

Supplementary Materials

Supplementary Methods

To identify potential microbiota markers that differentiate between the two subtypes of colorectal cancer or colorectal adenoma, we constructed classification models based on the top 30 different genera using two different methods, linear support vector machine and logistic regression, respectively. All analyses were carried out using the Python package ‘scikit-learn’¹.

The SelectFromModel method from scikit-learn was used for feature selection. The mean absolute coefficient value is set as a threshold parameter, and if the corresponding absolute coefficient values are below the mean absolute value, the features are considered unimportant and removed. Models were validated by 5-fold stratified cross-validation testing (we resampled dataset partitions 5 times). In each test, the accuracy of the model was examined using an area under the receiver operating characteristic curve.

Supplementary References

1. Pedregosa F, Varoquaux G, Gramfort A, et al. Scikit-learn: machine learning in Python. *JMLR* 2011; 12: 2825-2830.

Supplementary Table

Supplementary Table 1. Comparison of clinical characteristics between two subgroups in the colorectal cancer group

Variable	Type I (n = 77)	Type II (n = 53)	<i>P</i> value
Age, years			0.499
Mean (SD)	60.05 (9.98)	61.25 (9.69)	
Range	41-88	40-80	
Sex, No. (%)			0.212
Female	35 (45.5)	30 (56.6)	
Male	42 (54.5)	23 (43.4)	
Body mass index ^a , kg/m ²			0.489
Mean (SD)	23.75 (3.16)	23.37 (3.00)	
Range	17.03-33.33	17.02-30.85	
Education degree, No. (%)			0.990
Illiteracy	9 (11.7)	6 (11.3)	
Primary	12 (15.6)	8 (15.1)	
Middle	46 (59.7)	33 (62.3)	
High	10 (13.0)	6 (11.3)	
Physical activity, No. (%)			0.228
Heavy	12 (15.6)	12 (22.6)	
Medium	17 (22.1)	14 (26.4)	
Light	48 (62.3)	27 (51.0)	

Diseases history, No. (%)			
Hypertension			0.380
No	55 (71.4)	34 (64.2)	
Yes	22 (28.6)	19 (35.8)	
Coronary heart disease			0.201
No	74 (96.1)	48 (90.6)	
Yes	3 (3.9)	5 (9.4)	
Diabetes			0.677
No	70 (90.9)	47 (88.7)	
Yes	7 (9.1)	6 (11.3)	
TNM stage, No. (%)			0.422
Stage I-II	47 (61.0)	36 (67.9)	
Stage III-IV	30 (39.0)	17 (32.1)	
Differentiation grade, No. (%)			0.058
Unevaluable	0 (0.0)	1 (1.9)	
Low	0 (0.0)	3 (5.7)	
Medium	76 (98.7)	48 (90.6)	
High	1 (1.3)	1 (1.9)	
Lesion site, No. (%)			0.689
Proximal colon ^b	25 (32.5)	19 (35.8)	
Distal colon ^b and rectum	52 (67.5)	34 (64.2)	

Complete blood count			
Lymphocyte count, $\times 10^9/L$			0.818
Mean (SD)	1.88 (0.74)	1.85 (0.62)	
Range	0.75-4.47	0.55-3.6	
Neutrophil count, $\times 10^9/L$			0.656
Mean (SD)	3.97 (1.5)	3.84 (1.92)	
Range	1.37-8.24	1.2-12.34	
Platelet count, $\times 10^9/L$			0.073
Mean (SD)	239.52 (72.01)	218.02 (57.77)	
Range	100-418	88-347	
Hemoglobin, g/L			0.402
Mean (SD)	119.65 (25.19)	122.79 (17.44)	
Range	53-177	77-161	
Blood biochemistry			
Direct bilirubin, $\mu\text{mol/L}$			0.235
Mean (SD)	3.19 (1.70)	4.72 (11.08)	
Range	0.5-9.7	1-83	
Albumin, g/L			0.580
Mean (SD)	39.57 (3.41)	39.25 (3.11)	
Range	32-49	30-47	
Alanine transaminase, U/L			0.506
Mean (SD)	19.86 (11.6)	21.92 (23.4)	
Range	5-75	6-173	

Aspartate aminotransferase, U/L			0.411
Mean (SD)	21.45 (6.48)	23.26 (17.62)	
Range	13-42	11-136	
Alkaline phosphatase, U/L			0.048
Mean (SD)	69.97 (19.14)	63.83 (15.28)	
Range	20-153	42-102	
Lactic dehydrogenase, U/L			0.135
Mean (SD)	170.99 (41.68)	162.15 (25.09)	
Range	102-324	86-229	
Fasting blood-glucose, mmol/L			0.278
Mean (SD)	5.28 (1.05)	6 (5.69)	
Range	4-9	4-46	
Creatinine, μ mol/L			0.396
Mean (SD)	71.22 (14.19)	68.92 (16.34)	
Range	46-99	39-114	
Tumor markers			
Carcinoembryonic antigen, ng/ml			0.039
Mean (SD)	11.55 (23.83)	5.45 (7.19)	
Range	0.68-157.98	0.79-35.18	
Carbohydrate antigen 199, U/ml			0.719
Mean (SD)	58.41 (193.61)	46.9 (154.1)	
Range	2-999.99	2-922.02	

Abbreviations: SD, standard deviation.

^a Body mass index: weight (kg)/height (m)².

^b With the splenic flexure as the boundary, the proximal colon includes the cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure, while the distal colon includes the descending colon, sigmoid colon, and the rectosigmoid junction.

