

Table S1: Clinical characteristics of all subjects and paired subjects

Class	Microbiome test					Metabolome test				
	Pri_GD group (n=20)	HC group (n=45)	Eut_GD group (n=19)	P value (Pri_GD-HC)	P value (Eut_GD-HC)	Pri_GD group (n=15)	HC group (n=15)	Eut_GD group (n=15)	P value (Pri_GD-HC)	P value (Eut_GD-HC)
SEX(M/F)	2/18	9/36	3/16	0.480	1.000	2/13	4/11	2/13	0.651	0.651
Age (years, mean±SD)	37.3±8.01	41.58±11.02	39.42±10.90	1.24E-01	5.51E-01	36.53±8.90	34.60±10.53	37.00±10.76	5.47E-01	4.67E-01
BMI (kg/m ² , mean±SD)	21.17±1.79	22.30±2.13	21.80±1.62	3.72E-02	3.36E-01	21.00±1.90	22.24±2.16	21.71±1.79	1.71E-01	4.68E-01
Thyroid function										
fT3 (pg/mL, mean±SD)	11.72±7.94	2.87±0.38	2.82±0.45	1.59E-10	4.85E-01	12.73±8.95	2.74±0.37	2.83±0.49	3.05E-06	6.63E-01
fT4 (ng/mL, mean±SD)	2.57±0.92	1.06±0.14	1.10±0.16	3.44E-10	5.91E-01	2.74±0.94	1.05±0.16	1.12±0.17	4.54E-06	4.42E-01
TSH (uIU/mL, mean±SD)	0.003±0.007	2.016±0.988	1.210±0.646	1.59E-10	2.66E-03	0.00±0.01	1.87±1.04	1.20±0.60	3.04E-06	1.01E-01
TR_Ab (IU/L, mean±SD)	20.76±7.85	0.33±0.18	2.20±2.75	1.38E-10	8.37E-07	22.26±7.37	0.31±0.11	1.74±2.05	2.96E-06	5.23E-04
Blood routine										
WBC (10 ⁹ /L, mean±SD)	6.73±1.20	5.26±1.15	6.50±1.79	6.11E-05	4.67E-03	6.64±1.26	5.65±1.37	6.34±1.52	4.65E-02	2.37E-01
RBC (10 ¹² /L, mean±SD)	4.78±0.50	4.55±0.31	4.76±0.35	2.33E-02	1.91E-02	4.76±0.54	4.57±0.33	4.70±0.34	1.58E-01	2.21E-01
HGB (g/L, mean±SD)	132.85±12.49	139.98±6.62	138.74±8.22	1.88E-02	8.43E-01	132.27±14.43	141.67±7.01	137.33±7.97	5.86E-02	2.20E-01
HCT (%)	40.04±3.15	41.43±2.07	41.21±1.84	3.99E-02	7.74E-01	39.97±3.64	41.57±1.17	40.86±1.51	1.46E-01	1.98E-01
MCV (fl, mean±SD)	82.33±3.16	89.44±2.50	87.61±2.41	7.82E-10	1.90E-02	82.00±3.12	88.89±0.84	87.52±2.45	3.04E-06	7.43E-02
MCH (pg, mean±SD)	27.73±1.24	30.13±1.11	29.47±0.74	2.70E-08	1.43E-02	27.73±1.30	30.05±1.14	29.43±0.75	5.69E-05	1.40E-01
MCHC (g/L, mean±SD)	333.15±7.72	335.31±6.75	337.21±5.28	2.05E-01	2.96E-01	333.20±7.91	335.40±5.53	337.40±5.69	2.28E-01	1.09E-01
PLT (10 ⁹ /L, mean±SD)	267.94±52.35	244.01±40.03	267.16±54.95	7.21E-02	7.65E-02	269.99±55.05	241.29±28.13	267.87±62.06	7.12E-02	9.28E-02
PCT (%)	0.27±0.48	0.26±0.10	0.26±0.06	1.10E-01	9.11E-02	0.26±0.04	0.23±0.02	0.25±0.06	3.83E-02	2.18E-01

MPV (fl, mean±SD)	10.26±0.68	10.97±0.84	10.26±0.70	3.08E-03	5.94E-03
NEUT (10 ⁹ /L, mean±SD)	8.78±16.38	3.38±0.88	7.10±14.88	6.56E-02	2.74E-01
LYMP (10 ⁹ /L, mean±SD)	2.12±0.62	2.00±0.53	1.97±0.58	5.09E-01	7.35E-01
MONO (10 ⁹ /L, mean±SD)	0.35±0.08	0.28±0.09	0.26±0.08	2.38E-03	4.14E-01
EO (10 ⁹ /L, mean±SD)	0.09±0.08	0.10±0.07	0.10±0.09	6.48E-01	9.82E-01
BASO (10 ⁹ /L, mean±SD)	0.01±0.003	0.01±0.01	0.01±0.01	9.72E-01	2.21E-01
Liver function					
ALT (U/L, mean±SD)	26.97±13.50	18.78±8.77	16.83±10.28	2.66E-02	3.18E-01
AST (U/L, mean±SD)	26.53±5.67	22.29±8.68	20.53±6.04	4.78E-03	6.70E-01
TP (g/L, mean±SD)	70.97±2.51	77.31±5.11	77.01±4.89	2.66E-02	1.17E-02
ALB (g/L, mean±SD)	42.35±2.40	44.65±2.71	44.96±2.82	1.72E-06	2.85E-02
GLB (g/L, mean±SD)	28.60±3.16	26.65±4.05	32.17±4.07	6.06E-02	4.13E-05
GGT (U/L, mean±SD)	23.89±7.84	22.99±11.52	27.30±25.21	3.98E-01	7.08E-01
AKP/ALP (U/L, mean±SD)	134.85±70.67	80.61±20.76	105.67±28.36	3.42E-05	9.45E-04
TBIL (umol/L, mean±SD)	15.89±6.08	12.99±4.48	12.89±3.80	8.16E-02	8.95E-01
DBIL (umol/L, mean±SD)	3.27±1.12	2.40±0.75	2.91±2.23	1.37E-03	5.81E-01
IBIL (umol/L, mean±SD)	12.63±5.08	10.11±3.50	10.51±3.16	6.26E-02	7.02E-01
TBA (umol/L, mean±SD)	5.37±2.60	4.15±1.86	4.25±1.83	4.73E-02	9.94E-01
Blood fatty					
CHOL (mmol/L, mean±SD)	3.40±0.65	4.94±0.40	4.66±1.02	2.18E-09	8.69E-02
TG (mmol/L, mean±SD)	1.08±0.46	1.34±0.39	1.03±0.48	1.34E-02	1.69E-02
HDL (mmol/L, mean±SD)	1.11±0.21	1.19±0.11	1.28±0.28	4.64E-02	1.69E-01
ApoA (g/L, mean±SD)	1.44±0.25	1.46±0.09	1.77±0.52	2.37E-01	8.90E-04

10.35±0.61	10.94±0.71	10.07±0.60	3.40E-02	7.34E-03
10.60±18.70	3.37±0.92	7.75±16.77	5.38E-02	4.81E-01
2.13±0.60	1.85±0.42	1.97±0.65	2.06E-01	7.72E-01
0.35±0.08	0.25±0.07	0.25±0.07	1.03E-03	8.03E-01
0.10±0.08	0.09±0.06	0.12±0.09	9.34E-01	5.74E-01
0.01±0.00	0.01±0.01	0.02±0.01	9.80E-01	2.76E-01
26.95±14.11	25.69±6.86	15.32±8.12	7.87E-01	3.45E-03
25.84±5.34	29.17±10.15	20.11±5.70	3.19E-01	7.93E-03
70.71±2.62	70.95±4.81	76.67±5.18	6.78E-01	7.93E-03
42.70±2.34	46.71±2.61	44.30±2.60	5.33E-04	3.27E-02
27.99±3.41	24.20±3.70	32.37±4.24	6.18E-03	5.21E-05
22.96±7.93	33.21±11.02	21.25±10.17	8.42E-03	5.44E-03
139.76±81.15	89.80±12.85	103.42±23.13	3.81E-02	9.70E-02
15.80±6.32	16.03±3.19	13.31±4.09	3.95E-01	3.43E-02
3.23±1.17	2.89±0.62	2.60±0.87	3.50E-01	5.20E-01
12.57±5.23	12.16±2.89	10.71±3.41	8.52E-01	1.58E-01
5.29±2.58	4.05±1.81	4.53±1.96	2.05E-01	6.18E-01
3.29±0.53	4.99±0.49	4.78±0.93	6.77E-06	2.45E-01
0.94±0.34	1.26±0.30	1.07±0.47	9.52E-03	1.41E-01
1.13±0.21	1.18±0.10	1.28±0.25	2.13E-01	2.71E-01
1.44±0.22	1.47±0.11	1.70±0.42	1.90E-01	2.92E-02

ApoB (g/L, mean±SD)	0.54±0.16	0.93±0.08	0.76±0.20	8.44E-09	7.62E-05	0.51±0.09	0.93±0.09	0.78±0.19	3.04E-06	4.47E-03
LPa (mg/L, mean±SD)	43.38±41.16	118.51±83.77	86.68±88.91	4.52E-05	6.10E-02	35.20±39.67	151.88±109.89	79.37±79.79	2.05E-04	4.43E-02
LDL (mmol/L, mean±SD)	2.25±0.46	3.34±0.56	3.07±0.62	9.71E-09	3.62E-02	2.17±0.38	3.11±0.84	3.12±0.53	1.05E-04	3.00E-01

The Wilcoxon rank-sum test was used to compare age, BMI and clinical parameters between the groups. Fisher's exact test was used to compare sex distributions. Pearson Chi-Square, continuity correction or Fisher's Exact test were used to compare sex distributions based on sample size and expected count. Values are expressed as the mean ± SD. M/F, male/female; BMI, body mass index; fT3, free triiodothyronine; fT4, free thyroxine; TSH, thyroid-stimulating hormone; TR-Ab, thyrotropin receptor antibody; WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean cellular haemoglobin; MCHC, mean cellular haemoglobin contents; PCT, platelet crit; MPV, mean platelet volume; NEUT, neutrophil; LYMP, lymphocytic; MONO, monocyte; EO, eosinophil; BASO, basophil; ALT, alanine aminotransferase; AST, aspartate transaminase; TP, total protein; ALB, albumen; GLB, globulin; GGT, gamma-glutamyl transpeptidase; AKP, alkaline phosphatase; TBIL, total bilirubin; DBIL, direct bilirubin; IBIL, indirect bilirubin; TBA, total bile acid; CHOL, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; ApoA, apolipoprotein A; ApoB, apolipoprotein B; LPa, lipoprotein a; LDL, low-density lipoprotein. P value using scientific counting method.

Table S2: The different KEGG pathways between Pri_GD and HC groups

Level 1	Pri_GD mean	Eut_GD mean	HC mean	P value	Pfdr value
Cellular Processes	1522553	1170897	1199106	0.00428	0.00428
Environmental Information Processing	6344215	5799901	5273924	0.00021	0.00084
Genetic Information Processing	8230559	7593103	7143788	0.00034	0.000906667
Human Diseases	274606	253916	239539	0.0008	0.00128
Metabolism	18971195	17573165	16589384	0.00098	0.001306667
None	100051	89598	83146	0.0001	8.00E-04
Organismal Systems	301194	269015	263984	0.00138	0.001577143
Unclassified	5603818	5171234	4884057	0.00072	0.00128
Level 2	Pri_GD mean	Eut_GD mean	HC mean	P value	Pfdr value
Cancers	37647	34104	33543	0.00692	0.007758788
Immune System	37300	33421	33189	0.00692	0.007758788
Cell Motility	1247161	905057	944027	0.00468	0.005585806
Immune System Diseases	24612	21227	20595	0.00326	0.004020667
Nervous System	44806	41689	39719	0.00326	0.004020667
Excretory System	2351	2796	3155	0.00247	0.003409286
Metabolism	922330	867210	813679	0.00258	0.003409286
Xenobiotics Biodegradation and Metabolism	584149	561387	513169	0.00258	0.003409286
Carbohydrate Metabolism	4196281	3913393	3690511	0.00214	0.0031672
Cell Growth and Death	199149	190555	177757	0.00204	0.003145
Energy Metabolism	2336626	2187450	2056058	0.00153	0.002461304
Environmental Adaptation	86575	70494	70570	0.00132	0.00222

Metabolism of Terpenoids and Polyketides	638865	589664	560823	0.00108	0.001902857		
Poorly Characterized	1936409	1800554	1690451	0.00084	0.001554		
Cellular Processes and Signaling	1675715	1515861	1456464	0.00076	0.00148		
Folding, Sorting and Degradation	975221	894046	859340	0.00072	0.00148		
Metabolism of Other Amino Acids	556396	517346	485752	0.00076	0.00148		
Nucleotide Metabolism	1599509	1497300	1403716	0.00068	0.00148		
Replication and Repair	3586369	3336174	3141706	0.00061	0.00148		
Biosynthesis of Other Secondary Metabolites	387643	350246	333001	0.00042	0.001321429		
Enzyme Families	914143	832826	786715	0.0005	0.001321429		
Lipid Metabolism	1179190	1066748	1015689	0.0005	0.001321429		
Metabolic Diseases	39626	36892	34416	0.00045	0.001321429		
Amino Acid Metabolism	4078078	3734027	3504701	0.00029	0.001258		
Endocrine System	126830	115172	110789	0.00027	0.001258		
Genetic Information Processing	1069364	987609	923463	0.00026	0.001258		
Infectious Diseases	147989	137207	127622	0.00027	0.001258		
Membrane Transport	5616552	5180741	4671639	0.00017	0.001258		
Metabolism of Cofactors and Vitamins	1837498	1678604	1592806	0.00032	0.001258		
Signal Transduction	677262	569409	554362	0.00034	0.001258		
Transcription	1284700	1158929	1082208	0.00017	0.001258		
Translation	2384269	2203954	2060534	0.00032	0.001258		
Digestive System	3332	5443	6562	0	0		
Level 3	Pri_GD mean	Eut_GD mean	HC mean	P value (Pri_GD vs. HC)	Pfdr value (Pri_GD vs. HC)	Partial recovery (True/False)	P value (Pri_GD vs. Eut_GD)

