

Supplementary Tables

Supplementary Table 1. The model parameters of OPLS-DA in different comparative groups

WTND	A	r2x	r2x(cum)	r2y	r2y(cum)	q2	q2(cum)
vs. WTHFD	p1	0.254	0.254	0.961	0.961	0.833	0.833
	o1	0.191	0.444	0.028	0.028	0.0483	0.0483
	sum		0.444		0.989		0.881
WTHFD vs.	A	r2x	r2x(cum)	r2y	r2y(cum)	q2	q2(cum)
	WTHFDH	p1	0.339	0.339	0.967	0.967	0.878
		o1	0.195	0.534	0.022	0.0223	0.0223
AbND	A	r2x	r2x(cum)	r2y	r2y(cum)	q2	q2(cum)
	vs.	p1	0.31	0.31	0.915	0.915	0.836
	AbHFD	o1	0.371	0.682	0.0716	0.0716	0.109
		sum		0.682		0.987	0.944
AbHFD	A	r2x	r2x(cum)	r2y	r2y(cum)	q2	q2(cum)
	vs. AbHFDH	p1	0.208	0.208	0.891	0.891	0.697
		o1	0.208	0.416	0.103	0.103	0.0813
		sum		0.416		0.994	0.778
AbND	A	r2x	r2x(cum)	r2y	r2y(cum)	q2	q2(cum)
	vs. WTND	p1	0.249	0.249	0.872	0.872	0.764
		o1	0.355	0.604	0.122	0.122	0.156
		sum		0.604		0.994	0.919
AbHFD	A	r2x	r2x(cum)	r2y	r2y(cum)	q2	q2(cum)
	vs. WTHFD	p1	0.312	0.312	0.975	0.975	0.911
		o1	0.081	0.393	0.0242	0.0242	0.0281
		sum		0.393		0.999	0.939
AbHFDH vs.	A	r2x	r2x(cum)	r2y	r2y(cum)	q2	q2(cum)
	WTHFDH	p1	0.317	0.317	0.983	0.983	0.897
		o1	0.105	0.421	0.0157	0.0157	0.027
		sum		0.421		0.999	0.924

Supplementary Table 2. Relative abundance of OTUs showing differences between HFD and HFD+FBT groups in healthy mice

OUT ID	Relative abundance (%)			P value*			
	WTND	WTHFD	WTHFDH	ND	HFD	HFDH	sign
				vs.	HFD	HFDH	
OTU12 // Parabacteroides_goldsteinii	7.53	1.66	1.97	0.0390	1.0000	0.0520	☆
OTU593 // uncultured_bacterium_g_norank_f_Bacteroidales_S24-7_group	21.77	0.35	0.38	0.0090	1.0000	0.0120	
OTU594 // uncultured_bacterium_g_norank_f_Bacteroidales_S24-7_group	0.84	0.01	0.01	0.0080	1.0000	0.0130	
OTU600 // Lactobacillus_johnsonii	0.83	0.41	1.55	/	/	/	
OTU420 // unclassified_f_Erysipelotrichaceae	0.59	0.10	0.49	/	/	/	
OTU276 // Bacteroides_thetaiotaomicron	4.90	12.88	13.01	0.0170	1.0000	0.0280	
OTU415 // uncultured_bacterium_g_Lachnospiraceae_UCG-006	0.18	0.79	0.40	0.0050	0.4790	0.2510	☆
OTU401 // unclassified_g_[Eubacterium]_nodatum_group	0.08	0.90	0.50	0.0110	1.0000	0.0450	
OTU435 // unclassified_g_Lactobacillus	0.04	0.60	0.12	0.0090	0.5550	0.2970	☆
OTU270 // [Clostridium]_leptum_g_Ruminococcaceae_UCG-009	0.43	1.94	1.20	0.0030	0.4790	0.1750	☆
OTU443 // uncultured_bacterium_g_Intestinimonas	0.18	0.98	0.56	0.0040	0.5830	0.1550	☆
OTU461 // uncultured_bacterium_g_norank_f_Lachnospiraceae	0.02	0.94	0.49	0.0020	0.7000	0.0910	
OTU307 // unclassified_f_Ruminococcaceae	0.12	0.61	0.46	0.0070	1.0000	0.0240	
OTU442 // unclassified_g_Oscillibacter	0.08	0.49	0.30	0.0020	0.9130	0.0600	
OTU249 // uncultured_bacterium_g_Intestinimonas	0.30	0.45	0.42	/	/	/	
OTU465 // uncultured_bacterium_g_Lachnospiraceae_FCS020_group	0.22	0.35	0.24	/	/	/	
OTU416 // unclassified_g_Ruminiclostridium_5	0.21	0.93	0.11	0.1200	0.0090	1.0000	☆
OTU494 // Anaerotruncus_sp_G3_2012	0.22	0.72	0.15	0.1200	0.0090	1.0000	☆
OTU391 // unclassified_g_Blautia	0.35	3.59	0.64	/	/	/	
OTU366 // unclassified_g_Desulfovibrio	0.00	0.17	0.00	/	/	/	