Supplementary Table 2. Comparison of clinical characteristics between two subgroups in the colorectal adenoma group

Variable	Type I (n = 66)	Type II (n = 54)	<i>P</i> value
Age, years			0.461
Mean (SD)	58.44 (9.59)	59.81 (10.75)	
Range	41-83	40-84	
Sex, No. (%)			0.723
Female	26 (39.4)	23 (42.6)	
Male	40 (60.6)	31 (57.4)	
Body mass index ^a , kg/m ²			0.766
Mean (SD)	23.95 (3.28)	24.13 (3.42)	
Range	15.43-32.24	17.30-31.14	
Education degree, No. (%)			0.404
Illiteracy	2 (3.0)	3 (5.6)	
Primary	9 (13.6)	13 (24.1)	
Middle	39 (59.1)	26 (48.1)	
High	16 (24.2)	12 (22.2)	

Physical activity, No. (%)			0.966
Heavy	5 (7.6)	5 (9.3)	
Medium	13 (19.7)	12 (22.2)	
Light	48 (72.8)	37 (68.5)	
Diseases history, No. (%)			
Hypertension			0.889
No	46 (69.7)	37 (68.5)	
Yes	20 (30.3)	17 (31.5)	
Coronary heart disease			0.507
No	63 (95.5)	50 (92.6)	
Yes	3 (4.5)	4 (7.4)	
Diabetes			0.459
No	60 (90.9)	51 (94.4)	
Yes	6 (9.1)	3 (5.6)	
Lesion site, No. (%)			0.729
Proximal colon ^b	24 (36.4)	18 (33.3)	
Distal colon ^b and rectum	42 (63.6)	36 (66.7)	
Complete blood count			
Lymphocyte count, ×10 ⁹ /L			0.721
Mean (SD)	2.13 (0.74)	2.18 (0.72)	
Range	0.55-4.57	0.87-3.98	

Neutrophil count, $\times 10^9/L$			0.343
Mean (SD)	3.74 (1.22)	3.97 (1.48)	
Range	1.21-6.02	1.56-8.44	
Platelet count, $\times 10^9/L$			0.250
Mean (SD)	195.95 (50.94)	206.57 (48.86)	
Range	89-303	124-380	
Hemoglobin, g/L			0.734
Mean (SD)	140.11 (17.80)	139.19 (11.57)	
Range	71-172	115-157	
Blood biochemistry			
Direct bilirubin, $\mu\text{mol/L}$			0.744
Mean (SD)	3.62 (1.85)	3.44 (1.35)	
Range	1.2-9.1	1.7-7.3	
Albumin, g/L			0.642
Mean (SD)	40.08 (2.96)	39.08 (9.88)	
Range	34-45	4-49	
Alanine transaminase, U/L			0.160
Mean (SD)	27.17 (21.17)	19.34 (6.17)	
Range	12-121	8-28	
Aspartate aminotransferase, U/L			0.242
Mean (SD)	27.79 (21.44)	21.17 (7.13)	
Range	15-126	13-43	

Alkaline phosphatase, U/L			0.039
Mean (SD)	71.21 (24.61)	56.54 (14.65)	
Range	25-143	29-75	
Lactic dehydrogenase, U/L			0.265
Mean (SD)	167.08 (22.36)	175.4 (22.25)	
Range	133-220	145-241	
Fasting blood-glucose, mmol/L			0.695
Mean (SD)	5.01 (0.74)	4.88 (1.37)	
Range	4-7	2-9	
Creatinine, μ mol/L			0.277
Mean (SD)	78.78 (16.33)	73.11 (14.99)	
Range	43-111	51-97	
Tumor markers			
Carcinoembryonic antigen, ng/ml			0.008
Mean (SD)	3.55 (2.39)	2 (0.77)	
Range	1.03-9.28	0.88-3.81	
Carbohydrate antigen 199, U/ml			0.192
Mean (SD)	12.17 (13.11)	8.12 (4.7)	
Range	2-55.09	2-21.36	

Abbreviations: SD, standard deviation.

^a Body mass index: weight (kg)/height (m)².

^b With the splenic flexure as the boundary, the proximal colon includes the cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure, while the distal colon includes the descending colon, sigmoid colon, and the rectosigmoid junction.

Supplementary Table 3. Correlations between differential genera in type I colorectal cancer (Type I VS. Type II)

Genus 1	Genus 2	P value	Correlation coefficient
<i>Adlercreutzia</i>	<i>Christensenellaceae R-7 group</i>	0.028	0.251
<i>Adlercreutzia</i>	<i>Eubacterium coprostanoligenes group</i>	0.038	0.237
<i>Adlercreutzia</i>	<i>Oxalobacter</i>	0.001	0.361
<i>Eggerthella</i>	<i>Eubacterium ruminantium group</i>	0.001	-0.384
<i>Eggerthella</i>	<i>Coprococcus 2</i>	0.026	-0.254
<i>Eggerthella</i>	<i>Lachnoclostridium</i>	0.001	0.367
<i>Eggerthella</i>	<i>Lachnospiraceae UCG-001</i>	0.002	-0.345
<i>Eggerthella</i>	<i>Lachnospiraceae UCG-005</i>	0.046	-0.228
<i>Eggerthella</i>	<i>Marvinbryantia</i>	0.039	-0.236
<i>Eggerthella</i>	<i>Eubacterium coprostanoligenes group</i>	0.001	-0.362
<i>Eggerthella</i>	<i>Ruminiclostridium 6</i>	<0.001	-0.448
<i>Eggerthella</i>	<i>Ruminococcaceae UCG-002</i>	<0.001	-0.392
<i>Eggerthella</i>	<i>Ruminococcaceae UCG-009</i>	0.007	-0.305
<i>Eggerthella</i>	<i>Ruminococcaceae UCG-010</i>	<0.001	-0.503
<i>Eggerthella</i>	<i>Ruminococcaceae UCG-014</i>	<0.001	-0.412
<i>Eggerthella</i>	<i>Ruminococcus 1</i>	0.035	-0.241
<i>Eggerthella</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	<0.001	0.474
<i>Eggerthella</i>	<i>Victivallis</i>	0.001	-0.362

