

Untargeted metabolomics analysis reveals spatial metabolic heterogeneity in different intestinal segments of type 1 diabetic mice

Kaiyan Gong¹, Junli Chen¹, Xiaoli Yin¹, Mengjun Wu¹, Hong Zheng^{1,*} & Lingling Jiang^{2,3*}

¹School of Pharmaceutical Sciences, Wenzhou Medical University, Wenzhou 325035, China

²College of Science and Technology, Wenzhou-Kean University, Wenzhou 325060, China

³Wenzhou Municipal Key Laboratory for Applied Biomedical and Biopharmaceutical Informatics, Wenzhou-Kean University, Wenzhou 325060, China

*Corresponding author:

E-mail: 123zhenghong321@163.com (H.Z.); jianglingling@wku.edu.cn (L.L.J.).

Table S1. The detailed information on differential metabolites in the jejunum between T1D mice and age-matched controls.

Name	Mass (m/z)	RT (min)	Adducts	Formula	VIP	<i>p</i>	FC	KEGG	HMDB
S-Adenosyl-L-methionine	399.1436	12.44	M+H	C ₁₅ H ₂₂ N ₆ O ₅ S	1.39	0.00207	0.56	C00019	HMDB0001185
γ-Glutamylleucine	259.1292	8.17	M-H	C ₁₁ H ₂₀ N ₂ O ₅	3.49	0.00298	2.55	-	HMDB0011171
γ-Glutamyltyrosine	311.1233	9.10	M+H	C ₁₄ H ₁₈ N ₂ O ₆	1.32	0.00285	2.25	-	HMDB0011741
Serine	104.0353	9.94	M-H	C ₃ H ₇ NO ₃	1.20	0.00441	1.47	C00065	HMDB0000187
3-Sulfinio-L-alanine	152.0025	6.17	M-H	C ₃ H ₇ NO ₄ S	1.49	0.00015	0.28	C00606	HMDB0000996
Creatine	130.0615	9.38	M-H	C ₄ H ₉ N ₃ O ₂	1.58	<0.00001	0.54	C00300	HMDB0000064
L-Homoserine	102.0535	9.54	M-H ₂ O+H	C ₄ H ₉ NO ₃	1.03	0.00206	1.79	C00263	HMDB0000719
Betaine	118.0867	8.30	M+H	C ₅ H ₁₁ NO ₂	5.32	0.00056	0.61	-	HMDB0000043
L-Methionine	148.0443	8.18	M-H	C ₅ H ₁₁ NO ₂ S	2.04	0.00804	1.91	C00073	HMDB0000696
L-Proline	114.0565	8.65	M-H	C ₅ H ₉ NO ₂	1.73	0.00016	1.96	C00763	HMDB0003411
Pyroglutamic acid	128.0346	9.56	M-H	C ₅ H ₇ NO ₃	2.19	0.00299	1.79	C01879	HMDB0000267
L-Glutamate	148.0603	9.56	M+H	C ₅ H ₉ NO ₄	2.59	0.00168	1.92	C00025	HMDB0000148
L-Pipecolate	130.0870	11.95	M+H	C ₆ H ₁₁ NO ₂	4.07	0.00919	1.97	C00408	HMDB0000070
L-Lysine	147.1122	11.95	M+H	C ₆ H ₁₄ N ₂ O ₂	3.57	0.00858	1.99	C00047	HMDB0000182
Glycyl-isoleucine	187.1094	8.93	M-H	C ₈ H ₁₆ N ₂ O ₃	1.77	0.00532	4.95	-	HMDB0028844

L-Cystine	258.0644	9.00	M+NH ₄	C ₆ H ₁₂ N ₂ O ₄ S ₂	1.13	0.00706	0.43	C00491	HMDB0000192
L-Arginine	175.1195	11.82	M+H	C ₆ H ₁₄ N ₄ O ₂	10.97	0.00928	2.80	C00062	HMDB0000517
L-Histidine	154.0617	11.82	M-H	C ₆ H ₉ N ₃ O ₂	4.17	0.00844	1.62	C00135	HMDB0000177
L-Phenylalanine	164.0708	7.66	M-H	C ₉ H ₁₁ NO ₂	6.02	0.00909	1.55	C00079	HMDB0000159
L-Tyrosine	181.0709	8.47	M-H	C ₉ H ₁₁ NO ₃	1.56	0.00429	2.05	C00082	HMDB0000158
L-Lysopine	217.1193	8.77	M-H	C ₉ H ₁₈ N ₂ O ₄	2.10	0.00409	8.26	-	HMDB0033675
Coumarate	163.0398	8.46	M-H	C ₉ H ₈ O ₃	1.20	0.00466	1.97	C01772	HMDB0002641
(9Z)-Octadecenoic acid	265.2513	3.29	M-H ₂ O+H	C ₁₈ H ₃₄ O ₂	3.23	0.00057	7.18	-	HMDB0245277
Myristic acid	227.2015	3.33	M-H	C ₁₄ H ₂₈ O ₂	2.32	0.00271	7.08	C06424	HMDB0000806
(9Z)-Hexadecenoic acid	253.2171	3.31	M-H	C ₁₆ H ₃₀ O ₂	4.93	0.00201	17.41	C08362	HMDB0003229
Hexadecanal	263.2364	3.33	M+Na	C ₁₆ H ₃₂ O	4.74	0.00092	3.71	C00517	HMDB0001551
(9Z,12Z,15Z)-Octadecatrienoic acid	277.2174	3.36	M-H	C ₁₈ H ₃₀ O ₂	3.17	0.00607	2.72	-	HMDB0255900
Vaccenic acid	281.2489	3.24	M-H	C ₁₈ H ₃₄ O ₂	8.49	0.00695	3.85	C08367	HMDB0003231
cis-9,10-Epoxy stearic acid	299.2559	3.41	M+H	C ₁₈ H ₃₄ O ₃	1.18	0.00041	2.01	C19418	HMDB0247617
9,10-Dhome	314.2400	4.12	M-H	C ₁₈ H ₃₂ O ₄	1.01	0.00087	4.62	C14830	HMDB0004706
Oleamide	282.2803	3.35	M+H	C ₁₈ H ₃₅ NO	3.49	0.00021	0.40	C19670	HMDB0002117
15-Deoxy- δ -12,14-PGJ2	317.2112	4.24	M+H	C ₂₀ H ₂₈ O ₃	2.96	0.00007	0.44	C14717	HMDB0005079

δ-12-ProstaglandinJ2	352.2484	4.24	M+NH ₄	C ₂₀ H ₃₀ O ₄	1.22	0.00071	0.50	C05958	HMDB0004238
14,15-DiHETrE	319.2291	3.65	M-H ₂ O-H	C ₂₀ H ₃₄ O ₄	2.22	0.00046	0.48	C14775	HMDB0002265
Erucamide	338.3298	3.28	M+H	C ₂₂ H ₄₃ NO	2.00	0.00021	1.52	-	HMDB0244507
Stearidonic acid	277.2156	3.52	M+H	C ₁₈ H ₂₈ O ₂	2.98	0.00865	1.76	C16300	HMDB0006547
Arachidonoyl carnitine	448.3407	6.03	M+H	C ₂₇ H ₄₆ NO ₄	1.35	0.00882	0.64	-	HMDB0006455
MG 18:1	357.2997	3.29	M+H	C ₂₁ H ₄₀ O ₄	4.64	0.00052	12.74	-	HMDB0011567
Adenine	134.0477	7.17	M-H	C ₅ H ₅ N ₅	2.19	0.00679	0.13	C00147	HMDB0000034
L-Tryptophan	203.0835	7.68	M-H	C ₁₁ H ₁₂ N ₂ O ₂	1.36	0.00407	2.94	C00078	HMDB0000929
Phosphate	96.9602	10.31	M-H	H ₃ PO ₄	2.79	0.00253	2.08	C00009	HMDB0001429
Taurine	126.0218	8.56	M+H	C ₂ H ₇ NO ₃ S	3.04	0.00022	0.58	C00245	HMDB0000251
Ethanolamine	84.0436	9.55	M+Na	C ₂ H ₇ NO	1.80	0.00155	1.88	C00189	HMDB0000149
Cholinephosphate	184.0740	10.23	M+H	C ₅ H ₁₅ NO ₄ P	11.09	0.00496	0.56	C00588	HMDB0001565
D-Fructose-1-phosphate	259.0142	7.05	M-H	C ₆ H ₁₃ O ₉ P	1.09	0.00190	0.44	-	HMDB0060467
Arabinosyluracil	243.0616	6.77	M-H	C ₉ H ₁₂ N ₂ O ₆	3.24	0.00053	0.50	C00019	HMDB0246131

