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(J.Z., Y.N., L.Q., and Q.F contributed equally to this work)

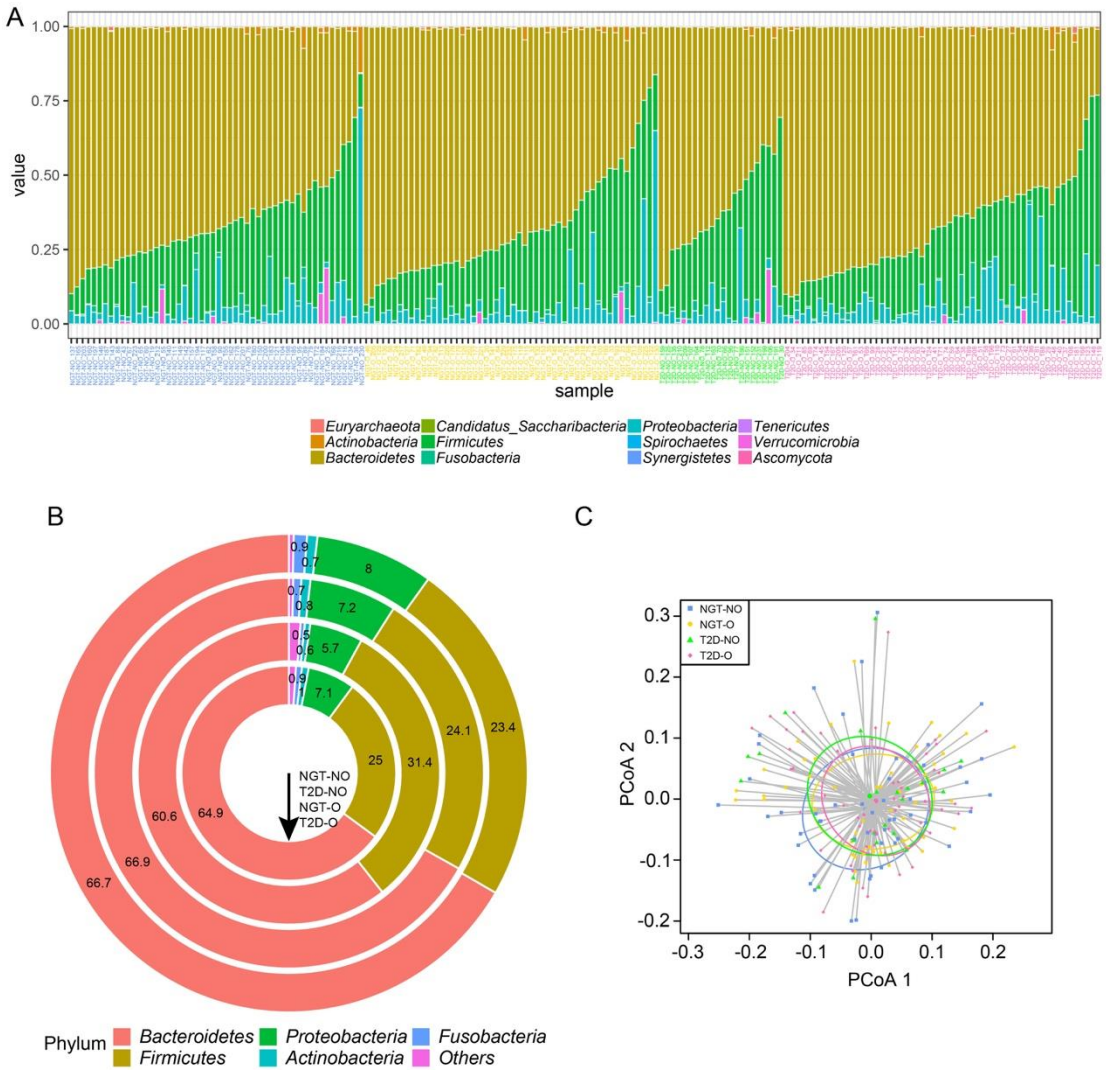

Figure S1. Taxonomic profiles of the gut microbiota for the four groups. (A) The taxonomic composition of the gut microbiota at the phylum level for all the samples. Samples were ordered and colored based on the affiliated groups: blue, NGT-NO; yellow, NGT-O; green, T2D-NO; pink, T2D-O. (B) The average relative abundances of gut microbiota phyla for the four groups shown as donut plot. The mean abundance of each phylum (only the top five most abundant) within each group was marked as percentage. Inner to outer rings: NGT-NO, T2D-NO, NGT-O and T2D-O. (C) Principal Coordinate Analysis (PCoA) plot based on weighted UniFrac distance for 4 different groups. NGT-NO, normal glucose tolerance-lean; NGT-O, normal glucose tolerance-abdominally obese; T2D-NO, type 2 diabetes-lean; T2D-O, type 2 diabetes-abdominally obese.