Ubiquitin system	937	1303	1210	0.04489	0.055521842	TRUE	0.08652
Naphthalene degradation	45000	43215	40892	0.04309	0.053577513	TRUE	0.46506
Huntington's disease	2772	3504	3566	0.04211	0.0526375	TRUE	0.09455
Isoquinoline alkaloid biosynthesis	19119	17684	17603	0.03882	0.048784492	TRUE	0.05426
Oxidative phosphorylation	402210	392686	367043	0.03587	0.045319624	TRUE	0.51812
Amino acid metabolism	73154	73156	64926	0.03424	0.043494054	FALSE	
Stilbenoid, diarylheptanoid and gingerol biosynthesis	134	150	158	0.03078	0.039311413	TRUE	0.35376
Biosynthesis of siderophore group nonribosomal peptides	8920	6679	7404	0.02708	0.034813388	TRUE	0.01341
Cell division	31286	30379	28018	0.02708	0.034813388	TRUE	0.44807
Primary bile acid biosynthesis	16320	14426	14042	0.02668	0.034813388	TRUE	0.05253
Tetracycline biosynthesis	56076	56948	49393	0.02711	0.034813388	FALSE	
Secondary bile acid biosynthesis	16295	14402	14011	0.02585	0.033937151	TRUE	0.05253
Bacterial toxins	45578	42570	39926	0.02516	0.033216854	TRUE	0.16006
Carotenoid biosynthesis	154	130	108	0.02495	0.033125706	TRUE	0.05786
Bisphenol degradation	34137	29533	29654	0.02252	0.030069318	TRUE	0.02285
Carbon fixation pathways in prokaryotes	332688	320798	304224	0.02161	0.029019143	TRUE	0.31177
Amino sugar and nucleotide sugar metabolism	563966	522380	505396	0.0206	0.027821839	TRUE	0.04605
Restriction enzyme	75240	64984	66894	0.02031	0.027588728	TRUE	0.01568
Biotin metabolism	59817	55187	53118	0.01996	0.02727093	TRUE	0.13644
Ion channels	2208	2814	1992	0.01799	0.024723099	FALSE	
NOD-like receptor signaling pathway	18279	16254	16310	0.01774	0.024522941	TRUE	0.03273
Pathways in cancer	18741	16938	16666	0.01718	0.023889349	TRUE	0.05253

Ether lipid metabolism	390	386	307	0.01675	0.02343006	TRUE	0.59341
Inositol phosphate metabolism	27533	27194	24929	0.01674	0.02343006	TRUE	0.61303
Other transporters	103491	95221	91927	0.01531	0.021673795	TRUE	0.10317
Glycosyltransferases	119584	109066	104534	0.01521	0.021662727	TRUE	0.0815
Glycan biosynthesis and metabolism	5141	6045	6168	0.0147	0.021064024	TRUE	0.13644
Energy metabolism	337203	311680	302528	0.01448	0.020876074	TRUE	0.07214
Fatty acid biosynthesis	185055	174444	163733	0.01383	0.020062037	TRUE	0.20609
Ethylbenzene degradation	6924	7813	8172	0.01359	0.019836335	TRUE	0.02459
Prostate cancer	18235	16215	16112	0.01341	0.019695938	TRUE	0.0305
Vitamin B6 metabolism	74130	70250	67154	0.0134	0.019695938	TRUE	0.19619
Phenylpropanoid biosynthesis	83474	72730	69022	0.01239	0.018428165	TRUE	0.02841
Propanoate metabolism	172031	167689	151434	0.01233	0.018428165	TRUE	0.50009
Primary immunodeficiency	24612	21227	20595	0.01215	0.018302885	TRUE	0.04307
Biosynthesis of ansamycins	57569	49207	49383	0.01169	0.017723548	TRUE	0.00974
Antigen processing and presentation	18200	16171	16000	0.01157	0.017655519	TRUE	0.0305
Glutamatergic synapse	44805	41688	39719	0.01143	0.017655519	TRUE	0.08654
Nitrogen metabolism	261019	243154	232177	0.01152	0.017655519	TRUE	0.09182
Progesterone-mediated oocyte maturation	18200	16171	16000	0.01157	0.017655519	TRUE	0.0305
Methane metabolism	511521	485765	446604	0.01052	0.016481333	TRUE	0.22697
Proximal tubule bicarbonate reclamation	2351	2796	3155	0.01002	0.015882215	TRUE	0.12226
Staphylococcus aureus infection	882	2142	765	0.01007	0.015882215	FALSE	
Amoebiasis	3624	3918	2864	0.00943	0.015123129	FALSE	
Ubiquinone and other terpenoid-quinone biosynthesis	20350	23768	26509	0.00946	0.015123129	TRUE	0.144

Butirosin and neomycin biosynthesis	30222	26096	25909	0.00844	0.013678621	TRUE	0.03273
Carbon fixation in photosynthetic organisms	271463	247182	239426	0.0083	0.013545139	TRUE	0.0305
Cyanoamino acid metabolism	126585	113103	108088	0.00781	0.012834615	TRUE	0.02841
Flagellar assembly	239908	161090	175993	0.00775	0.012825704	TRUE	0.00541
Arachidonic acid metabolism	1993	3095	3240	0.00757	0.012616667	TRUE	0.10317
Drug metabolism - other enzymes	123685	115792	111227	0.00742	0.012455	TRUE	0.09182
Prenyltransferases	116201	108362	104144	0.0069	0.011665468	TRUE	0.05605
Synthesis and degradation of ketone bodies	18243	13289	13739	0.00681	0.011596739	TRUE	0.00454
Pyruvate metabolism	406509	379940	354483	0.00657	0.011269708	TRUE	0.12226
Galactose metabolism	349225	319885	305434	0.0062	0.010713235	TRUE	0.05976
Carbohydrate metabolism	80555	74938	69308	0.00594	0.010566296	TRUE	0.19619
Cell cycle - Caulobacter	198979	190174	177602	0.00604	0.010566296	TRUE	0.16858
Chaperones and folding catalysts	398210	366128	354496	0.00599	0.010566296	TRUE	0.04025
Sulfur metabolism	122697	105307	103804	0.00607	0.010566296	TRUE	0.01451
One carbon pool by folate	252232	230626	223395	0.00563	0.010099618	TRUE	0.03273
beta-Alanine metabolism	76354	70256	65749	0.00552	0.009978462	TRUE	0.10925
Metabolism of cofactors and vitamins	36336	36720	31952	0.00536	0.009978462	FALSE	
Mismatch repair	327743	305708	288498	0.00551	0.009978462	TRUE	0.07214
Pentose phosphate pathway	377774	349621	330055	0.00541	0.009978462	TRUE	0.05976
RNA degradation	179999	166719	160319	0.00544	0.009978462	TRUE	0.04025
Carbohydrate digestion and absorption	1343	2168	1846	0.00483	0.0090992	TRUE	0.00219
Lipid biosynthesis proteins	234468	211945	205120	0.00484	0.0090992	TRUE	0.04605
Chloroalkane and chloroalkene degradation	74623	72806	63399	0.00476	0.009094309	TRUE	0.53648
Folate biosynthesis	128872	129245	117545	0.00466	0.009014754	FALSE	

Transcription machinery	411960	370203	359684	0.00468	0.009014754	TRUE	0.02943
Bacterial motility proteins	542875	373354	401035	0.0046	0.009008333	TRUE	0.00454
Histidine metabolism	275239	247824	237818	0.00449	0.00892605	TRUE	0.02122
Peroxisome	61017	57562	54667	0.00452	0.00892605	TRUE	0.16006
Protein export	233982	215470	206527	0.00446	0.00892605	TRUE	0.0376
Protein folding and associated processing	228854	219290	202220	0.00431	0.008731466	TRUE	0.31177
DNA replication	254824	239615	225384	0.00424	0.008664348	TRUE	0.09737
Fluorobenzoate degradation	107	140	80	0.00397	0.008245614	FALSE	
Taurine and hypotaurine metabolism	38876	36286	34202	0.004	0.008245614	TRUE	0.0492
Pertussis	2333	3342	3813	0.00382	0.008015179	TRUE	0.04307
Tryptophan metabolism	43481	40918	37140	0.0038	0.008015179	TRUE	0.22697
Biosynthesis of vancomycin group antibiotics	22859	21933	20224	0.00372	0.007947273	TRUE	0.29852
Glutathione metabolism	60855	59419	54927	0.00372	0.007947273	TRUE	0.5181
Insulin signaling pathway	44270	38656	37280	0.00371	0.007947273	TRUE	0.04605
Lysine degradation	46236	40294	39097	0.00346	0.007599065	TRUE	0.0197
Tropane, piperidine and pyridine alkaloid biosynthesis	47180	41554	40960	0.00346	0.007599065	TRUE	0.0124
DNA replication proteins	487298	455280	430104	0.00333	0.007452857	TRUE	0.07214
Lipid metabolism	66834	58838	55812	0.00329	0.007434135	TRUE	0.0305
Alanine, aspartate and glutamate metabolism	451901	417326	396073	0.00322	0.007346602	TRUE	0.04307
Lipoic acid metabolism	2292	3082	3631	0.00321	0.007346602	TRUE	0.03508
Others	360966	333463	309365	0.0032	0.007346602	TRUE	0.0815
Type I diabetes mellitus	20013	18867	17613	0.00318	0.007346602	TRUE	0.16858
Xylene degradation	24996	24693	20831	0.00291	0.006907576	TRUE	0.78951

RNA transport	69443	61534	57679	0.00283	0.006786224	TRUE	0.04605
Plant-pathogen interaction	86575	70493	70571	0.00271	0.006565464	TRUE	0.00454
Vibrio cholerae pathogenic cycle	30234	26345	26244	0.00268	0.006560417	TRUE	0.01239
Valine, leucine and isoleucine degradation	72744	64372	62995	0.0026	0.006431579	TRUE	0.00826
Bacterial chemotaxis	270324	198829	203371	0.0025	0.0064	TRUE	0.00264
Dioxin degradation	25077	24982	20974	0.00256	0.0064	TRUE	0.88827
Function unknown	477555	439946	410874	0.00247	0.0064	TRUE	0.0767
Glycolysis / Gluconeogenesis	458044	419886	396361	0.00245	0.0064	TRUE	0.02841
Nitrotoluene degradation	39271	36343	31510	0.00256	0.0064	TRUE	0.22697
Phosphatidylinositol signaling system	31675	28454	27037	0.00248	0.0064	TRUE	0.03273
Polycyclic aromatic hydrocarbon degradation	53053	48115	45690	0.00251	0.0064	TRUE	0.04605
Translation factors	212546	198303	187664	0.00252	0.0064	TRUE	0.05253
Tyrosine metabolism	131003	124392	114495	0.00229	0.006257558	TRUE	0.23796
Selenocompound metabolism	143011	133590	124354	0.00224	0.006192941	TRUE	0.0767
Atrazine degradation	6020	6917	4632	0.00218	0.006126786	FALSE	
Biosynthesis of unsaturated fatty acids	42549	39622	36377	0.00216	0.006126786	TRUE	0.11561
Chromosome	668116	606048	579661	0.00209	0.006126786	TRUE	0.02841
D-Glutamine and D-glutamate metabolism	57661	53152	50733	0.00216	0.006126786	TRUE	0.03509
General function prediction only	1458879	1360590	1279577	0.00219	0.006126786	TRUE	0.0678
Homologous recombination	372772	348413	328031	0.00202	0.006126786	TRUE	0.0492
Pyrimidine metabolism	729210	681105	642124	0.00216	0.006126786	TRUE	0.06368
Terpenoid backbone biosynthesis	245721	222114	212344	0.00215	0.006126786	TRUE	0.01693
Germination	22736	20681	18480	0.00194	0.005998684	TRUE	0.1559
Bacterial secretion system	213341	199956	189760	0.00191	0.005984667	TRUE	0.10925

