.96	0.99	1.44	0.98	0.99	
3-Methylpentanoic acid	2.21	0.21	0.65	1.21	0.56	0.99	1.11	1.00	1.00	



Supplementary Figure 1 Dietary intakes and physical activity during 6 months intervention among 217 participants included in the gut microbiota study.



Supplementary Figure 2 Anthropometrics data and blood biomarkers during 6 months intervention among 217 participants included in the gut

microbiota study. TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.



Supplementary Figure 3 Clustering of gut microbiota into Enterotypes at OTU-level using Jensen-Shannon distance. (A) shows two clusters are most naturally existed in the dataset by PAM method. The *x*-axis shows cluster number, the *y*-axis shows Calinski-Harabasz index. (B) shows the clustering of the first two principal components. (C) Relative abundance of bacterial taxa characteristic of each Enterotype. Boxes represent the interquartile range (IQR) and the line inside represents the median. Whiskers denote the lowest and highest values within $1.5 \times IQR$. (D) Proportions of enterotypes before and after the intervention in each group. No statistically significant were observed before and after the intervention in each group by chi-square test.



▲ Lower-fat diet ● Moderate-fat diet ■ Higher-fat diet

Supplementary Figure 4 PCoA score plots based on Bray-Cutis distance at baseline and month 6 among the three groups at phylum (A), genus (B) and OTU (C) level, respectively. PCoA, principal coordinate analysis; PERMANOVA, permutational multivariate analysis of variance; OTU, operational taxonomic unit.



Supplementary Figure 5 Changes of the most responding phylum (A) and genera (B) among the three intervention groups. *p<0.05, **p<0.01.



Supplementary Figure 6 OPLS-DA score plots comparing total fecal metabolites at baseline (A) and month 6 (B) among three diet group. The p values are evaluated by CV-ANOVA. A p value of less than 0.05 means that global faecal metabolite composition were significantly different among groups. OPLS-DA, orthogonal projection to latent structure-discriminant analysis; CV-ANOVA, cross-validation analysis of variance.

A. Median Chain Fatty Acids

Lower-fat diet (R2X=0.708, Q2=-0.003, p=1) Moderate-fat diet (R2X=0.663, Q2=-0.248, p=1) Higher-fat diet (R2X=0.741, Q2=-0.070, p=1)



C. Long-chain Unsaturated Fatty Aeids

1.05585 * to[1]

-2

-4 -6 -8

-10

Lower-fat diet (R2X=0.447, Q2=-0.058, p=1) Moderate-fat diet (R2X=0.455, O2=-0.169, p=1) Higher-fat diet (R2X=0.490, O2=-0.093, p=0.12)



R2X[1] = 0.073 R2Xo[1] = 0.374 Ellipse: Hotelling's T2 (95%) R2X[1] = 0.107 R2X0[1] = 0.348 Ellipse: Hotelling's 12 (95%) R2X[1] = 0.100 R2Xo[1] = 0.391 Ellipse: Hotelline's T2 (95%

B. Long-chain Saturated Fatty Acids

Lower-fat diet (R2X=0.630, Q2=-0.016, p=1) Moderate-fat diet (R2X=0.275, Q2=-0.108, p=1) Higher-fat diet (R2X=0.704, Q2=0.240, p<0.001)



D. Amino Acids

Lower-fat diet (R2X=0.771, Q2=-0.072, p=1) Moderate-fat diet (R2X=0.702, Q2=-0.135, p=1) Higher-fat diet (R2X=0.754, Q2=-0.105, p=1)



F. Organic Acids and Derivatives

E. Amino Acids Metabolites Lower-fat diet (R2X=0.467, Q2=0.207, p=0.001) Moderate-fat diet (R2X=0.354, Q2=-0.330, p=1) Higher-fat diet (R2X=0.450, Q2=0.027, p=0.72) Lower-fat diet (R2X=0.484, Q2=-0.082, p=1) Moderate-fat diet (R2X=0.438, O2=-0.177, p=1) Higher-fat diet (R2X=0.519, Q2=-0.193, p=1) 1.13565 * to[1] 011 (o[1] D .04384 2236 0466 05663 -2 -2 -2 -8 -8 -10 -10 -10 -10 -10 -3 -2 -1 2 -3 -2 -1 0 2 -3 -2 -1 Ó 2 1 -3 -2 -1 0 2 3 -3 -2 -1 2 0 0 0 1.07832 * t[1] 1.11457 * t[1] 1.10709 * t[1] 1.04873 * t[1] 1.16827 * t[1] 1.12092 * t[1] R2X[1] - 0.061 R2Xo[1] - 0.423 Ellipse: Hotelling's 12 (95%) R2X[1] - 0.052 R2X0[1] - 0.415 Ellipse: Hotelling's T2 (95%) R2X[1] - 0.062 R2Xo[1] - 0.292 Ellipse: Hotelling's 12 (95%) R2X[1] - 0.050 R2Xo[1] - 0.401 Ellipse: Hotelling's 12 (95%) R2X[1] - 0.049 R2Xo[1] - 0.389 Ellipse: Hotelling's 12 (95%) R2X[1] - 0.042 R2X0[1] - 0.478 Ellipse: Hotelling's 12 (95% baseline 📕 month 6

Supplementary Figure 7 OPLS-DA score plots comparing the fecal metabolites before and after the diet intervention in each group, stratified by faecal metabolite categories. (A) shows the median chain fatty acids category. (B) shows the long-chain saturated fatty acids category. (C) shows the long-chain unsaturated fatty acids category. (D) shows the amino acids category. (E) shows the amino acids derivatives category, (F) shows the organic acids and derivatives category. A p value of less than 0.05 means that global faecal metabolite composition changed significantly after the intervention in this group. P values are evaluated by CV-ANOVA. OPLS-DA, orthogonal projection to latent structurediscriminant analysis; CV-ANOVA, cross-validation analysis of variance.



Supplementary Figure 8 Changes of the most responding fecal metabolites among the three intervention groups. *p<0.05, **p<0.01.