

# **Multi-omics gut microbiome signatures in obese women: role of diet and uncontrolled eating behavior**

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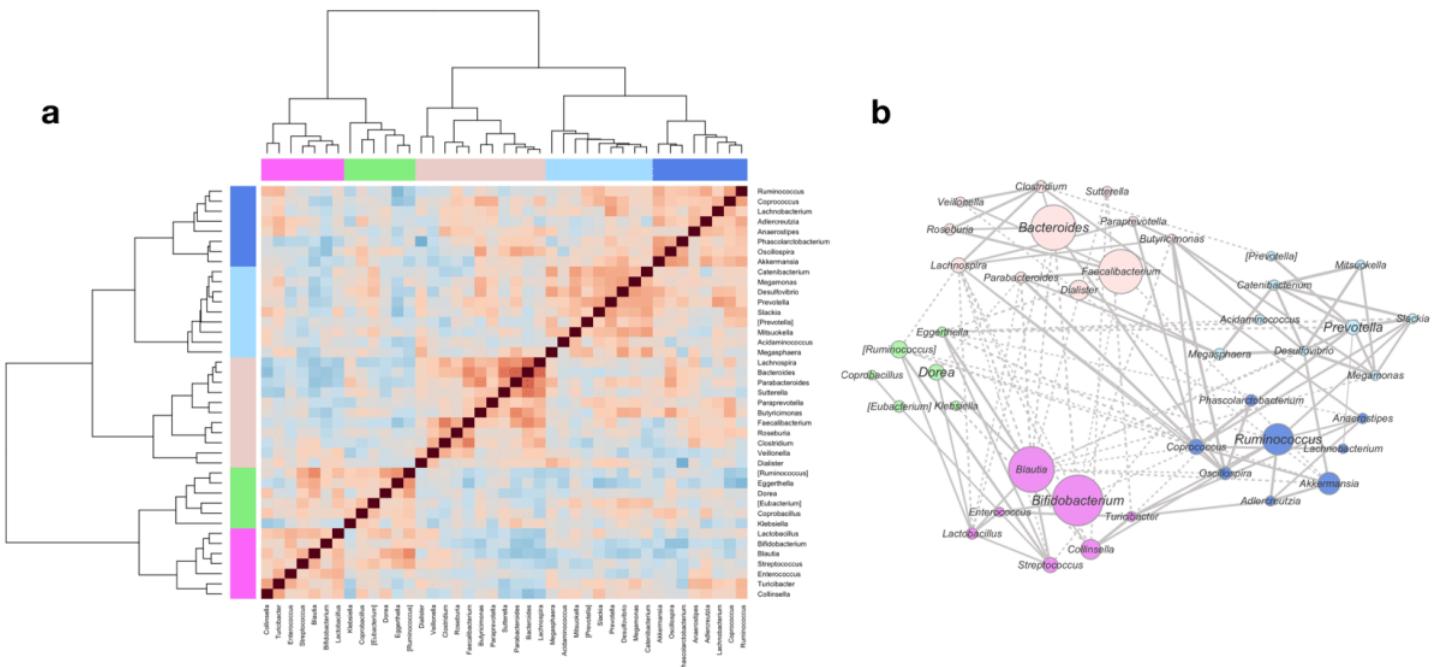
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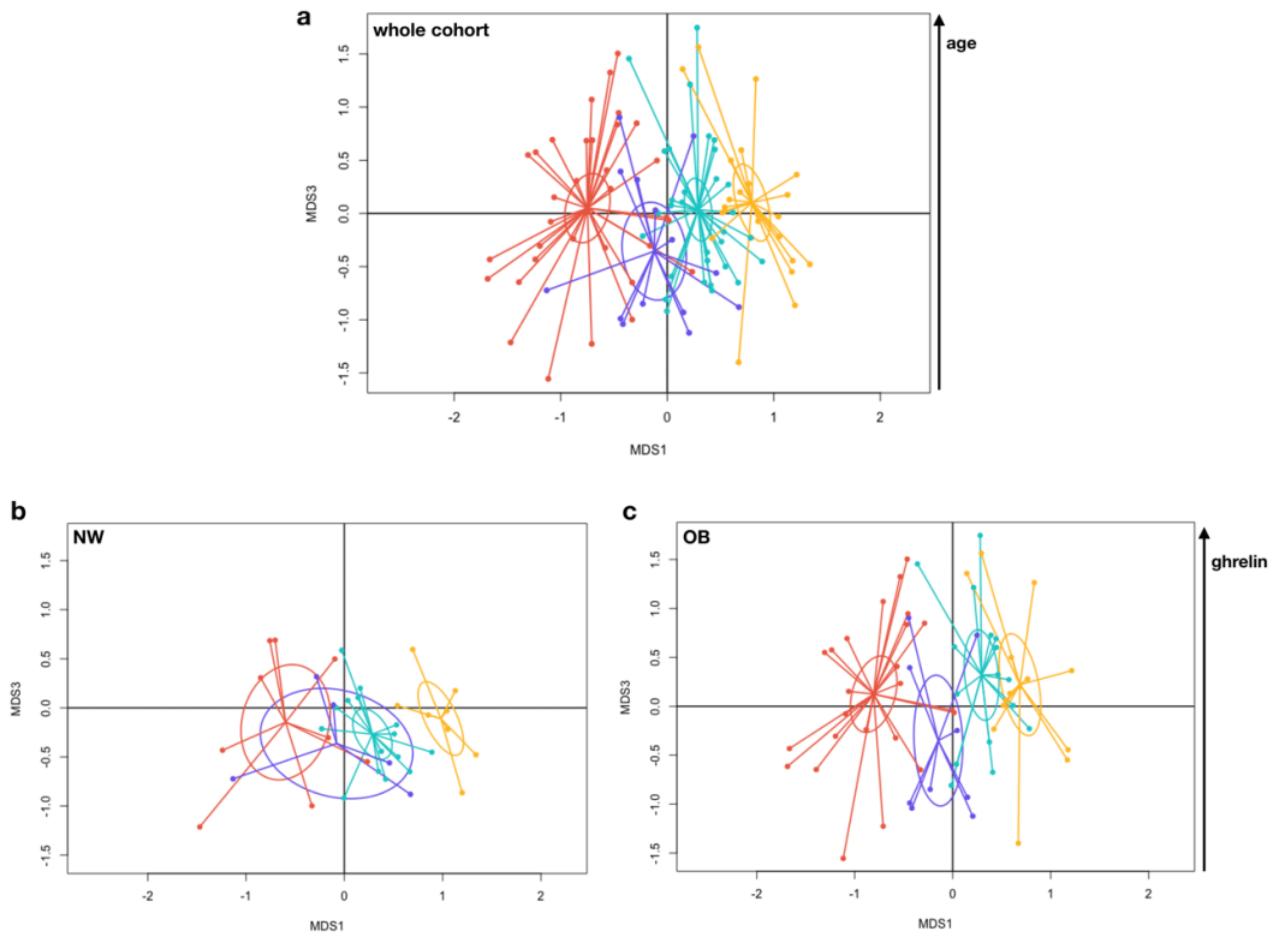
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## Supplementary Material