Alzheimer's disease	19154	17688	16658	0.00184	0.005843243	TRUE	0.05426
Glycerolipid metabolism	178985	162257	149891	0.00184	0.005843243	TRUE	0.04307
Mineral absorption	520	795	1086	0.00182	0.005843243	TRUE	0.20607
Inorganic ion transport and metabolism	78395	66936	65636	0.00175	0.005792254	TRUE	0.00974
Peptidases	778181	711268	674273	0.00171	0.005740714	TRUE	0.03273
Bacterial invasion of epithelial cells	130	184	100	0.00162	0.005517391	FALSE	
Base excision repair	175866	165169	153343	0.00159	0.005517391	TRUE	0.09737
Bladder cancer	130	184	100	0.00162	0.005517391	FALSE	
Nucleotide excision repair	163173	151659	142198	0.00153	0.005517391	TRUE	0.05605
Purine metabolism	870300	816185	761594	0.00158	0.005517391	TRUE	0.09182
Arginine and proline metabolism	543941	493959	466277	0.0015	0.005507813	TRUE	0.0305
Nicotinate and nicotinamide metabolism	183213	168221	158486	0.00145	0.00540873	TRUE	0.02644
Tuberculosis	66677	59532	57065	0.0014	0.005306452	TRUE	0.01568
Other ion-coupled transporters	511935	465064	449056	0.00133	0.00512377	TRUE	0.01056
Amino acid related enzymes	619254	573861	537289	0.00129	0.0050525	TRUE	0.03509
beta-Lactam resistance	17811	15670	14759	0.00129	0.0050525	TRUE	0.04025
Cytoskeleton proteins	194064	171776	163633	0.00124	0.005024138	TRUE	0.02459
Two-component system	632169	526981	514767	0.00123	0.005024138	TRUE	0.00541
Aminoacyl-tRNA biosynthesis	506543	466692	434477	0.00112	0.004951786	TRUE	0.04307
Chlorocyclohexane and chlorobenzene degradation	3750	4130	2732	0.00097	0.004951786	FALSE	
Cysteine and methionine metabolism	393762	359327	339456	0.00096	0.004951786	TRUE	0.02644
DNA repair and recombination proteins	1136335	1063936	994135	0.00116	0.004951786	TRUE	0.06368
Glycine, serine and threonine metabolism	319745	298903	278698	0.00117	0.004951786	TRUE	0.09182

Glyoxylate and dicarboxylate metabolism	209456	191896	180518	0.00097	0.004951786	TRUE	0.04605
Phenylalanine, tyrosine and tryptophan biosynthesis	382514	342922	322610	0.00098	0.004951786	TRUE	0.02122
Polyketide sugar unit biosynthesis	86232	80210	74218	0.00118	0.004951786	TRUE	0.09737
Porphyrin and chlorophyll metabolism	487917	432820	409309	0.00093	0.004951786	TRUE	0.02459
PPAR signaling pathway	41473	38243	36518	0.00111	0.004951786	TRUE	0.0815
Proteasome	19473	17919	16494	0.00095	0.004951786	TRUE	0.08654
Protein kinases	135962	121553	112438	0.00103	0.004951786	TRUE	0.04025
Riboflavin metabolism	98070	86453	84368	0.00118	0.004951786	TRUE	0.01568
Ribosome	954652	895364	834618	0.00094	0.004951786	TRUE	0.07214
Secretion system	513299	439040	422618	0.00109	0.004951786	TRUE	0.00974
Sporulation	447493	384508	357884	0.00116	0.004951786	TRUE	0.0197
Starch and sucrose metabolism	503473	453044	423793	0.00097	0.004951786	TRUE	0.03509
Streptomycin biosynthesis	123662	115037	106908	0.00111	0.004951786	TRUE	0.11561
Translation proteins	371094	341612	321016	0.0008	0.004947368	TRUE	0.02644
Butanoate metabolism	228706	212143	196106	0.00077	0.004890541	TRUE	0.0678
Peptidoglycan biosynthesis	342636	321158	296679	0.00076	0.004890541	TRUE	0.09182
Replication, recombination and repair proteins	322788	301045	275935	0.00075	0.004890541	TRUE	0.10317
RNA polymerase	65836	61592	56415	0.00068	0.0047	TRUE	0.10925
D-Alanine metabolism	40321	37893	35119	0.00065	0.004628788	TRUE	0.0815
African trypanosomiasis	785	1073	365	0.00063	0.004626563	FALSE	
Novobiocin biosynthesis	57125	52054	49064	0.00062	0.004626563	TRUE	0.0197
Ribosome Biogenesis	621164	563307	529082	0.00056	0.004386667	TRUE	0.02122
Benzoate degradation	82519	76568	69984	0.0005	0.004213793	TRUE	0.05976

Chagas disease (American trypanosomiasis)	767	1058	347	0.00051	0.004213793	FALSE	
Ribosome biogenesis in eukaryotes	19917	18744	17027	0.00052	0.004213793	TRUE	0.144
Epithelial cell signaling in Helicobacter pylori infection	42558	39612	36060	0.00045	0.004067308	TRUE	0.10925
Lysine biosynthesis	395197	360614	333656	0.00041	0.004067308	TRUE	0.03509
Sulfur relay system	123068	108447	101319	0.00043	0.004067308	TRUE	0.01451
Thiamine metabolism	239476	212480	201200	0.00045	0.004067308	TRUE	0.00974
Type II diabetes mellitus	19613	18025	16803	0.00044	0.004067308	TRUE	0.02459
Pantothenate and CoA biosynthesis	285858	260145	242492	0.00033	0.003692857	TRUE	0.02644
Glycerophospholipid metabolism	274987	239503	228358	0.0003	0.003525	TRUE	0.00496
Lipopolysaccharide biosynthesis proteins	43266	52964	56684	0.00028	0.003463158	TRUE	0.02459
Transcription factors	805202	725566	664710	0.00026	0.003463158	TRUE	0.0305
Transporters	3170883	2938967	2624727	0.00028	0.003463158	TRUE	0.10317
Valine, leucine and isoleucine biosynthesis	340357	310939	282145	0.00026	0.003463158	TRUE	0.05976
ABC transporters	1525607	1424297	1265472	0.00021	0.00329	TRUE	0.09737
Photosynthesis	217398	196115	181261	0.00015	0.002685714	TRUE	0.02459
Photosynthesis proteins	217632	196426	181515	0.00016	0.002685714	TRUE	0.02459
Apoptosis	50	236	32	0.00011	0.002545833	FALSE	
Geraniol degradation	2759	4012	4525	0.00013	0.002545833	TRUE	0.02459
Signal transduction mechanisms	218001	200791	181589	0.00012	0.002545833	TRUE	0.04307
C5-Branched dibasic acid metabolism	145868	134479	119463	0.00009	0.00235	TRUE	0.12226
Fatty acid metabolism	89529	84411	75546	0.00006	0.0017625	TRUE	0.18664
Lipopolysaccharide biosynthesis	13203	22357	29725	0.00001	0.000335714	TRUE	0.0124
Protein digestion and absorption	1469	2480	3630	0.00001	0.000335714	TRUE	0.0076

Cellular antigens	2579	4295	5992	0	0	TRUE	0. 00541
Glycosaminoglycan degradation	7051	8117	13803	0	0	TRUE	0. 0815
Glycosphingolipid biosynthesis - ganglio series	2869	4125	9156	0	0	TRUE	0. 01145
Lysosome	15225	17725	22654	0	0	TRUE	0. 03273
Steroid hormone biosynthesis	671	1216	2602	0	0	TRUE	0. 0038

Table S3: The different fecal metabolites between Pri_GD and HC groups

ID	Pattern	Pri_GD mean	HC mean	VIP	FC (Pri_GD/HC)	P value	Metabolic names
n111	neg	5.8334	70.0384	1.42467	0.083288771	0.0044	5alpha,9alpha-epidioxy-cholest-7-en-3beta,6alpha-diol
n115	neg	1.3808	14.7979	1.56265	0.093310317	0.0292	5-Hydroxymethyluracil
n14	neg	0.46	1.6934	1.03559	0.271624764	0.0254	1,25-dihydroxy-2,4-dinor-1,3-secovitamin D3 / 1,25-dihydroxy-2,4-dinor-1,3-secocholecalciferol
n155	neg	0.4006	2.2121	1.49592	0.181111114	0.0345	Campesterol
n181	neg	7.9205	41.4859	1.00763	0.190920978	0.0295	D-Maltose
n20	neg	1.312	12.3516	2.11567	0.106220461	0.0205	10-Hydroxy-3,7-dimethyl-2E,6E-decadienoic acid
n21	neg	7.4587	58.7861	1.33812	0.126877891	0.0079	11-acetoxy-3beta,6alpha-dihydroxy-9,11-seco-5alpha-cholest-7-en-9-one.
n212	neg	0.7298	3.6116	2.25323	0.202068765	0.0422	L-3-Phenyllactic acid
n242	neg	61.9932	274.0992	1.14221	0.22617072	0.0464	Mycolipenic acid (C25)
n248	neg	0.0055	0.9418	2.92629	0.005828924	0.0075	Neuraminic acid
n27	neg	6.4177	71.855	1.09566	0.089315187	0.0108	15-HETE-G
n273	neg	5.7085	2.2079	2.25268	2.585503907	0.0397	PC(22:1(13Z)/24:1(15Z))
n3	neg	3.5344	56.0297	1.57131	0.063080995	0.0422	(1R,2R)-3-oxo-2-pentyl-cyclopentanehexanoic acid
n327	neg	7.013	79.4306	1.27705	0.088291372	0.007	Protometagenin
n33	neg	6.8851	43.1682	1.06186	0.159494641	0.0109	19-(3-methyl-butanoyloxy)-villanovane-13alpha,17-diol
n336	neg	0.2341	1.2199	1.85747	0.191858718	0.0415	Salicyluric acid
n343	neg	20.5078	142.4227	1.49742	0.143992249	0.032	Taurocholic acid
n345	neg	19.6947	125.4303	1.48689	0.157017165	0.0191	Tauroursodeoxycholic acid
n352	neg	0.5488	4.065	2.05912	0.135015158	0.0184	Thymidine
n356	neg	8.6886	40.6168	2.44587	0.213916195	0.0011	Ustilagic acid

n36	neg	0.4818	4.1113	1.53793	0.117183852	0.0214	1alpha,25-dihydroxy-24-oxo-22-oxavitamin D3 / 1alpha,25-dihydroxy-24-oxo-22-oxacholecalciferol
n38	neg	3.3499	36.0529	1.42069	0.092916917	0.0128	1alpha,25-dihydroxy-2alpha-(3-hydroxypropoxy)-19-norvitamin D3 / 1alpha,25-dihydroxy-2alpha-(3-hydroxypropoxy)-19-norcholecalciferol
n46	neg	1.5518	24.1995	2.19923	0.064126049	0.0453	1beta-butyl-1alpha,25-dihydroxyvitamin D3 / 1beta-butyl-1alpha,25-dihydroxycholecalciferol
n56	neg	0.9393	6.8185	2.09515	0.137752756	0.0254	24,24-Difluoro-25-hydroxy-26,27-dimethylvitamin D3
n63	neg	2.6164	28.2398	1.31344	0.092649536	0.0324	26,27-diethyl-1alpha,25-dihydroxyvitamin D3 / 26,27-diethyl-1alpha,25-dihydroxycholecalciferol
n64	neg	1.4904	21.1839	1.77725	0.070353711	0.0111	26,27-dinor-3alpha,6alpha,12alpha-trihydroxy-5beta-cholestan-24-one
n7	neg	0.5927	6.411	1.70428	0.092445488	0.0163	(24R,25S)-25,26-epoxy-1alpha,24-dihydroxy-27-norvitamin D3 / (24R,25S)-25,26-epoxy-1alpha,24-dihydroxy-27-norcholecalciferol
n70	neg	2.8164	47.1302	1.85513	0.059757738	0.0304	2alpha-(3-Hydroxypropyl)-1alpha,25-dihydroxy-19-norvitamin D3
n71	neg	24.8796	186.8705	1.10325	0.133138213	0.0095	2-deoxyecdysone
n83	neg	12.9388	90.4312	2.23255	0.143078809	0.0004	32,35-anhydrobacteriohopan-11-ene-tetrol
n86	neg	3.1904	31.124	2.23316	0.102507345	0.0323	3alpha,7alpha,12alpha,25-Tetrahydroxy-5beta-cholestan-26-oic acid
p1006	pos	6.9529	39.9708	3.16729	0.185514411	0.0197	PA(O-16:0/22:2(13Z,16Z))
p1089	pos	25.321	85.5748	1.4872	0.315591898	0.0357	PG(13:0/19:1(9Z))
p1097	pos	40.5726	19.08	1.06391	2.268176192	0.0082	PG(16:1(9Z)/20:4(5Z,8Z,11Z,14Z))
p110	pos	47.4172	191.4739	1.22437	0.264151169	0.0044	13,14-dihydroxy-docosanoic acid
p1104	pos	6.5435	20.7821	1.387	0.33583419	0.0053	PG(19:1(9Z)/0:0)
p1105	pos	29.2104	99.769	1.34427	0.312298237	0.0016	PG(20:0/0:0)
p114	pos	42.4036	139.8642	1.21157	0.323375647	0.0275	14,15-HxA3-C(11S)
p1221	pos	85.4103	41.4933	1.07151	2.195640292	0.0004	PS(O-16:0/14:1(9Z))