OTU447 // uncultured_organism_g_Ruminococcaceae_UCG-010	0.08	0.23	0.34	/	/	/	
OTU438 // unclassified_f_Ruminococcaceae	0.09	0.07	0.21	/	/	/	
OTU121 // uncultured_bacterium_g_Lachnospiraceae_NK4A136_group	0.27	0.11	0.68	1.0000	0.0090	0.1190	★
OTU578 // unclassified_g_Alistipes	0.15	0.06	0.32	1.0000	0.0360	0.3390	★
OTU572 // uncultured_bacterium_g_norank_f_Lachnospiraceae	0.44	0.09	0.72	/	/	/	
OTU545 // uncultured_organism_g_[Eubacterium]_ventriosum_group	0.05	0.12	0.16	1.0000	0.0690	0.1540	
OTU454 // uncultured_bacterium_g_norank_f_Bacteroidales_S24-7_group	0.40	0.22	1.15	0.9130	0.0020	0.0600	★
OTU323 // uncultured_Bacteroidales_bacterium_g_norank_f_Bacteroidales_S24-7_group	0.00	1.25	12.01		1.0000	0.0050	0.0100
OTU389 // uncultured_bacterium_g_Clostridium_sensu_stricto_1	0.03	0.02	0.30	1.0000	0.0140	0.0270	★
OTU369 // uncultured_bacterium_g_norank_f_Lachnospiraceae	0.10	0.59	0.88	0.0910	0.7020	0.0025	
OTU577 // unclassified_g_Lachnospiraceae_NK4A136_group	0.09	0.37	0.99	0.0980	1.0000	0.0110	
OTU529 // unclassified_f_Lachnospiraceae	0.28	1.61	1.95	0.0330	1.0000	0.0030	
OTU274 // unclassified_g_norank_f_Lachnospiraceae	0.11	1.18	0.65	0.1050	1.0000	0.0850	
OTU456 // unclassified_g_norank_f_Clostridiales_vadinBB60_group	0.02	0.11	0.14	0.2460	0.9440	0.0180	
OTU412 // unclassified_f_Lachnospiraceae	0.02	0.03	0.71	1.0000	0.0550	0.0050	
OTU557 // unclassified_g_norank_f_Lachnospiraceae	0.09	0.10	0.24	/	/	/	
OTU320 // uncultured_bacterium_g_Lachnospiraceae_NK4A136_group	0.01	0.01	2.57	1.0000	0.0270	0.0020	★
OTU352 // unclassified_g_norank_f_Clostridiales_vadinBB60_group	0.04	0.06	0.27	/	/	/	

Note: The OTUs significantly increased in group WTHFDH compared to WTHFD or significantly decreased in group WTHFD compared to WTND are shown in red; On the contrary, the OTUs are shown in green; The OTUs significantly increased in group WTHFDH, in which significantly decreased in group WTHFD are shown signed with "★", while those insignificantly decreased in group WTHFD yet insignificantly changed in group WTHFDH compared to WTND are signed with "☆". On the contrary, the OTUs are shown in green with "★" or green with "☆". Other OTUs that had no significant changes are shown in grey. *P values were calculated using Kruskal-Wallis test with Bonferroni's correction. Significant P values (<0.05) are shown in red, yellow, or green.