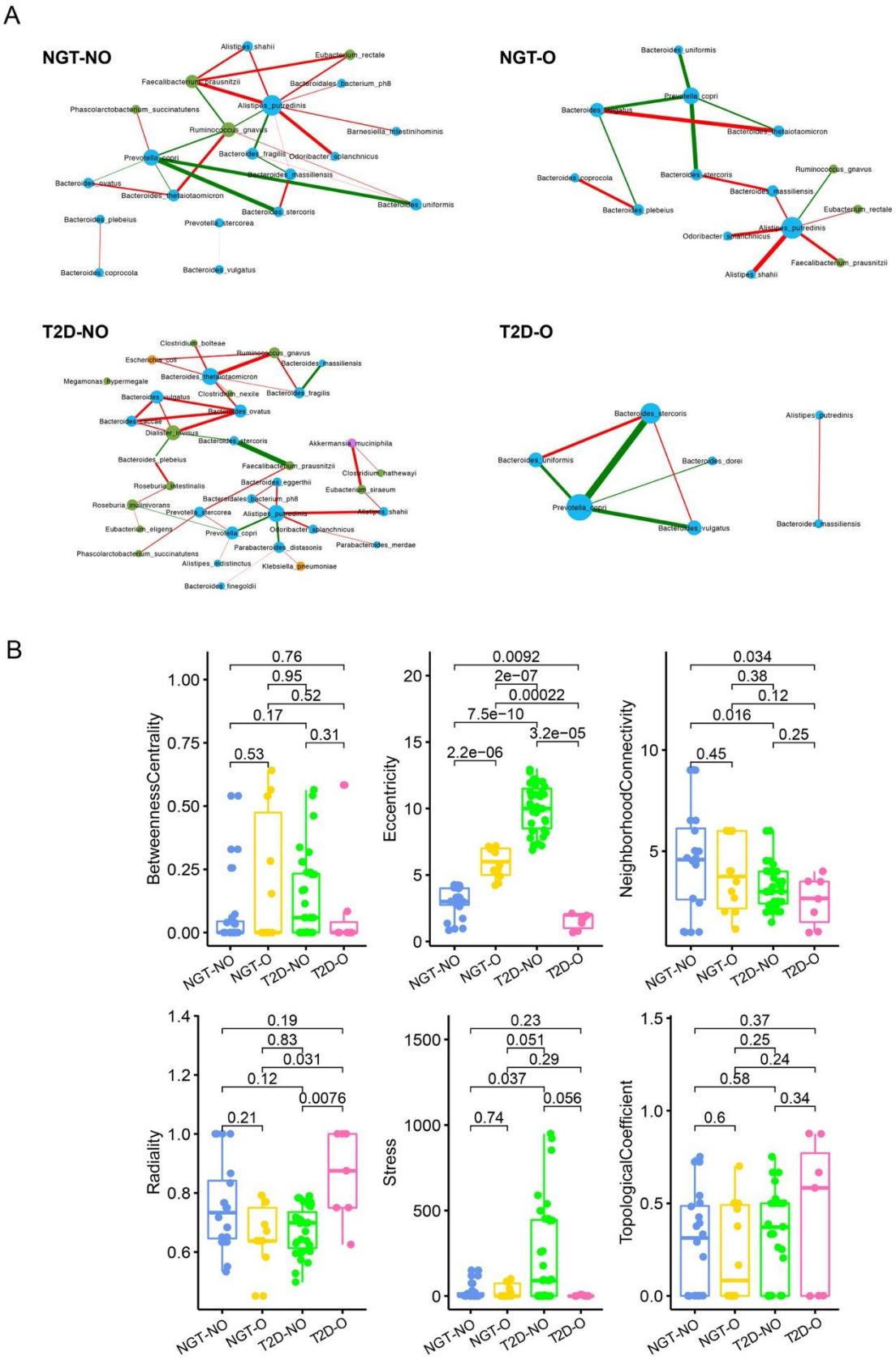

Figure S2. Bacteria-bacteria co-abundance networks in different groups. (A) Microbial co-abundance was calculated with Spearman's rank-based correlations for prevalent species (present in more than 50% of the samples) within each group. The edges represent significantly (P<0.05) positive

(red) or negative (green) correlations and the edge width is proportional to the absolute value of correlations. Nodes are colored based on their affiliated phyla and the node size is proportional to the average relative abundance of species. (B) Comparison of co-abundance network topological properties for the four groups. Statistical p values determined from Wilcoxon rank-sum tests are marked in pairwise manner. Boxplots show median (centerlines), lower/upper quartiles (box limits), whiskers (the last data points 1.5 times IQR from the lower or upper quartiles), and notches (95% confidence interval for the medians). NGT-NO, normal glucose tolerance-lean; NGT-O, normal glucose tolerance-abdominally obese; T2D-NO, type 2 diabetes-lean; T2D-O, type 2 diabetes-abdominally obese.