p1249	pos	18.5503	72.8051	3.76545	0.271771944	0.0093	Rifamycin B
p1288	pos	37.3733	103.2862	3.45444	0.385952876	0.0183	Sulfated Dihydromenaquinone-9
p131	pos	14.5966	47.6371	1.23822	0.326836409	0.0018	16,16-dimethyl-PGE1
p1346	pos	13.0292	37.842	1.65438	0.367253625	0.0035	Thromboxane B3
p1357	pos	12.6093	29.3074	1.04125	0.458917858	0.0034	Tuftsia
p1358	pos	2.022	11.8964	1.40837	0.181079778	0.0393	Tyramine
p1365	pos	148.7342	438.9666	1.19834	0.361416315	0.0022	VD 2716
p142	pos	7.9961	30.9673	1.56726	0.275370426	0.0257	17-oxo-20Z-hexacosenoic acid
p163	pos	0.6287	6.0774	2.27755	0.110260236	0.0085	1alpha,25-dihydroxy-2beta-(4-hydroxybutoxy)vitamin D3 / 1alpha,25-dihydroxy-2beta-(4-hydroxybutoxy)cholecalciferol
p164	pos	29.4087	75.1233	1.00043	0.417564481	0.006	1alpha,25-dihydroxy-2beta-(6-hydroxyhexyl)vitamin D3 / 1alpha,25-dihydroxy-2beta-(6-hydroxyhexyl)cholecalciferol
p166	pos	88.9645	195.2022	1.06556	0.486139523	0.0002	1alpha,25-dihydroxy-9,11-didehydro-3-deoxyvitamin D3 / 1alpha,25-dihydroxy-9,11-didehydro-3-deoxycholecalciferol
p168	pos	3.9417	14.3871	3.52004	0.292092991	0.0322	1alpha,25-Dihydroxyvitamin D3 25-trimethylsilyl ether
p17	pos	19.6203	47.2906	1.07072	0.442543662	0.0028	(1S)-1-hydroxy-23-oxo-24,25,26,27-tetranorcalciol
p185	pos	5.8764	13.7086	1.19694	0.457223223	0.0051	2,3-Dinor-6-keto-prostaglandin F1 a
p19	pos	17.0943	67.4905	1.23894	0.270150915	0.0202	(20R)-24-Hydroxygeminivitamin D3
p2	pos	57.5777	200.3503	1.37238	0.306543783	0.0004	(-)-Fusicoplugin A
p214	pos	38.5241	13.4519	1.05325	3.054599769	0.0303	24-hydroxy-tetracosanoic acid
p228	pos	378.0491	867.8545	1.01987	0.46465419	0.0022	27-Nor-5b-cholestane-3a,7a,12a,24,25-pentol
p239	pos	112.3806	248.6731	1.02846	0.482048283	0.0025	2beta,3alpha,7alpha,12alpha-Tetrahydroxy-5beta-cholestan-26-oic acid
p281	pos	483.7366	237.8967	1.10053	2.168948287	0.0003	3,7,11,15-Tetramethyl-6,10,14-hexadecatrien-1-ol
p347	pos	13.9799	65.6737	1.09016	0.227031004	0.0294	4E,6E,10Z-Hexadecatrien-1-ol

p373	pos	27.7336	67.9072	1.03543	0.435621582	0.0097	5a-Cholestane-3a,7a,12a,23,25-pentol
p375	pos	4.1177	17.6865	3.77152	0.24833385	0.0011	5alpha-Cholesterol
p389	pos	7.5536	0.6124	2.26536	13.15458429	0.0184	6,7-dihydroxy-4-oxo-2-heptenoic acid
p398	pos	14.3446	3.3594	2.57919	4.554454307	0.0098	6-Chloroapigenin
p399	pos	0.4314	14.3191	3.38831	0.032094924	0.0087	6-dehydrotestosterone 17-glucosiduronic acid
p413	pos	9.9673	4.2371	1.20267	2.50920455	0.0003	7,7-dimethyl-5Z,8Z-eicosadienoic acid
p433	pos	7.2974	20.7377	1.35727	0.375318618	0.0097	8'-apo-beta-carotenol
p436	pos	4.7571	11.6455	1.12616	0.435712519	0.0019	8-Epiiridotrial glucoside
p441	pos	1.7376	7.1959	1.84876	0.257248251	0.0353	8S-hydroxy-2E-Decene-4,6-diynoic acid
p443	pos	58.3005	35.0559	1.02199	1.773945001	0	8Z-Heptadecene
p449	pos	3.3423	38.7926	2.70941	0.091832065	0.0409	9,11alpha-epoxy-6alpha-acetoxy-cholest-7-en-3beta,5alpha,19-triol
p45	pos	4.0297	6.7228	1.6554	0.638877503	0.0495	(3'-sulfo)Galbeta-Cer(d18:1/16:0(2OH))
p453	pos	3.2607	8.1926	2.75445	0.424515493	0.0027	9-chloro-10-hydroxy-octadecanoic acid
p457	pos	16.1305	44.1143	1.28539	0.390013991	0.0098	9-hydroxy-10E,14Z-octadecadien-12-ynoic acid
p532	pos	200.7481	57.7877	1.0278	3.705427879	0.0477	Behenic acid
p533	pos	19.9768	10.7797	1.02704	1.976724792	0.0001	Behenoyl-EA
p538	pos	73.3183	207.3943	1.28209	0.37708929	0	Briantheine W
p539	pos	4.3088	16.101	1.35455	0.285447106	0.0002	Bufalin
p551	pos	7.444	187.1127	1.85398	0.042428915	0.0186	Capric acid
p554	pos	10.3689	42.0959	1.77494	0.262671058	0.0426	Cer(d16:1/17:0)
p574	pos	64.9189	29.4665	1.05529	2.350002226	0.0083	cholesteryl beta-D-glucoside
p588	pos	62.1282	125.032	1.06218	0.530024787	0.0006	Coproporphyrin III
p612	pos	3.6181	9.1294	1.37574	0.422690366	0.0055	Deoxyuridine
p617	pos	12.7436	72.6211	2.5315	0.187165234	0.0159	DG(13:0/20:4(5Z,8Z,11Z,14Z)/0:0)[iso2]

p629	pos	312.2669	843.4651	1.06343	0.394899897	0.0062	DG(15:0/16:1(9Z)/0:0)
p632	pos	71.054	211.7024	1.57095	0.358004953	0.0066	DG(15:0/18:3(6Z,9Z,12Z)/0:0)
p657	pos	9.2134	22.1357	2.18416	0.443911252	0.0208	diamino-pimelic acid
p693	pos	2.5073	24.8215	1.31368	0.107717892	0.0107	Epicatechin 3',4'-dimethyl ether
p701	pos	4.3358	17.0819	1.51443	0.270740734	0.0014	Erycristin
p712	pos	2533.1423	70.372	2.30675	38.39623042	0.0088	Etioline
p748	pos	8.8275	34.1918	1.48267	0.27536117	0.013	Glycocholic acid 3-glucuronide
p755	pos	94.6285	247.697	1.03946	0.40749887	0.0125	Grandiflorone
p758	pos	13.1046	4.1983	1.57229	3.329459475	0.0007	Guibourtinidol-(4alpha->6)-catechin
p759	pos	1.2457	4.0112	1.38275	0.331203805	0.0034	Guibourtinidol-7-methyl ether
p801	pos	35.6802	85.7829	1.02339	0.443661025	0.0052	Kazinol H
p829	pos	33.7517	11.7672	3.26269	3.059438397	0.0109	Liothyronine
p872	pos	6.4017	55.6542	2.16577	0.12264099	0.0456	methyl-10-hydroperoxy-8E,12Z,15Z-octadecatrienoate
p874	pos	12.1257	32.2292	1.2522	0.401303745	0.0053	MG(0:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)
p887	pos	29.9183	189.548	1.23718	0.168349941	0.0374	Myriocin

Table S4: The different fecal metabolites between Eut_GD and HC groups

ID	Pattern	Eut_GD mean	HC mean	m/z	VIP	P value	FC (Eut_GD/HC)	Metabolic names
n107	neg	12.3204	1.1283	341.1027242	2.32644	0.008328676	10.91899266	5,6,7,8-Tetramethoxyflavone
n132	neg	7.3253	26.8665	439.0850103	1.38585	0.039747616	0.272655677	9,10-dibromo-stearic acid
n20	neg	0.9905	12.3516	423.2746852	2.23239	0.016476361	0.0801901	10-Hydroxy-3,7-dimethyl-2E,6E-decadienoic acid
n21	neg	17.5715	58.7861	521.3478322	2.02985	0.034095018	0.298905835	11-acetoxy-3beta,6alpha-dihydroxy-9,11-seco-5alpha-cholest-7-en-9-one.
n212	neg	0.8796	3.6116	331.1183199	1.48295	0.047402296	0.243538782	L-3-Phenyllactic acid
n294	neg	2.6028	8.0813	867.5312014	1.94355	0.046301857	0.322076067	PG(18:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))
n297	neg	19.4814	141.761	805.5606198	2.15374	0.037891494	0.137423955	PG(0-16:0/20:2(11Z,14Z))
n327	neg	23.0372	79.4306	491.3007652	1.70969	0.036305533	0.290029569	Protometagenin
n356	neg	13.1653	40.6168	783.4018759	1.82953	0.008397192	0.324134097	Ustilagic acid
p102	pos	113.3146	333.8649	371.257492	1.16551	0.036060644	0.339402623	12alpha-Hydroxy-3-oxocholesterol-4-en-24-oic Acid
p1029	pos	21.0104	38.8742	672.4199126	1.13194	0.012537758	0.540470414	PC(16:0/9:0(CHO))
p1030	pos	0.2054	5.3577	268.6717728	3.35347	0.0185949	0.038346237	PC(16:1(9Z)/2:0)
p1045	pos	1.7796	10.6086	396.2505467	3.86648	0.037657364	0.167750165	PC(0-10:1(9E)/0:0)
p1056	pos	46.5792	7.9295	189.0218726	1.5171	0.010835067	5.874196554	p-Cresol sulfate
p1057	pos	43.0315	160.1165	628.3957506	2.04894	0.049849425	0.268751115	PE(12:0/14:1(9Z))
p1089	pos	28.5134	85.5748	703.4900227	3.1294	0.045097904	0.333198569	PG(13:0/19:1(9Z))
p1093	pos	18.1514	35.6262	451.2448803	1.11997	0.02372336	0.509496196	PG(15:1(9Z)/0:0)
p1105	pos	37.1895	99.769	523.3387979	1.35451	0.004855459	0.372756395	PG(20:0/0:0)
p1116	pos	199.6687	3710.697	819.5901509	3.52676	0.01146753	0.053808941	PG(0-20:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))

p1145	pos	5.7969	31.5573	875.5601956	2.88765	0.005378334	0.18369505	PI (13:0/22:0)
p1160	pos	26.1624	52.589	310.147347	1.0227	0.010618669	0.497489003	PI (20:5 (5Z, 8Z, 11Z, 14Z, 17Z) /0:0)
p1161	pos	43.9644	116.0338	657.3958648	1.17422	0.035399205	0.378893145	PI (22:0/0:0)
p1213	pos	2.3533	10.5892	850.5550188	2.31308	0.029038382	0.222234079	PS (17:1 (9Z) /22:2 (13Z, 16Z))
p1220	pos	2.9564	11.7893	411.7679519	2.81573	0.001855337	0.250768959	PS (22:6 (4Z, 7Z, 10Z, 13Z, 16Z, 19Z) /17:0)
p1221	pos	100.1396	41.4933	709.5123381	1.25426	0.000176231	2.413394082	PS (0-16:0/14:1 (9Z))
p1231	pos	63.4761	216.2129	499.209875	1.56487	0.024010866	0.293581598	punaglandin 4
p1249	pos	24.8276	72.8051	773.3471778	2.74813	0.019452536	0.341014616	Rifamycin B
p126	pos	3.1152	37.4968	299.2003896	3.23924	0.042004012	0.083078231	15-Deoxy-d-12, 14-PGJ2
p1288	pos	20.9086	103.2862	883.5895271	3.31389	0.000634591	0.202433953	Sulfated Dihydromenaquinone-9
p1293	pos	131.142	35.3332	416.3520408	1.59518	0.024513713	3.711584091	Teinemine
p181	pos	36.8241	18.3589	666.52283	1.07628	0.00063966	2.005787834	1-tetradecanyl-2-(8-[3]-ladderane-octanyl)-sn-glycerophosphoethanolamine
p185	pos	6.8391	13.7086	365.1941479	1.35673	0.009557546	0.498892368	2,3-Dinor-6-keto-prostaglandin F1 a
p268	pos	1.2165	16.2883	171.1166478	4.15416	0.034217974	0.074686829	2-tridecene-4,7-diynal
p28	pos	181.6463	92.6607	485.3611184	1.08138	0.000747754	1.960338436	(22R)-1alpha,25-dihydroxy-22-methoxy-26,27-dimethyl-23,23,24,24-tetradehydro-24a-homovitamin D3 / (22R)-1alpha,25-dihydroxy-22-methoxy-26,27-dimethyl-23,23,24,24-tetradehydro-24a-homocholecalciferol
p290	pos	2370.3735	7575.7859	373.2735203	1.34143	0.008170164	0.312888125	3alpha,12alpha-Dihydroxy-5beta-chol-6-en-24-olic Acid

p291	pos	171.5722	444.1017	429.2603476	1.21168	0.015879006	0.386335394	3alpha,12beta-Dihydroxy-11-oxo-5beta-cholan-24-oic Acid
p307	pos	15.1269	37.3313	171.0764553	1.05167	0.014196832	0.405207396	3-Hydroxyanthranilic acid
p328	pos	0.5666	2.0245	201.1631665	3.03816	0.009034523	0.279857383	4(15),7(11)-Oppositadien-12-al
p329	pos	0.7821	4.1326	145.1011783	3.91908	0.02068755	0.189246207	4,10-undecadiynal
p331	pos	0.0771	0.5119	405.3511702	2.80227	0.016167432	0.150620865	4,4'-Diapo-zeta-carotene
p345	pos	2.3734	4.5097	110.0597784	1.27143	0.000226117	0.526293203	4-Aminophenol
p37	pos	2.5485	9.7544	271.6791419	2.42285	0.030128761	0.261269899	(25R)-3alpha,7alpha-dihydroxy-5beta-cholestan-27-oyl taurine
p372	pos	9.7146	68.016	259.168929	2.00539	0.00849575	0.142827825	5,8,11-heptadecatriynoic acid
p382	pos	6.5899	22.4898	336.2533783	2.86836	0.041429516	0.293017179	5-KETE (5-oxo-6E,8Z,11Z,14Z-eicosatetraenoic acid)
p398	pos	12.4684	3.3594	305.0343773	2.13438	0.010461355	3.711501912	6-Chloroapigenin
p402	pos	28.7949	110.2208	245.1531663	1.4359	0.003624781	0.261247021	6E,8E,12E,14E-Hexadecatetraen-10-ynoic acid
p413	pos	9.4076	4.2371	319.299306	1.03629	0.003989001	2.220289037	7,7-dimethyl-5Z,8Z-eicosadienoic acid
p414	pos	9.3897	35.0688	297.1844269	1.2167	0.025911412	0.267750587	7,8,7',8'-Tetradehydroastaxanthin
p419	pos	1.8336	8.9617	205.1583269	2.839	0.032200865	0.204606756	7E,9E,11-Dodecatrienyl acetate
p436	pos	5.3917	11.6455	327.143423	1.8839	0.003899319	0.462988916	8-Epiiridotrial glucoside
p45	pos	4.3351	6.7228	813.5510404	1.02461	0.03598899	0.644836272	(3'-sulfo)Galbeta-Cer(d18:1/16:0(20H))
p456	pos	27.3197	7.1552	346.2588095	1.69021	0.039854833	3.818158176	9-hydroperoxy-12,13-epoxy-10-octadecenoic acid
p457	pos	18.1987	44.1143	293.2255823	1.20068	0.009671446	0.412535055	9-hydroxy-10E,14Z-octadecadien-12-ynoic acid
p510	pos	5.5334	37.5799	287.2006823	2.58553	0.030116358	0.147242815	Androstenedione