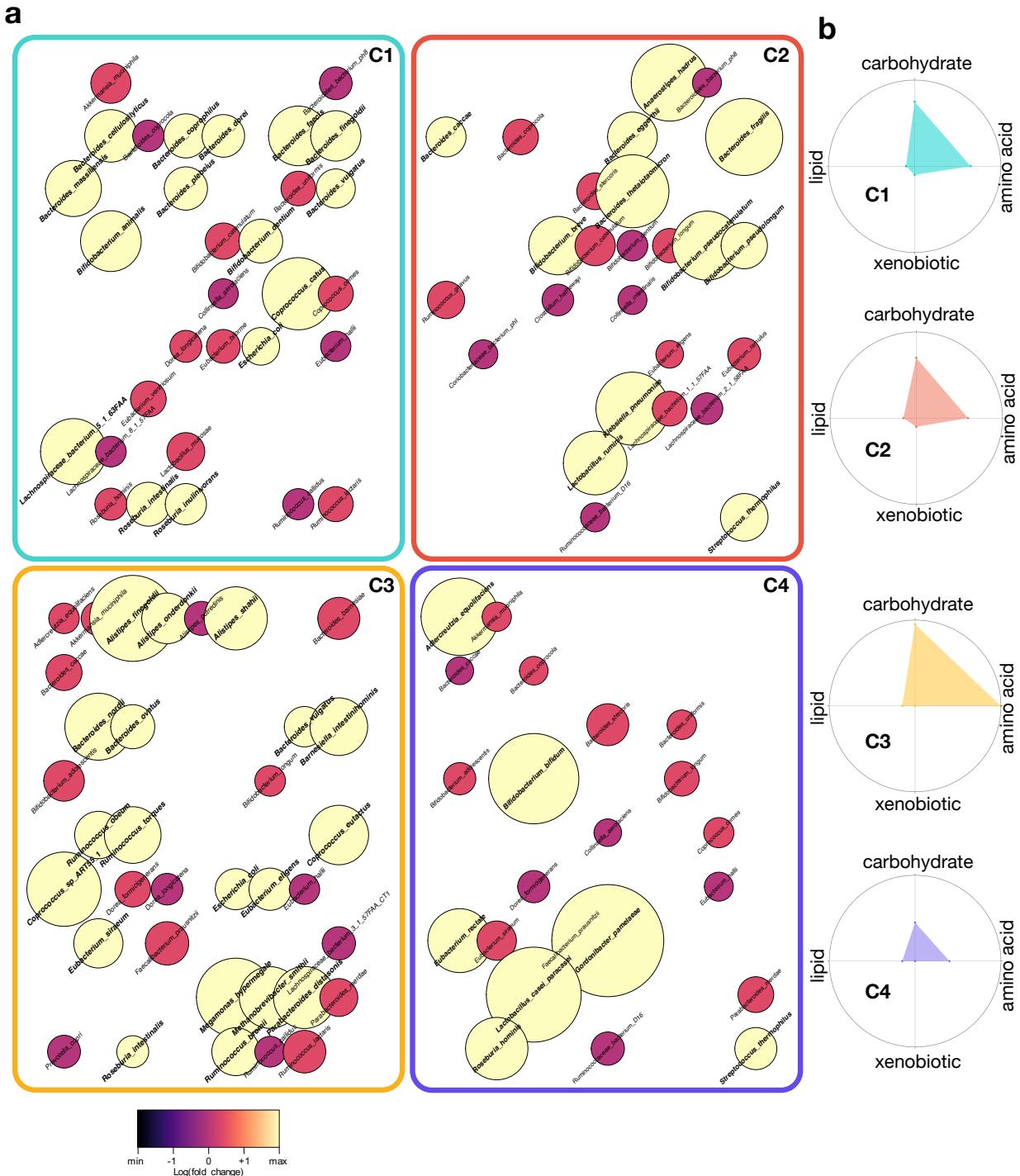
**Figure S1. Assignment of bacterial co-abundance groups (CAGs).** CAGs were assigned according to the heat plot **(a)** showing Kendall correlations between genera clustered by the Spearman correlation coefficient and Ward linkage hierarchical clustering. **(b)** Wiggum plot correlation between the five CAGs identified. Circle size is proportional to the genus relative abundance and the connections between nodes represent significant correlations between genera (Kendall, FDR < 0.05). Positive correlations are represented by continuous lines, while negative correlations are represented by dashed lines. Thickness of the lines is proportional to the significance of the correlation.



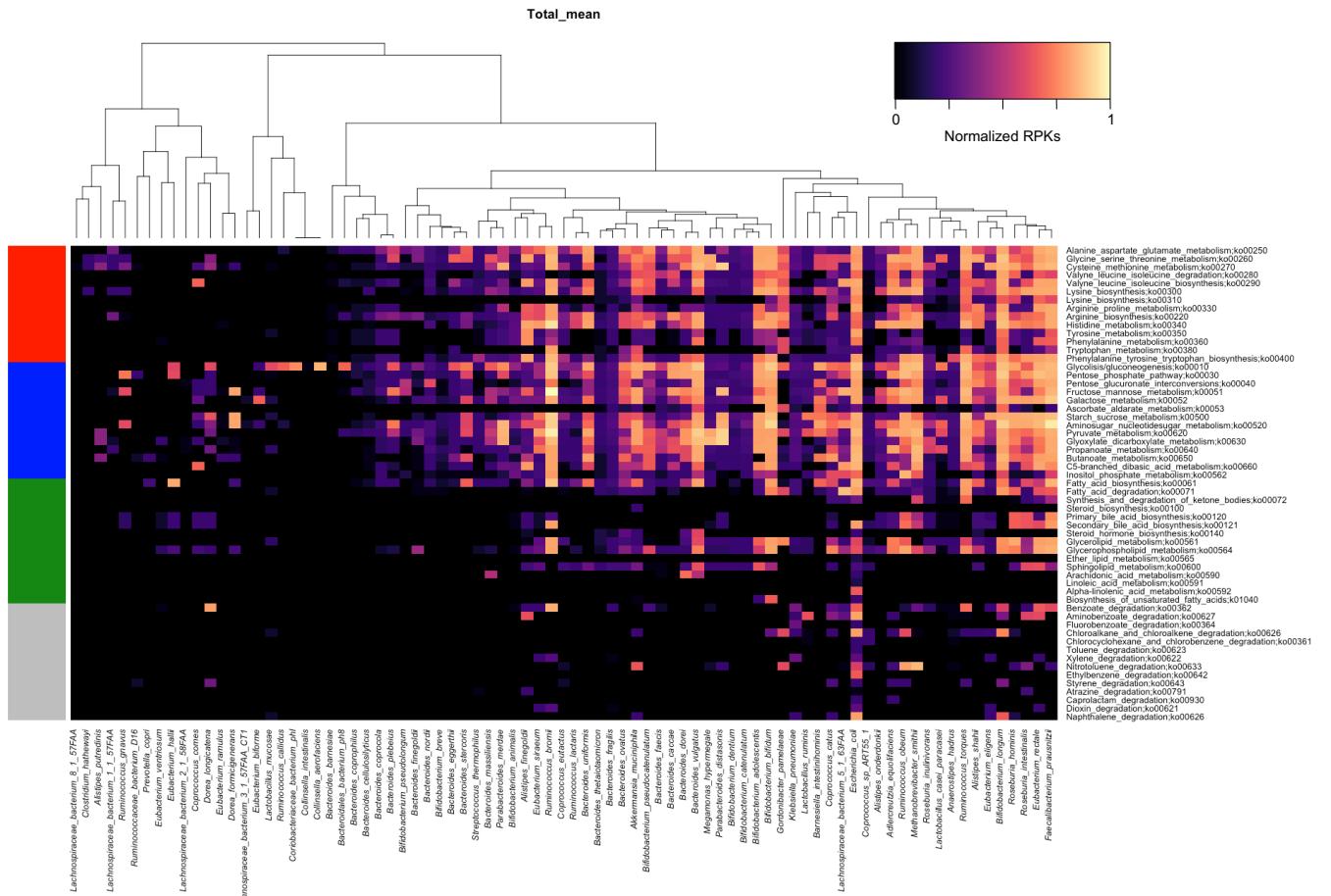
**Figure S2. Associations of the microbiota profiles with host metadata.** Unweighted UniFrac PCoA of the fecal microbiota in the whole cohort (**a**), as well as in normal-weight women (NW, **b**) and overweight/obese women (OB, **c**), stratified according to the four microbiota clusters (C1-C4, see Fig. 3). The host variables significantly associated with the axes are highlighted. MDS, multidimensional scaling.