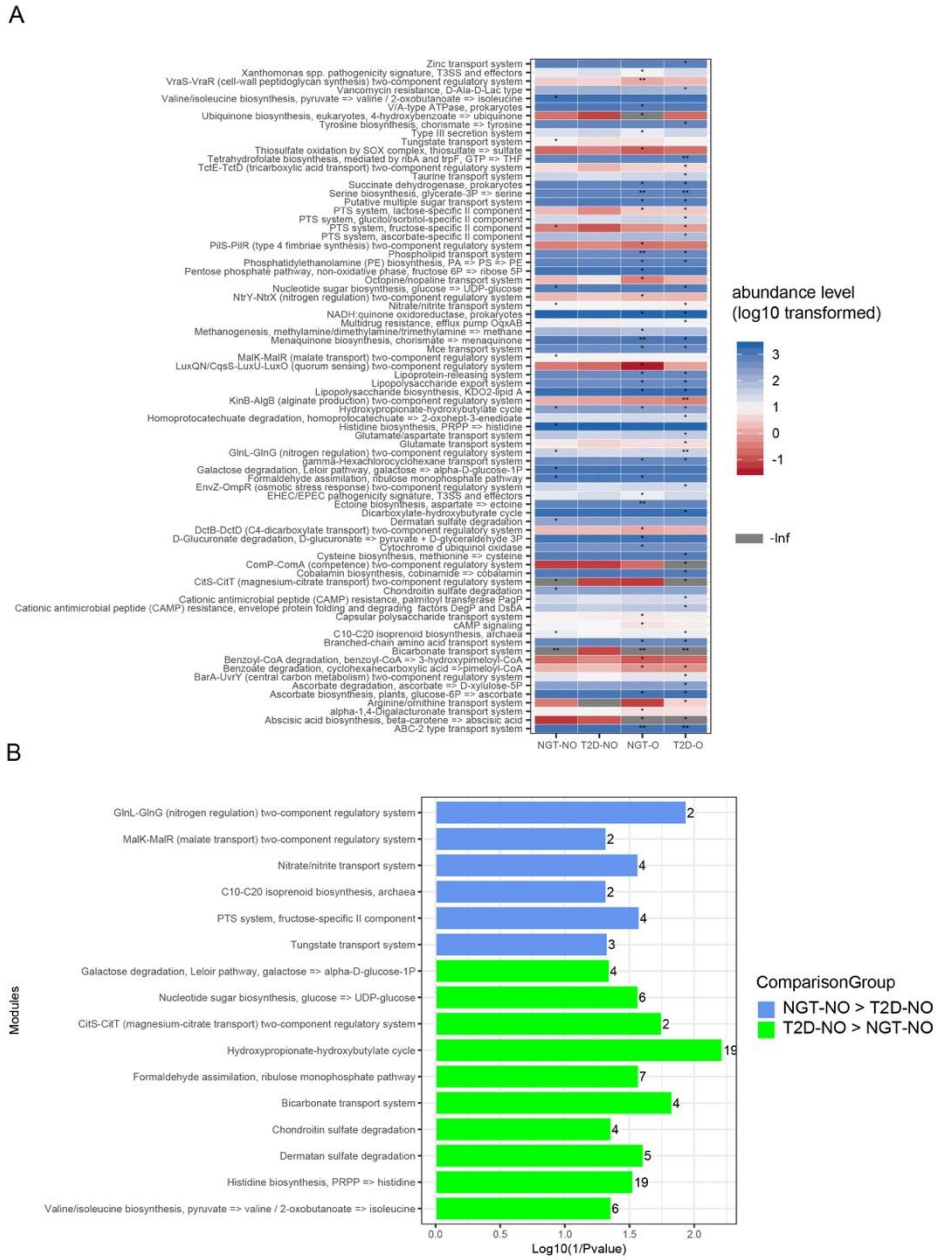

Figure S3. Gut microbiota KEGG module enrichment analysis. (A) Differentially abundance gut microbial KEGG modules comparing the T2D-NO group against each of the other three groups. *, P < 0.05, Wilcoxon rank-sum test when comparing against T2D-NO. For visualization purpose, the relative abundances of functional modules were log10-transformed. (B) KEGG modules significantly enriched in either NGT-NO (blue) or T2D-NO (green) groups. The number of KEGG Orthologs within each KEGG module was marked along the corresponding bar. NGT-NO, normal glucose tolerance-lean; T2D-NO, type 2 diabetes-lean