<i>Eggerthella</i>	<i>Oxalobacter</i>	0.011	-0.289
<i>Porphyromonas</i>	<i>Lachnospiraceae NK4A136 group</i>	0.015	-0.276
<i>Porphyromonas</i>	<i>Hydrogenoanaerobacterium</i>	0.039	0.236
<i>Prevotella 2</i>	<i>Lachnospiraceae NK4A136 group</i>	0.022	-0.260
<i>Prevotella 2</i>	<i>Lachnospiraceae UCG-001</i>	0.021	-0.262
<i>Prevotella 2</i>	<i>Ruminiclostridium 9</i>	0.025	0.256
<i>Prevotella 2</i>	<i>Ruminococcus 1</i>	0.008	-0.299
<i>Christensenellaceae R-7 group</i>	<i>Eubacterium ruminantium group</i>	0.004	0.326
<i>Christensenellaceae R-7 group</i>	<i>Coprococcus 2</i>	<0.001	0.485
<i>Christensenellaceae R-7 group</i>	<i>Lachnoclostridium</i>	0.002	-0.340
<i>Christensenellaceae R-7 group</i>	<i>Lachnospiraceae UCG-001</i>	0.001	0.374
<i>Christensenellaceae R-7 group</i>	<i>Lachnospiraceae UCG-005</i>	0.048	0.226
<i>Christensenellaceae R-7 group</i>	<i>Marvinbryantia</i>	<0.001	0.405
<i>Christensenellaceae R-7 group</i>	<i>Peptococcus</i>	0.001	0.387
<i>Christensenellaceae R-7 group</i>	<i>Eubacterium coprostanoligenes group</i>	<0.001	0.412
<i>Christensenellaceae R-7 group</i>	<i>Hydrogenoanaerobacterium</i>	<0.001	0.586
<i>Christensenellaceae R-7 group</i>	<i>Ruminiclostridium 6</i>	<0.001	0.444
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae NK4A214 group</i>	<0.001	0.497
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-002</i>	<0.001	0.521
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-009</i>	0.003	0.336
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-010</i>	<0.001	0.653

<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-014</i>	<0.001	0.573
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcus 1</i>	0.002	0.342
<i>Christensenellaceae R-7 group</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.030	-0.248
<i>Christensenellaceae R-7 group</i>	<i>Victivallis</i>	<0.001	0.445
<i>Christensenellaceae R-7 group</i>	<i>Oxalobacter</i>	0.001	0.375
<i>Christensenellaceae R-7 group</i>	<i>Cloacibacillus</i>	0.029	0.249
<i>Eubacterium ruminantium group</i>	<i>Coproccoccus 2</i>	<0.001	0.420
<i>Eubacterium ruminantium group</i>	<i>Lachnoclostridium</i>	0.002	-0.344
<i>Eubacterium ruminantium group</i>	<i>Lachnospiraceae NK4A136 group</i>	0.034	0.242
<i>Eubacterium ruminantium group</i>	<i>Lachnospiraceae UCG-001</i>	<0.001	0.430
<i>Eubacterium ruminantium group</i>	<i>Marvinbryantia</i>	0.022	0.261
<i>Eubacterium ruminantium group</i>	<i>Eubacterium coprostanoligenes group</i>	0.017	0.272
<i>Eubacterium ruminantium group</i>	<i>Ruminiclostridium 6</i>	<0.001	0.526
<i>Eubacterium ruminantium group</i>	<i>Ruminococcaceae UCG-002</i>	0.026	0.254
<i>Eubacterium ruminantium group</i>	<i>Ruminococcaceae UCG-009</i>	0.001	0.373
<i>Eubacterium ruminantium group</i>	<i>Ruminococcaceae UCG-010</i>	0.003	0.332
<i>Eubacterium ruminantium group</i>	<i>Ruminococcaceae UCG-014</i>	<0.001	0.433
<i>Eubacterium ruminantium group</i>	<i>Ruminococcus 1</i>	0.003	0.334
<i>Eubacterium ruminantium group</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	<0.001	-0.401
<i>Eubacterium ruminantium group</i>	<i>Victivallis</i>	0.031	0.247
<i>Eubacterium ruminantium group</i>	<i>Escherichia Shigella</i>	0.043	-0.231