Table S2. The detailed information on differential metabolites in the ileum between T1D mice and age-matched controls.

Name	Mass (m/z)	RT (min)	Adducts	Formula	VIP	<i>p</i>	FC	KEGG	HMDB
5'-Methylthioadenosine	298.0954	5.94	M+H	C ₁₁ H ₁₅ N ₅ O ₃ S	1.28	0.00673	1.92	C00170	HMDB0001173
Creatine	130.0624	9.37	M-H	C ₄ H ₉ N ₃ O ₂	2.27	0.00035	0.63	C00300	HMDB0000064
Betaine	235.1661	8.29	2M+H	C ₅ H ₁₁ NO ₂	10.23	0.00252	0.31	-	HMDB0000043
Ornithine	133.0983	12.13	M+H	C ₅ H ₁₂ N ₂ O ₂	1.08	0.00366	1.47	C00077	HMDB0000214
<i>N</i> -Acetyl-L-glutamic acid	188.0566	5.94	M-H	C ₇ H ₁₁ NO ₅	1.42	0.02270	1.71	C00624	HMDB0001138
S-Carboxymethyl-L-cysteine	178.0194	6.33	M-H	C ₅ H ₉ NO ₄ S	1.28	0.03469	0.58	-	HMDB0029415
<i>N</i> -Methyl-L-proline	152.0208	9.36	M+Na	C ₆ H ₁₁ NO ₂	1.13	0.00039	0.66	-	HMDB0094696
L-Cystine	258.0647	8.99	M+NH ₄	C ₆ H ₁₂ N ₂ O ₄ S ₂	1.83	0.00204	0.47	C00491	HMDB0000192
N ₆ -Methyl-L-lysine	161.1277	12.18	M+H	C ₇ H ₁₆ N ₂ O ₂	1.02	0.00387	0.43	C02728	HMDB0002038
Symmetric dimethylarginine	201.1350	11.22	M-H	C ₈ H ₁₈ N ₄ O ₂	1.11	0.06739	0.74	-	HMDB0003334
3-Chloro-L-tyrosine	214.0244	9.34	M-H	C ₉ H ₁₀ ClNO ₃	2.32	0.00574	0.61	-	HMDB0001885
L-Lysopine	217.1189	11.30	M-H	C ₉ H ₁₈ N ₂ O ₄	1.18	0.00068	2.22	-	HMDB0033675
Thiamine	265.2513	3.28	M+H	C ₁₂ H ₁₇ N ₄ OS	3.13	0.00003	2.57	C00378	HMDB0000235
L-Octanoylcarnitine	310.1983	6.32	M+Na	C ₁₅ H ₂₉ NO ₄	1.00	0.00592	0.55	C02838	HMDB0000791
Hexadecenoic acid	253.2173	3.28	M-H	C ₁₆ H ₃₀ O ₂	7.34	0.00067	12.53	C08362	HMDB0003229

Isopalmitic acid	279.2318	2.82	M+Na	C ₁₆ H ₃₂ O ₂	1.06	0.00421	3.02	-	HMDB0031068
FA 17:3;O	279.1967	3.81	M-H	C ₁₇ H ₂₈ O ₃	1.88	0.06558	0.78	-	-
Linolenic acid	279.2318	3.44	M+H	C ₁₈ H ₃₀ O ₂	4.36	0.00005	1.99	C06427	HMDB0001388
FA 18:3;(2OH)	293.2120	3.42	M+FA-H	C ₁₈ H ₃₀ O ₃	1.97	0.00458	2.02	-	-
FA 18:2;O	295.2286	3.38	M-H	C ₁₈ H ₃₂ O ₃	2.32	0.00205	3.14	C14762	HMDB0004667
13-HPODE	311.2229	4.13	M-H	C ₁₈ H ₃₂ O ₄	1.14	0.07900	1.66	-	HMDB0062637
9,12,13-trihydroxyoctadeca-10,15-dienoic acid	472.3196	4.19	M+H	C ₁₈ H ₃₂ O ₅	1.36	0.00101	0.63	-	HMDB0241542
FA 18:1	281.2498	3.23	M-H	C ₁₈ H ₃₄ O ₂	13.04	0.00066	3.16	-	-
FA 18:1;1O	297.2454	3.38	M-H	C ₁₈ H ₃₄ O ₃	1.61	0.00222	2.57	-	-
FA 18:1;2O	313.2373	4.12	M-H	C ₁₈ H ₃₄ O ₄	2.21	0.06920	3.23	C14829	HMDB0004705
9,12,13-trihydroxyoctadec-15-enoic acid	353.2668	3.43	2M+NH ₄	C ₁₈ H ₃₄ O ₅	2.45	0.00273	2.02	-	-
Arachidonic acid	303.2344	3.24	M-H	C ₂₀ H ₃₂ O ₂	6.13	0.07809	0.75	C00219	HMDB0001043
Icosatrienoic acid	305.2473	3.27	M-H	C ₂₀ H ₃₄ O ₂	2.15	0.06062	0.74	C03242	HMDB0002925
Icosenoic acid	309.2792	3.19	M-H	C ₂₀ H ₃₈ O ₂	2.72	0.00033	5.17	C16526	HMDB0002231
Docosahexaenoic acid	327.2337	3.21	M-H	C ₂₂ H ₃₂ O ₂	1.76	0.00073	0.51	-	HMDB0251558
3-Hydroxyisovaleric acid	117.0549	5.19	M-H	C ₅ H ₁₀ O ₃	1.04	0.00012	0.24	-	HMDB0000754