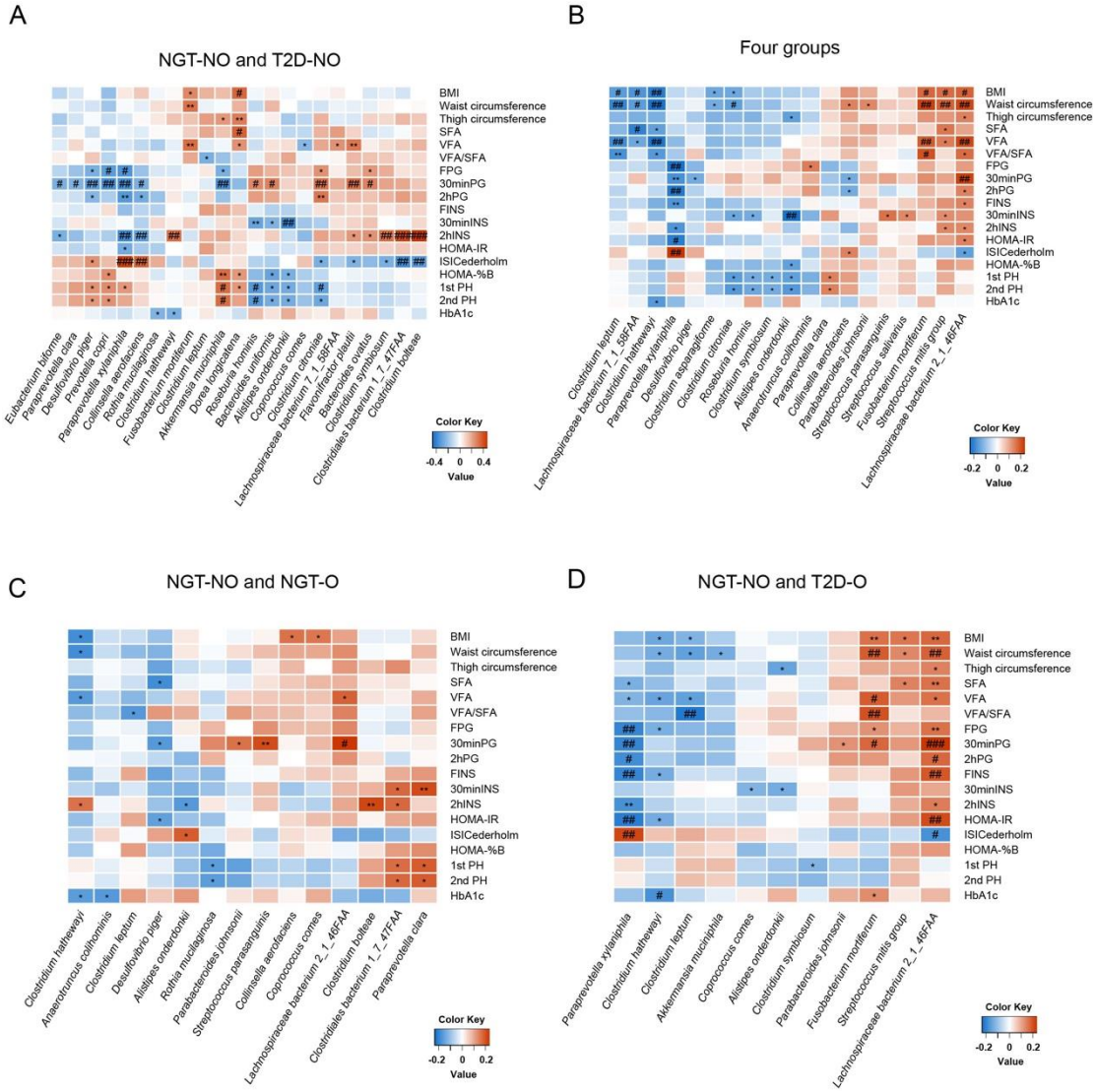

Figure S4. Correlations between specific gut bacteria and clinical indices among different groups. Spearman's rank-based correlations were calculated between prevalent species (>30% in at least one group) and clinical metadata for samples from (A) T2D-NO and NGT-NO groups; (B) all four groups; (C) NGT-O and NGT-NO groups; (D) T2D-O and NGT-NO groups. Only species with at least one significant correlation ($P < 0.05$) were included. Red, positive correlations; blue, negative correlations. #, FDR-corrected P< 0.1; ##, FDR-corrected P <0.05; ###, FDR-corrected P< 0.01; *, P< 0.05; **, P< 0.01; ***, P< 0.001. BMI, body mass index; FINS, fasting serum insulin; FPG, fasting plasma glucose; HOMA-%B, homeostasis model assessment of insulin secretion; HOMA-IR, homeostasis model assessment of insulin resistance; 30min PG, 30min plasma glucose during OGTT; 30min INS, 30min serum insulin during OGTT; 2hPG, 2-h plasma glucose during OGTT; 2hINS, 2-h serum insulin during OGTT; NGT-NO, normal glucose tolerance-lean; NGT-O, normal glucose tolerance-abdominally obese; SFA, subcutaneous abdominal fat area; T2D-NO, type 2 diabetes-lean; T2D-O, type 2 diabetes-abdominally obese; VFA, visceral abdominal fat area. 1st PH, first-phase insulin release; 2nd PH, second-phase insulin release.

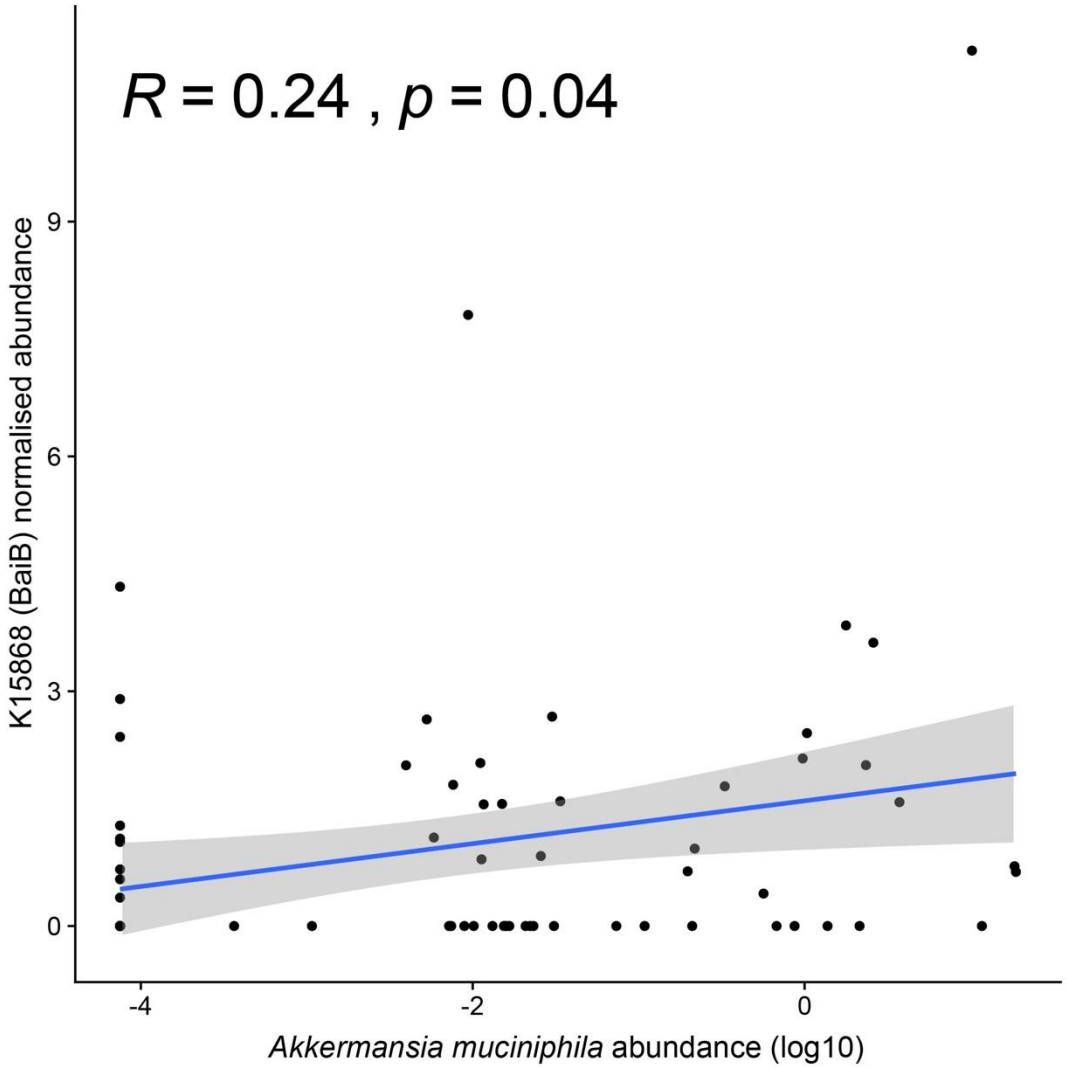

Figure S5. Scatter plot showing the correlation between *Akkermansia muciniphila* and gut microbial gene K15868. All samples from NGT-NO and T2D-NO groups were used for Spearman's rank correlation estimation. For visualization purpose, the relative abundances of Akkermansia muciniphila were log10-transformed. The abundance of bacterial gene K15868 was quantified in an RPKM-like manner (normalized by both the library size and the gene length). NGT-NO, normal glucose tolerance-lean; T2D-NO, type 2 diabetes-lean.