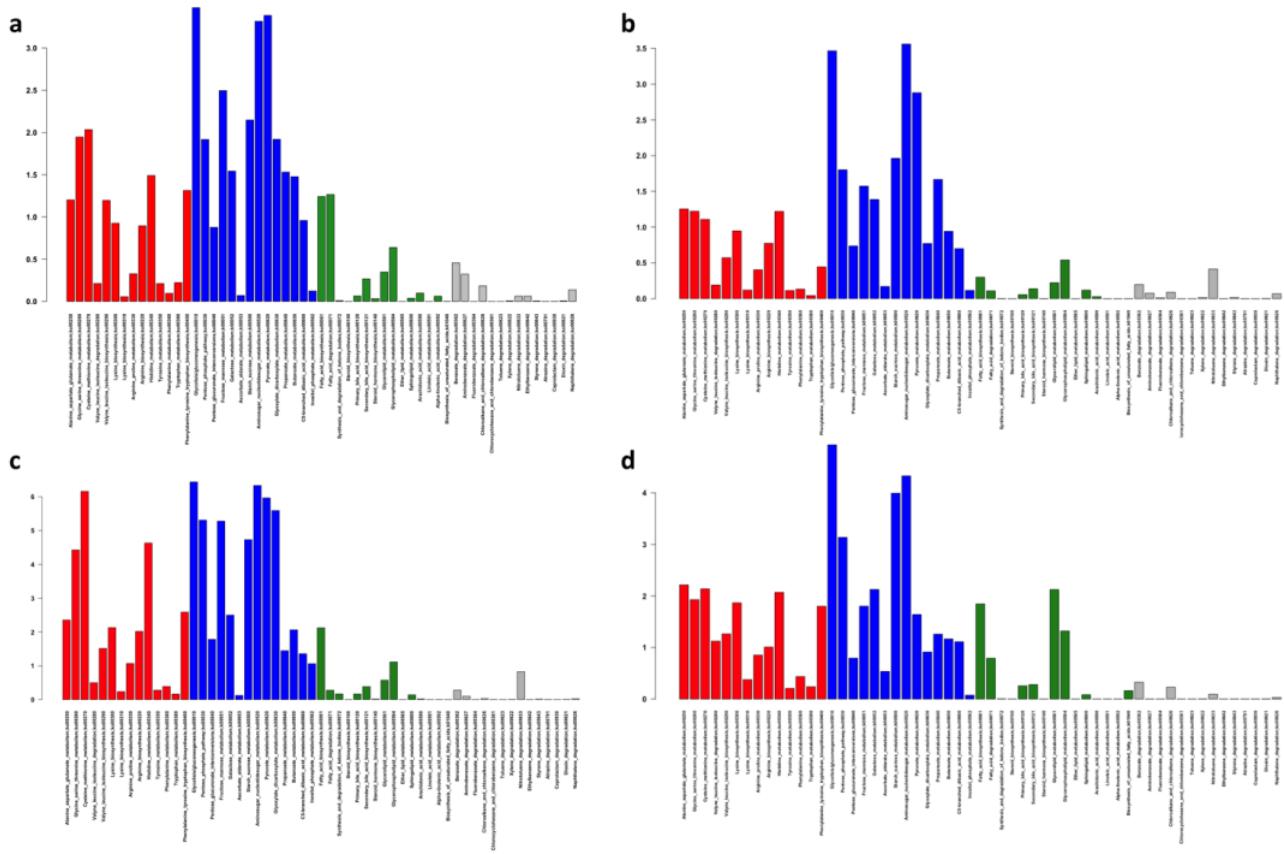
**Figure S3. Distribution of eating behavior-based study groups across the four microbiome clusters (C1-C4).** Women were stratified based on addictive eating behavior into 4 groups: NW\_NA (normal-weight, non-addicted), O\_LA (overweight/obese, low-addicted), O\_HA (overweight/obese, high-addicted), and O\_DHA (overweight/obese, high-addicted with food addiction diagnosis). See Methods for further details on stratification.



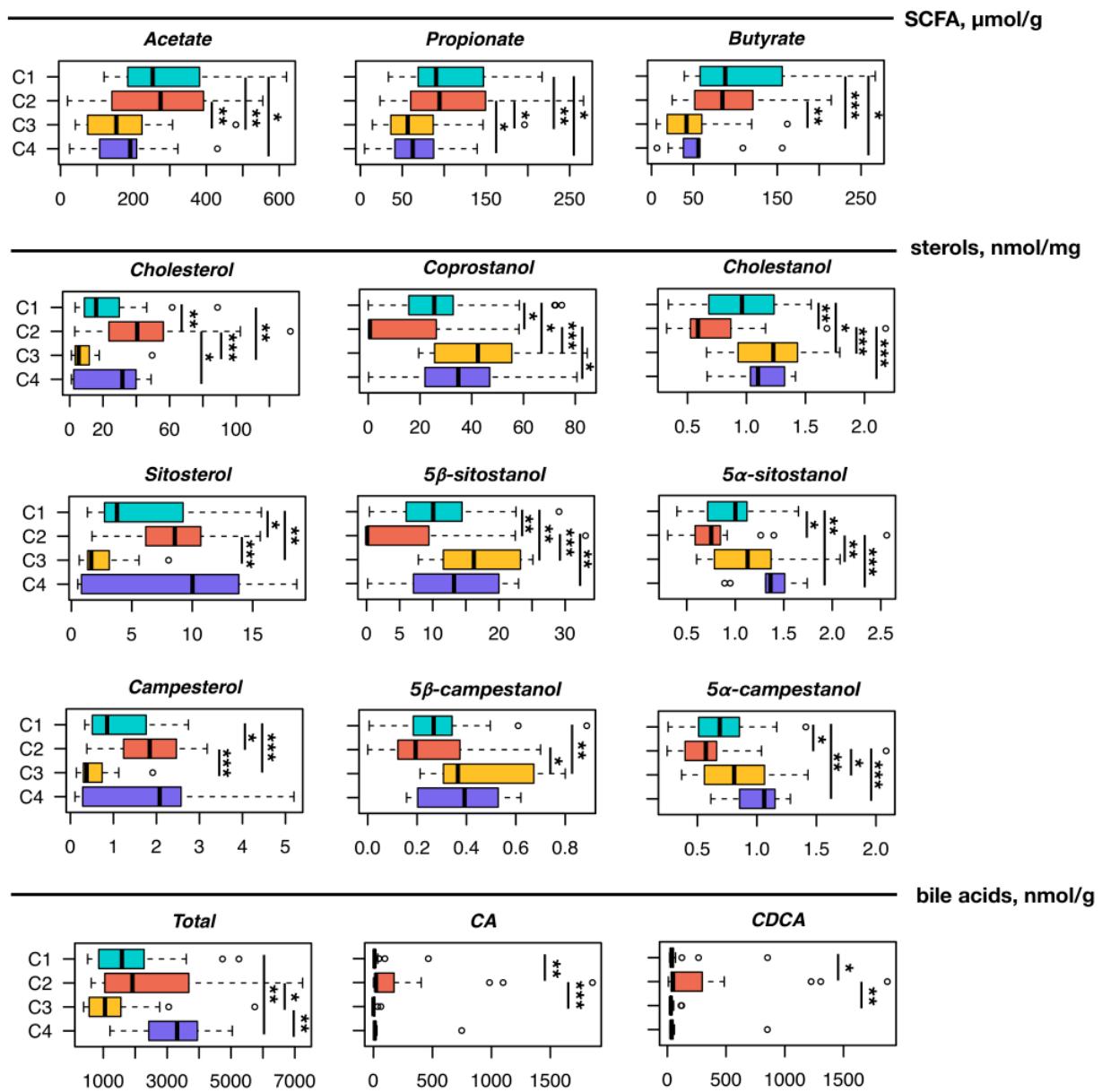
**Figure S4. The transcriptionally active fraction of the gut microbiome differs according to obesity and uncontrolled eating behavior.** (a) Bubble charts showing the transcriptionally active microbial species within the four microbiome configurations (clusters C1-C4). Circle sizes and colors indicate the transcriptional over-abundance of a given species compared to its average normalized abundance in the whole cohort using log<sub>2</sub> transformation. (b) Spider plots showing the number of active species for each metabolism (i.e., carbohydrate, lipid, amino acid and xenobiotic metabolism). Species were counted as “active” when present with log<sub>2</sub> normalized abundance > 1 in at least 1/3 of the pathways comprised in the specific metabolic category.