Supplementary Table 3. Relative abundance of matabolites showing differences between HFD and HFD+FBT groups in healthy mice

Metabolites	Relative abundance (%)			P value*			HFD vs. ND		HFDH vs. HFD		
	WTND	WTHFD	WTHFDH	HFD	HFDH	HFDH	Effect	Trend	Fold	Trend	Fold
				vs. ND	vs. HFD	vs. ND	of FBT	change	change	change	change
LysoPC(P-16:0)	0.61	0.58	0.47	/	/	/		↓	0.96	↓	0.81
Bis(2-ethylhexyl) phthalate	0.46	0.35	0.19	0.703	0.281	0.012		↓	0.75	↓	0.55
10,11-dihydro-20-trihydroxy-leukotriene B4	3.61	1.46	0.46	0.351	0.175	0.002		↓	0.40	↓	0.32
Aliskiren	2.79	1.65	0.92	0.390	0.136	0.001		↓	0.59	↓	0.56
LysoPE(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	7.30	7.25	5.44	1.000	0.092	0.080		↓	0.99	↓	0.75
LysoPC(22:5(4Z,7Z,10Z,13Z,16Z))	6.19	6.10	4.91	/	/	/		↓	0.98	↓	0.81
PE(18:0/0:0)	5.05	4.99	3.89	1.000	0.120	0.039		↓	0.99	↓	0.78
LysoPE(18:0/0:0)	3.54	6.05	5.41	/	/	/		↑	1.71	↓	0.89
Oleamide	0.52	0.60	0.14	1.000	0.011	0.017	☆	↑	1.15	↓ *	0.23
Janthitrem C	1.09	0.71	0.89	/	/	/		↓	0.65	↑	1.26
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:2(9Z,12Z))	0.63	0.39	0.58	0.013	0.027	0.787	★	↓ *	0.61	↑ *	1.49
PC(20:3(8Z,11Z,14Z)/16:0)	0.71	0.50	0.64	0.028	0.223	1.000	☆	↓ *	0.71	↑	1.27
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/20:4(5Z,8Z,11Z,14Z))	0.36	0.16	0.27	0.021	0.198	1.000	☆	↓ *	0.44	↑	1.68
LysoPC(22:5(7Z,10Z,13Z,16Z,19Z))	1.38	0.88	1.44	/	/	/		↓	0.64	↑	1.64
LysoPC(20:3(5Z,8Z,11Z))	13.22	10.06	13.41	0.092	0.052	1.000		↓	0.76	↑	1.33
Lactosylceramide (d18:1/12:0)	1.15	0.95	1.26	0.175	0.060	1.000		↓	0.83	↑	1.32
LysoPC(22:1(13Z))	0.30	0.08	0.07	0.024	1.000	0.004		↓ *	0.26	↓	0.93
LysoPE(20:1(11Z)/0:0)	3.15	1.58	1.60	/	/	/		↓	0.50	↑	1.01
LysoPC(18:1(11Z))	10.85	7.19	7.36	/	/	/		↓	0.66	↑	1.02
1-Heptadecanoylglycerophosphoethanolamine	0.67	0.34	0.38	0.015	0.838	0.251	☆	↓ *	0.51	↑	1.11