Table S1 Statistical comparison of microbial community alpha and beta diversity

Comparisons	Alpha diversity			Beta diversity (Weighted UniFrac)	
	Simpson	Shannon	Evenness	R^2	*P*
NGT-NO vs T2D-NO	0.527	0.474	0.46	0.023	0.108
NGT-NO vs NGT-O	0.723	0.587	0.619	0.006	0.733
NGT-NO vs T2D-O	0.107	0.096	0.066	0.009	0.424
T2D-NO vs NGT-O	0.411	0.335	0.274	0.039	0.030
T2D-NO vs T2D-O	0.041	0.049	0.02	0.045	0.012
NGT-O vs T2D-O	0.324	0.419	0.292	0.003	0.918

Statistical comparisons of alpha diversity and beta diversity (weighted UniFrac distances) were performed using Wilcoxon rank-sum test and permutational multivariate analysis of variance (PERMANOVA), respectively. NGT-NO, normal glucose tolerance-lean; NGT-O, normal glucose tolerance-abdominally obese; T2D-NO, type 2 diabetes-lean; T2D-O, type 2 diabetes-abdominally obese.

Table S2 Anthropometric parameters and biochemical indexes among the subgroup for investigating serum BAs (n=80)

Variables	NGT-NO (n=20)	NGT-O (n=20)	T2D-NO (n=20)	T2D-O (n=20)	*P* (subgroup vs. total cohort)				*P* (Four Groups)
					NGT-NO	NGT-O	T2D-NO	T2D-O	
Male/female	10/10	10/10	10/10	10/10					-
Age (year)	55.2 ± 6.6	56.7 ± 5.6	59.4 ± 5.0	58.0 ± 7.5	0.62	0.63	0.77	0.95	0.182
VFA (cm^2) §	51.3 (41.2, 71.6)	138.0 (129.8, 171.3) *†	63.7 (41.1, 75.5)	184.0 (145.9, 213.9) *†	0.62	0.84	0.84	0.57	< 0.001
SFA (cm^2) §	82.8 (66.3, 91.3)	197.5 (142.4, 232.2) *†	77.6 (63.4, 91.5)	196.5 (170.0, 243.5) *†	0.19	0.89	0.62	0.09	< 0.001
BMI (kg/m^2)	20.8 ± 1.5	27.7 ± 2.1*†	21.5 ± 2.3	28.5 ± 2.7*†	0.29	0.95	0.36	0.59	< 0.001
FPG (mmol/L) §	5.6 (5.3, 5.7)	5.7 (5.4, 6.0) †	7.2 (6.7, 7.6)*	7.1 (6.8, 7.5)*‡	0.54	0.54	0.83	0.62	< 0.001
2hPG (mmol/L) §	6.4 (5.5, 7.0)	6.7 (5.7, 7.2) †	12.1 (9.3, 17.0) *	12.5 (11.6, 15.7) *‡	0.44	0.85	0.69	0.58	< 0.001
HbA1c (%) §	5.3 (5.1, 5.5)	5.4 (5.1, 5.7) †	5.9 (5.4, 6.9)*	6.1 (5.6, 6.3)*	0.49	0.61	0.86	0.65	0.001
FINS (μU/mL) §	3.6 (1.9, 5.3)	7.2 (6.0, 9.6)*†	4.3 (2.7, 6.4)	9.5 (8.0, 11.8)*†	0.55	0.08	0.45	0.05	< 0.001
2hINS (μU/mL) §	25.9 (17.9, 32.7)	31.6 (20.6, 56.4)	41.9 (22.6, 49.5)	81.3 (50.3, 93.1) *†‡	0.89	0.61	0.73	0.75	< 0.001
HOMA-IR §	0.8 (0.5, 1.3)	1.9 (1.5, 2.3)*	1.4 (0.9, 2.2) *	3.1 (2.6, 3.7)*†‡	0.59	0.06	0.48	0.03	< 0.001
HOMA-%B §	35.4 (17.1, 54.1)	71.1 (55.7, 82.5) *†	23.6 (16.1, 29.4)	52.3 (39.8, 56.9) *†	0.48	0.21	0.43	0.35	< 0.001
1st PH	569.0 ± 51.0	950.7 ± 130.2 †	-125.1 ± 85.1*	410.1 ± 153.0†‡	0.07	0.83	0.34	0.59	< 0.001

2nd PH	175.6 ± 10.7	271.4 ± 29.0*†	41.7 ± 16.9*	158.0 ± 30.6†‡	0.06	0.90	0.33	0.43	< 0.001

Data are means ± SD or median (interquartile range). Data are means ± SEM for 1st PH or 2nd PH. Statistical significance between subgroup and the corresponding whole group was determined with Student' *t* test. Statistical significance among four groups was determined with ANOVA with Bonferroni multiple-comparison analysis. **§** Log transformed before analysis. BMI, body mass index; FINS, fasting serum insulin; FPG, fasting plasma glucose; HOMA-%B, homeostasis model assessment of insulin secretion; HOMA-IR, homeostasis model assessment of insulin resistance; 2hPG, 2-h plasma glucose; 2hINS, 2-h serum insulin; NGT-NO, normal glucose tolerance-lean; NGT-O, normal glucose tolerance-abdominally obese; SFA, subcutaneous abdominal fat area; T2D-NO, type 2 diabetes-lean; T2D-O, type 2 diabetes-abdominally obese; VFA, visceral abdominal fat area. 1st PH, first-phase insulin release; 2nd PH, second-phase insulin release. * vs NGT-NO, $P < 0.05$; † vs T2D-NO, $P < 0.05$； ‡, vs NGT-O, $P < 0.05$.