<i>Eubacterium ventriosum</i> group	<i>Lachnoclostridium</i>	0.025	-0.255
<i>Eubacterium ventriosum</i> group	<i>Lachnospiraceae</i> UCG-001	0.030	0.248
<i>Eubacterium ventriosum</i> group	<i>Lachnospiraceae</i> UCG-005	0.002	0.345
<i>Eubacterium ventriosum</i> group	<i>Ruminiclostridium</i> 6	0.045	0.229
<i>Eubacterium ventriosum</i> group	<i>Ruminiclostridium</i> 9	0.001	-0.373
<i>Eubacterium ventriosum</i> group	<i>Ruminococcaceae</i> NK4A214 group	0.049	0.225
<i>Eubacterium ventriosum</i> group	<i>Ruminococcus</i> 1	0.011	0.289
<i>Coprococcus</i> 2	<i>Lachnoclostridium</i>	0.004	-0.322
<i>Coprococcus</i> 2	<i>Lachnospiraceae</i> NK4A136 group	0.022	0.262
<i>Coprococcus</i> 2	<i>Lachnospiraceae</i> UCG-001	<0.001	0.528
<i>Coprococcus</i> 2	<i>Lachnospiraceae</i> UCG-005	0.044	0.230
<i>Coprococcus</i> 2	<i>Marvinbryantia</i>	0.031	0.246
<i>Coprococcus</i> 2	<i>Peptococcus</i>	0.027	0.251
<i>Coprococcus</i> 2	<i>Eubacterium coprostanoligenes</i> group	0.013	0.283
<i>Coprococcus</i> 2	<i>Hydrogenoanaerobacterium</i>	0.002	0.346
<i>Coprococcus</i> 2	<i>Ruminiclostridium</i> 6	0.002	0.351
<i>Coprococcus</i> 2	<i>Ruminococcaceae</i> NK4A214 group	0.002	0.352
<i>Coprococcus</i> 2	<i>Ruminococcaceae</i> UCG-002	0.010	0.292
<i>Coprococcus</i> 2	<i>Ruminococcaceae</i> UCG-009	0.025	0.256
<i>Coprococcus</i> 2	<i>Ruminococcaceae</i> UCG-010	<0.001	0.527
<i>Coprococcus</i> 2	<i>Ruminococcaceae</i> UCG-014	<0.001	0.537

<i>Coprococcus</i> 2	<i>Ruminococcus</i> 1	<0.001	0.411
<i>Coprococcus</i> 2	<i>Erysipelotrichaceae Incertae Sedis</i>	0.001	-0.386
<i>Coprococcus</i> 2	<i>Escherichia Shigella</i>	0.026	-0.253
<i>Lachnospiraceae</i> UCG-001	<i>Lachnospiraceae</i> UCG-001	0.014	-0.279
<i>Lachnospiraceae</i> UCG-001	<i>Eubacterium coprostanoligenes</i> group	0.004	-0.322
<i>Lachnospiraceae</i> UCG-001	<i>Hydrogenoanaerobacterium</i>	0.029	-0.250
<i>Lachnospiraceae</i> UCG-001	<i>Ruminiclostridium</i> 6	0.026	-0.253
<i>Lachnospiraceae</i> UCG-001	<i>Ruminococcaceae</i> NK4A214 group	<0.001	-0.416
<i>Lachnospiraceae</i> UCG-001	<i>Ruminococcaceae</i> UCG-002	0.003	-0.336
<i>Lachnospiraceae</i> UCG-001	<i>Ruminococcaceae</i> UCG-009	0.002	-0.356
<i>Lachnospiraceae</i> UCG-001	<i>Ruminococcaceae</i> UCG-010	<0.001	-0.393
<i>Lachnospiraceae</i> UCG-001	<i>Ruminococcaceae</i> UCG-014	0.014	-0.279
<i>Lachnospiraceae</i> UCG-001	<i>Ruminococcus</i> 1	0.001	-0.358
<i>Lachnospiraceae</i> UCG-001	<i>Erysipelotrichaceae Incertae Sedis</i>	<0.001	0.589
<i>Lachnospiraceae</i> UCG-001	<i>Victivallis</i>	0.007	-0.306
<i>Lachnospiraceae</i> UCG-001	<i>Escherichia Shigella</i>	<0.001	0.388
<i>Lachnospiraceae</i> UCG-001	<i>Lachnospiraceae</i> UCG-001	0.001	0.373
<i>Lachnospiraceae</i> UCG-001	<i>Ruminiclostridium</i> 9	0.001	-0.357
<i>Lachnospiraceae</i> UCG-001	<i>Ruminococcaceae</i> UCG-014	0.027	0.252
<i>Lachnospiraceae</i> UCG-001	<i>Ruminococcus</i> 1	0.023	0.259
<i>Lachnospiraceae</i> UCG-001	<i>Erysipelotrichaceae Incertae Sedis</i>	0.011	-0.290

<i>Lachnospiraceae NK4A136 group</i>	<i>Escherichia Shigella</i>	0.033	-0.243
<i>Lachnospiraceae UCG-001</i>	<i>Lachnospiraceae UCG-005</i>	0.001	0.368
<i>Lachnospiraceae UCG-001</i>	<i>Peptococcus</i>	0.007	0.303
<i>Lachnospiraceae UCG-001</i>	<i>Eubacterium coprostanoligenes group</i>	0.012	0.286
<i>Lachnospiraceae UCG-001</i>	<i>Ruminiclostridium 6</i>	0.003	0.334
<i>Lachnospiraceae UCG-001</i>	<i>Ruminiclostridium 9</i>	0.003	-0.330
<i>Lachnospiraceae UCG-001</i>	<i>Ruminococcaceae NK4A214 group</i>	0.001	0.382
<i>Lachnospiraceae UCG-001</i>	<i>Ruminococcaceae UCG-002</i>	<0.001	0.394
<i>Lachnospiraceae UCG-001</i>	<i>Ruminococcaceae UCG-010</i>	<0.002	0.432
<i>Lachnospiraceae UCG-001</i>	<i>Ruminococcaceae UCG-014</i>	<0.003	0.403
<i>Lachnospiraceae UCG-001</i>	<i>Ruminococcus 1</i>	<0.001	0.479
<i>Lachnospiraceae UCG-001</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.002	-0.351
<i>Lachnospiraceae UCG-001</i>	<i>Oxalobacter</i>	0.035	0.240
<i>Lachnospiraceae UCG-005</i>	<i>Marvinbryantia</i>	0.012	0.286
<i>Lachnospiraceae UCG-005</i>	<i>Ruminococcaceae UCG-002</i>	0.028	0.251
<i>Lachnospiraceae UCG-005</i>	<i>Ruminococcaceae UCG-014</i>	0.002	0.349
<i>Marvinbryantia</i>	<i>Hydrogenoanaerobacterium</i>	0.016	0.273
<i>Marvinbryantia</i>	<i>Ruminiclostridium 6</i>	0.034	0.242
<i>Marvinbryantia</i>	<i>Ruminococcaceae NK4A214 group</i>	0.015	0.275
<i>Marvinbryantia</i>	<i>Ruminococcaceae UCG-002</i>	<0.001	0.457
<i>Marvinbryantia</i>	<i>Ruminococcaceae UCG-009</i>	0.003	0.337