LysoPC(16:1(9Z))		14.85	4.82	4.92	0.006	1.000	0.017		↓ **	0.32	↑ 1.02
PC(20:2(11Z,14Z)/14:1(9Z))		1.05	0.47	0.52	0.003	1.000	0.033		↓ **	0.45	↑ 1.09
PC(20:4(5Z,8Z,11Z,14Z)/16:1(9Z))		0.81	0.36	0.42	0.002	0.768	0.069	☆	↓ **	0.44	↑ 1.17
LysoPC(20:1(11Z))		1.07	0.40	0.43	0.002	0.991	0.045		↓ **	0.38	↑ 1.07
6-(4-ethyl-3-hydroxyphenoxy)-3,4,5-trihydroxyoxane-2-carboxylic acid		0.28	0.06	0.13	0.000	0.136	0.198	☆	↓ ***	0.22	↑ 2.09
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/16:1(9Z))		0.67	0.25	0.33	0.003	0.479	0.175	☆	↓ **	0.37	↑ 1.33
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:1(9Z))		0.35	0.13	0.17	0.001	0.251	0.175	☆	↓ **	0.36	↑ 1.33
LysoPC(20:4(5Z,8Z,11Z,14Z))		28.24	26.45	31.41	0.641	0.005	0.175	☆	↓	0.94	↑ ** 1.19
LysoPC(20:4(8Z,11Z,14Z,17Z))		3.65	4.15	5.78	1.000	0.060	0.007		↑	1.14	↑ 1.39
PE(18:1(9Z)/0:0)		3.54	6.05	5.41	0.006	1.000	0.069	☆	↑ **	1.71	↓ 0.89
1-Linoleoylglycerophosphocholine		47.08	52.04	52.13	0.092	1.000	0.033		↑	1.11	↑ 1.00
3a,7a-Dihydroxy-5b-cholestane		0.36	0.62	0.64	0.092	1.000	0.033		↑	1.73	↑ 1.03
1-Hydroxy-2,12,15-heneicosatrien-4-one		0.07	0.09	0.18	0.991	0.314	0.028		↑	1.38	↑ 1.98
Asn Lys Ala Val Gly		0.12	0.50	0.54	0.039	1.000	0.002		↑ *	4.14	↑ 1.09
Cytochalasin Ppho		0.02	0.34	0.36	0.028	1.000	0.004		↑ ***	22.13	↑ 1.08
3-Indolepropionic acid		0.03	0.02	0.04	0.390	0.002	0.198	☆	↓	0.69	↑ ** 1.83

Note: Trend ↑ , ↓ denote that the metabolite content increased and decreased, respectively. * denotes that the difference is significant ($p < 0.05$), **denotes that the difference is highly significant ($p < 0.01$), and *** denotes that the difference is highly significant ($p < 0.001$).The metabolites significantly increased in group WTHFDH or significantly decreased in group WTHFD,in which different changes of metabolites exist in WTHFDH and WTDN groups compared with group WTHFD,are shown in red; On the contrary, the metabolites are shown in green; The metabolites significantly increased in group WTHFDH while significantly decreased in group WTHFD are shown in red with "★".On the contrary, the metabolites are shown in green with "★". The metabolites shown in red or green towards or beyond the levels in group WTND are signed with "☆". Other metabolites that had no significant changes are shown in grey. *P values were calculated using Kruskal–Wallis test with Bonferroni's correction. Significant P values (<0.05) are shown in red, yellow,or green.

Supplementary Table 4. Relative abundance of matabolics showing differences between HFD and HFD+FBTgroups in microbiota-depleted mice