2-Methylglutaric acid	145.0512	5.33	M-H	C ₆ H ₁₀ O ₄	2.22	0.02486	0.54	-	HMDB0000422
1-Oleoyl monoglyceride	357.3020	3.28	M+H	C ₂₁ H ₄₀ O ₄	4.65	0.00001	3.54	-	HMDB0011567
DG 34:2	610.5395	2.81	M+NH ₄	C ₃₇ H ₆₈ O ₅	1.29	0.00768	2.45	-	HMDB0007215
DG 40:7	684.5492	2.79	M+ACN+H	C ₄₃ H ₇₀ O ₅	1.46	0.00184	0.31	-	-
LPE 13:1	408.2200	4.15	M+FA-H	C ₁₈ H ₃₆ NO ₇ P	1.19	0.01061	0.62	-	-
LPE 13:0	410.2358	4.14	M+FA-H	C ₁₈ H ₃₈ NO ₇ P	2.50	0.00142	0.48	-	-
LPE 14:0	424.2563	5.50	M-H	C ₁₉ H ₄₀ NO ₇ P	2.07	0.00440	0.55	-	HMDB0011500
LPA 17:0	423.2506	5.50	M-H	C ₂₀ H ₄₁ O ₇ P	4.63	0.00403	0.56	-	-
LPE 16:1	450.2622	5.93	M-H	C ₂₁ H ₄₂ NO ₇ P	1.96	0.00073	3.12	-	HMDB0011504
LPA 19:0	451.2789	5.51	M-H	C ₂₂ H ₄₅ O ₇ P	6.84	0.00887	0.51	-	HMDB0114746
LPC 14:0	468.3071	5.92	M+H	C ₂₂ H ₄₆ NO ₇ P	5.71	0.00016	1.51	-	HMDB0010379
LPE 18:1	478.2920	5.86	M-H	C ₂₃ H ₄₆ NO ₇ P	2.52	0.09121	1.49	-	HMDB0011506
LPC 16:1	494.3244	5.88	M+H	C ₂₄ H ₄₈ NO ₇ P	7.57	<0.000001	2.10	C04230	HMDB0010383
LPC 17:1	508.3458	5.85	M+H	C ₂₅ H ₅₀ NO ₇ P	1.97	0.00240	1.49	-	-
PS O-19:0	538.3185	5.86	M-H	C ₂₅ H ₅₀ NO ₉ P	1.02	0.00425	1.69	-	-
LPC 17:0	510.3547	5.84	M+H	C ₂₅ H ₅₂ NO ₇ P	2.61	0.00175	0.73	C04230	HMDB0012108
LPC 18:1	522.3557	5.81	M+H	C ₂₆ H ₅₂ NO ₇ P	7.04	0.00907	1.31	C04230	HMDB0010385

LPI 18:2	595.2455	5.95	M-H	C ₂₇ H ₄₉ O ₁₂ P	3.09	0.02177	4.88	-	HMDB0240597
LPG 22:6	555.2716	5.51	M-H	C ₂₈ H ₄₅ O ₉ P	2.42	0.08612	0.51	-	-
β-Glycerophosphoric acid	171.0055	10.18	M-H	C ₃ H ₉ O ₆ P	1.51	0.07323	2.46	C02979	HMDB00002520
PG 38:6	793.5006	4.21	M-H	C ₄₄ H ₇₅ O ₁₀ P	1.02	0.00057	0.49	-	HMDB0116584
PC 36:4	782.5703	5.60	M+H	C ₄₄ H ₈₀ NO ₈ P	7.80	0.00126	0.69	-	HMDB00008074
Lactate	89.0242	5.47	M-H	C ₃ H ₆ O ₃	7.34	0.00777	0.73	C00186	HMDB00000190
Adenine	134.0473	7.16	M-H	C ₅ H ₅ N ₅	3.10	0.00380	0.34	C00147	HMDB00000034
Phosphate	96.9694	9.66	M-H	H ₃ O ₄ P	2.74	0.03192	0.85	C00009	HMDB00001429
Taurine	124.0071	8.53	M-H	C ₂ H ₇ NO ₃ S	4.90	0.01971	0.90	C00245	HMDB00000251
Anandamide	348.2902	3.53	M+H	C ₂₂ H ₃₇ NO ₂	1.36	0.00676	0.54	C11695	HMDB00004080
SM d30:1	705.5078	3.22	M-H	C ₃₅ H ₇₁ N ₂ O ₆ P	1.04	0.00107	0.35	-	-
α-D-Glucosamine1-phosphate	258.0372	10.18	M-H	C ₆ H ₁₄ NO ₈ P	2.70	0.07138	2.74	-	HMDB00001109
β-N-Acetylglucosamine	256.0505	8.98	M+Cl	C ₈ H ₁₅ NO ₆	4.47	0.00009	0.42	C03878	HMDB00000803
Lactamide	90.0547	9.33	M+NH4	C ₃ H ₇ NO ₂	1.27	0.00063	0.76	-	HMDB0253942
Inosine	268.0766	7.37	M-H	C ₁₀ H ₁₂ N ₄ O ₅	1.30	0.07985	0.62	C00294	HMDB00000195
Cer 12:1;3O/11:0;(2OH)	416.3388	6.16	M+H	C ₂₃ H ₄₅ NO ₅	1.66	0.00645	0.51	-	-
Car 18:4	420.3091	3.35	M+Na	C ₂₅ H ₄₁ NO ₄	3.27	0.00152	0.66	-	-

Cer 12:0;20/16:0	456.4018	5.99	M+ACN+H	C ₂₈ H ₅₇ NO ₃	1.03	0.00030	0.46	-	-
Cer 13:1;30/24:2;(2OH)	608.5221	2.82	2M+NH ₄	C ₃₇ H ₆₉ NO ₅	1.38	0.00432	3.82	-	-
Epiandrosterone	291.2303	2.95	M+H	C ₁₉ H ₃₀ O ₂	1.13	0.00222	1.75	C07635	HMDB0000365
<i>N</i> -acetyl-O-methyltyrosine	236.0933	5.49	M-H	C ₁₂ H ₁₅ NO ₄	3.38	0.00953	0.62	C00170	HMDB0001173

Table S3. The detailed information on differential metabolites in the cecum between T1D mice and age-matched controls.

Name	Mass (m/z)	RT (min)	Adducts	Formula	VIP	<i>p</i>	FC	KEGG	HMDB
L-Cystine	258.0622	9.00	M+NH ₄	C ₆ H ₁₂ N ₂ O ₄ S ₂	1.45	0.00400	0.24	C00491	HMDB0000192
<i>N</i> -Acetylaspartate	174.0409	5.96	M-H	C ₆ H ₉ NO ₅	1.83	0.00814	0.63	C01042	HMDB0000812
3-Methylhistidine	170.0921	11.30	M+H	C ₇ H ₁₁ N ₃ O ₂	1.04	0.00279	1.40	C01152	HMDB0000479
<i>N</i> -Acetylglutamate	188.0361	5.56	M-H	C ₇ H ₁₁ NO ₅	1.08	0.00569	2.17	C00624	HMDB0001138
3-Chloro-L-tyrosine	214.8908	9.61	M-H	C ₉ H ₁₀ ClNO ₃	1.22	0.00037	0.47	-	HMDB0001885
Pantothenic acid	218.1037	5.63	M-H	C ₉ H ₁₇ NO ₅	5.76	0.00332	0.67	-	HMDB0250782
9,10-Epoxy-18-hydroxy-octadecanoic acid	337.2365	5.33	M+H	C ₂₀ H ₃₂ O ₄	1.24	0.00120	0.64	C19620	HMDB0302107
Leukotriene A4	319.2256	4.14	M+H	C ₂₀ H ₃₀ O ₃	1.54	0.00351	0.55	C00909	HMDB0001337
5,6-DHET	361.2358	4.16	M+Na	C ₂₀ H ₃₄ O ₄	2.12	0.00168	0.36	C14772	HMDB0002343
Eicosadienoic acid	307.2634	3.24	M-H	C ₂₀ H ₃₆ O ₂	1.82	0.00087	0.58	C16525	HMDB0005060