<i>Marvinbryantia</i>	<i>Ruminococcaceae</i> UCG-010	0.002	0.351
<i>Marvinbryantia</i>	<i>Ruminococcaceae</i> UCG-014	0.002	0.348
<i>Marvinbryantia</i>	<i>Ruminococcus</i> 1	0.018	0.269
<i>Marvinbryantia</i>	<i>Victivallis</i>	0.002	0.341
<i>Peptococcus</i>	<i>Hydrogenoanaerobacterium</i>	<0.001	0.439
<i>Peptococcus</i>	<i>Ruminococcaceae</i> UCG-002	0.008	0.299
<i>Peptococcus</i>	<i>Ruminococcaceae</i> UCG-010	0.001	0.384
<i>Peptococcus</i>	<i>Ruminococcaceae</i> UCG-014	0.011	0.290
<i>Peptococcus</i>	<i>Erysipelotrichaceae</i> Incertae Sedis	0.016	-0.275
<i>Eubacterium coprostanoligenes</i> group	<i>Hydrogenoanaerobacterium</i>	0.010	0.292
<i>Eubacterium coprostanoligenes</i> group	<i>Ruminiclostridium</i> 6	<0.001	0.426
<i>Eubacterium coprostanoligenes</i> group	<i>Ruminococcaceae</i> NK4A214 group	<0.001	0.540
<i>Eubacterium coprostanoligenes</i> group	<i>Ruminococcaceae</i> UCG-002	<0.001	0.440
<i>Eubacterium coprostanoligenes</i> group	<i>Ruminococcaceae</i> UCG-009	0.001	0.380
<i>Eubacterium coprostanoligenes</i> group	<i>Ruminococcaceae</i> UCG-010	<0.001	0.396
<i>Eubacterium coprostanoligenes</i> group	<i>Ruminococcaceae</i> UCG-014	0.048	0.226
<i>Eubacterium coprostanoligenes</i> group	<i>Ruminococcus</i> 1	0.001	0.364
<i>Eubacterium coprostanoligenes</i> group	<i>Erysipelotrichaceae</i> Incertae Sedis	0.011	-0.288
<i>Eubacterium coprostanoligenes</i> group	<i>Victivallis</i>	0.007	0.306
<i>Hydrogenoanaerobacterium</i>	<i>Ruminiclostridium</i> 6	0.002	0.355
<i>Hydrogenoanaerobacterium</i>	<i>Ruminococcaceae</i> NK4A214 group	<0.001	0.476

<i>Hydrogenoanaerobacterium</i>	<i>Ruminococcaceae</i> UCG-002	<0.001	0.438
<i>Hydrogenoanaerobacterium</i>	<i>Ruminococcaceae</i> UCG-010	<0.001	0.453
<i>Hydrogenoanaerobacterium</i>	<i>Ruminococcaceae</i> UCG-014	<0.001	0.420
<i>Hydrogenoanaerobacterium</i>	<i>Victivallis</i>	0.012	0.284
<i>Hydrogenoanaerobacterium</i>	<i>Oxalobacter</i>	0.004	0.324
<i>Hydrogenoanaerobacterium</i>	<i>Cloacibacillus</i>	0.011	0.290
<i>Ruminiclostridium</i> 6	<i>Ruminococcaceae</i> NK4A214 group	0.038	0.237
<i>Ruminiclostridium</i> 6	<i>Ruminococcaceae</i> UCG-002	0.009	0.296
<i>Ruminiclostridium</i> 6	<i>Ruminococcaceae</i> UCG-009	0.001	0.359
<i>Ruminiclostridium</i> 6	<i>Ruminococcaceae</i> UCG-010	<0.001	0.522
<i>Ruminiclostridium</i> 6	<i>Ruminococcaceae</i> UCG-014	<0.001	0.420
<i>Ruminiclostridium</i> 6	<i>Ruminococcus</i> 1	0.002	0.355
<i>Ruminiclostridium</i> 6	<i>Erysipelotrichaceae</i> Incertae Sedis	0.027	-0.252
<i>Ruminiclostridium</i> 6	<i>Victivallis</i>	<0.001	0.398
<i>Ruminiclostridium</i> 6	<i>Pyramidobacter</i>	0.035	0.240
<i>Ruminococcaceae</i> NK4A214 group	<i>Ruminococcaceae</i> UCG-002	<0.001	0.582
<i>Ruminococcaceae</i> NK4A214 group	<i>Ruminococcaceae</i> UCG-009	<0.001	0.424
<i>Ruminococcaceae</i> NK4A214 group	<i>Ruminococcaceae</i> UCG-010	<0.001	0.413
<i>Ruminococcaceae</i> NK4A214 group	<i>Ruminococcaceae</i> UCG-014	0.001	0.366
<i>Ruminococcaceae</i> NK4A214 group	<i>Ruminococcus</i> 1	<0.001	0.520
<i>Ruminococcaceae</i> NK4A214 group	<i>Erysipelotrichaceae</i> Incertae Sedis	0.003	-0.333