metabolites	Relative abundance (%)			P value*`			AbHFD vs.		AbHFDH vs.		
	AbND	AbHFD	AbHFDH	HFD	HFDH	HFDH	Effect	Trend	Fold	Trend	Fold
				vs.	vs.	vs.	of	change	change	change	change
				ND	HFD	ND	FBT				
LysoPC(16:1(9Z))	11.39	3.29	3.03	0.036	1.000	0.004		↓**	0.29	↓	0.92
1-Linoleoylglycerophosphocholine	41.26	50.42	51.24	0.026	1.000	0.019		↑*	1.22	↑	1.02
LysoPC(18:1(11Z))	8.41	6.13	6.22	/	/	/		↓	0.73	↑	1.02
PE(18:1(9Z)/0:0)	2.71	3.32	4.78	1.000	0.109	0.011		↑	1.23	↑	1.44
10,11-dihydro-20-trihydroxy-leukotriene B4	1.58	0.26	0.23	0.067	1.000	0.010		↓	0.16	↓	0.89
LysoPE(20:1(11Z)/0:0)	2.34	1.25	1.18	/	/	/		↓	0.53	↓	0.94
Aliskiren	1.53	1.06	0.64	/	/	/		↓	0.69	↓	0.60
LysoPC(20:1(11Z))	0.66	0.30	0.25	/	/	/		↓	0.46	↓	0.82
PC(20:2(11Z,14Z)/14:1(9Z))	0.89	0.31	0.28	/	/	/		↓**	0.34	↓	0.90
PC(20:4(5Z,8Z,11Z,14Z)/16:1(9Z))	0.72	0.24	0.23	0.049	1.000	0.015		↓*	0.34	↓	0.94
Asn Lys Ala Val Gly	0.08	0.29	0.28	0.005	1.000	0.035		↓***	3.67	↓	0.94
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/16:1(9Z))	0.77	0.26	0.16	1.000	0.059	0.007		↓	0.33	↓	0.64
Cytochalasin Ppho	0.01	0.18	0.16	0.006	1.000	0.029		↑***	25.13	↓	0.86
1-Heptadecanoylglycerophosphoethanolamine	0.54	0.26	0.25	/	/	/		↓	0.48	↓	0.96
6-(4-ethyl-3-hydroxyphenoxy)-3,4,5-trihydroxyoxane-2-carboxylic acid	0.18	0.18	0.25	/	/	/		↑	1.04	↑	1.39
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:1(9Z))	0.28	0.13	0.12	/	/	/		↓	0.47	↓	0.87
LysoPC(22:1(13Z))	0.18	0.05	0.04	/	/	/		↓*	0.31	↓	0.83
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:2(9Z,12Z))	0.67	0.40	0.29	/	/	/		↓	0.59	↓	0.73
3a,7a-Dihydroxy-5b-cholestane	0.27	0.97	0.96	0.013	1.000	0.023		↑*	3.57	↓	0.99

LysoPC(20:4(5Z,8Z,11Z,14Z))	27.63	31.12	29.08	/	/	/	↑	1.13	↓	0.93
LysoPC(20:3(5Z,8Z,11Z))	12.73	11.08	9.51	/	/	/	↓	0.87	↓	0.86
LysoPE(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	4.61	6.12	5.23	/	/	/	↑	1.33	↓	0.85
LysoPC(20:4(8Z,11Z,14Z,17Z))	3.77	5.17	5.03	/	/	/	↑	1.37	↓	0.97
LysoPC(22:5(4Z,7Z,10Z,13Z,16Z))	4.11	4.42	4.64	/	/	/	↑	1.07	↑	1.05
LysoPE(18:0/0:0)	4.11	4.42	4.64	/	/	/	↑	1.07	↑	1.05
PE(18:0/0:0)	3.96	3.83	4.16	/	/	/	↓	0.97	↑	1.09
LysoPC(22:5(7Z,10Z,13Z,16Z,19Z))	1.66	1.46	1.19	/	/	/	↓	0.88	↓	0.81
Oleamide	2.48	1.61	2.26	/	/	/	↓	0.65	↑	1.40
Lactosylceramide (d18:1/12:0)	1.14	0.98	0.82	/	/	/	↓	0.87	↓	0.83
Janthitrem C	1.40	1.28	1.03	/	/	/	↓	0.92	↓	0.80
Bis(2-ethylhexyl) phthalate	1.28	0.49	0.46	0.026	1.000	0.019	↓*	0.38	↓*	0.95
PC(20:3(8Z,11Z,14Z)/16:0)	0.71	0.44	0.42	/	/	/	↓	0.63	↓	0.95
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/20:4(5Z,8Z,11Z,14Z))	0.42	0.19	0.12	/	/	/	↓	0.45	↓	0.62
LysoPC(P-16:0)	0.37	0.41	0.42	/	/	/	↑	1.09	↑	1.03
1-Hydroxy-2,12,15-heneicosatrien-4-one	0.06	0.27	0.33	0.026	1.000	0.006	↑*	4.29	↑	1.21
3-Indolepropionic acid	0.00	0.00	0.00	1.000	0.021	0.062	↑	1.13	↑*	1.79