13-Docosenamide	338.2678	4.20	M+H	C ₂₂ H ₄₃ NO	1.25	0.00633	0.74	-	HMDB0244507
Citramalic acid	207.0488	5.56	M+CH ₃ COO	C ₅ H ₈ O ₅	2.60	0.00429	3.16	C00815	HMDB0000426
LPE 13:0	410.2355	4.14	M-H	C ₁₈ H ₃₈ NO ₇ P	3.39	0.00025	0.46	-	-
LPE 16:1	450.2619	5.89	M-H	C ₂₁ H ₄₂ NO ₇ P	2.26	0.00024	2.31	-	-
PC 16:0	496.3412	5.88	M+H	C ₂₄ H ₅₀ NO ₇ P	11.07	0.00538	0.83	C04230	HMDB0010382
LPC 17:0	510.3521	5.83	M+H	C ₂₅ H ₅₂ NO ₇ P	2.36	0.00465	0.73	C04230	HMDB0012108
LPC 18:0	524.3699	5.81	M+H	C ₂₆ H ₅₄ NO ₇ P	9.26	0.00418	0.75	-	HMDB0011128
PC 36:4	782.5692	5.62	M+H	C ₄₄ H ₈₀ NO ₈ P	5.47	0.00361	0.64	-	HMDB0008074
2-Methyl-3-hydroxypropanoate	254.0346	7.73	M-H	C ₁₁ H ₁₃ NO ₆	2.42	0.00779	0.42	-	HMDB0059748
5-Hydroxyindoleacetic acid	190.0533	5.51	M-H	C ₁₀ H ₉ NO ₃	2.66	0.00341	1.92	-	HMDB0000763
2-Acetolactate	131.0356	6.20	M-H	C ₅ H ₈ O ₄	1.00	0.00012	0.47	C00900	HMDB0006833
Phosphate	96.9698	9.67	M-H	H ₃ O ₄ P	5.86	0.00013	0.54	C00009	HMDB0001429
Glyceric acid	281.9804	9.56	M+NH ₄ -2H	C ₃ H ₈ O ₁₀ P ₂	1.16	0.00063	0.63	C00236	HMDB0001270
Taurine	124.0066	8.53	M-H	C ₂ H ₇ NO ₃ S	8.08	0.00011	0.80	C00245	HMDB0000251
L-3-Hydroxykynurenine	223.0761	8.41	M-H	C ₁₀ H ₁₂ N ₂ O ₄	1.32	0.00374	0.49	C03227	HMDB0011631
Arabinonic acid	225.0608	10.23	M+CH ₃ COO	C ₅ H ₁₀ O ₆	1.71	0.00372	0.64	C00878	HMDB0000539
1-Deoxy-D-xylulose5-phosphate	273.0391	10.02	M+CH ₃ COO	C ₅ H ₁₁ O ₇ P	4.20	0.00769	0.60	C11437	HMDB0001213

β -N-Acetylglucosamine	256.0497	8.96	M+Cl	C ₈ H ₁₅ NO ₆	4.69	0.00546	0.18	C03878	HMDB0000803
Hyodeoxycholic acid	785.5908	4.45	2M+H	C ₂₄ H ₄₀ O ₄	3.49	0.00260	0.29	-	HMDB0000733
NAGly19:0;O	783.5719	5.72	M+NH ₄	C ₄₉ H ₈₃ NO ₅	3.79	0.00219	0.64	C00491	HMDB0005096

Table S4. The detailed information on differential metabolites in the colon between T1D mice and age-matched controls.

Name	Mass (m/z)	RT (min)	Adducts	Formula	VIP	<i>p</i>	FC	KEGG	HMDB
LPC 16:0	540.3291	5.79	M+HCOO	C ₂₄ H ₅₀ NO ₇ P	3.31	0.00787	0.75	C04230	HMDB0010382
3-Methylxanthine	165.0398	8.85	M-H	C ₆ H ₆ N ₄ O ₂	1.77	0.00276	0.56	C16357	HMDB0001886
FA 24:4	359.2944	3.21	M-H	C ₂₄ H ₄₀ O ₂	1.07	0.00178	0.44	-	-
Methylisocitric acid	207.0498	7.50	M+H	C ₇ H ₁₀ O ₇	1.37	0.00082	0.53	C04593	HMDB0006471
L-Citrulline	193.1248	9.14	M+NH ₄	C ₆ H ₁₃ N ₃ O ₃	1.02	0.00075	0.37	C00327	HMDB0000904
Asymmetric dimethylarginine	203.1495	11.26	M+H	C ₈ H ₁₈ N ₄ O ₂	4.31	0.00476	0.70	C03626	HMDB0001539
S-Hydroxymethyl-glutathione	374.0356	8.52	M+K-2H	C ₁₁ H ₁₉ N ₃ O ₇ S	1.70	0.00149	0.68	C14180	HMDB0004662
Dihomo- γ -linolenic acid	306.2502	3.27	M-H	C ₂₀ H ₃₄ O ₂	2.70	0.00305	0.34	C03242	HMDB0002925
13-L-Hydroperoxylinoleic acid	335.2204	4.24	M+Na	C ₁₈ H ₃₂ O ₄	1.35	0.00083	0.69	C04717	HMDB0003871
15,16-DiHODE	335.2204	5.21	M+Na	C ₁₈ H ₃₂ O ₄	1.10	0.00018	0.66	-	HMDB0010208
5,6-EET	321.2403	3.42	M+H	C ₂₀ H ₃₂ O ₃	1.61	0.00569	0.52	-	HMDB0246887
Bovinic acid	304.2337	3.69	M+Na	C ₁₈ H ₃₂ O ₂	1.52	0.00009	0.47	C04056	HMDB0003797

DG O-23:1	444.4040	6.07	M+NH ₄	C ₂₆ H ₅₀ O ₄	1.52	0.00004	0.65	-	-
α-Linolenic acid	279.2299	3.41	M+H	C ₁₈ H ₃₀ O ₂	1.30	0.00016	2.19	C06427	HMDB0001388
Icosadienoic acid	307.2611	3.19	M-H	C ₂₀ H ₃₆ O ₂	1.46	0.00187	0.56	-	-
Leukotriene A4	301.2145	3.74	M+H	C ₂₀ H ₂₈ O ₂	1.14	0.00901	0.70	C00909	HMDB0244343
Prostaglandin E2	351.2153	4.22	M-H	C ₂₀ H ₃₂ O ₅	1.05	0.00189	0.50	C00584	HMDB0001220
Prostaglandin J2	335.2208	4.24	M+H	C ₂₀ H ₃₀ O ₄	3.05	0.00044	0.60	C05957	HMDB0002710
Stearidonic acid	278.2205	3.47	M+H	C ₁₈ H ₂₈ O ₂	1.84	0.00840	1.93	C16300	HMDB0006547
Car 18:0	428.3737	6.01	M+H	C ₂₅ H ₄₉ NO ₄	3.58	0.00001	0.41	-	-
MG 18:1	357.2990	3.25	M+H	C ₂₁ H ₄₀ O ₄	3.66	0.00253	4.83	-	HMDB0000848"
LPC 15:1	480.4002	5.95	M+H	C ₂₃ H ₄₆ NO ₇ P	1.52	0.00015	0.38	-	HMDB0011567
LPC 16:2	492.3056	5.86	M+H	C ₂₄ H ₄₆ NO ₇ P	1.66	0.00016	0.56	-	-
LPC 24:2	604.4296	5.71	M+H	C ₃₂ H ₆₂ NO ₇ P	1.87	0.00338	0.48	-	-
LPC 24:5	598.3889	5.71	M+H	C ₃₂ H ₅₆ NO ₇ P	1.35	0.00236	0.57	-	-
LPE 16:0	454.2916	5.87	M+H	C ₂₁ H ₄₄ NO ₇ P	5.75	0.00632	0.73	-	-
LPE 28:7	608.4573	5.69	M+H	C ₃₃ H ₅₄ NO ₇ P	1.18	0.00738	0.58	-	HMDB0011473
LPG 22:6	555.2731	5.50	M+HCOO	C ₂₄ H ₄₇ O ₉ P	1.29	0.00030	0.56	-	-
PC 36:4	782.5703	5.56	M+H	C ₄₄ H ₈₀ NO ₈ P	5.07	0.00087	0.74	-	-