<i>Ruminococcaceae NK4A214 group</i>	<i>Victivallis</i>	0.018	0.270
<i>Ruminococcaceae NK4A214 group</i>	<i>Oxalobacter</i>	0.009	0.294
<i>Ruminococcaceae UCG-002</i>	<i>Ruminococcaceae UCG-009</i>	<0.001	0.475
<i>Ruminococcaceae UCG-002</i>	<i>Ruminococcaceae UCG-010</i>	<0.001	0.531
<i>Ruminococcaceae UCG-002</i>	<i>Ruminococcaceae UCG-014</i>	0.001	0.370
<i>Ruminococcaceae UCG-002</i>	<i>Ruminococcus 1</i>	0.001	0.356
<i>Ruminococcaceae UCG-002</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	<0.001	-0.491
<i>Ruminococcaceae UCG-002</i>	<i>Victivallis</i>	0.001	0.372
<i>Ruminococcaceae UCG-002</i>	<i>Oxalobacter</i>	<0.001	0.416
<i>Ruminococcaceae UCG-009</i>	<i>Ruminococcaceae UCG-010</i>	<0.001	0.456
<i>Ruminococcaceae UCG-009</i>	<i>Ruminococcaceae UCG-014</i>	0.012	0.285
<i>Ruminococcaceae UCG-009</i>	<i>Ruminococcus 1</i>	0.020	0.265
<i>Ruminococcaceae UCG-009</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.008	-0.302
<i>Ruminococcaceae UCG-009</i>	<i>Victivallis</i>	0.003	0.332
<i>Ruminococcaceae UCG-009</i>	<i>Escherichia Shigella</i>	0.014	-0.278
<i>Ruminococcaceae UCG-010</i>	<i>Ruminococcaceae UCG-014</i>	<0.001	0.559
<i>Ruminococcaceae UCG-010</i>	<i>Ruminococcus 1</i>	0.001	0.359
<i>Ruminococcaceae UCG-010</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	<0.001	-0.408
<i>Ruminococcaceae UCG-010</i>	<i>Victivallis</i>	<0.001	0.550
<i>Ruminococcaceae UCG-010</i>	<i>Oxalobacter</i>	<0.001	0.447
<i>Ruminococcaceae UCG-014</i>	<i>Ruminococcus 1</i>	0.009	0.296

<i>Ruminococcaceae UCG-014</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.005	-0.318
<i>Ruminococcaceae UCG-014</i>	<i>Victivallis</i>	<0.001	0.397
<i>Ruminococcaceae UCG-014</i>	<i>Oxalobacter</i>	0.032	0.244
<i>Ruminococcus 1</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.004	-0.323
<i>Ruminococcus 1</i>	<i>Victivallis</i>	0.011	0.287
<i>Ruminococcus 1</i>	<i>Pyramidobacter</i>	0.029	0.250
<i>Erysipelotrichaceae Incertae Sedis</i>	<i>Escherichia Shigella</i>	<0.001	0.400
<i>Victivallis</i>	<i>Oxalobacter</i>	0.002	0.346
<i>Oxalobacter</i>	<i>Cloacibacillus</i>	<0.001	0.495

Supplementary Table 4. Correlations between differential genera in type II colorectal cancer
(Type II VS. Type I)

Genus 1	Genus 2	P value	Correlation coefficient
<i>Adlercreutzia</i>	<i>Ruminiclostridium 6</i>	0.020	0.318
<i>Eggerthella</i>	<i>Lachnoclostridium</i>	<0.001	0.566
<i>Eggerthella</i>	<i>Ruminiclostridium 6</i>	0.005	-0.377
<i>Eggerthella</i>	<i>Ruminococcaceae UCG-014</i>	0.045	-0.276
<i>Eggerthella</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	<0.001	0.494
<i>Eggerthella</i>	<i>Escherichia Shigella</i>	0.032	-0.296
<i>Eggerthella</i>	<i>Pyramidobacter</i>	0.016	0.331
<i>Porphyromonas</i>	<i>Prevotella 2</i>	0.014	0.336
<i>Porphyromonas</i>	<i>Christensenellaceae R-7 group</i>	0.036	0.289
<i>Porphyromonas</i>	<i>Ruminiclostridium 6</i>	0.001	0.439
<i>Porphyromonas</i>	<i>Ruminococcaceae NK4A214 group</i>	0.024	0.310
<i>Porphyromonas</i>	<i>Ruminococcaceae UCG-002</i>	0.001	0.442
<i>Porphyromonas</i>	<i>Ruminococcaceae UCG-010</i>	0.044	0.278
<i>Porphyromonas</i>	<i>Ruminococcaceae UCG-014</i>	0.008	0.359
<i>Porphyromonas</i>	<i>Victivallis</i>	0.035	0.290
<i>Porphyromonas</i>	<i>Escherichia Shigella</i>	0.019	0.321
<i>Prevotella 2</i>	<i>Eubacterium ruminantium group</i>	0.031	0.296
<i>Prevotella 2</i>	<i>Ruminiclostridium 6</i>	0.039	0.285