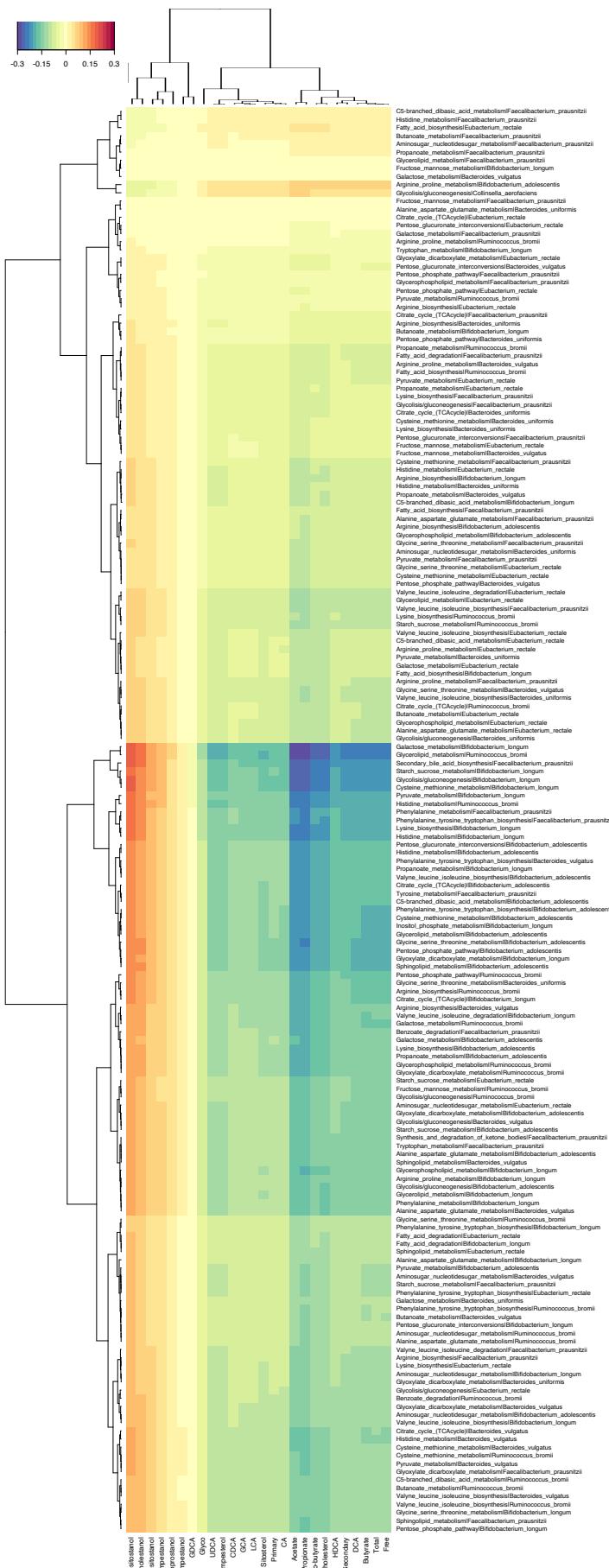
**Figure S5. The metabolic activities of the gut microbiome are broadly taxonomically distributed.** Transcription ratios of 57 KEGG pathways related to amino acid (red), carbohydrate (blue), lipid (green), and xenobiotic (grey) metabolisms that were most prevalently transcribed among the species detected by metagenomics. A given pathway-species combination in the heatmap represents the transcript abundance averaged over all samples that measured an RNA/DNA ratio for that species. All the pathway-species combinations in at least 1 sample were considered. Columns in the heatmap were ordered based on Ward linkage clustering on a Spearman distance matrix of DNA-normalized transcript abundance profiles for each species. Normalized RPKs correspond to DNA-normalized (RNA:DNA ratio) transcript reads per kilobases.



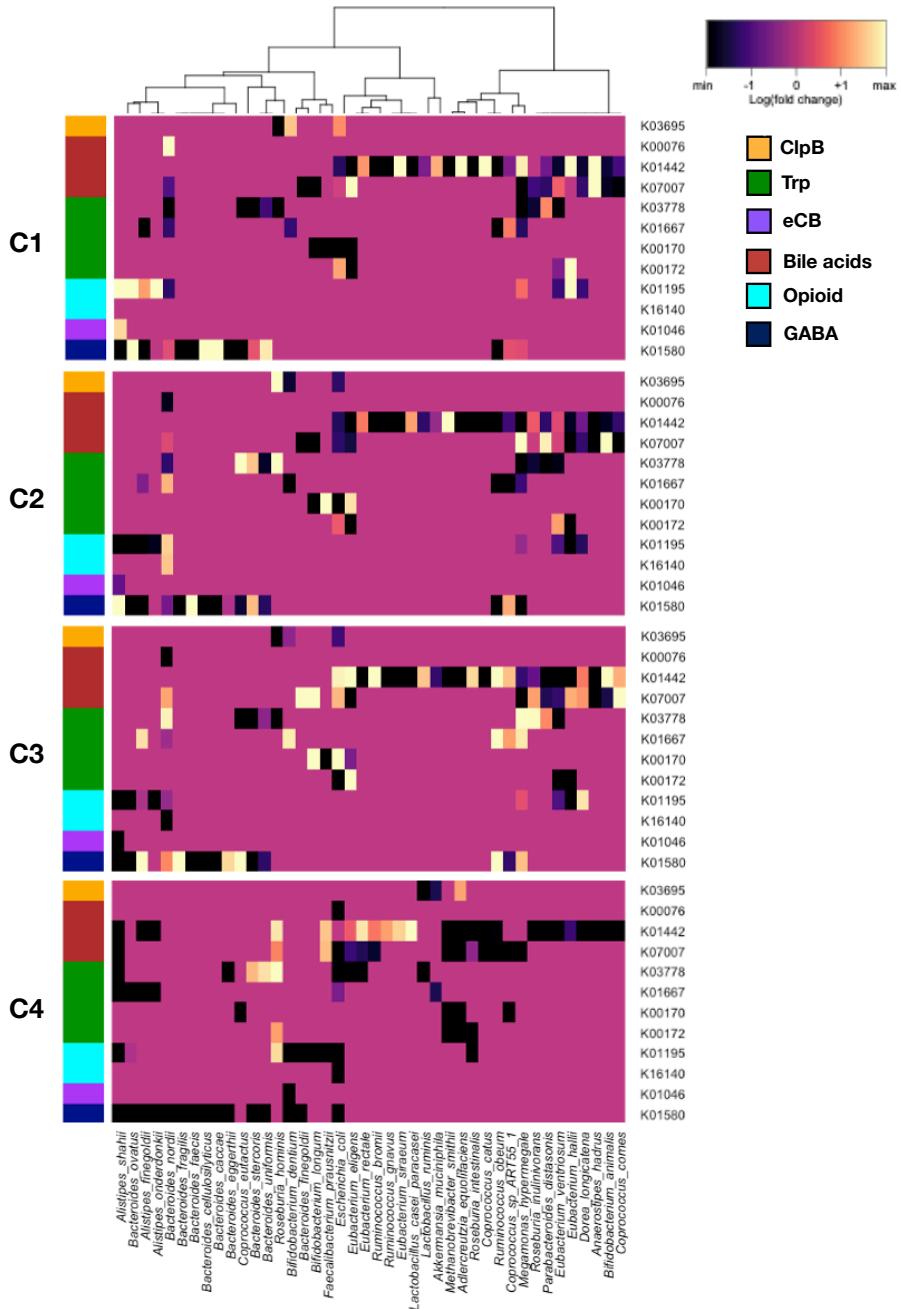
**Figure S6. Metabolic activities of the four microbiota clusters according to metatranscriptomic analysis.** Expression levels of the 57 identified KEGG pathways related to amino acid (red), carbohydrate (blue), lipid (green), and xenobiotic (grey) metabolisms that were most prevalently transcribed among the species detected by metagenomics, for the microbiome clusters C1 (a), C2 (b), C3 (c) and C4 (d).



**Figure S7. Fecal lipidomic profiles of the four microbiota clusters (C1-C4).** Boxplots showing the amount distribution of short-chain fatty acids (SCFAs, upper panel), sterols (middle panel) and bile acids (lower panel) significantly different between the four microbiota clusters. CA, cholic acid; CDCA, chenodeoxycholic acid; GDCA, glycocholic acid; Glyco, glycoconjugates. See [50] for further details on fecal lipidomics analysis. \*,  $p \leq 0.05$ ; \*\*,  $p \leq 0.01$ ; \*\*\*,  $p \leq 0.001$ ; Wilcoxon test.



**Figure S8. Associations between the transcriptionally active fraction of the gut microbiome and lipidomics measures.** Hierarchical clustering obtained with complete linkage method and Pearson correlation as distance, performed on the sparse partial least square (sPLS) regression of transcriptionally active pathways and species of the gut microbiome and host lipids. CA, cholic acid; CDCA, chenodeoxycholic acid; DCA, deoxycholic acid; GCA, glycocholic acid; GDCA, glycodeoxycholic acid; HDCA, hyodeoxycholic acid; LCA, lithocholic acid; UDCA, ursodeoxycholic acid.



**Figure S9. Transcriptional activities of microbiome configurations specifically related to food intake, energy expenditure and neuroendocrine signaling.** Average RNA:DNA ratio for each cluster (C1-C4) with respect to the whole cohort, of a selection of key genes involved in ClpB (orange), bile acid (brown), tryptophan (green), opioid (cyan), eCB (violet), and GABA (navy) production, divided by the assigned microbial species. Phylogenetic tree on the top of the heatmap was built using hierarchical Ward linkage clustering based on the Spearman correlation coefficients of the average DNA-normalized transcript abundance profiles for the species with detectable transcriptomes in the whole cohort.

**Table S1. Genus-level distribution and differences in the gut microbiota profiles among the four clusters (C1-C4).** For each genus, the mean relative abundance and sem (standard error of the mean) are reported, along with Wilcoxon test *p* values (significant values in bold).