Table S3 Bile acids and branched-chain amino acids levels among the subgroup (n=80)

Variables	NGT-NO (n=20)	NGT-O (n=20)	T2D-NO (n=20)	T2D-O (n=20)	*P*
βUCA (nmol/L)§	0.2 (0.1, 0.3)	0.7 (0.2, 1.6)*	0.5 (0.3, 1.3)*	0.4 (0.2, 1.0)	0.004
UCA (nmol/L)§	0.2 (0.1, 0.5)	0.4 (0.1, 1.6)	0.5 (0.3, 1.5)*	0.4 (0.2, 0.7)	0.099
GUDCA (nmol/L)§	19.5 (10.6, 34.0)	24.0 (15.8, 47.0)	34.6 (19.8, 91.4)*	39.7 (17.1, 60.4)	0.052
GHCA (nmol/L)§	2.0 (1.4, 3.2)	1.6 (0.8, 2.5)	1.5 (1.0, 2.2)	2.3 (1.0, 3.0)	0.478
GCA (nmol/L)§	15.7 (8.9, 25. 9)	19.2 (13.4, 38.1)	17.2 (5.9, 51.7)	36.8 (22.1, 64.9)*†	0.006
TUDCA (nmol/L)§	0.5 (0.4, 0.8)	0.8 (0.5, 1.6)	0.6 (0.5, 2.1)	1.0 (0.6, 2.1)*	0.044
TaMCA (nmol/L)§	0.8 (0.4, 1.3)	0.4 (0.2, 0.6)	0.4 (0.2, 0.9)	0.9 (0.4, 1.3)‡	0.041
THCA (nmol/L)§	0.4 (0.4, 0.5)	0.4 (0.4, 0.5)	0.4 (0.3, 0.4)	0.4 (0.4, 0.6)	0.382
TCA (nmol/L)§	1.3 (0.6, 1.8)	2.3 (1.2, 3.9)	1.0 (0.5, 5.9)	3.5 (2.1, 9.9)*†	0.001
AlloLCA (nmol/L)§	0.5 (0.3, 1.0)	0.3 (0.2, 0.3)*†	0.4 (0.3, 0.8)	0.3 (0.3, 0.4)	< 0.001
isoLCA (nmol/L)§	2.9 (0.7, 7.9)	0.4 (0.1, 1.3)*†	3.3 (0.3, 6.2)	1.8 (0.2, 5.7)	0.022
LCA (nmol/L)§	2.9 (0.9, 6.5)	1.1 (0.1, 3.2)	2.2 (0.5, 6.1)	3.9 (0.8, 6.4)	0.067
NorDCA (nmol/L)§	0.9 (0.4, 1.7)	0.3 (0.0, 0.6)*	0.4 (0.2, 1.3)	0.5 (0.3, 1.4)‡	0.007
7_ketoLCA (nmol/L)§	4.4 (1. 8, 9.8)	2.2 (0.9, 8.6)	4.5 (3.0, 7.3)	4.5 (2.1, 7.3)	0.368
12_ketoLCA (nmol/L)§	2.3 (1.5, 4.6)	0.9 (0.2, 1.7)*†	1.9 (1.1, 5.0)	2.2 (1.3, 5.8)‡	0.006
CDCA (nmol/L)§	152.7 (80.0, 342.2)	89.2 (40.0, 289.0)	116.8 (73.2, 197.2)	128.5 (53.4, 371.4)	0.815
DCA (nmol/L)§	127.8 (67.7, 226.1)	69.3 (13.9, 114.3)	86.2 (35.4, 142.2)	110.0 (38. 7, 252.2)	0.068
GLCA (nmol/L)§	1.4 (0.7, 2.6)	0.7 (0.1, 2.2)†	2.3 (0.6, 5.3)	2.3 (0.8, 8.2)‡	0.032
LCA_3S (nmol/L)§	3.8 (1.8, 5.5)	0.6 (0.2, 2.7)*†	2.3 (1.2, 6.2)	2.0 (0.7, 5.2)	0.003
6_ketoLCA (nmol/L)§	0.7 (0.6, 0.9)	0.6 (0.4, 0.8)†	0.8 (0.6, 1.3)	0.8 (0.7, 1.0)	0.020
βCDCA (nmol/L)§	17.8 (14.8, 20.4)	24.6 (14.6, 38.3)	35.4 (25.1, 71.6)*	29.2 (23.2, 68.3)*	0.004
βDCA (nmol/L)§	13.9 (3.4, 22.7)	8.2 (2.0, 14.6)	11.4 (5.7, 22.9)	16.1 (4.7, 29.8)	0.146
UDCA (nmol/L)§	27.7 (15.8, 51.2)	26.2 (11.7, 67.7)	43. 2 (18.3, 92.1)	43.2 (17.3, 59.1)	0.603
HDCA (nmol/L)§	0.8 (0.2, 1.3)	0.2 (0.0, 0.5)	0.4 (0.1, 0.7)	0.5 (0.2, 1.2)	0.073
NorCA (nmol/L)§	1.1 (0.6, 1.7)	1.2 (0.7, 1.8)	1.4 (1.0, 2.2)	2.0 (1.1, 4.5)*	0.028
7_DHCA (nmol/L)§	0.7 (0.1, 3.1)	0.7 (0.1, 2.2)	0.9 (0.1, 2. 7)	0.8 (0.2, 1.9)	0.978
3-DHCA (nmol/L)§	0.4 (0.2, 1.2)	0.7 (0.3, 1.2)	1.2 (0.3, 1.5)	0.6 (0.2, 1.0)	0.273
βCA (nmol/L)§	0.4 (0.2, 0.7)	0.9 (0.6, 2.8)*	1.5 (0.6, 3.8)*	1.2 (0.4, 2.8)*	0.002