PC O-38:5	794.6026	5.54	M+H	C ₄₆ H ₈₄ NO ₇ P	1.73	0.00059	0.66	-	HMDB0008074
LPC 17:0	568.3580	5.75	M+Hac-H	C ₂₅ H ₅₂ NO ₇ P	2.61	0.00407	0.66	C04230	HMDB0013432
LPC 18:1	580.3584	5.69	M+Hac-H	C ₂₆ H ₅₂ NO ₇ P	1.16	0.00946	0.54	-	HMDB0012108
LPC 20:4	602.4119	5.71	M+Hac-H	C ₂₈ H ₅₀ NO ₇ P	1.38	0.00006	0.45	C04230	HMDB0002815
LPI 18:0	599.3210	5.86	M-H	C ₂₇ H ₅₃ O ₁₂ P	3.81	0.00008	0.38	-	HMDB0010395
Lactic acid	89.0241	5.39	M-H	C ₃ H ₆ O ₃	2.26	0.00158	0.50	C00186	HMDB0240261
Phosphate	96.9697	9.64	M-H	H ₃ O ₄ P	3.25	0.00015	0.75	C00009	HMDB0000190
Phenol sulfate	172.9921	1.75	M-H	C ₆ H ₆ O ₄ S	2.79	0.00723	0.31	C02180	HMDB0001429
Phosphonoacetate	176.9363	9.65	M+K-2H	C ₂ H ₅ O ₅ P	2.42	0.00108	0.66	C05682	HMDB0060015
Taurine	126.0215	8.57	M+H	C ₂ H ₇ NO ₃ S	3.90	0.00541	0.72	C00245	HMDB00004110
<i>N</i> -Acetyl-9-O-acetylneuraminic acid	350.1070	7.09	M-H	C ₁₃ H ₂₁ NO ₁₀	3.02	0.00048	0.36	-	HMDB0000251
SM 40:8;2O	795.6066	5.54	M+Na	C ₄₅ H ₇₇ N ₂ O ₆ P	1.17	0.00195	0.67	-	HMDB0000794
alltrans-Retinal	285.2201	3.67	M+H	C ₂₀ H ₂₈ O	1.16	0.00022	0.53	C00376	-
4-Thiouridine	261.0539	5.69	M-H	C ₉ H ₁₂ N ₂ O ₅ S	1.54	0.00907	0.40	-	HMDB0001358
Cer 12:0;2O/20:0	512.3344	5.97	M+H	C ₃₂ H ₆₅ NO ₃	2.12	0.00059	0.48	-	HMDB0246588
Cer 12:1;3O/11:0;(2OH)	416.3364	6.14	M+H	C ₂₃ H ₄₅ NO ₅	1.15	0.00173	0.46	-	-

Cer 13:1;3O/28:3;(2OH)	662.5711	2.77	M+H	C ₄₁ H ₇₅ NO ₅	1.71	0.00339	0.19	-	-
CerP 12:2;2O/16:4	524.3710	5.77	M+H	C ₂₈ H ₄₆ NO ₆ P	9.27	0.00640	0.75	-	-
Lauryl sulfate	265.2526	3.26	M-H	C ₁₂ H ₂₆ O ₄ S	2.64	0.00269	2.89	-	-
NAGlySer12:0;O	361.2352	4.19	M+H	C ₁₇ H ₃₂ N ₂ O ₆	1.60	0.00156	0.58	-	-
Tauropine	196.0272	8.43	M-H	C ₅ H ₁₁ NO ₅ S	1.14	0.00024	0.45	C04230	-

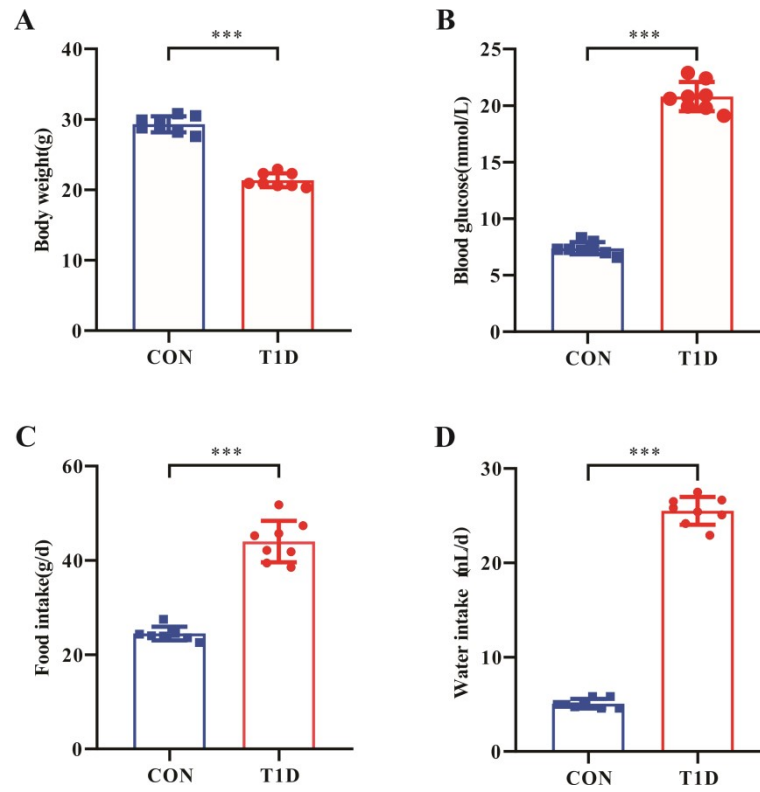


Figure S1. Streptozotocin-induced type 1 diabetic mouse model. Changes in (A) body weight, (B) blood glucose level, (C) daily food intake and (D) daily water intake between CON and T1D mice. The significance of the differences between CON and T1D mice was assessed by two-tailed unpaired student's t-test. Significant level: *** $p < 0.001$. Group: CON, normal control mice; T1D, type 1 diabetic mice.