p52	pos	9.8243	21.0854	198.1157957	1.08017	0.010130888	0.465929687	(6RS)-22-hydroxy-23,24,25,26,27-pentanorvitamin D3 6,19-sulfur dioxide adduct / (6RS)-22-hydroxy-23,24,25,26,27-pentanorcholecalciferol 6,19-sulfur dioxide adduct
p53	pos	8.4755	44.8008	197.1080135	1.44513	0.020868421	0.189182616	(6RS)-22-oxo-23,24,25,26,27-pentanorvitamin D3 6,19-sulfur dioxide adduct / (6RS)-22-oxo-23,24,25,26,27-pentanorcholecalciferol 6,19-sulfur dioxide adduct
p532	pos	133.982	57.7877	358.3677469	1.03393	0.038010817	2.318520693	Behenic acid
p564	pos	581.7952	224.1733	560.501531	1.20512	0.003660198	2.595291592	Ceramide (d18:1/16:0)
p568	pos	0.7576	3.0677	185.1322704	2.13521	0.013363574	0.246943484	Chamazulene
p574	pos	91.9171	29.4665	571.3981211	1.14815	0.009354184	3.119378704	cholesteryl beta-D-glucoside
p578	pos	2.5005	8.7556	147.1167638	3.35444	0.035137872	0.285584336	cis-Jasmone
p597	pos	183.0873	45.6099	272.1278654	1.19752	0.0344685	4.014198839	Dalbergichromene
p601	pos	48.3109	16.4401	316.2844858	1.32511	0.023703313	2.938599419	Dehydrophytosphingosine
p609	pos	9.978	84.9995	313.216058	2.39395	0.02973526	0.117389383	Deoxycorticosterone
p610	pos	16.92	27.9888	268.1039991	1.07083	0.046319147	0.604526856	Deoxyguanosine
p611	pos	2.604	5.9813	207.1050185	1.26157	0.043797223	0.435348662	Deoxypyridinoline
p612	pos	2.9783	9.1294	211.0711201	2.38911	0.001532512	0.326230796	Deoxyuridine
p657	pos	9.2309	22.1357	403.1810259	1.11996	0.01131364	0.417013671	diamino-pimelic acid
p693	pos	3.2469	24.8215	301.1061996	1.14001	0.012655655	0.130808351	Epicatechin 3',4'-dimethyl ether
p695	pos	2.7781	103.0147	923.3159501	3.30447	0.049989847	0.026967995	Epimedokoreanoside I
p721	pos	2.0874	11.8536	684.4589922	2.91393	0.012944686	0.176100052	Galbeta1-3GalNAcbeta1-4Galbeta1-4Glcbeta-Cer (d18:1/26:0)

p733	pos	2.4016	40.5317	617.3613849	1.29039	0.043659048	0.059252776	Gestrinone
p749	pos	12.0163	33.2723	667.2292766	1.87284	0.03071236	0.361149209	Glycogen
p803	pos	2.9938	27.8566	868.5096368	4.02135	0.004695133	0.1074717	KDNalpha2-3Galbeta1-4(Fucalpha1-3)GlcNAcbeta1-3Galbeta1-4Glcbeta-Cer(d18:1/24:0)
p812	pos	75.3495	27.7176	884.607136	1.44518	0.043888349	2.718468276	LacCer(d18:1/16:0)
p862	pos	57.9857	18.929	550.4824419	1.54715	0.011870587	3.063329635	Mayolene-16
p918	pos	45.2664	133.8532	619.4092333	2.21068	0.045791884	0.338179346	NeuAcalpha2-3Galbeta1-4Glcbeta-Cer(d18:1/22:0)
p969	pos	4.9213	25.8078	669.482675	2.49688	0.005556869	0.19069207	PA(14:1(9Z)/18:0)

Table S5: The different fecal metabolites between Pri_GD and Eut_GD groups

ID	Pattern	Pri_GD mean	Eut_GD mean	m/z	VIP	P value	FC (Pri_GD/Eut_GD)	Metabolic names
n111	neg	5.8334	29.5023	477.3217373	1.4223	0.015362185	0.197727152	5alpha,9alpha-epidioxy-cholest-7-en-3beta,6alpha-diol
n180	neg	1.7699	4.5586	599.525591	1.44248	0.009221864	0.388264008	DL-2-hydroxy stearic acid
n3	neg	3.5344	15.3354	535.3998913	2.5898	0.041783386	0.230473805	(1R,2R)-3-oxo-2-pentyl-cyclopentanehexanoic acid
n301	neg	351.5126	717.5824	773.5705164	1.95767	0.049984322	0.489856756	PG(0-20:0/17:2(9Z,12Z))
n322	neg	2.1822	4.0255	825.4705067	1.35642	0.017148012	0.542107748	PPA(18:1(9Z)/18:1(9Z))
n33	neg	6.8851	21.7608	467.3017655	1.13358	0.013715919	0.316398246	19-(3-methyl-butanoyloxy)-villanovane-13alpha,17-diol
n38	neg	3.3499	12.3551	523.3631724	1.44021	0.030121964	0.271136405	1alpha,25-dihydroxy-2alpha-(3-hydroxypropoxy)-19-norvitamin D3 / 1alpha,25-dihydroxy-2alpha-(3-hydroxypropoxy)-19-norcholecalciferol
n64	neg	1.4904	9.2723	451.3060429	1.12792	0.013480558	0.160732833	26,27-dinor-3alpha,6alpha,12alpha-trihydroxy-5beta-cholestan-24-one
n70	neg	2.8164	18.1145	507.3683181	1.90024	0.017540004	0.155477253	2alpha-(3-Hydroxypropyl)-1alpha,25-dihydroxy-19-norvitamin D3
p1039	pos	135.7251	20.6135	800.5936207	3.03055	0.044728529	6.584290376	PC(22:5(4Z,7Z,10Z,13Z,16Z)/P-18:1(11Z))
p1109	pos	83.0837	125.1627	531.271768	1.00644	0.003479151	0.663805684	PG(20:5(5Z,8Z,11Z,14Z,17Z)/0:0)
p124	pos	10.338	25.0024	277.2160528	1.59298	0.009786351	0.413479732	15(16)-EpODE
p1240	pos	40.1364	2.3425	757.1995175	5.18152	0.037305178	17.13363905	Quercetin 3-(2G-(E)-p-coumaroylrutinoside)
p1269	pos	3.1561	10.686	324.2871121	2.66667	0.019492089	0.295352961	Sphinganine
p1280	pos	96.4235	313.9539	428.3725928	1.41586	0.008901659	0.307126254	Stearoylcarnitine
p1285	pos	187.9603	364.7384	485.3241567	1.07451	0.024867903	0.515329111	Stoloniferone F

p1369	pos	9.4614	19.7541	455.3877209	3.22069	0.009790592	0.478957612	Vitamin D3 butyrate
p1372	pos	3.0466	7.9132	206.0446043	2.14376	0.032310894	0.385005199	Xanthurenic acid
p139	pos	22.8441	38.9385	413.2001922	2.20198	0.049628549	0.586671803	17-Hydroxypregnenolone sulfate
p142	pos	8.5275	39.6894	431.3507216	2.38573	0.018941883	0.2148553	17-oxo-20Z-hexacosenoic acid
p166	pos	94.8955	198.6322	381.3149313	1.0619	0.006020999	0.477744817	1alpha,25-dihydroxy-9,11-didehydro-3-deoxyvitamin D3 / 1alpha,25-dihydroxy-9,11-didehydro-3-deoxycholecalciferol
p186	pos	58.5315	126.5092	989.5406781	1.68641	0.040088755	0.462666389	2',4',6',3,4-Pentahydroxy-3'-geranyl-5-prenyldihydrochalcone
p19	pos	18.2326	61.3973	519.402871	1.82263	0.018811105	0.296961459	(20R)-24-Hydroxygeminivitamin D3
p194	pos	4.5547	1.0787	258.2425328	2.73888	0.016388985	4.222305911	2,5-dimethyl-2E-tridecenoic acid
p2	pos	61.4161	118.3094	461.2514262	1.00492	0.008896074	0.519114843	(-)-Fusicoplagin A
p228	pos	403.2522	749.0876	461.3236093	1.03084	0.000813303	0.53832453	27-Nor-5b-cholestane-3a,7a,12a,24,25-pentol
p229	pos	80.4944	172.1927	499.3262466	1.29483	0.00674381	0.467466891	27-nor-campestan-3beta,4beta,5alpha,6alpha,7beta,8beta,14alpha,15alpha,24-nonol
p271	pos	21.5974	48.6193	268.2633133	1.12249	0.018351734	0.444213343	3,4,7,11-Tetramethyl-6E,10Z-tridecadienal
p288	pos	15.8562	29.314	469.4031983	1.2167	0.035368807	0.54090986	32:6(14Z,17Z,20Z,23Z,26Z,29Z)
p292	pos	12.9928	27.6289	438.3576197	2.09414	0.024873696	0.470261779	3Alpha,7Alpha,12Alpha-trihydroxy-27-nor-5Beta-cholestan-24-one
p322	pos	3.7889	10.2007	207.1737271	1.19338	0.022912092	0.371429804	3-oxo-13-Tetradecenal
p327	pos	644.7194	1564.4532	160.1330453	1.73076	0.005232623	0.412105259	3-tert-butyl-3-butenic acid
p345	pos	3.9405	2.3734	110.0597784	1.28423	0.026290081	1.660244086	4-Aminophenol
p347	pos	14.91	59.0978	254.2475112	1.58905	0.019176205	0.252293126	4E,6E,10Z-Hexadecatrien-1-ol
p354	pos	4.6612	8.4259	177.091275	1.55817	0.003666171	0.553196639	4'-O-Methylbavachalcone

p36	pos	24.742	47.9086	457.2929631	1.04781	0.021374656	0.516441937	(24R)-1alpha, 24, 25-trihydroxy-22-oxavitamin D3 / (24R)-1alpha, 24, 25-trihydroxy-22-oxacholecalciferol
p361	pos	2.3324	5.0537	193.1221647	2.81044	0.024161909	0.461531958	5,11-dodecadiynoic acid
p371	pos	3.7269	8.8452	254.2841303	2.96469	0.024021489	0.421348958	5,7-Heptadecadiene
p373	pos	29.5818	66.6154	470.3834271	1.31049	0.014466972	0.444069086	5a-Cholestane-3a, 7a, 12a, 23, 25-pentol
p374	pos	24.0432	76.0579	454.3885455	1.15129	0.033817913	0.316116886	5alpha-Cholestane-3alpha, 7alpha, 16alpha, 26-tetrol
p384	pos	13.9378	34.7433	419.3132764	1.17552	0.018997581	0.401163367	5-methyl-2-undecenoic acid
p50	pos	32.1743	55.8745	480.3502653	1.03056	0.006930071	0.575832491	(6R)-6-methylvitamin D3 6,19-sulfur dioxide adduct / (6R)-6-methylcholecalciferol 6,19-sulfur dioxide adduct
p539	pos	4.596	13.2138	387.2526052	1.50631	0.003215592	0.347817766	Bufalin
p554	pos	11.0574	42.5224	546.4860823	1.29654	0.028069798	0.260036205	Cer(d16:1/17:0)
p555	pos	23.6191	82.9319	534.4863742	1.09708	0.009753519	0.284800409	Cer(d18:0/14:0)
p560	pos	22.4831	51.0193	532.4701937	1.50795	0.046009586	0.440678865	Cer(d18:1/14:0)
p564	pos	236.8867	581.7952	560.501531	1.33327	0.004777596	0.407165133	Ceramide (d18:1/16:0)
p566	pos	101.645	345.8254	586.516424	1.41784	0.019051513	0.293919947	Ceramide (d18:1/9Z-18:1)
p617	pos	13.5921	259.3068	592.4929034	4.39541	0.035945307	0.052417236	DG(13:0/20:4(5Z, 8Z, 11Z, 14Z)/0:0) [iso2]
p629	pos	333.0843	855.0032	575.4631365	1.02607	0.023919427	0.389570802	DG(15:0/16:1(9Z)/0:0)
p755	pos	100.9363	203.0588	651.2938377	1.23851	0.024673454	0.497078876	Grandiflorone
p758	pos	13.9782	6.1444	564.1874294	1.40087	0.005344014	2.274941831	Guibourtinidol-(4alpha->6)-catechin
p796	pos	30.1823	89.6563	613.4417581	1.19459	0.039955572	0.336644871	Jurubine
p817	pos	60.4657	145.6934	280.2633553	1.27349	0.042941675	0.415020506	Lepadin D
p829	pos	36.0011	15.9085	668.8241707	2.54599	0.039780717	2.263005351	Liothyronine
p862	pos	16.2148	57.9857	550.4824419	2.77041	0.009802404	0.279634456	Mayolene-16
p874	pos	12.9337	26.7227	403.2841933	1.09205	0.032354176	0.483996394	MG(0:0/22:6(4Z, 7Z, 10Z, 13Z, 16Z, 19Z)/0:0)

p888	pos	3.4295	12.5631	211.2053902	3.92291	0.007933819	0.272981484	Myristic acid
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Table S6: KEGG pathways of differential metabolite annotation between Pri_GD and HC groups