Note: Trend ↑, ↓ denote that the metabolite content increased and decreased, respectively. * denotes that the difference is significant ($p < 0.05$), **denotes that the difference is highly significant ($p < 0.01$), and *** denotes that the difference is highly significant ($p < 0.001$).The metabolites significantly increased in group WTHFDH or significantly decreased in group WTHFD,in which different changes of metabolites exist in WTHFDH and WTDN groups compared with group WTHFD,are shown in red; On the contrary, the metabolites are shown in green; The metabolites significantly increased in group WTHFDH while significantly decreased in group WTHFD are shown in red with "★".On the contrary, the metabolites are shown in green with "★". The metabolites shown in red or green towards or beyond the levels in group WTND are signed with "☆". Other metabolites that had no significant changes are shown in grey. *P values were calculated using Kruskal-Wallis test with Bonferroni's correction. Significant P values (<0.05) are shown in red, yellow,or green.

	AbND	AbHFD	AbHFDH	WTND	WTHFD	WTHFDH	lower(AB vs. WT)			
PC(20:2(11Z,14Z)/14:1(9Z))	0.89	0.31	0.28	1.05	0.47	0.52	0.15	0.35	0.46	0.32
LysoPC(20:1(11Z))	0.66	0.30	0.25	1.07	0.40	0.43	0.38	0.25	0.42	0.35

3-Indolepropionic acid	0.00	0.00	0.00	0.03	0.02	0.04	0.96	0.94	0.94	0.94
PC(20:4(5Z,8Z,11Z,14Z)/16:1(9Z))	0.72	0.24	0.23	0.81	0.36	0.42	0.11	0.32	0.46	0.30
LysoPE(20:1(11Z)/0:0)	2.34	1.25	1.18	3.15	1.58	1.60	0.26	0.21	0.26	0.24
LysoPC(16:1(9Z))	11.39	3.29	3.03	14.85	4.82	4.92	0.23	0.32	0.38	0.31
1-Heptadecanoylglycerophosphoethanolamine	0.54	0.26	0.25	0.67	0.34	0.38	0.20	0.26	0.35	0.27

Supplementary Table 5. Metabolites values involved in glycerophospholipid metabolism showing differences between HFD and HFD+FBT groups in healthy mice and microbiota-depleted mice

Metabolites	Average values			P value*		Average values			P value*	
	WTND	WTHFD	WTHFDH	WTHFD		AbND	AbHFD	AbHFDH	AbHFD	
				vs.	vs.				vs.	vs.
				WTND	WTHFD				AbND	AbHFD
C04230 (1-Acyl-sn-glycero-3-phosphocholine)	80.52	72.35	85.67	0.3481	0.0804	77.94	81.91	74.83	0.9463	0.8403
C00157 (Phosphatidylcholine)	5.937	3.548	4.392	0.0009	0.2606	5.905	3.337	2.86	0.0916	0.9073
C00350 (Phosphatidylethanolamine)	4.507	4.686	4.481	0.8626	0.8233	3.975	3.882	3.893	0.9923	>0.9999

Note: *P values were calculated using Tukey's HSD test. Significant P values (<0.05) are shown in grey.

Supplementary Table 6. Primer sequences for qRT-PCR analysis, related to Figures 8

Genes	Forward Primer Sequence	Reverse Primer Sequence
<i>AhR</i>	ACCGGCTGAACACAGAGTTA	CCATTCA CGGCCATCAAAGA
<i>Cyp1a1</i>	CAGGCTGACTCTGAACTTGC	AGACCAAGAGCTGATGCAGT
<i>Pemt</i>	AGCAGAGAACTCGGAAGCTG	CCAGGAAGTAGGTGGTGTTGG
<i>Fasn</i>	TCGGGTGTGGTGGTTGGT	GGCGTGAGATGTGTTGCTGAGG
<i>β-actin</i>	GCTGTCCCTGTATGCCTCTG	TGATGTCACGCACGATTCC