Genus	relative abundances								p values					
	mean C1	sem C1	mean C2	sem C2	mean C3	sem C3	mean C4	sem C4	C1 vs C2	C1 vs C3	C1 vs C4	C2 vs C3	C2 vs C4	C3 vs C4
<i>Anaerotruncus</i>	0.0038	0.0013	0.0049	0.0017	0.03	0.0077	0.019	0.0094	0.8	<b>0.0004</b>	0.07	<b>0.0001</b>	0.1	0.1
<i>Coprococcus</i>	0.023	0.0094	0.032	0.013	0.048	0.021	0.2	0.11	0.7	0.6	<b>0.03</b>	0.4	<b>0.02</b>	0.2
<i>Eggerthella</i>	0.026	0.011	0.32	0.081	0.054	0.034	0.13	0.048	<b>8.00E-06</b>	0.3	<b>0.002</b>	<b>0.0006</b>	0.3	<b>0.03</b>
<i>Butyrivibrio</i>	0.034	0.0076	0.062	0.03	0.14	0.056	0.0054	0.0027	0.08	<b>0.03</b>	<b>0.02</b>	<b>0.002</b>	0.5	<b>0.0009</b>
<i>Lachnobacterium</i>	0.035	0.017	0.013	0.0061	0.081	0.058	0.0046	0.0027	<b>0.03</b>	0.8	<b>0.05</b>	<b>0.03</b>	0.7	<b>0.05</b>
<i>[Prevotella]</i>	0.057	0.049	0	0	0.13	0.11	0	0	0.07	0.2	0.2	<b>0.005</b>	NA	0.06
<i>Slackia</i>	0.059	0.019	0.042	0.021	0.18	0.093	0.16	0.11	0.1	0.1	0.4	<b>0.007</b>	0.7	0.09
<i>Desulfovibrio</i>	0.061	0.034	0.022	0.016	0.2	0.081	0.0062	0.0054	0.4	0.1	0.3	<b>0.03</b>	0.7	0.06
<i>Veillonella</i>	0.094	0.026	0.3	0.2	0.01	0.0033	0.024	0.014	0.5	<b>0.0004</b>	<b>0.009</b>	<b>0.004</b>	<b>0.05</b>	0.7
<i>Adlercreutzia</i>	0.19	0.057	0.074	0.028	0.13	0.033	0.29	0.063	<b>0.0002</b>	0.5	<b>0.04</b>	<b>0.005</b>	<b>0.0001</b>	<b>0.02</b>
<i>Turicibacter</i>	0.21	0.1	0.16	0.073	0.091	0.026	0.28	0.095	<b>0.02</b>	0.5	0.3	0.2	<b>0.04</b>	0.08
<i>Catenibacterium</i>	0.26	0.17	0.13	0.13	0.5	0.29	0	0	0.4	0.1	0.1	<b>0.01</b>	0.3	<b>0.01</b>
<i>Anaerostipes</i>	0.3	0.042	0.19	0.043	0.23	0.057	0.24	0.082	<b>0.02</b>	0.1	0.1	0.3	0.3	0.7
<i>Parabacteroides</i>	0.4	0.064	0.6	0.17	0.42	0.066	0.079	0.035	0.2	0.7	<b>0.0001</b>	0.1	0.07	<b>0.00004</b>
<i>Phascolarctobacterium</i>	0.48	0.1	0.25	0.12	1.06	0.27	0.33	0.22	<b>0.01</b>	0.2	<b>0.05</b>	<b>0.002</b>	0.8	<b>0.01</b>
<i>Roseburia</i>	0.62	0.11	0.46	0.099	0.21	0.049	0.24	0.061	0.1	<b>0.001</b>	<b>0.02</b>	0.4	0.8	0.4
<i>Clostridium</i>	0.67	0.077	0.83	0.14	0.37	0.09	0.25	0.074	0.6	<b>0.006</b>	<b>0.002</b>	0.04	<b>0.02</b>	0.4
<i>[Ruminococcus]</i>	0.99	0.14	2.94	0.59	0.84	0.16	1.37	0.25	<b>0.001</b>	0.4	0.1	<b>0.0008</b>	0.1	<b>0.04</b>
<i>Akkermansia</i>	1.5	0.31	0.39	0.21	6.74	1.71	4.9	1.88	<b>0.00009</b>	<b>0.03</b>	0.9	<b>0.00006</b>	0.05	0.3
<i>Lachnospira</i>	1.54	0.36	1.48	0.41	1.13	0.22	0.32	0.14	0.3	0.8	<b>0.0004</b>	0.4	<b>0.04</b>	<b>0.002</b>
<i>Collinsella</i>	1.73	0.21	2.02	0.42	1.95	0.33	4.92	0.91	0.4	0.8	<b>0.001</b>	0.5	<b>0.003</b>	<b>0.005</b>
<i>Coprococcus</i>	1.75	0.3	0.33	0.074	2.38	0.5	0.94	0.31	<b>3.00E-07</b>	0.4	0.03	<b>2.00E-06</b>	0.03	<b>0.02</b>
<i>Prevotella</i>	2.23	0.72	0.18	0.12	1.89	0.7	0.083	0.034	<b>0.002</b>	0.6	0.08	<b>0.0002</b>	0.3	<b>0.02</b>
<i>Bifidobacterium</i>	5.55	0.9	11.14	1.38	4.59	1.05	17.84	3.51	<b>0.001</b>	0.4	<b>0.0002</b>	<b>0.00008</b>	<b>0.05</b>	<b>0.0002</b>
<i>Ruminococcus</i>	5.87	0.46	2.45	0.71	5.36	0.91	6.47	1.11	<b>1.00E-06</b>	0.1	0.7	<b>0.00009</b>	<b>0.001</b>	0.3
<i>Blautia</i>	7.33	0.81	10.68	1.51	3.86	0.61	8.39	1.32	0.1	<b>0.001</b>	0.6	<b>0.00007</b>	0.5	<b>0.003</b>
<i>Bacteroides</i>	8.44	0.98	9.07	1.62	7.68	1.82	2.84	1	0.5	0.2	<b>0.0004</b>	0.9	0.09	<b>0.02</b>
<i>Faecalibacterium</i>	10.43	0.83	7.61	1.03	5.99	0.97	3.05	0.75	<b>0.05</b>	<b>0.0004</b>	<b>6.00E-07</b>	0.5	<b>0.03</b>	<b>0.04</b>

**Table S2. Food description and average frequency of daily consumption for each microbiota cluster (C1 to C4).**

Food	Description	Food category	Microbiota group			
			C1	C2	C3	C4
biscuits and sweet snacks	Biscuits, packaged cakes or pastries	Snacks	0.385	0.417	0.215	0.567
cheese	Grated, sliced or spreadable cheese	Cheese	0.25	0.312	0.288	0.333
chocolate	Chocolate candy and bars	Snacks	0.244	0.231	0.182	0.183
eggs	Boiled or fried eggs	Eggs	0.11	0.099	0.092	0.088
fried food	Fried food	Other	0.111	0.077	0.082	0.11
fried potatoes	Fried potatoes	Vegetable	0.084	0.099	0.067	0.076
homemade sandwiches	Hamburger, hotdog, kebab, wrap, falafel	Cereal	0.198	0.149	0.206	0.152
ice cream	Ice cream, milk and fruit based bars	Snacks	0.138	0.135	0.123	0.062
meat	Fresh and fried meat	Meat Products	0.088	0.117	0.086	0.138
milk and yoghurt	Milk and plain sweetened yoghurt	Dairy Products	0.481	0.664	0.464	0.683
not homemade sandwiches	Hamburger, hotdog, kebab, wrap, falafel	Cereal	0.076	0.064	0.092	0.112
olive oil	Vegetable dressing	Fat and oils	0.658	0.784	0.561	0.776
pizza	Pizza	Cereal	0.146	0.14	0.185	0.133
sausages	Cold cuts and preserved meat product	Meat Products	0.038	0.072	0.029	0.043
seasonings and condiments	Butter, margarine on bread, pesto, ragù	Condiments	0.214	0.244	0.089	0.217
slide ham	Cold cuts and preserved meat product	Meat Products	0.116	0.139	0.12	0.167
sweet and salty snacks	Packaged cakes or savoury pastries and fritters	Snacks	0.204	0.244	0.155	0.16
sweetened drinks	Sweetened soft beverages	Drinks	0.118	0.195	0.092	0.1
wine	Alcoholic beverages	Drinks	0.189	0.172	0.273	0.16

**Table S3. Summary of dietary groups and microbiota clusters for each of the 100 enrolled women.** Women were stratified based on addictive eating behavior into 4 groups: NW\_NA (normal-weight, non-addicted), O\_LA (overweight/obese, low-addicted), O\_HA (overweight/obese, high-addicted), and O\_DHA (overweight/obese, high-addicted with food addiction diagnosis). For microbiota clusters and dietary groups, see Fig. 3 and Fig. 5, respectively.