Level 1	Level 2	Level 3	P value (enrichment analysis at the level 3)	Pathway ID	Num. of Metabolites	Metabolic names
Environmental Information Processing	Membrane transport	ABC transporters	2.46E-01	ko02010	1	D-Maltose
Metabolism	Lipid metabolism	alpha-Linolenic acid metabolism	1.13E-01	ko00592	1	PC(22:1(13Z)/24:1(15Z))
Metabolism	Lipid metabolism	Arachidonic acid metabolism	1.72E-01	ko00590	1	PC(22:1(13Z)/24:1(15Z))
Human Diseases	Immune diseases	Autoimmune thyroid disease	9.88E-03	ko05320	1	Liothyronine
Cellular Processes	Cell motility	Bacterial chemotaxis	3.14E-02	ko02030	1	D-Maltose
Organismal Systems	Digestive system	Bile secretion	1.70E-03	ko04976	3	6-dehydrotestosterone 17-glucosiduronic acid;Liothyronine;Taurocholic acid
Metabolism	Metabolism of terpenoids and polyketides	Biosynthesis of ansamycins	7.40E-02	ko01051	1	Rifamycin B
Metabolism	Global and overview maps	Biosynthesis of antibiotics	1.84E-01	ko01130	1	Rifamycin B
Metabolism	Global and overview maps	Biosynthesis of secondary metabolites	–	ko01110	4	PC(22:1(13Z)/24:1(15Z));Tyramine;Campesterol;Coproporphyrin III
Metabolism	Lipid metabolism	Biosynthesis of unsaturated fatty acids	1.37E-01	ko01040	1	Behenic acid

Metabolism	Metabolism of terpenoids and polyketides	Brassinosteroid biosynthesis	6.76E-02	ko00905	1	Campesterol
Organismal Systems	Digestive system	Carbohydrate digestion and absorption	6.76E-02	ko04973	1	D-Maltose
Organismal Systems	Digestive system	Cholesterol metabolism	2.67E-02	ko04979	1	Taurocholic acid
Human Diseases	Cancers: Overview	Choline metabolism in cancer	3.14E-02	ko05231	1	PC (22:1 (13Z) /24:1 (15Z))
Metabolism	Lipid metabolism	Cutin, suberine and wax biosynthesis	6.54E-02	ko00073	1	Behenic acid
Metabolism	Lipid metabolism	Fatty acid biosynthesis	1.32E-01	ko00061	1	Capric acid
Metabolism	Lipid metabolism	Glycerophospholipid metabolism	1.36E-01	ko00564	1	PC (22:1 (13Z) /24:1 (15Z))
Metabolism	Metabolism of terpenoids and polyketides	Insect hormone biosynthesis	6.10E-02	ko00981	1	2-deoxyecdysone
Metabolism	Biosynthesis of other secondary metabolites	Isoquinoline alkaloid biosynthesis	2.28E-01	ko00950	1	Tyramine
Metabolism	Lipid metabolism	Linoleic acid metabolism	6.97E-02	ko00591	1	PC (22:1 (13Z) /24:1 (15Z))
Metabolism	Global and overview maps	Metabolic pathways	–	ko01100	9	6-dehydrotestosterone 17-glucosiduronic acid;Thymidine;Taurocholic acid;Coproporphyrin III;PC (22:1 (13Z) /24:1 (15Z)) ;Campesterol;Liothyronine;Capric acid;D-Maltose

Metabolism	Energy metabolism	Methane metabolism	1.85E-01	ko00680	1	Tyramine
Environmental Information Processing	Signaling molecules and interaction	Neuroactive ligand-receptor interaction	3.71E-02	ko04080	2	Tyramine;Liothyronine
Metabolism	Carbohydrate metabolism	Pentose and glucuronate interconversions	1.39E-01	ko00040	1	6-dehydrotestosterone 17-glucosiduronic acid
Metabolism	Amino acid metabolism	Phenylalanine metabolism	1.69E-01	ko00360	1	L-3-Phenyllactic acid
Environmental Information Processing	Membrane transport	Phosphotransferase system (PTS)	1.41E-01	ko02060	1	D-Maltose
Metabolism	Metabolism of cofactors and vitamins	Porphyrin and chlorophyll metabolism	2.63E-01	ko00860	1	Coproporphyrin III
Metabolism	Lipid metabolism	Primary bile acid biosynthesis	1.07E-01	ko00120	1	Taurocholic acid
Organismal Systems	Digestive system	Protein digestion and absorption	1.05E-01	ko04974	1	Tyramine
Metabolism	Nucleotide metabolism	Pyrimidine metabolism	1.37E-02	ko00240	2	Deoxyuridine;Thymidine
Organismal Systems	Nervous system	Retrograde endocannabinoid signaling	4.98E-02	ko04723	1	PC(22:1(13Z)/24:1(15Z))
Metabolism	Lipid metabolism	Secondary bile acid biosynthesis	9.08E-02	ko00121	1	Taurocholic acid
Metabolism	Carbohydrate metabolism	Starch and sucrose metabolism	1.07E-01	ko00500	1	D-Maltose
Metabolism	Lipid metabolism	Steroid biosynthesis	1.13E-01	ko00100	1	Campesterol

Organismal Systems	Sensory system	Taste transduction	7.62E-02	ko04742	1	D-Maltose
Metabolism	Metabolism of other amino acids	Taurine and hypotaurine metabolism	7.40E-02	ko00430	1	Taurocholic acid
Organismal Systems	Environmental adaptation	Thermogenesis	6.10E-02	ko04714	1	Liothyronine
Organismal Systems	Endocrine system	Thyroid hormone signaling pathway	2.91E-02	ko04919	1	Liothyronine
Organismal Systems	Endocrine system	Thyroid hormone synthesis	5.21E-02	ko04918	1	Liothyronine
Metabolism	Biosynthesis of other secondary metabolites	Tropane, piperidine and pyridine alkaloid biosynthesis	1.46E-01	ko00960	1	L-3-Phenyllactic acid
Metabolism	Metabolism of terpenoids and polyketides	Type I polyketide structures	6.10E-02	ko01052	1	Rifamycin B
Metabolism	Amino acid metabolism	Tyrosine metabolism	1.83E-02	ko00350	2	Tyramine;Liothyronine

Table S7: KEGG pathways of differential metabolite annotation between Eut_GD and HC groups

Level 1	Level 2	Level 3	P value (enrichment analysis at the level 3)	Pathway ID	Num. of Metabolites	Metabolic names
Organismal Systems	Endocrine system	Adipocytokine signaling pathway	1.91E-02	ko04920	1	Ceramide (d18:1/16:0)
Human Diseases	Endocrine and metabolic diseases	AGE-RAGE signaling pathway in diabetic complications	2.94E-02	ko04933	1	Ceramide (d18:1/16:0)
Organismal Systems	Endocrine system	Aldosterone synthesis and secretion	5.14E-02	ko04925	1	Deoxycorticosterone
Metabolism	Xenobiotics biodegradation and metabolism	Aminobenzoate degradation	1.64E-02	ko00627	2	3-Hydroxyanthranilic acid;4-Aminophenol
Metabolism	Lipid metabolism	Arachidonic acid metabolism	1.53E-01	ko00590	1	15-Deoxy-d-12,14-PGJ2
Metabolism	Metabolism of terpenoids and polyketides	Biosynthesis of ansamycins	6.48E-02	ko01051	1	Rifamycin B
Metabolism	Global and overview maps	Biosynthesis of antibiotics	2.32E-01	ko01130	1	Rifamycin B
Metabolism	Global and overview maps	Biosynthesis of secondary metabolites	–	ko01110	1	Glycogen
Metabolism	Lipid metabolism	Biosynthesis of unsaturated fatty acids	1.22E-01	ko01040	1	Behenic acid
Organismal Systems	Digestive system	Carbohydrate digestion and absorption	5.91E-02	ko04973	1	Glycogen
Metabolism	Energy metabolism	Carbon fixation in photosynthetic	5.52E-02	ko00710	1	Glycogen

		organisms				
Metabolism	Lipid metabolism	Cutin, suberine and wax biosynthesis	5.72E-02	ko00073	1	Behenic acid
Organismal Systems	Endocrine system	Glucagon signaling pathway	5.33E-02	ko04922	1	Glycogen
Human Diseases	Endocrine and metabolic diseases	Insulin resistance	1.04E-03	ko04931	2	Ceramide (d18:1/16:0);Glycogen
Organismal Systems	Endocrine system	Insulin signaling pathway	1.07E-02	ko04910	1	Glycogen
Human Diseases	Infectious diseases: Parasitic	Leishmaniasis	1.70E-02	ko05140	1	Ceramide (d18:1/16:0)
Metabolism	Global and overview maps	Metabolic pathways	–	ko01100	7	Ceramide (d18:1/16:0);Glycogen;LacCer(d18:1/16:0);Androstenedione;3-Hydroxyanthranilic acid;Deoxyguanosine;Deoxycorticosterone
Metabolism	Global and overview maps	Microbial metabolism in diverse environments	–	ko01120	3	3-Hydroxyanthranilic acid;4-Aminophenol;Androstenedione
Cellular Processes	Cell growth and death	Necroptosis	2.53E-02	ko04217	1	Ceramide (d18:1/16:0)
Organismal Systems	Nervous system	Neurotrophin signaling pathway	1.49E-02	ko04722	1	Ceramide (d18:1/16:0)
Organismal Systems	Endocrine system	Ovarian steroidogenesis	4.94E-02	ko04913	1	Androstenedione

Human Diseases	Cancers: Overview	Pathways in cancer	7.05E-02	ko05200	1	Androstenedione
Metabolism	Amino acid metabolism	Phenylalanine metabolism	1.50E-01	ko00360	1	L-3-Phenyllactic acid
Organismal Systems	Endocrine system	Prolactin signaling pathway	2.32E-02	ko04917	1	Androstenedione
Human Diseases	Cancers: Specific types	Prostate cancer	2.32E-02	ko05215	1	Androstenedione
Metabolism	Nucleotide metabolism	Purine metabolism	1.82E-01	ko00230	1	Deoxyguanosine
Metabolism	Nucleotide metabolism	Pyrimidine metabolism	1.39E-01	ko00240	1	Deoxyuridine
Metabolism	Lipid metabolism	Sphingolipid metabolism	1.77E-03	ko00600	2	Ceramide (d18:1/16:0);LacCer (d18:1/16:0)
Environmental Information Processing	Signal transduction	Sphingolipid signaling pathway	3.75E-02	ko04071	1	Ceramide (d18:1/16:0)
Metabolism	Carbohydrate metabolism	Starch and sucrose metabolism	9.42E-02	ko00500	1	Glycogen
Metabolism	Xenobiotics biodegradation and metabolism	Steroid degradation	4.55E-02	ko00984	1	Androstenedione
Metabolism	Lipid metabolism	Steroid hormone biosynthesis	1.77E-02	ko00140	2	Androstenedione;Deoxycorticosterone
Metabolism	Biosynthesis of other secondary metabolites	Tropane, piperidine and pyridine alkaloid biosynthesis	1.30E-01	ko00960	1	L-3-Phenyllactic acid
Metabolism	Amino acid metabolism	Tryptophan metabolism	1.64E-01	ko00380	1	3-Hydroxyanthranilic acid
Metabolism	Metabolism of	Type I polyketide structures	5.33E-02	ko01052	1	Rifamycin B

	terpenoids and polyketides					
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Table S8: KEGG pathways of differential metabolite annotation between Pri_GD and Eut_GD groups