<i>Prevotella 2</i>	<i>Ruminococcaceae UCG-014</i>	0.001	0.442
<i>Prevotella 2</i>	<i>Oxalobacter</i>	0.004	0.385
<i>Prevotella 2</i>	<i>Cloacibacillus</i>	0.044	0.278
<i>Christensenellaceae R-7 group</i>	<i>Lachnospiraceae NK4A136 group</i>	0.015	0.332
<i>Christensenellaceae R-7 group</i>	<i>Marvinbryantia</i>	0.047	0.274
<i>Christensenellaceae R-7 group</i>	<i>Eubacterium coprostanoligenes group</i>	0.032	0.296
<i>Christensenellaceae R-7 group</i>	<i>Ruminiclostridium 9</i>	0.016	0.331
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae NK4A214 group</i>	0.007	0.369
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-002</i>	0.009	0.354
<i>Christensenellaceae R-7 group</i>	<i>Cloacibacillus</i>	0.008	0.359
<i>Eubacterium ruminantium group</i>	<i>Coprococcus 2</i>	<0.001	0.525
<i>Eubacterium ruminantium group</i>	<i>Ruminococcaceae UCG-014</i>	<0.001	0.578
<i>Eubacterium ventriosum group</i>	<i>Lachnospiraceae NK4A136 group</i>	<0.001	0.479
<i>Eubacterium ventriosum group</i>	<i>Lachnospiraceae UCG-001</i>	0.006	0.370
<i>Eubacterium ventriosum group</i>	<i>Lachnospiraceae UCG-005</i>	0.034	0.292
<i>Eubacterium ventriosum group</i>	<i>Marvinbryantia</i>	0.005	0.378
<i>Eubacterium ventriosum group</i>	<i>Eubacterium coprostanoligenes group</i>	0.001	0.438
<i>Eubacterium ventriosum group</i>	<i>Ruminiclostridium 9</i>	0.024	0.310
<i>Eubacterium ventriosum group</i>	<i>Cloacibacillus</i>	0.006	0.371
<i>Coprococcus 2</i>	<i>Ruminococcaceae UCG-014</i>	0.016	0.328
<i>Lachnoclostridium</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	<0.001	0.480

<i>Lachnospiraceae NK4A136 group</i>	<i>Marvinbryantia</i>	0.025	0.309
<i>Lachnospiraceae NK4A136 group</i>	<i>Eubacterium coprostanoligenes group</i>	0.002	0.424
<i>Lachnospiraceae UCG-001</i>	<i>Eubacterium coprostanoligenes group</i>	0.019	0.322
<i>Lachnospiraceae UCG-001</i>	<i>Cloacibacillus</i>	0.018	0.323
<i>Lachnospiraceae UCG-005</i>	<i>Marvinbryantia</i>	0.007	0.368
<i>Marvinbryantia</i>	<i>Ruminiclostridium 9</i>	0.032	0.295
<i>Eubacterium coprostanoligenes group</i>	<i>Ruminococcaceae NK4A214 group</i>	0.026	0.307
<i>Eubacterium coprostanoligenes group</i>	<i>Ruminococcaceae UCG-002</i>	0.003	0.407
<i>Eubacterium coprostanoligenes group</i>	<i>Ruminococcaceae UCG-009</i>	0.002	0.407
<i>Eubacterium coprostanoligenes group</i>	<i>Ruminococcaceae UCG-010</i>	0.042	0.280
<i>Hydrogenoanaerobacterium</i>	<i>Ruminococcaceae NK4A214 group</i>	0.004	0.388
<i>Hydrogenoanaerobacterium</i>	<i>Ruminococcaceae UCG-009</i>	0.002	0.408
<i>Hydrogenoanaerobacterium</i>	<i>Oxalobacter</i>	0.042	0.280
<i>Ruminiclostridium 6</i>	<i>Ruminococcaceae UCG-014</i>	<0.001	0.565
<i>Ruminiclostridium 6</i>	<i>Ruminococcus 1</i>	0.006	0.370
<i>Ruminiclostridium 6</i>	<i>Escherichia Shigella</i>	0.001	0.429
<i>Ruminiclostridium 9</i>	<i>Ruminococcaceae UCG-009</i>	0.017	0.327
<i>Ruminococcaceae NK4A214 group</i>	<i>Ruminococcaceae UCG-002</i>	0.001	0.445
<i>Ruminococcaceae NK4A214 group</i>	<i>Ruminococcaceae UCG-010</i>	0.042	0.281
<i>Ruminococcaceae NK4A214 group</i>	<i>Victivallis</i>	0.031	0.297
<i>Ruminococcaceae NK4A214 group</i>	<i>Oxalobacter</i>	0.014	0.335

<i>Ruminococcaceae</i> UCG-002	<i>Ruminococcaceae</i> UCG-010	0.014	0.337
<i>Ruminococcaceae</i> UCG-002	<i>Ruminococcus</i> 1	0.026	0.305
<i>Ruminococcaceae</i> UCG-009	<i>Victivallis</i>	0.001	0.429
<i>Ruminococcaceae</i> UCG-010	<i>Victivallis</i>	<0.001	0.588
<i>Ruminococcaceae</i> UCG-014	<i>Ruminococcus</i> 1	0.023	0.312
<i>Ruminococcaceae</i> UCG-014	<i>Escherichia Shigella</i>	<0.001	0.502
<i>Ruminococcus</i> 1	<i>Victivallis</i>	0.045	0.276
<i>Erysipelotrichaceae</i> Incertae Sedis	<i>Pyramidobacter</i>	0.010	0.352