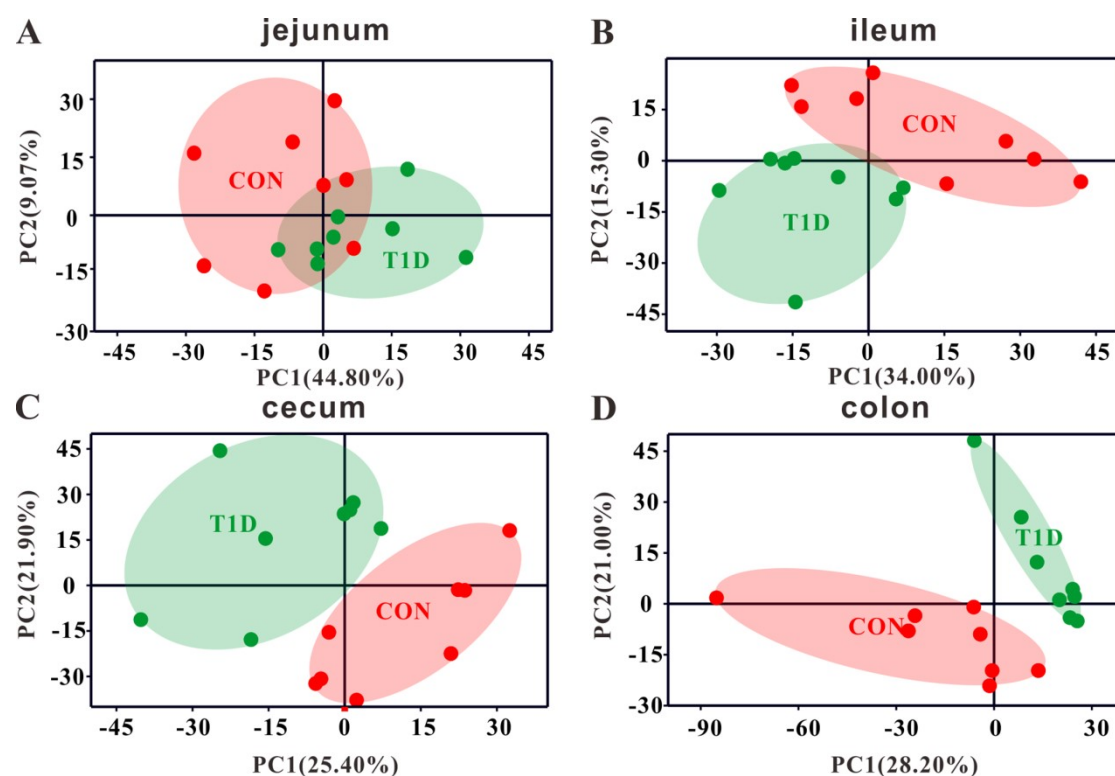


Figure S2. Changes in metabolic patterns in different intestinal segments of T1D mice. Principal component analyses were carried out to examine the overall changes of metabolic patterns analyzed by LC-MS-based untargeted metabolomics analysis under the negative ion model in the (A) jejunum, (B) ileum, (C) cecum and (D) colon between CON and T1D mice between CON and T1D mice. Group: CON, normal control mice; T1D, type 1 diabetic mice.

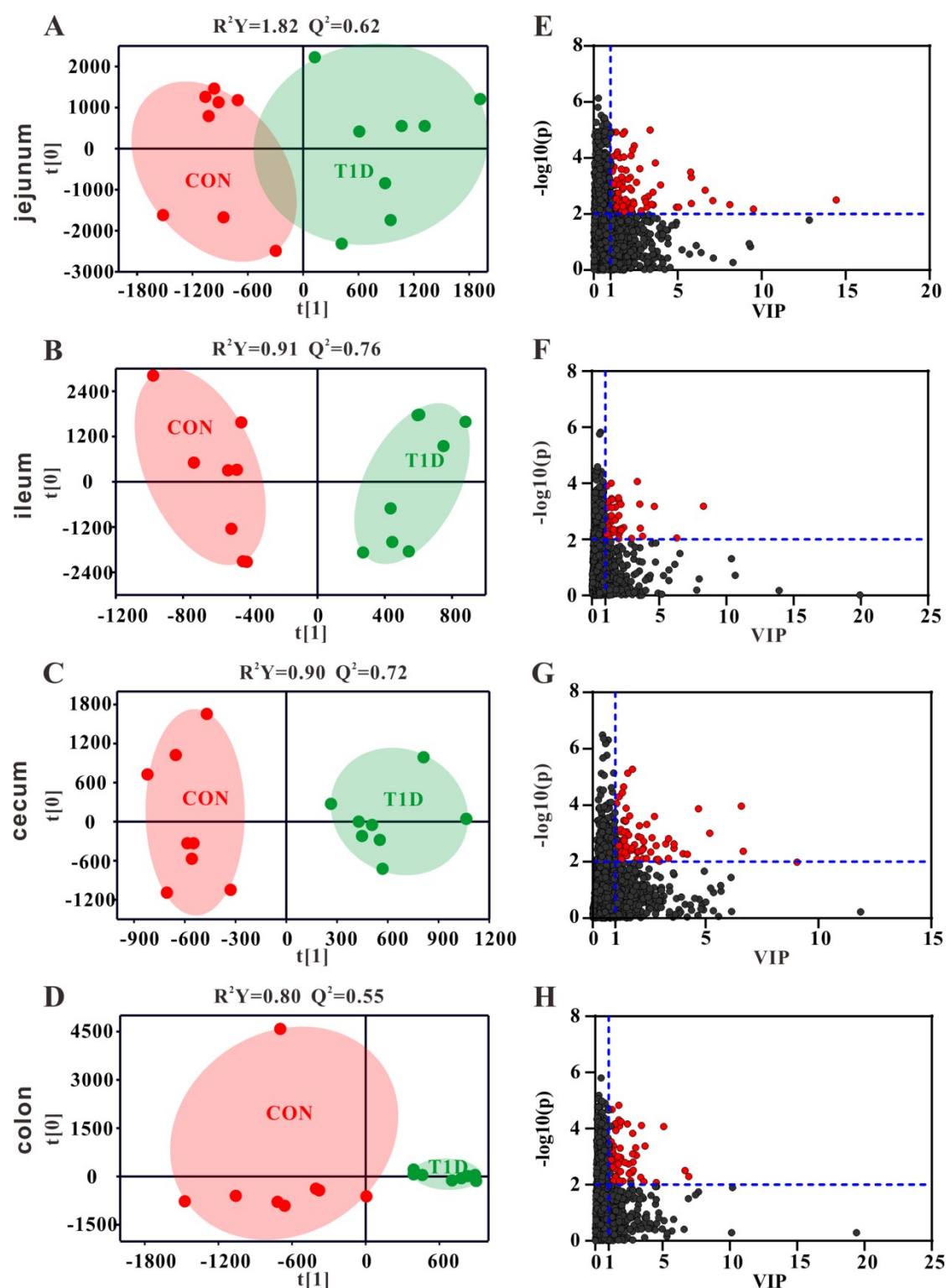


Figure S3. Identification of important differential metabolites in different intestinal segments of T1D mice. Orthogonal projection to latent structures-discriminant analyses were used to maximize the metabolic separation analyzed by LC-MS-based untargeted metabolomics analysis under the negative ion model in the (A) jejunum, (B) ileum, (C) cecum and (D) colon between CON and T1D mice and identify important

metabolites by the variable importance in the projection (VIP) and p values. The metabolic signals with $VIP > 1.0$ and $-\log_{10}(p) > 2.0$ were selected and show as red points in the (E) jejunum, (F) ileum, (G) cecum and (H) colon. Group: CON, normal control mice; T1D, type 1 diabetic mice.