Level 1	Level 2	Level 3	P value (enrichment analysis at the level 3)	Pathway ID	Num. of Metabolites	Metabolic names
Organismal Systems	Endocrine system	Adipocytokine signaling pathway	5.50E-05	ko04920	2	Ceramide (d18:1/16:0);Ceramide (d18:1/9Z-18:1)
Human Diseases	Endocrine and metabolic diseases	AGE-RAGE signaling pathway in diabetic complications	1.38E-04	ko04933	2	Ceramide (d18:1/16:0);Ceramide (d18:1/9Z-18:1)
Metabolism	Lipid metabolism	alpha-Linolenic acid metabolism	6.38E-02	ko00592	1	PC(22:5 (4Z, 7Z, 10Z, 13Z, 16Z) /P-18:1 (11Z))
Metabolism	Xenobiotics biodegradation and metabolism	Aminobenzoate degradation	1.14E-01	ko00627	1	4-Aminophenol
Metabolism	Lipid metabolism	Arachidonic acid metabolism	1.01E-01	ko00590	1	PC(22:5 (4Z, 7Z, 10Z, 13Z, 16Z) /P-18:1 (11Z))
Human Diseases	Immune diseases	Autoimmune thyroid disease	5.29E-03	ko05320	1	Liothyronine
Organismal Systems	Digestive system	Bile secretion	1.19E-01	ko04976	1	Liothyronine
Metabolism	Global and overview maps	Biosynthesis of secondary metabolites	–	ko01110	1	PC(22:5 (4Z, 7Z, 10Z, 13Z, 16Z) /P-18:1 (11Z))
Human Diseases	Cancers: Overview	Choline metabolism in cancer	1.70E-02	ko05231	1	PC(22:5 (4Z, 7Z, 10Z, 13Z, 16Z) /P-18:1 (11Z))
Metabolism	Lipid metabolism	Fatty acid biosynthesis	7.54E-02	ko00061	1	Myristic acid
Metabolism	Lipid metabolism	Glycerophospholipid metabolism	7.77E-02	ko00564	1	PC(22:5 (4Z, 7Z, 10Z, 13Z, 16Z) /P-18:1 (11Z))
Human Diseases	Endocrine and	Insulin resistance	3.81E-04	ko04931	2	Ceramide (d18:1/16:0);Ceramide

	metabolic diseases					(d18:1/9Z-18:1)
Human Diseases	Infectious diseases: Parasitic	Leishmaniasis	4.28E-05	ko05140	2	Ceramide (d18:1/16:0);Ceramide (d18:1/9Z-18:1)
Metabolism	Lipid metabolism	Linoleic acid metabolism	3.85E-02	ko00591	1	PC(22:5(4Z, 7Z, 10Z, 13Z, 16Z)/P-18:1(11Z))
Metabolism	Global and overview maps	Metabolic pathways	–	ko01100	6	Ceramide (d18:1/9Z-18:1);PC(22:5(4Z, 7Z, 10Z, 13Z, 16Z)/P-18:1(11Z));Ceramide (d18:1/16:0);Sphinganine;Myristic acid;Liothyronine
Metabolism	Global and overview maps	Microbial metabolism in diverse environments	–	ko01120	1	4-Aminophenol
Cellular Processes	Cell growth and death	Necroptosis	1.01E-04	ko04217	2	Ceramide (d18:1/16:0);Ceramide (d18:1/9Z-18:1)
Environmental Information Processing	Signaling molecules and interaction	Neuroactive ligand-receptor interaction	1.49E-01	ko04080	1	Liothyronine
Organismal Systems	Nervous system	Neurotrophin signaling pathway	3.22E-05	ko04722	2	Ceramide (d18:1/16:0);Ceramide (d18:1/9Z-18:1)
Organismal Systems	Nervous system	Retrograde endocannabinoid signaling	2.72E-02	ko04723	1	PC(22:5(4Z, 7Z, 10Z, 13Z, 16Z)/P-18:1(11Z))
Metabolism	Lipid metabolism	Sphingolipid metabolism	6.08E-06	ko00600	3	Ceramide (d18:1/16:0);Ceramide (d18:1/9Z-18:1);Sphinganine
Environmental Information	Signal transduction	Sphingolipid signaling pathway	1.23E-06	ko04071	3	Ceramide (d18:1/16:0);Ceramide (d18:1/9Z-18:1);Sphinganine

Processing						
Organismal Systems	Environmental adaptation	Thermogenesis	3.35E-02	ko04714	1	Liothyronine
Organismal Systems	Endocrine system	Thyroid hormone signaling pathway	1.57E-02	ko04919	1	Liothyronine
Organismal Systems	Endocrine system	Thyroid hormone synthesis	2.85E-02	ko04918	1	Liothyronine
Metabolism	Amino acid metabolism	Tryptophan metabolism	1.09E-01	ko00380	1	Xanthurenic acid
Metabolism	Amino acid metabolism	Tyrosine metabolism	1.05E-01	ko00350	1	Liothyronine

Table S9: Partial recovery of differential KEGG pathways in Eut_GD group

ID	KEGG pathway names	HC mean	Pri_GD mean	Eut_GD mean	P value (Pri_GD vs. Eut_GD)	Partial recovery (True/False)
KEGG 2	ABC transporters	1073125.93	1546075.73	1447582.60	0.00003	TRUE
KEGG 4	African trypanosomiasis	214.60	917.00	867.13	0.0014	TRUE
KEGG 5	Alanine, aspartate and glutamate metabolism	362177.20	456447.80	426468.33	0.00024	TRUE
KEGG 7	Alzheimer's disease	15213.87	19292.53	18199.40	0.00012	TRUE
KEGG 8	Amino acid metabolism	53271.40	75392.93	74737.80	0.00007	TRUE
KEGG 9	Amino acid related enzymes	489356.20	624449.73	589503.73	0.00011	TRUE
KEGG 10	Amino sugar and nucleotide sugar metabolism	459047.27	567906.00	538268.33	0.00046	TRUE
KEGG 11	Aminoacyl-tRNA biosynthesis	391118.80	510228.47	480463.13	0.00012	TRUE
KEGG 12	Aminobenzoate degradation	25911.07	29806.53	30847.67	0.01074	FALSE
KEGG 13	Amoebiasis	1959.13	3979.60	3713.80	0.00002	TRUE
KEGG 15	Antigen processing and presentation	14716.07	18148.73	16823.67	0.00098	TRUE
KEGG 16	Apoptosis	32.07	51.60	284.93	0.01701	FALSE
KEGG 17	Arachidonic acid metabolism	3883.47	2089.60	3573.13	0.00394	TRUE
KEGG 18	Arginine and proline metabolism	419815.73	547854.60	507084.20	0.00012	TRUE
KEGG 19	Ascorbate and aldarate metabolism	19961.07	24821.87	26859.47	0.01359	FALSE
KEGG 20	Atrazine degradation	2792.47	6454.80	7142.73	0.00001	FALSE
KEGG 21	Bacterial chemotaxis	194547.07	260307.33	208838.20	0.01359	TRUE
KEGG 23	Bacterial motility proteins	401948.53	513687.20	399159.40	0.04425	TRUE
KEGG 24	Bacterial secretion system	176867.87	213699.33	207151.20	0.00024	TRUE
KEGG 25	Bacterial toxins	35008.47	46552.40	43232.40	0.00039	TRUE
KEGG 27	Base excision repair	137062.13	177732.47	170132.13	0.00007	TRUE

KEGG 28	Benzoate degradation	61826.40	82971.93	77961.60	0.00007	TRUE
KEGG 29	beta-Alanine metabolism	59672.27	76772.33	72931.93	0.00131	TRUE
KEGG 30	beta-Lactam resistance	13326.87	17856.80	16358.33	0.00028	TRUE
KEGG 31	Biosynthesis and biodegradation of secondary metabolites	16071.53	20381.13	21294.00	0.00659	FALSE
KEGG 32	Biosynthesis of ansamycins	44986.00	56553.20	50953.73	0.00151	TRUE
KEGG 34	Biosynthesis of unsaturated fatty acids	31690.00	42327.67	40789.33	0.00028	TRUE
KEGG 35	Biosynthesis of vancomycin group antibiotics	18287.00	23343.27	22318.40	0.00011	TRUE
KEGG 36	Biotin metabolism	48782.80	60321.93	57578.40	0.00098	TRUE
KEGG 37	Bisphenol degradation	26514.00	33954.53	30270.00	0.00302	TRUE
KEGG 39	Butanoate metabolism	177713.07	230439.87	216167.47	0.00021	TRUE
KEGG 40	Butirosin and neomycin biosynthesis	24458.73	29972.60	26723.93	0.0023	TRUE
KEGG 41	C5-Branched dibasic acid metabolism	104061.13	147800.60	136523.27	0.00006	TRUE
KEGG 44	Carbohydrate metabolism	60138.73	81754.47	75553.73	0.00024	TRUE
KEGG 45	Carbon fixation in photosynthetic organisms	220254.53	271338.27	254318.07	0.00062	TRUE
KEGG 46	Carbon fixation pathways in prokaryotes	275941.20	337876.73	329407.20	0.00039	TRUE
KEGG 47	Carotenoid biosynthesis	86.93	149.80	136.13	0.00263	TRUE
KEGG 48	Cell cycle - Caulobacter	159342.00	201848.87	195148.87	0.00012	TRUE
KEGG 49	Cell division	24113.73	32081.20	31219.80	0.00011	TRUE
KEGG 51	Cellular antigens	7645.73	2715.47	4678.20	0.00002	TRUE
KEGG 52	Chagas disease (American trypanosomiasis)	199.13	899.27	851.93	0.00151	TRUE
KEGG 53	Chaperones and folding catalysts	332285.73	399402.93	379205.07	0.00098	TRUE
KEGG 54	Chloroalkane and chloroalkene degradation	49309.20	77134.00	73225.60	0.00001	TRUE

KEGG 55	Chlorocyclohexane and chlorobenzene degradation	1664.00	4053.67	3996.80	0.00001	TRUE
KEGG 56	Chromosome	534431.33	669253.13	626313.20	0.00028	TRUE
KEGG 57	Citrate cycle (TCA cycle)	139178.67	155293.00	155634.33	0.00449	FALSE
KEGG 58	Cyanoamino acid metabolism	101418.20	127510.87	114436.67	0.00151	TRUE
KEGG 59	Cysteine and methionine metabolism	312272.20	396361.00	368064.00	0.00021	TRUE
KEGG 60	Cytoskeleton proteins	148386.87	194417.87	176841.00	0.00021	TRUE
KEGG 61	D-Alanine metabolism	31988.27	40560.93	39172.33	0.00017	TRUE
KEGG 63	D-Glutamine and D-glutamate metabolism	47049.27	58145.27	54717.40	0.00033	TRUE
KEGG 64	Dioxin degradation	15653.87	25522.80	25250.87	0.00003	TRUE
KEGG 65	DNA repair and recombination proteins	901404.00	1148294.60	1092853.33	0.00012	TRUE
KEGG 66	DNA replication	205660.00	258101.47	245555.93	0.00033	TRUE
KEGG 67	DNA replication proteins	394678.40	492122.13	466755.87	0.00033	TRUE
KEGG 68	Drug metabolism - cytochrome P450	3961.00	5784.87	6178.33	0.01359	FALSE
KEGG 69	Drug metabolism - other enzymes	104626.53	124322.00	118801.40	0.00062	TRUE
KEGG 71	Energy metabolism	277062.67	338474.00	320683.67	0.00098	TRUE
KEGG 72	Epithelial cell signaling in Helicobacter pylori infection	31906.40	43106.27	41035.67	0.00005	TRUE
KEGG 73	Ether lipid metabolism	205.60	368.00	373.27	0.00046	FALSE
KEGG 75	Fatty acid biosynthesis	143067.67	186592.13	179264.07	0.00017	TRUE
KEGG 76	Fatty acid metabolism	68480.07	90536.47	85574.40	0.00006	TRUE
KEGG 79	Flavonoid biosynthesis	231.07	408.53	445.73	0.01209	FALSE
KEGG 81	Folate biosynthesis	105837.13	132242.40	132112.13	0.00021	TRUE
KEGG 82	Fructose and mannose metabolism	297618.53	382464.33	370245.07	0.00033	TRUE

KEGG 83	Function unknown	370706.53	479732.60	453249.20	0.00028	TRUE
KEGG 85	Galactose metabolism	279230.13	352816.53	326037.60	0.00033	TRUE
KEGG 86	General function prediction only	1153580.93	1469192.20	1399037.53	0.00017	TRUE
KEGG 87	Geraniol degradation	5270.53	2473.80	4668.93	0.00004	TRUE
KEGG 88	Germination	15206.40	22928.73	21232.33	0.00009	TRUE
KEGG 89	Glutamatergic synapse	35438.27	45315.53	42694.00	0.00021	TRUE
KEGG 90	Glutathione metabolism	52282.40	61550.07	61253.13	0.00113	TRUE
KEGG 91	Glycan biosynthesis and metabolism	6305.53	5148.93	6416.53	0.00449	TRUE
KEGG 92	Glycerolipid metabolism	129409.53	179702.93	166037.47	0.00017	TRUE
KEGG 93	Glycerophospholipid metabolism	210073.73	273301.93	247741.67	0.00033	TRUE
KEGG 94	Glycine, serine and threonine metabolism	253275.80	322718.73	306495.67	0.00017	TRUE
KEGG 95	Glycolysis / Gluconeogenesis	357031.27	460494.93	430855.53	0.00015	TRUE
KEGG 96	Glycosaminoglycan degradation	17861.67	7464.60	8515.33	0.00001	TRUE
KEGG 97	Glycosphingolipid biosynthesis - ganglio series	12380.60	2971.73	4657.47	0	TRUE
KEGG 99	Glycosyltransferases	98715.60	119188.67	114735.33	0.00581	TRUE
KEGG 100	Glyoxylate and dicarboxylate metabolism	163844.67	209908.40	196872.07	0.00021	TRUE
KEGG 101	Histidine metabolism	214857.53	275834.60	255769.40	0.00028	TRUE
KEGG 102	Homologous recombination	298405.40	376687.67	358156.87	0.00015	TRUE
KEGG 104	Inorganic ion transport and metabolism	62792.47	77001.20	69940.47	0.00394	TRUE
KEGG 105	Inositol phosphate metabolism	22246.60	28209.47	27392.73	0.00024	TRUE
KEGG 106	Insulin signaling pathway	33867.47	43831.47	39976.47	0.00098	TRUE
KEGG 107	Ion channels	1502.53	2401.80	2753.67	0.01708	FALSE
KEGG 108	Isoquinoline alkaloid biosynthesis	17379.40	19315.40	18256.33	0.0191	TRUE
KEGG 109	Limonene and pinene degradation	18264.53	22949.47	22690.33	0.00302	TRUE