βMCA (nmol/L)§	1.0 (0.6, 1.4)	0.7 (0.4, 1.0)	0.9 (0.6, 2.4)	0.7 (0.4, 1.2)	0.254
HCA (nmol/L)§	7.1 (4.0, 13.0)	4.8 (1.5, 9.6)	5.5 (3.3, 10.5)	4.3 (1.3, 7.0)	0.157
CA (nmol/L)§	78.4 (17.4, 349.2)	48.2 (14.6, 169.6)	53.9 (20.1, 104.4)	25.8 (14.8, 150.7)	0.657
GCDCA (nmol/L)§	130.3 (51.3, 181.3)	130.3 (74.0, 214.3)	138.9 (87.0, 294.9)	277.0 (110.6, 380.8)*	0.029
GDCA (nmol/L)§	29.8 (15.5, 43.6)	15.5 (6.8, 35.8)	25.6 (11.8, 51.0)	60.9 (27.4, 103.7)‡	0.017
TCDCA (nmol/L)§	5.6 (2.5, 8.4)	9.1 (4.8, 18.6)	7.3 (2.9, 39.8)	13.5 (6.6, 34.9)*	0.018
TDCA (nmol/L)§	2.3 (1.7, 4.1)	1.8 (0.9, 3.3)	2.2 (1.1, 7.0)	4.0 (2.1, 13.2)‡	0.029
GLCA_3S (nmol/L)§	57.7 (28.7, 95.7)	16.1 (2.9, 39.2)†	52.5 (13.7, 80.0)	55.5 (27.1, 101.2)‡	0.022
CDCA_3Gln (nmol/L)§	4.5 (3.1, 11.4)	4.4 (2.1, 10.9)	5.5 (2.8, 8.7)	5.5 (2.8, 17.1)	0.673
Valine (μmol/L)	151.1 ± 24.7	207.1 ± 45.7 *†	178.8 ± 28.4 *	225.4 ± 35.7 *†	< 0.001
Leucine (μmol/L)	96.3 ± 15.0	125.7 ± 27.2 *†	109.2 ± 19.6	133.6 ± 22.0 *†	< 0.001
Isoleucine (μmol/L)	42.2 ± 7.4	56.7 ± 16.3*†	48.8 ± 9.6	62.8 ± 13.2*†	< 0.001

Data are median (interquartile range). Statistical significance was determined with ANOVA with Bonferroni multiple-comparison analysis. § Log transformed before analysis. * vs NGT-NO, $P < 0.05$; † vs T2D-NO, $P < 0.05$; ‡, vs NGT-O, $P < 0.05$.

NGT-NO, normal glucose tolerance-lean; NGT-O, normal glucose tolerance-abdominally obese; T2D-NO, type 2 diabetes-lean; T2D-O, type 2 diabetes-abdominally obese; βUCA, β-ursocholic acid; UCA, ursocholic acid; GUDCA, glycoursodeoxycholic acid; GHCA, glycohyocholic acid; GCA, glycocholic acid; TUDCA, tauroursodeoxycholic acid; TαMCA, tauro α-muricholic acid; THCA, taurohyocholic acid; TCA, taurocholic acid; alloLCA, allolithocholic acid; isoLCA, isolithocholic acid; LCA, lithocholic acid; NorDCA, 23-nordeoxycholic acid; 7-ketoLCA, 7-ketolithocholic acid; 12-ketoLCA, 12-ketolithocholic acid; CDCA, chenodeoxycholic acid; DCA, deoxycholic acid; GLCA, glycolithocholic acid; LCA-3S, lithocholic acid-3-sulfate; 6-ketoLCA, 6-ketolithocholic acid; βCDCA, 3β-chenodeoxycholic acid; βDCA, 3β-deoxycholic acid; UDCA, ursodeoxycholic acid; HDCA, α-hyodeoxycholic acid; NorCA, norcholic acid; 7-DHCA, 7-ketodeoxycholic acid; 3-DHCA, 3-dehydrocholic acid; βCA, 3β-cholic acid; βMCA, β-muricholic acid; HCA, hyocholic acid; CA, cholic acid; GCDCA, glycochenodeoxycholic acid; GDCA, glycodeoxycholic acid; TCDCA, taurochenodeoxycholic acid; TDCA, taurodeoxycholic acid; GLCA-3S, glycolithocholic acid-3-sulfate; CDCA-3Gln, chenodeoxycholic acid-3-β-d-glucuronide.

Table S4 Bile acids levels of mice (n=31)