SampleID	Group	Microbiota cluster	Diet group
NEU10B	O_LA	C3	D1
NEU116B	O HA	C2	D3
NEU117B	O NA	C4	D3
NEU118B	O NA	C2	D1
NEU119B	O LA	C2	D1
NEU11B	O NA	C4	D1
NEU127B	O LA	C4	D3
NEU129B	O NA	C2	D2
NEU12B	O LA	C2	D1
NEU134B	O HA	C3	D2
NEU139B	O NA	C1	D3
NEU13B	O LA	C1	D3
NEU144B	O NA	C3	D2
NEU14B	O LA	C4	D1
NEU152B	O NA	C1	D1
NEU153B	O LA	C4	D1
NEU155B	O LA	C3	D3
NEU160B	O NA	C2	D1
NEU161B	O LA	C1	D1
NEU163B	O LA	C4	D1
NEU164B	O LA	C2	D3
NEU167B	O NA	C3	D2
NEU16B	O HA	C2	D1
NEU170B	O NA	C1	D2
NEU172B	O NA	C2	D1
NEU174B	O HA	C2	D2
NEU176B	O NA	C1	D2
NEU177B	O LA	C3	D3
NEU178B	O HA	C3	D1
NEU179B	O LA	C1	D1
NEU17B	O HA	C2	D1
NEU180B	O LA	C1	D2
NEU18B	O HA	C1	D1
NEU19B	O HA	C3	D1
NEU1B	O NA	C3	D3
NEU20B	O HA	C3	D3
NEU21B	O HA	C4	D1
NEU22B	O HA	C2	D1
NEU23B	O HA	C2	D1
NEU25B	O NA	C1	D1
NEU26B	O NA	C1	D1
NEU27B	O LA	C3	D3
NEU28B	O NA	C1	D3
NEU29B	O NA	C2	D1
NEU2B	O NA	C2	D1
NEU30B	O NA	C1	D1
NEU31B	O LA	C1	D3
NEU32B	O HA	C3	D2
NEU33B	O HA	C3	D3
NEU34B	O NA	C2	D3
NEU35B	O LA	C2	D3
NEU36B	O NA	C2	D2
NEU37B	O NA	C2	D1
NEU38B	O NA	C2	D1
NEU39B	O LA	C2	D3
NEU3B	O LA	C1	D3
NEU4B	O LA	C4	D1
NEU5B	O NA	C2	D1
NEU6B	O NA	C2	D1
NEU7B	O NA	C3	D3
NEU8B	O HA	C1	D1
NEU9B	O LA	C2	D1

SampleID	Group	Microbiota cluster	Diet group
NC120B	NW_NA	C1	D1
NC121B	NW_NA	C2	D2
NC122B	NW_NA	C1	D3
NC123B	NW_NA	C1	D3
NC124B	NW_NA	C2	D3
NC125B	NW_NA	C2	D3
NC126B	NW_NA	C1	D1
NC128B	NW_NA	C2	D1
NC130B	NW_NA	C2	D1
NC131B	NW_NA	C1	D1
NC132B	NW_NA	C1	D3
NC133B	NW_NA	C3	D3
NC135B	NW_NA	C2	D1
NC136B	NW_NA	C1	D1
NC137B	NW_NA	C4	D2
NC138B	NW_NA	C4	D1
NC140B	NW_NA	C1	D3
NC141B	NW_NA	C3	D2
NC142B	NW_NA	C1	D2
NC143B	NW_NA	C4	D2
NC145B	NW_NA	C1	D2
NC146B	NW_NA	C3	D3
NC147B	NW_NA	C1	D1
NC148B	NW_NA	C2	D2
NC149B	NW_NA	C4	D1
NC150B	NW_NA	C3	D1
NC151B	NW_NA	C1	D2
NC154B	NW_NA	C4	D1
NC156B	O HA	C4	D3
NC157B	NW_NA	C3	D1
NC159B	NW_NA	C1	D2
NC162B	NW_NA	C3	D1
NC165B	NW_NA	C2	D2
NC166B	NW_NA	C1	D1
NC168B	NW_NA	C3	D2
NC171B	NW_NA	C1	D1
NC173B	NW_NA	C3	D2
NC175B	NW_NA	C2	D1

**Table S4. Loading scores obtained from sPLS correlation analysis between metatranscriptomics and lipidomics datasets.** UDCA, ursodeoxycholic acid; HDCA, hyodeoxycholic acid; GCA, glycocholic acid; CA, cholic acid; CDCA, chenodeoxycholic acid; GDCA, glycodeoxycholic acid; DCA, deoxycholic acid; LCA, lithocholic acid; Free, free bile acids; Glyco, glycine-conjugated bile acids; Primary, primary bile acids; Secondary, secondary bile acids; Total, total bile acids. See also Fig. 9.