KEGG 110	Linoleic acid metabolism	20060.93	26448.07	24569.13	0.00062	TRUE
KEGG 111	Lipid biosynthesis proteins	190259.40	234458.67	218650.27	0.00046	TRUE
KEGG 112	Lipid metabolism	49070.53	66643.87	61428.93	0.00046	TRUE
KEGG 113	Lipoic acid metabolism	3926.47	2400.93	2997.93	0.02648	TRUE
KEGG 114	Lipopolysaccharide biosynthesis	38497.80	13325.13	26114.13	0.00004	TRUE
KEGG 115	Lipopolysaccharide biosynthesis proteins	62841.60	44087.53	57402.93	0.00046	TRUE
KEGG 116	Lysine biosynthesis	298402.33	398534.40	368977.80	0.00009	TRUE
KEGG 117	Lysine degradation	36360.87	45412.20	42401.13	0.00345	TRUE
KEGG 118	Lysosome	25578.73	16198.40	17887.60	0.00033	TRUE
KEGG 119	MAPK signaling pathway - yeast	11199.80	14157.87	13642.80	0.00113	TRUE
KEGG 122	Metabolism of cofactors and vitamins	27033.60	37427.60	37889.00	0.00002	FALSE
KEGG 123	Metabolism of xenobiotics by cytochrome P450	3951.47	5740.73	6090.53	0.01439	FALSE
KEGG 124	Methane metabolism	377505.53	520291.27	495371.67	0.00009	TRUE
KEGG 125	Mineral absorption	1138.80	528.47	918.13	0.00953	TRUE
KEGG 126	Mismatch repair	260676.47	331065.13	313950.87	0.00046	TRUE
KEGG 127	Naphthalene degradation	36022.07	45905.13	43677.87	0.00024	TRUE
KEGG 128	N-Glycan biosynthesis	4646.00	5877.07	6175.40	0.0362	FALSE
KEGG 129	Nicotinate and nicotinamide metabolism	144416.87	184048.13	173124.80	0.00024	TRUE
KEGG 130	Nitrogen metabolism	211035.47	262978.27	249372.87	0.00062	TRUE
KEGG 131	Nitrotoluene degradation	23921.27	40381.33	37166.13	0.00002	TRUE
KEGG 132	NOD-like receptor signaling pathway	15135.40	18237.47	16911.87	0.00264	TRUE
KEGG 134	Novobiocin biosynthesis	44976.93	57472.40	53409.07	0.00021	TRUE
KEGG 135	Nucleotide excision repair	129395.87	164984.40	155308.93	0.00012	TRUE
KEGG 136	Nucleotide metabolism	9804.60	12381.40	11634.27	0.00844	TRUE

KEGG 137	One carbon pool by folate	210281.00	253080.40	238376.73	0.00113	TRUE
KEGG 139	Other ion-coupled transporters	423406.00	511776.73	480178.53	0.00084	TRUE
KEGG 140	Other transporters	83385.80	103441.60	98373.73	0.00131	TRUE
KEGG 141	Others	271344.13	363752.93	341015.73	0.00033	TRUE
KEGG 142	Oxidative phosphorylation	325245.00	409440.67	402309.07	0.00039	TRUE
KEGG 143	Pantothenate and CoA biosynthesis	220346.27	287659.87	266605.07	0.00011	TRUE
KEGG 144	Pathways in cancer	15242.67	18639.87	17706.60	0.00131	TRUE
KEGG 146	Pentose and glucuronate interconversions	162245.73	204964.00	195899.20	0.00033	TRUE
KEGG 147	Pentose phosphate pathway	291947.53	379876.13	357045.00	0.00028	TRUE
KEGG 148	Peptidases	613432.93	782975.53	731086.47	0.00017	TRUE
KEGG 149	Peptidoglycan biosynthesis	265810.33	346475.53	330657.53	0.00006	TRUE
KEGG 150	Peroxisome	52885.47	61752.80	58192.13	0.00131	TRUE
KEGG 151	Pertussis	4349.20	1803.53	3910.80	0.00151	TRUE
KEGG 152	Phenylalanine metabolism	51915.07	62752.07	60131.60	0.00098	TRUE
KEGG 153	Phenylalanine, tyrosine and tryptophan biosynthesis	292095.00	383446.27	352626.00	0.00028	TRUE
KEGG 154	Phenylpropanoid biosynthesis	65367.53	83999.93	72567.00	0.00345	TRUE
KEGG 155	Phosphatidylinositol signaling system	24966.07	31657.87	29514.67	0.00053	TRUE
KEGG 156	Phosphonate and phosphinate metabolism	10132.20	12964.40	12827.00	0.00174	TRUE
KEGG 157	Phosphotransferase system (PTS)	138568.87	192118.53	184395.73	0.00072	TRUE
KEGG 158	Photosynthesis	166272.27	217960.07	202172.67	0.00012	TRUE
KEGG 159	Photosynthesis proteins	166537.07	218163.20	202490.80	0.00012	TRUE
KEGG 160	Plant-pathogen interaction	66853.33	84807.47	73789.27	0.00747	TRUE
KEGG 161	Polycyclic aromatic hydrocarbon degradation	41611.73	53138.27	49956.87	0.00012	TRUE

KEGG 162	Polyketide sugar unit biosynthesis	67630.20	87410.67	82343.13	0.00024	TRUE
KEGG 164	Porphyrin and chlorophyll metabolism	368753.00	491272.40	447428.80	0.00017	TRUE
KEGG 165	PPAR signaling pathway	35452.20	42116.47	38585.27	0.00046	TRUE
KEGG 166	Prenyltransferases	98272.40	117192.07	111742.47	0.00072	TRUE
KEGG 167	Primary bile acid biosynthesis	12122.67	16247.93	14690.07	0.00084	TRUE
KEGG 168	Primary immunodeficiency	18997.80	24358.73	21937.80	0.00511	TRUE
KEGG 169	Prion diseases	944.73	1239.33	1443.13	0.0191	FALSE
KEGG 170	Progesterone-mediated oocyte maturation	14716.07	18148.73	16823.67	0.00098	TRUE
KEGG 171	Propanoate metabolism	129053.13	174722.60	171744.47	0.00009	TRUE
KEGG 172	Prostate cancer	14828.40	18187.53	16873.60	0.00131	TRUE
KEGG 173	Proteasome	14961.00	19768.07	18087.00	0.00007	TRUE
KEGG 174	Protein digestion and absorption	4892.87	1686.13	2481.27	0.00004	TRUE
KEGG 175	Protein export	190451.60	235312.93	222558.67	0.00033	TRUE
KEGG 176	Protein folding and associated processing	181025.53	231429.00	226784.27	0.00017	TRUE
KEGG 177	Protein kinases	97808.20	135426.93	125244.33	0.00017	TRUE
KEGG 180	Purine metabolism	692210.93	879408.87	838868.60	0.00017	TRUE
KEGG 181	Pyrimidine metabolism	588426.53	736027.33	700139.93	0.00021	TRUE
KEGG 182	Pyruvate metabolism	310401.80	410018.20	389015.53	0.00015	TRUE
KEGG 184	Replication, recombination and repair proteins	244195.00	326005.20	310659.47	0.00007	TRUE
KEGG 185	Restriction enzyme	66009.80	74665.20	68451.40	0.02944	TRUE
KEGG 187	Riboflavin metabolism	81872.27	97639.00	90590.20	0.00581	TRUE
KEGG 188	Ribosome	759709.40	966150.73	919294.93	0.00006	TRUE
KEGG 189	Ribosome Biogenesis	482826.60	622291.80	582354.67	0.00015	TRUE
KEGG 190	Ribosome biogenesis in eukaryotes	15434.93	20189.73	19046.40	0.00007	TRUE

KEGG 191	RIG-I-like receptor signaling pathway	555.07	856.93	1027.47	0.00174	FALSE
KEGG 192	RNA degradation	149213.20	181435.67	171576.07	0.00046	TRUE
KEGG 193	RNA polymerase	50788.47	66749.93	63170.93	0.00012	TRUE
KEGG 194	RNA transport	49947.13	69181.47	64326.60	0.00046	TRUE
KEGG 195	Secondary bile acid biosynthesis	12122.67	16247.93	14690.07	0.00084	TRUE
KEGG 196	Secretion system	392937.73	503712.53	459620.93	0.00264	TRUE
KEGG 197	Selenocompound metabolism	113212.80	144006.33	137023.47	0.00033	TRUE
KEGG 198	Signal transduction mechanisms	160032.00	219630.80	205123.40	0.00006	TRUE
KEGG 199	Sphingolipid metabolism	84106.67	94010.87	84051.07	0.04881	TRUE
KEGG 200	Sporulation	302544.00	448738.67	394019.27	0.00028	TRUE
KEGG 201	Staphylococcus aureus infection	522.27	916.13	2460.00	0.00394	FALSE
KEGG 202	Starch and sucrose metabolism	387357.33	507310.00	461073.27	0.00012	TRUE
KEGG 203	Steroid hormone biosynthesis	3558.00	707.67	1376.47	0	TRUE
KEGG 204	Stilbenoid, diarylheptanoid and gingerol biosynthesis	55.80	99.20	187.80	0.02105	FALSE
KEGG 205	Streptomycin biosynthesis	98369.20	125389.07	117521.07	0.00024	TRUE
KEGG 206	Styrene degradation	2577.20	4685.13	4818.27	0.00015	FALSE
KEGG 207	Sulfur metabolism	99064.33	120920.13	109362.67	0.00659	TRUE
KEGG 208	Sulfur relay system	91067.47	122523.13	112065.20	0.00028	TRUE
KEGG 210	Taurine and hypotaurine metabolism	31500.20	39160.00	37170.20	0.00039	TRUE
KEGG 211	Terpenoid backbone biosynthesis	197091.27	246323.47	228996.33	0.00046	TRUE
KEGG 212	Tetracycline biosynthesis	37489.40	57587.40	57936.67	0.00004	FALSE
KEGG 213	Thiamine metabolism	186241.00	239971.33	218621.60	0.00028	TRUE
KEGG 215	Transcription factors	580123.47	808600.87	740510.00	0.00017	TRUE

KEGG 216	Transcription machinery	331178.33	413790.27	380451.27	0.00053	TRUE
KEGG 218	Translation factors	172121.13	214479.73	204464.53	0.00017	TRUE
KEGG 219	Translation proteins	292518.40	373308.67	351810.60	0.00012	TRUE
KEGG 220	Transporters	2223498.20	3207046.80	2982098.07	0.00004	TRUE
KEGG 221	Tropane, piperidine and pyridine alkaloid biosynthesis	38988.80	47054.80	42907.67	0.00302	TRUE
KEGG 222	Tryptophan metabolism	32424.53	43289.20	42584.60	0.00024	TRUE
KEGG 223	Tuberculosis	53352.13	66654.13	61385.73	0.00039	TRUE
KEGG 224	Two-component system	478018.67	619668.40	547685.53	0.0023	TRUE
KEGG 225	Type I diabetes mellitus	16201.60	20276.67	19184.67	0.00021	TRUE
KEGG 226	Type II diabetes mellitus	15449.13	19736.07	18592.40	0.00021	TRUE
KEGG 227	Tyrosine metabolism	101751.80	132559.93	127010.53	0.00007	TRUE
KEGG 228	Ubiquinone and other terpenoid-quinone biosynthesis	30987.20	20054.93	25182.73	0.00024	TRUE
KEGG 229	Ubiquitin system	1414.67	1079.27	1127.33	0.04003	TRUE
KEGG 230	Valine, leucine and isoleucine biosynthesis	248556.20	343611.80	316511.87	0.00006	TRUE
KEGG 231	Valine, leucine and isoleucine degradation	62080.27	71978.07	66891.33	0.01359	TRUE
KEGG 232	Vibrio cholerae pathogenic cycle	25890.80	29950.07	27234.93	0.01074	TRUE
KEGG 233	Vitamin B6 metabolism	63367.33	74458.40	72169.27	0.00174	TRUE
KEGG 234	Xylene degradation	15488.13	25436.53	24906.13	0.00002	TRUE
KEGG 235	Zeatin biosynthesis	17353.67	19661.20	19056.73	0.00511	TRUE

Table S10: The features list of prediction models 2 and 3

Clssfier list	Eut_GD mean	Pri_GD mean	HC mean	Model 4
p2	118.309352	61.41614067	200.350306	Yes
p142	39.65886667	8.531987333	30.97931267	
p228	749.0875933	403.2522267	867.8544933	Yes
p345	2.374533333	3.940666667	4.51	Yes
p539	13.21378446	4.595988993	16.10101803	Yes
p564	581.7952087	236.8867233	224.1733493	Yes
p617	259.4046667	13.56313333	72.61133333	
p758	6.148666667	13.982	4.200933333	Yes
p862	58.00666667	16.1986	18.92733333	Yes
n38	12.35146667	3.345733333	36.04710667	
n111	29.50473333	5.836266667	70.05933333	
<i>Eubacterium_rectale</i>	3043.733333	4883.933333	3194.266667	
<i>Bacteroides</i>	1836.6	1191.533333	7086.733333	Yes
<i>Coprococcus_3</i>	135.3333333	204.2	65.86666667	Yes
<i>Dialister</i>	735.9333333	225.8	646.8	Yes
<i>Erysipelotrichaceae_UCG-003</i>	343.2666667	619.7333333	144	Yes
<i>Intestinibacter</i>	437.5333333	229.6	214.8666667	
<i>Lachnospiraceae_ND3007</i>	116.0666667	195.2666667	79.2	Yes
<i>Prevotella_9</i>	2077.666667	586.6	3172.666667	Yes
<i>Ruminococcus_1</i>	501.9333333	423.8666667	281.4666667	