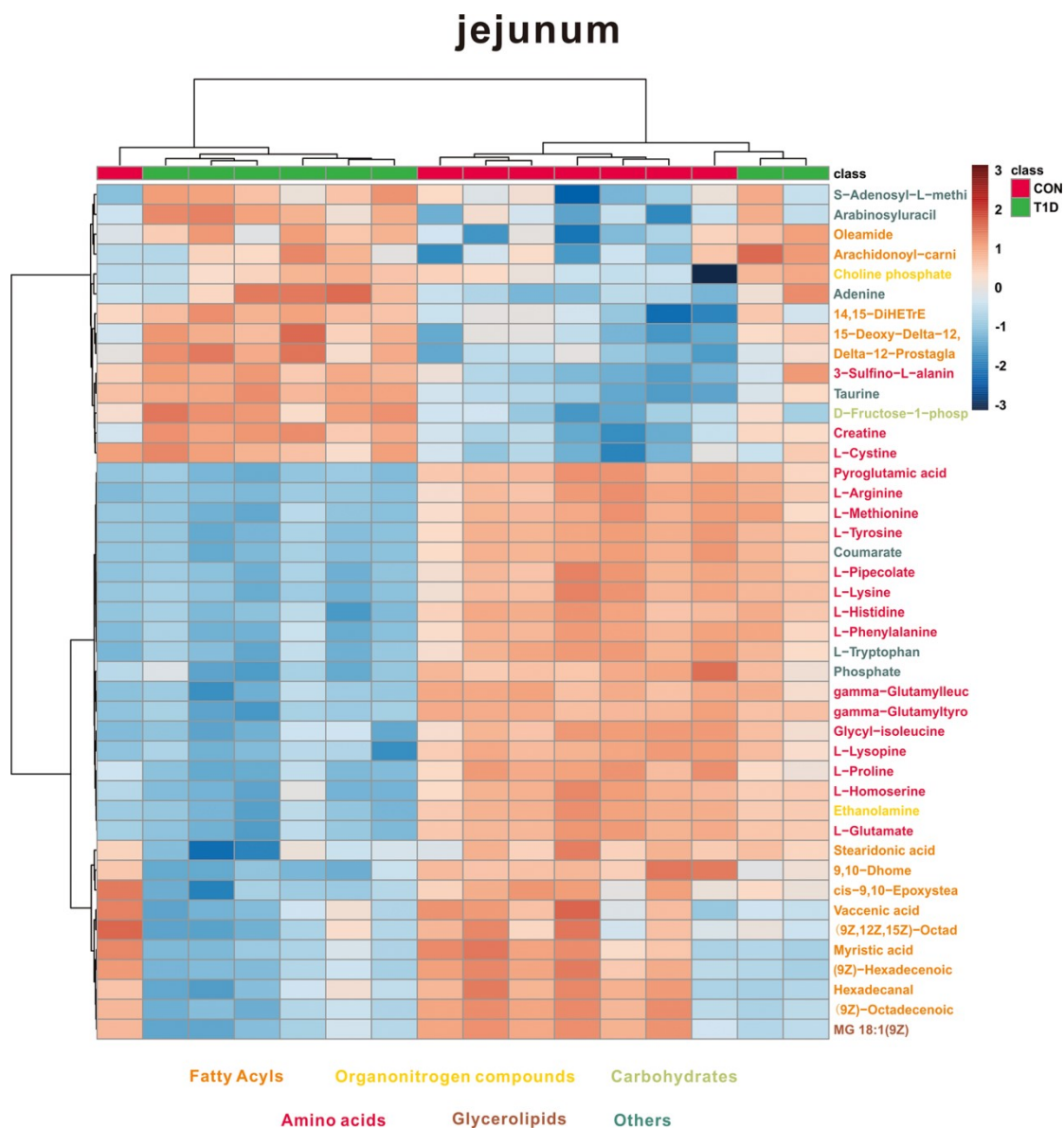


Figure S4. Metabolic changes in the jejunum of T1D mice. Heatmap showing alterations of identified differential metabolites between CON and T1D mice analyzed by LC-MS-based untargeted metabolomics analysis under both the positive and negative ion models. Group: CON, normal control mice; T1D, type 1 diabetic mice.

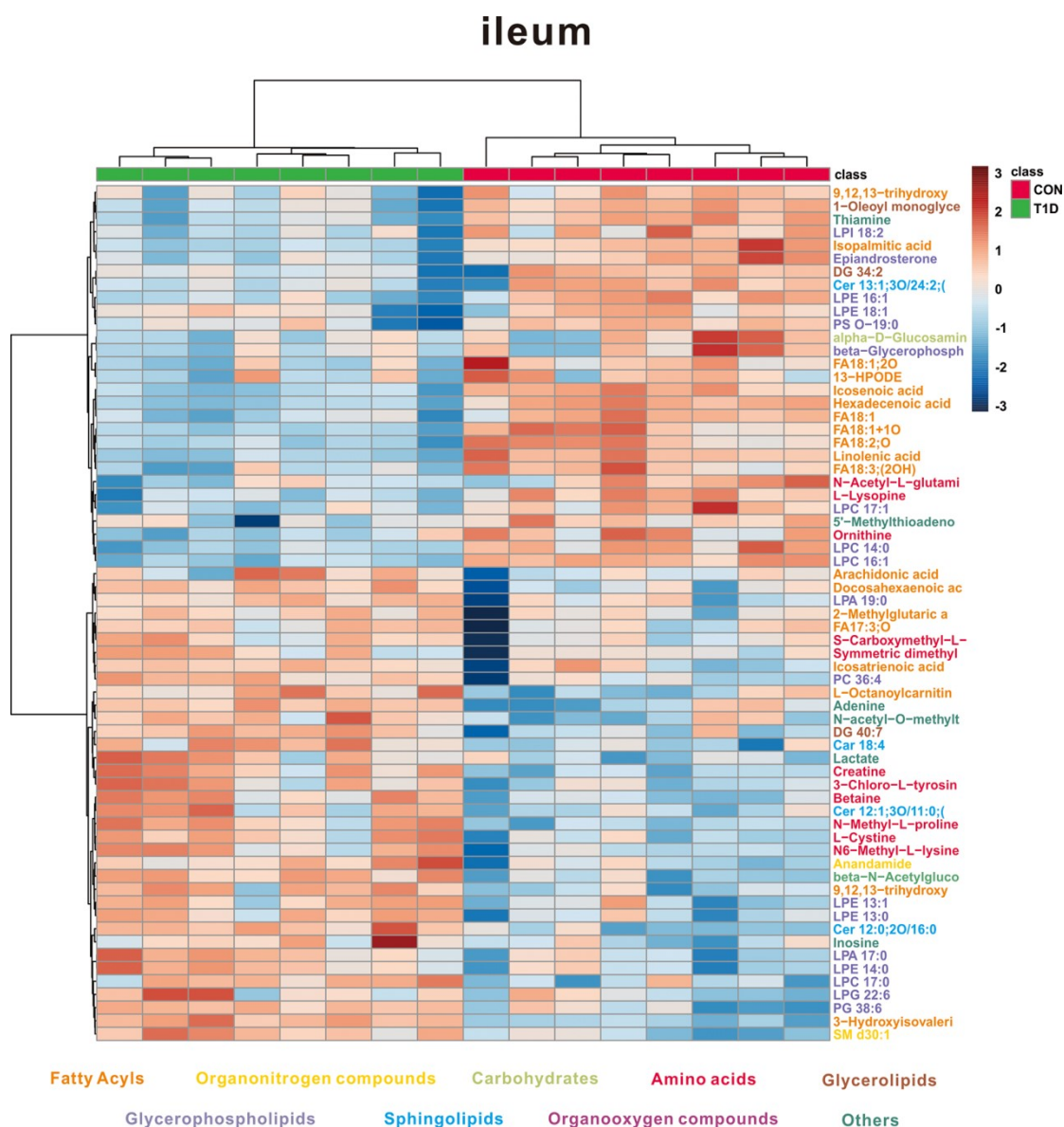


Figure S5. Metabolic changes in the ileum of T1D mice. Heatmap showing alterations of identified differential metabolites between CON and T1D mice analyzed by LC-MS-based untargeted metabolomics analysis under both the positive and negative ion models. Group: CON, normal control mice; T1D, type 1 diabetic mice.