	comp1	comp2		comp1	comp2
Alanine_aspartate glutamate_metabolism  <i>Bacteroides_uniformis</i>	0.009235	0.04616256	Glyoxylate_dicarboxylate_metabolism  <i>Eubacterium_rectale</i>	-0.0018626	-0.0259434
Alanine_aspartate metabolism  <i>Bacteroides_vulgaris</i>	-0.0520611	-0.097455	Glyoxylate_dicarboxylate_metabolism  <i>Faecalibacterium_prausnitzii</i>	0.15205264	-0.0005026
Alanine_aspartate glutamate_metabolism  <i>Bifidobacterium_adolescentis</i>	0.0855606	-0.057281	Glyoxylate_dicarboxylate_metabolism  <i>Ruminococcus_bromii</i>	0.03103988	-0.0607227
Alanine_aspartate glutamate_metabolism  <i>Bifidobacterium_longum</i>	0.1528817	0.01184153	Histidine_metabolism  <i>Bacteroides_uniformis</i>	-0.0371093	-0.05323
Alanine_aspartate glutamate_metabolism  <i>Eubacterium_rectale</i>	-0.0137712	-0.0794428	Histidine_metabolism  <i>Bacteroides_vulgaris</i>	-0.0304953	-0.0840892
Alanine_aspartate glutamate_metabolism  <i>Faecalibacterium_prausnitzii</i>	0.14664802	0.0194782	Histidine_metabolism  <i>Bifidobacterium_adolescentis</i>	-0.0312191	-0.048457
Alanine_aspartate glutamate_metabolism  <i>Ruminococcus_bromii</i>	-0.0391005	-0.0701839	Histidine_metabolism  <i>Bifidobacterium_longum</i>	-0.0598143	-0.1302051
Aminosugar_nucleotidesugar metabolism  <i>Bacteroides_uniformis</i>	-0.0166901	-0.0101881	Histidine_metabolism  <i>Eubacterium_rectale</i>	-0.0504765	-0.0841557
Aminosugar_nucleotidesugar metabolism  <i>Bacteroides_vulgaris</i>	-0.0359378	-0.0556378	Histidine_metabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0202314	0.0205647
Aminosugar_nucleotidesugar metabolism  <i>Bifidobacterium_adolescentis</i>	0.03401977	0.06051082	Histidine_metabolism  <i>Ruminococcus_bromii</i>	0.0425901	-0.0804564
Aminosugar_nucleotidesugar metabolism  <i>Bifidobacterium_longum</i>	0.16476177	-0.01687818	Inositol_phosphate_metabolism  <i>Bifidobacterium_longum</i>	-0.0183562	-0.1097688
Aminosugar_nucleotidesugar metabolism  <i>Eubacterium_rectale</i>	-0.0095053	-0.1217103	Lysine biosynthesis  <i>Bacteroides_uniformis</i>	-0.048137	-0.1029858
Aminosugar_nucleotidesugar metabolism  <i>Faecalibacterium_prausnitzii</i>	0.02032995	-0.04422082	Lysine biosynthesis  <i>Bifidobacterium_adolescentis</i>	0.02015933	0.01680654
Aminosugar_nucleotidesugar metabolism  <i>Ruminococcus_bromii</i>	-0.0430462	-0.065318	Lysine biosynthesis  <i>Bifidobacterium_longum</i>	0.0760526	0.1552683
Arginine biosynthesis  <i>Bacteroides_uniformis</i>	0.17587216	0.01734575	Lysine biosynthesis  <i>Eubacterium_rectale</i>	0.02126343	-0.0921349
Arginine biosynthesis  <i>Bacteroides_vulgaris</i>	-0.04415	-0.0850094	Lysine biosynthesis  <i>Faecalibacterium_prausnitzii</i>	0.13341229	-0.0173083
Arginine biosynthesis  <i>Bifidobacterium_adolescentis</i>	0.17454724	0.01654483	Lysine biosynthesis  <i>Ruminococcus_bromii</i>	0.12420193	-0.0249484
Arginine biosynthesis  <i>Bifidobacterium_longum</i>	0.17555978	0.00256697	Pentose glucuronate_+E19	-0.0069456	-0.0172927
Arginine biosynthesis  <i>Eubacterium_rectale</i>	0.19039125	0.02537051	Pentose glucuronate_interconversions  <i>Bifidobacterium_adolescentis</i>	0.00663459	-0.0593316
Arginine biosynthesis  <i>Faecalibacterium_prausnitzii</i>	0.15123445	-0.016064	Pentose glucuronate_interconversions  <i>Bifidobacterium_longum</i>	-0.0051937	-0.0319584
Arginine biosynthesis  <i>Ruminococcus_bromii</i>	-0.0451281	-0.1084412	Pentose glucuronate_interconversions  <i>Eubacterium_rectale</i>	0.20427309	0.06553809
Arginine_proline metabolism  <i>Bacteroides_vulgatus</i>	-0.0532033	-0.112923	Pentose glucuronate_interconversions  <i>Faecalibacterium_prausnitzii</i>	0.14343372	0.05493857
Arginine_proline metabolism  <i>Bifidobacterium_adolescentis</i>	0.10478334	0.2295757	Pentose_phosphate_pathway  <i>Bacteroides_uniformis</i>	0.00811933	0.04530707
Arginine_proline metabolism  <i>Bifidobacterium_longum</i>	-0.0367454	-0.0869794	Pentose_phosphate_pathway  <i>Bacteroides_vulgaris</i>	-0.0045012	0.0111527
Arginine_proline metabolism  <i>Eubacterium_rectale</i>	0.1014597	-0.0562661	Pentose_phosphate_pathway  <i>Bifidobacterium_adolescentis</i>	-0.0484244	-0.0878174
Arginine_proline metabolism  <i>Faecalibacterium_prausnitzii</i>	0.05237896	-0.0650532	Pentose_phosphate_pathway  <i>Bifidobacterium_longum</i>	0.12240484	-0.074938
Arginine_proline metabolism  <i>Ruminococcus_bromii</i>	0.00157108	0.02449597	Pentose_phosphate_pathway  <i>Eubacterium_rectale</i>	0.18759885	0.02499292
Benzoate_degradation  <i>Faecalibacterium_prausnitzii</i>	-0.0118867	-0.1170003	Pentose_phosphate_pathway  <i>Faecalibacterium_prausnitzii</i>	0.15597607	0.03684897
Benzoate_degradation  <i>Ruminococcus_bromii</i>	-0.0390719	-0.0685037	Pentose_phosphate_pathway  <i>Ruminococcus_bromii</i>	0.0220488	-0.111932
Butanoate_methabolism  <i>Bacteroides_vulgatus</i>	-0.0382804	-0.06815137	Phenylalanine_metabolism  <i>Bifidobacterium_longum</i>	-0.0540729	-0.1256542
Butanoate_methabolism  <i>Bifidobacterium_longum</i>	-0.0038901	-0.1393872	Phenylalanine_metabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0271721	-0.1023913
Butanoate_methabolism  <i>Eubacterium_rectale</i>	0.03020697	-0.0690874	Phenylalanine_tyrosine_tryptophan_biosynthesis  <i>Bacteroides_vulgatus</i>	-0.0619938	-0.1662977
Butanoate_methabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0369	-0.0111378	Phenylalanine_tyrosine_tryptophan_biosynthesis  <i>Bifidobacterium_adolescentis</i>	-0.0503946	-0.1011115
Butanoate_methabolism  <i>Ruminococcus_bromii</i>	-0.0273715	-0.0793332	Phenylalanine_tyrosine_tryptophan_biosynthesis  <i>Bifidobacterium_longum</i>	-0.0264878	-0.0627147
C5-branched_dibasic_acid_methabolism  <i>Bifidobacterium_adolescentis</i>	-0.04459568	-0.0990028	Phenylalanine_tyrosine_tryptophan_biosynthesis  <i>Eubacterium_rectale</i>	-0.0459295	-0.0911387
C5-branched_dibasic_acid_methabolism  <i>Bifidobacterium_longum</i>	0.16868302	0.02599513	Phenylalanine_tyrosine_tryptophan_biosynthesis  <i>Faecalibacterium_prausnitzii</i>	-0.0767918	-0.1693213
C5-branched_dibasic_acid_methabolism  <i>Eubacterium_rectale</i>	0.02757989	-0.0595254	Phenylalanine_tyrosine_tryptophan_biosynthesis  <i>Ruminococcus_bromii</i>	-0.0358508	-0.0531026
C5-branched_dibasic_acid_methabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0042805	0.00776443	Propanoate_methabolism  <i>Bacteroides_vulgatus</i>	-0.0292632	-0.0406072
C5-branched_dibasic_acid_methabolism  <i>Ruminococcus_bromii</i>	-0.0268406	-0.0795628	Propanoate_methabolism  <i>Bifidobacterium_adolescentis</i>	0.05747076	-0.0349505
Citrate_cycle_[TCacycle]  <i>Bacteroides_uniformis</i>	0.01203061	0.0459165	Propanoate_methabolism  <i>Bifidobacterium_longum</i>	-0.0218885	-0.0670602
Citrate_cycle_[TCacycle]  <i>Bacteroides_vulgatus</i>	-0.0365719	-0.0724681	Propanoate_methabolism  <i>Eubacterium_rectale</i>	-0.0213239	-0.0245049
Citrate_cycle_[TCacycle]  <i>Bifidobacterium_adolescentis</i>	0.0473634	-0.0579925	Propanoate_methabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0021203	-0.0306922
Citrate_cycle_[TCacycle]  <i>Bifidobacterium_longum</i>	-0.0393426	-0.0976341	Propanoate_methabolism  <i>Ruminococcus_bromii</i>	-0.0121883	0.01073714
Citrate_cycle_[TCacycle]  <i>Eubacterium_rectale</i>	0.18700245	0.1251242	Pyruvate_methabolism  <i>Bacteroides_uniformis</i>	-0.0428595	-0.0641322
Citrate_cycle_[TCacycle]  <i>Faecalibacterium_prausnitzii</i>	-0.0329655	-0.0110352	Pyruvate_methabolism  <i>Bacteroides_vulgatus</i>	-0.0364955	-0.0702486
Citrate_cycle_[TCacycle]  <i>Ruminococcus_bromii</i>	-0.0384286	-0.0482036	Pyruvate_methabolism  <i>Bifidobacterium_adolescentis</i>	0.15290735	0.00405458
Cysteine_methionine_methabolism  <i>Bacteroides_uniformis</i>	0.0534738	-0.1084937	Pyruvate_methabolism  <i>Bifidobacterium_longum</i>	-0.0224948	-0.1010304