Variables (nmol/l)	Control (n=8)	HS-water (n=7)	HS-hk AKK (n=8)	HS-AKK (n=8)	*P*
TUDCA§	4.8 (3.5, 5.6)	5.8 (5.4, 12.3)	5.3 (4.4, 6.2)	6 (5.3, 8.4)	0.237
THDCA§	4.9 (4.1, 5.8)	5.9 (4.7, 8.3)	3.9 (2.7, 5.9)	5.2 (3.8, 6.4)	0.340
TωMCA§	75.5 (58.9, 101.9)	66.5 (35.7, 71)	57.7 (24.6, 87.6)	98.2 (46.4, 146.5)	0.593
TαMCA§	42.6 (27.4, 61.6)	12.2 (8.9, 50.6)	16.5 (9.8, 25.2)	35.5 (25, 55.1)	0.230
TβMCA§	72.7 (42, 87.1)	53.6 (38.4, 172.3)	90.3 (49.9, 153.8)	192.5 (105.2, 437.9)	0.061
TCA§	34.7 (18.5, 40.3)	18.8 (7.8, 44.1)	22.8 (16.8, 33.1)	34 (27.7, 56.8)	0.816
LCA§	3.8 (3.4, 5.1)	5.3 (4.2, 6) ‡	3.3 (2.5, 4.3)	2.5 (2.2, 3.1)	0.009
NorDCA§	3.9 (2.8, 4.4)	9 (5.1, 12.1)	4.2 (2.7, 5.6)	2.7 (2.4, 3.7)	0.057
12_ketoLCA§	3.4 (2.7, 4.4)	4.8 (4.2, 5.8)	4.2 (2.5, 5)	2.7 (2.5, 3.2)	0.074
CDCA§	10.5 (5.6, 15.7)	13.1 (6.2, 16.1)	4.7 (1.8, 9.3)	4.2 (2.2, 7)	0.438
DCA§	35.5 (25.8, 124.7)	104.2 (65.9, 106.7)	43.2 (16.3, 92.3)	31.1 (24.7, 32.2)	0.082
UDCA§	18.9 (12.4, 31.2)	26.2 (10.3, 31.4)	9.2 (5.5, 19.1)	5.7 (4.7, 11.5)	0.095
HDCA§	9 (7.5, 14.6)	21.5 (10.9, 24.8) ‡	6 (4.6, 9.3)	4.8 (3.6, 6.2)	0.004
3_DHCA§	4.9 (3.9, 5.9)	3.7 (3.5, 4)	3.7 (3.3, 4.3)	3.5 (3.1, 3.7)	0.152
ωMCA§	185.7 (113.5, 228.4)	210.2 (147.4, 228.5)	87.2 (68.5, 110.9)	129.4 (100.2, 187.9)	0.048
αMCA§	12 (8.3, 15.5)	6.9 (4.6, 9.6)	3.6 (2.8, 7.3)	3.6 (3.2, 6.7)	0.062
βMCA§	101.3 (60, 188.6)	120.7 (90.7, 211.4)	88.1 (52.7, 125)	107.1 (93.4, 174.5)	0.669
ACA§	12.4 (7, 24.4)	13.2 (7.6, 23.2)	4.3 (2, 8.2)	6.3 (5, 8.5)	0.237
CA§	82 (28.7, 111.2)	32.2 (21.3, 64.4)	14.2 (4.3, 32.5)	4.4 (3, 24.3)	0.065
TCDCA§	4.3 (3.4, 5.6)	3.3 (2.8, 4.2)	3.4 (2.6, 4)	3.5 (3.1, 4.2)	0.639
TDCA§	8.1 (5.8, 16.5)	21 (9.4, 32.8)	9.9 (4.4, 23.6)	5 (4, 10.7)	0.246
UCA§	3.5 (2.9, 8.9)	3 (2.8, 3.4)	2.8 (2.6, 4.1)	3 (2.8, 4)	0.161
6_ketoLCA§	2.5 (2.2, 2.8)	2.8 (2.7, 3.5)	2.5 (2.2, 3.2)	2 (1.9, 2.4)	0.075
muroCA§	2.3 (2.2, 3.8)	6.5 (3.1, 8.2) ‡	2.8 (2.3, 4.3)	1.9 (1.8, 2)	0.054
βDCA§	1.9 (0.9, 3.4)	1.9 (1.7, 3)	1.7 (0.1, 3.6)	0.5 (0.3, 1.1)	0.149
HCA§	3.5 (2.5, 4.2)	1.3 (1.3, 1.6) †	1.4 (1.3, 1.4) †	1.6 (1.6, 1.8) †	< 0.001
βCDCA§	1.3 (0.6, 1.7)	3.6 (2.8, 4.5) †‡	1.8 (0.5, 3.6)	1.1 (0.9, 1.4)	0.028

Data are median (interquartile range). Statistical significance was determined with ANOVA with Bonferroni multiple-comparison analysis. § Log transformed before analysis. † vs control, $P < 0.05$; ‡, vs HS-AKK, $P < 0.05$. Mice fed the HS diet were treated with drinking water (HS-water) or water with viable (HS-AKK) or heat-killed A. muciniphila (HS-hk AKK). TUDCA, tauroursodeoxycholic acid; THDCA, taurohyodeoxycholic acid; T**ω**MCA, tauro ω- muricholate; TαMCA, tauro α-muricholate; TβMCA, tauro β-muricholate; TCA, taurocholic acid; LCA, lithocholic acid; NorDCA, 3α,12α-dihydroxynorcholanate\23-nordeoxycholic acid; 12_ketoLCA, 12-ketolithocholic acid; CDCA, chenodeoxycholic acid; DCA, deoxycholic acid; UDCA, ursodeoxycholic acid; HDCA, α-hyodeoxycholic acid; 3_DHCA, 3-dehydrocholic acid; **ω**MCA, **ω**-muricholic acid; aMCA, α-muricholic acid; bMCA, β-muricholic acid; ACA, Allocholic acid; CA, cholic acid; TCDCA, taurochenodeoxycholate; TDCA, taurodeoxycholate; UCA, ursocholic acid; 6_ketoLCA, 6-ketolithocholic acid;

muroCA, murocholic acid; βDCA, 3β-deoxycholic acid; HCA, γ- muricholic acid\hyocholic acid; βCDCA, 3β-chenodeoxycholic acid.

Table S5 The sequences of primers used in this study

Gene	Forward	Reverse
Akkermansia muciniphila	CAGCACGTGAAGGTGGGGAC	CCTTGCGGTTGGCTTCAGAT
mPGC1-α	AGACAAATGTGCTTCCAAAAAGAA	GAAGAGATAAAGTTGTTGGTTTGGC
mG6Pase	GTGGCAGTGGTCGGAGACT	ACGGGCGTTGTCCAAAC
mPEPCK	CACCATCACCTCCTGGAAGA	GGGTGCAGAATCTCGAGTTG
mFBP2	ACCCTGACCCGTTACGTTATG	ACATTCACGCTCCCCGAAATC
mCEBPα	TGGACAAGAACAGCAACGAGTAC	GCAGTTGCCCATGGCCTTGAC
mCEBPβ	CAAGCTGAGCGACGAGTACA	AGCTGCTCCACCTTCTTCTG
mCpt1	CAGAGGATGGACACTGTAAAGG	CGGCACTTCTTGATCAAGCC
mFoxo1	ACATTTCGTCCTCGAACCAGCTCA	ATTTCAGACAGACTGGGCAGCGTA
mPDK4	GATTGACATCCTGCCTGACC	CATGGAACTCCACCAAATCC
mGAPDH	TGATGGGTGTGAACCACGAG	GGGCCATCCACAGTCTTCTG
mFGF15	GAGGACCAAAACGAACGAAATT	ACGTCCTTGATGGCAATCG
mCyclophilin	GGAGATGGCACAGGAGGAA	GCCCGTAGTGCTTCAGCTT