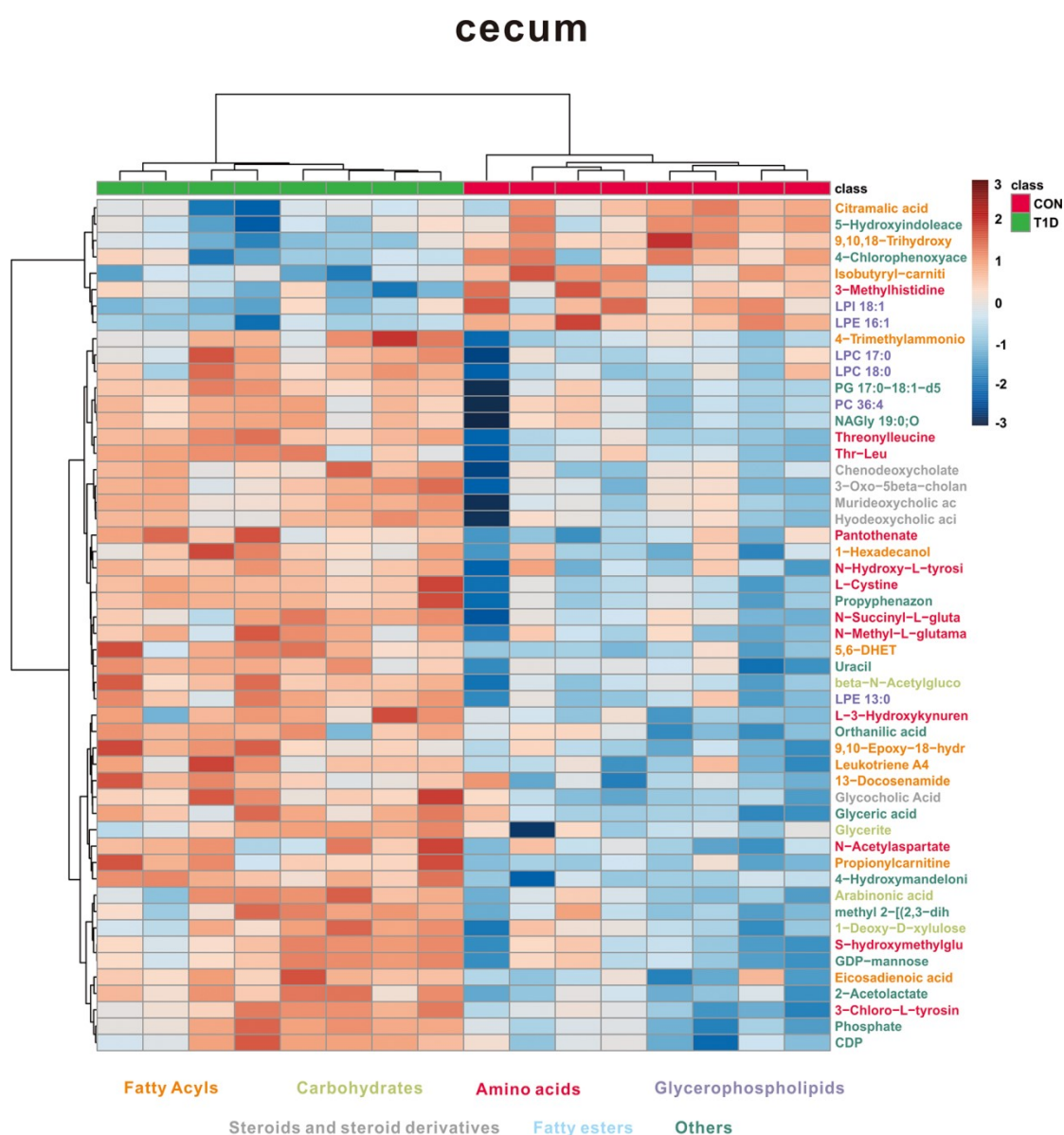


Figure S6. Metabolic changes in the cecum of T1D mice. Heatmap showing alterations of identified differential metabolites between CON and T1D mice analyzed by LC-MS-based untargeted metabolomics analysis under both the positive and negative ion models. Group: CON, normal control mice; T1D, type 1 diabetic mice.

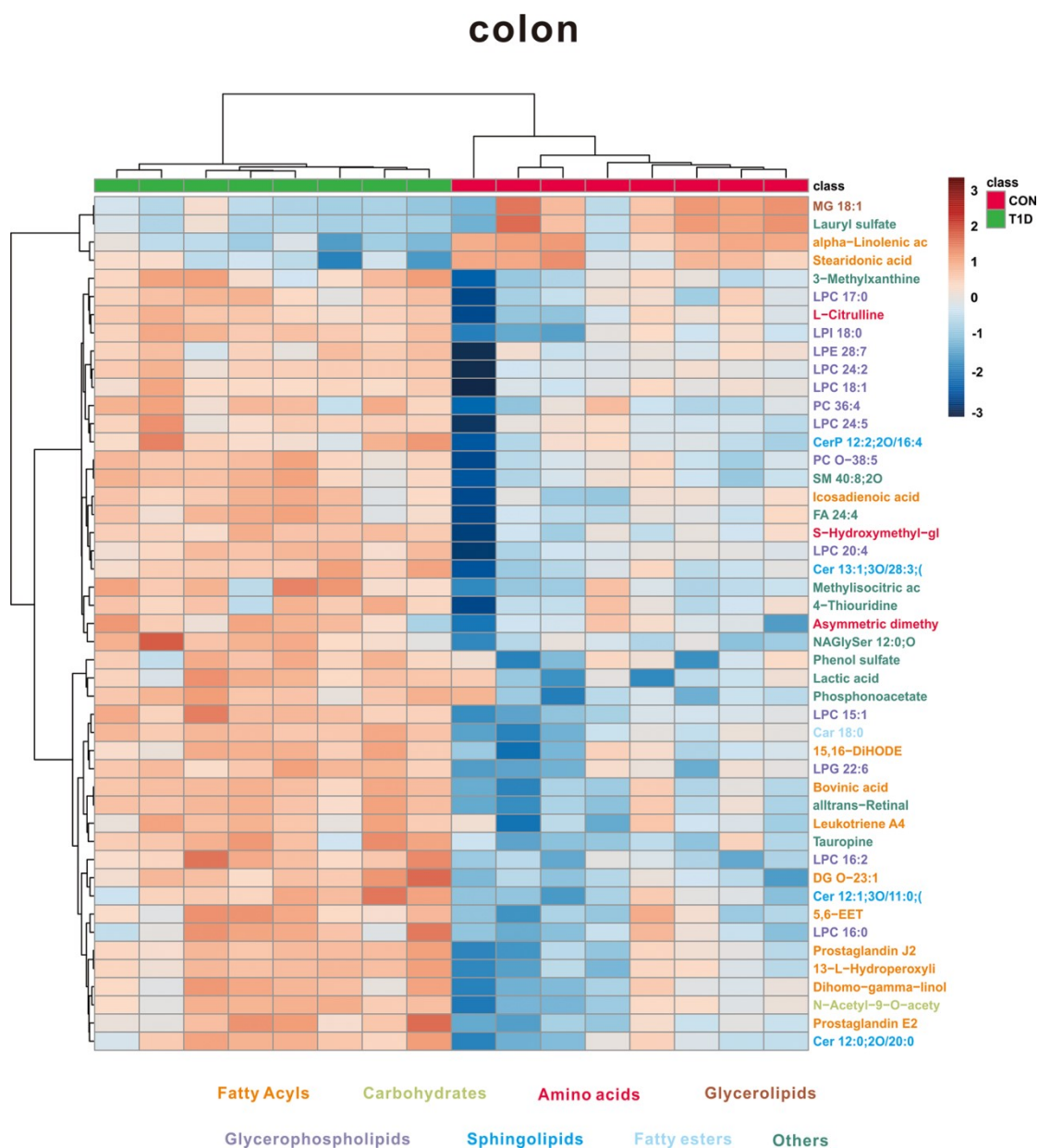


Figure S7. Metabolic changes in the colon of T1D mice. Heatmap showing alterations of identified differential metabolites between CON and T1D mice analyzed by LC-MS-based untargeted metabolomics analysis under both the positive and negative ion models. Group: CON, normal control mice; T1D, type 1 diabetic mice.