Cysteine_methionine_methabolism  <i>Bacteroides_vulgatus</i>	-0.0391717	-0.0734806	Pyruvate_methabolism  <i>Eubacterium_rectale</i>	-0.0518731	-0.1182136
Cysteine_methionine_methabolism  <i>Bifidobacterium_adolescentis</i>	0.02683465	-0.0895375	Pyruvate_methabolism  <i>Faecalibacterium_prausnitzii</i>	0.05191536	0.08941692
Cysteine_methionine_methabolism  <i>Bifidobacterium_longum</i>	-0.0732872	-0.1677291	Pyruvate_methabolism  <i>Ruminococcus_bromii</i>	-0.0313049	0.01081404
Cysteine_methionine_methabolism  <i>Eubacterium_rectale</i>	0.16930047	-0.011449	Secondary_bile_acid_biosynthesis  <i>Faecalibacterium_prausnitzii</i>	-0.0708559	-0.1898972
Cysteine_methionine_methabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0574743	-0.0478324	Sphingolipid_methabolism  <i>Bacteroides_vulgatus</i>	-0.0707435	-0.1558627
Cysteine_methionine_methabolism  <i>Ruminococcus_bromii</i>	-0.0459592	-0.0823733	Sphingolipid_methabolism  <i>Bifidobacterium_adolescentis</i>	-0.0480328	-0.1020751
Fatty_acid_biosynthesis  <i>Bifidobacterium_longum</i>	-0.054355	-0.1331028	Sphingolipid_methabolism  <i>Eubacterium_rectale</i>	0.00302496	0.00268982
Fatty_acid_biosynthesis  <i>Eubacterium_rectale</i>	0.01180928	0.0446595	Sphingolipid_methabolism  <i>Faecalibacterium_prausnitzii</i>	0.02724378	-0.0687131
Fatty_acid_biosynthesis  <i>Faecalibacterium_prausnitzii</i>	0.13161096	0.01468158	Starch_sucrose_methabolism  <i>Bifidobacterium_adolescentis</i>	0.10931292	0.02872667
Fatty_acid_biosynthesis  <i>Ruminococcus_bromii</i>	0.17714228	0.00963077	Starch_sucrose_methabolism  <i>Bifidobacterium_longum</i>	0.05843321	-0.097843
Fatty_acid_degradation  <i>Bifidobacterium_longum</i>	-0.0331333	-0.0450722	Starch_sucrose_methabolism  <i>Eubacterium_rectale</i>	0.02423033	-0.0692128
Fatty_acid_degradation  <i>Eubacterium_rectale</i>	-0.0518408	-0.1097163	Starch_sucrose_methabolism  <i>Faecalibacterium_prausnitzii</i>	0.12795212	-0.0511098
Fatty_acid_degradation  <i>Faecalibacterium_prausnitzii</i>	0.0090592	0.0112093	Starch_sucrose_methabolism  <i>Ruminococcus_bromii</i>	-0.0032485	-0.0397679
Fructose_mannose_methabolism  <i>Bacteroides_vulgatus</i>	0.02085311	0.06321988	Synthesis_and_degradation_of_ketone_bodies  <i>Faecalibacterium_prausnitzii</i>	-0.0397837	-0.1345995
Fructose_mannose_methabolism  <i>Bifidobacterium_longum</i>	-0.07099683	0.15969279	Tryptophan_methabolism  <i>Bifidobacterium_longum</i>	0.05427486	0.12993406
Fructose_mannose_methabolism  <i>Eubacterium_rectale</i>	-0.0370269	-0.0419938	Tryptophan_methabolism  <i>Faecalibacterium_prausnitzii</i>	0.0423289	0.1350475
Fructose_mannose_methabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0282621	-0.0004705	Tyrosine_methabolism  <i>Bifidobacterium_prausnitzii</i>	-0.0647138	-0.1234953
Fructose_mannose_methabolism  <i>Ruminococcus_bromii</i>	-0.0364744	-0.0801744	Valine_leucine_isoleucine_biosynthesis  <i>Bacteroides_uniformis</i>	-0.03669219	-0.0414563
Galactose_methabolism  <i>Bacteroides_uniformis</i>	-0.047041	-0.0751224	Valine_leucine_isoleucine_biosynthesis  <i>Bacteroides_vulgaris</i>	-0.0172274	-0.0506811
Galactose_methabolism  <i>Bifidobacterium_vulgatus</i>	0.03692171	0.10931652	Valine_leucine_isoleucine_biosynthesis  <i>Eubacterium_rectale</i>	-0.0191291	-0.0752678
Galactose_methabolism  <i>Bifidobacterium_adolescentis</i>	0.06467799	0.0436452	Valine_leucine_isoleucine_biosynthesis  <i>Faecalibacterium_prausnitzii</i>	0.12890713	-0.0390076
Galactose_methabolism  <i>Eubacterium_rectale</i>	0.03833331	-0.1000509	Valine_leucine_isoleucine_biosynthesis  <i>Eubacterium_rectale</i>	0.02421914	-0.0658155
Galactose_methabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0268155	-0.0431515	Valine_leucine_isoleucine_biosynthesis  <i>Faecalibacterium_prausnitzii</i>	-0.0273044	-0.070694
Galactose_methabolism  <i>Ruminococcus_bromii</i>	0.05279556	0.07212299	Valine_leucine_isoleucine_biosynthesis  <i>Ruminococcus_bromii</i>	-0.0281565	-0.0877044
Galactose_methabolism  <i>Bifidobacterium_adolescentis</i>	0.01570023	-0.1021153	Valine_leucine_isoleucine_degradation  <i>Bifidobacterium_longum</i>	-0.0533973	-0.167613
Glycerolipid_methabolism  <i>Bifidobacterium_longum</i>	-0.0480968	-0.1046292	Valine_leucine_isoleucine_degradation  <i>Eubacterium_rectale</i>	-0.0543576	-0.1103114
Glycerolipid_methabolism  <i>Eubacterium_rectale</i>	-0.05140826	-0.0778977	Valine_leucine_isoleucine_degradation  <i>Faecalibacterium_prausnitzii</i>	-0.0004455	-0.1226966
Glycerolipid_methabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0512837	-0.1034357	UDCA	0.0318571	0.18728833
Glycerolipid_methabolism  <i>Ruminococcus_bromii</i>	-0.074291	-0.1840143	HDCA	0.12381823	0.22497026
Glycerophospholipid_methabolism  <i>Bifidobacterium_adolescentis</i>	0.00107726	0.01120388	GCA	0.26273764	0.16915474
Glycerophospholipid_methabolism  <i>Bifidobacterium_longum</i>	-0.0322393	-0.06940925	CA	0.05983688	0.17612961
Glycerophospholipid_methabolism  <i>Eubacterium_rectale</i>	0.02161453	0.04345353	CDCA	0.09461606	0.166439
Glycerophospholipid_methabolism  <i>Faecalibacterium_prausnitzii</i>	0.017490803	0.01309418	GDCA	0.63568879	0.01496889
Glycerophospholipid_methabolism  <i>Ruminococcus_bromii</i>	-0.0339757	-0.0988365	DCA	0.07808238	0.23783547
Glycine_serine_threonine_methabolism  <i>Bacteroides_uniformis</i>	-0.0518845	-0.08069933	LCA	0.13910779	0.16952029
Glycine_serine_threonine_methabolism  <i>Bacteroides_vulgaris</i>	-0.0321992	-0.04054949	Free	0.09889973	0.24130769
Glycine_serine_threonine_methabolism  <i>Bifidobacterium_adolescentis</i>	-0.0472385	-0.1053129	Glyco	0.49128508	0.107967
Glycine_serine_threonine_methabolism  <i>Bifidobacterium_longum</i>	0.02529456	-0.09686989	Primary	0.10273992	0.17421446
Glycine_serine_threonine_methabolism  <i>Eubacterium_rectale</i>	0.01854273	0.03127098	Secondary	0.05929263	0.2314309
Glycine_serine_threonine_methabolism  <i>Faecalibacterium_prausnitzii</i>	-0.0498555	-0.0392114	Total	0.10274423	0.24103386
Glycine_serine_threonine_methabolism  <i>Ruminococcus_bromii</i>	0.15703109	-0.0227147	Cholesterol	-0.045817	0.26048194
Glycolysis/gluconeogenesis  <i>Bacteroides_uniformis</i>	0.09945992	-0.0004881	Coprostanol	0.04587252	-0.057621
Glycolysis/gluconeogenesis  <i>Bacteroides_vulgaris</i>	-0.0354176	-0.0764224	Cholestanol	-0.0064043	-0.1737653
Glycolysis/gluconeogenesis  <i>Bifidobacterium_adolescentis</i>	0.05982939	-0.017426	S $\alpha$ -sitostanol	0.02353579	-0.1898743
Glycolysis/gluconeogenesis  <i>Bifidobacterium_longum</i>	0.04242188	-0.0863507	S $\beta$ -sitostanol	0.09345976	-0.1293211
Glycolysis/gluconeogenesis  <i>Eubacterium_rectale</i>	0.03219151	0.10454868	Campesterol	-0.034006	0.18740311
Glycolysis/gluconeogenesis  <i>Faecalibacterium_prausnitzii</i>	0.00479905	-0.0763129	S $\alpha$ -campesterol	-0.0353578	-0.0182533
Glycolysis/gluconeogenesis  <i>Eubacterium_rectale</i>	0.11917693	-0.030391	S $\beta$ -campesterol	0.06164568	-0.1049988
Glycolysis/gluconeogenesis  <i>Ruminococcus_bromii</i>	0.12179793	-0.0460131	Acetate	0.25021637	0.28911942
Glycolyate_dicarboxylate_methabolism  <i>Bacteroides_uniformis</i>	-0.065306	0.09429493	Propionate	0.28235266	0.20704989
Glycolyate_dicarbox					

**Table S5. Summary of the main distinctive features of the four microbiota clusters in terms of clinical, dietary and lipidomic profiles.** BITE, Bulimic Investigatory Test Edinburgh; NDT, non-distinctive tracts; SCFAs, short-chain fatty acids.

	microbiota profile			
	C1	C2	C3	C4
<b>clinical characteristics</b>	NDT	↑ uric acid, BITE severity score	NDT	↑BITE symptoms score ↓ uric acid
<b>diet</b>	↑ fiber intake	↑ energy intake ↓ fiber, fat intake	NDT	↑ energy, carbohydrate intake ↓ fat intake
<b>lipidomics</b>	↑ SCFAs	↑ SCFAs, cholesterol, bile acids	↑ converted sterols ↓ SCFAs	↑bile acids ↓ SCFAs