Supplementary Table 5. Correlations between differential genera in type I colorectal adenoma (Type I VS. Type II)

Genus 1	Genus 2	P value	Correlation coefficient
<i>Actinomyces</i>	<i>Lactococcus</i>	0.001	0.394
<i>Actinomyces</i>	<i>Lachnoclostridium</i>	0.002	0.369
<i>Actinomyces</i>	<i>Erysipelatoclostridium</i>	0.001	0.394
<i>Actinomyces</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.031	0.265
<i>Adlercreutzia</i>	<i>Coprobacter</i>	0.021	0.283
<i>Adlercreutzia</i>	<i>Eubacterium brachy group</i>	<0.001	0.435
<i>Adlercreutzia</i>	<i>Lactonifactor</i>	0.005	0.345
<i>Adlercreutzia</i>	<i>Ruminiclostridium 6</i>	0.044	0.249
<i>Adlercreutzia</i>	<i>Ruminococcaceae NK4A214 group</i>	0.004	0.351
<i>Adlercreutzia</i>	<i>Fusobacterium</i>	0.017	-0.294
<i>Adlercreutzia</i>	<i>Oxalobacter</i>	0.019	0.289
<i>Coprobacter</i>	<i>Eubacterium brachy group</i>	0.010	0.315
<i>Coprobacter</i>	<i>Lachnoclostridium</i>	0.009	0.320
<i>Bacillus</i>	<i>Lactococcus</i>	0.001	0.398
<i>Bacillus</i>	<i>Escherichia Shigella</i>	0.010	0.316
<i>Bacillus</i>	<i>Candidatus Saccharimonas</i>	0.035	0.259
<i>Enterococcus</i>	<i>Escherichia Shigella</i>	<0.001	0.423
<i>Lactococcus</i>	<i>Lachnoclostridium</i>	0.039	0.255
<i>Lactococcus</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.024	0.278

<i>Lactococcus</i>	<i>Escherichia Shigella</i>	0.020	0.286
<i>Lactococcus</i>	<i>Candidatus Saccharimonas</i>	0.040	0.253
<i>Christensenellaceae R-7 group</i>	<i>Eubacterium brachy group</i>	0.009	0.319
<i>Christensenellaceae R-7 group</i>	<i>Family XIII UCG-001</i>	0.011	0.313
<i>Christensenellaceae R-7 group</i>	<i>Coprococcus 2</i>	<0.001	0.480
<i>Christensenellaceae R-7 group</i>	<i>Lachnoclostridium</i>	0.028	-0.270
<i>Christensenellaceae R-7 group</i>	<i>Ruminiclostridium 6</i>	0.001	0.395
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae NK4A214 group</i>	<0.001	0.485
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-002</i>	<0.001	0.605
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-005</i>	<0.001	0.739
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-010</i>	<0.001	0.665
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-014</i>	<0.001	0.541
<i>Christensenellaceae R-7 group</i>	<i>Oxalobacter</i>	0.001	0.387
<i>Eubacterium brachy group</i>	<i>Lactonifactor</i>	<0.001	0.551
<i>Eubacterium brachy group</i>	<i>Ruminococcaceae UCG-005</i>	0.017	0.294
<i>Eubacterium brachy group</i>	<i>Ruminococcaceae UCG-010</i>	0.027	0.273
<i>Eubacterium brachy group</i>	<i>Oxalobacter</i>	<0.001	0.450
<i>Family XIII UCG-001</i>	<i>Ruminococcaceae NK4A214 group</i>	0.002	0.380
<i>Family XIII UCG-001</i>	<i>Ruminococcaceae UCG-002</i>	0.020	0.286
<i>Family XIII UCG-001</i>	<i>Ruminococcaceae UCG-005</i>	<0.001	0.435
<i>Family XIII UCG-001</i>	<i>Ruminococcaceae UCG-010</i>	0.015	0.298

<i>Family XIII UCG-001</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.022	-0.282
<i>Family XIII UCG-001</i>	<i>Fusobacterium</i>	0.030	-0.268
<i>Coprococcus 2</i>	<i>Ruminiclostridium 6</i>	0.001	0.399
<i>Coprococcus 2</i>	<i>Ruminococcaceae NK4A214 group</i>	0.002	0.381
<i>Coprococcus 2</i>	<i>Ruminococcaceae UCG-002</i>	0.033	0.263
<i>Coprococcus 2</i>	<i>Ruminococcaceae UCG-005</i>	0.002	0.369
<i>Coprococcus 2</i>	<i>Ruminococcaceae UCG-010</i>	<0.001	0.527
<i>Coprococcus 2</i>	<i>Ruminococcaceae UCG-014</i>	0.002	0.373
<i>Coprococcus 2</i>	<i>Fusobacterium</i>	0.028	-0.270
<i>Coprococcus 2</i>	<i>Oxalobacter</i>	0.027	0.271
<i>Lachnoclostridium</i>	<i>Ruminiclostridium 6</i>	0.049	-0.244
<i>Lachnoclostridium</i>	<i>Ruminococcaceae NK4A214 group</i>	0.038	-0.257
<i>Lachnoclostridium</i>	<i>Ruminococcaceae UCG-014</i>	0.023	-0.280
<i>Lachnoclostridium</i>	<i>Erysipelatoclostridium</i>	0.008	0.322
<i>Lachnoclostridium</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.025	0.275
<i>Lactonifactor</i>	<i>Ruminococcaceae UCG-005</i>	0.038	0.256
<i>Lactonifactor</i>	<i>Erysipelatoclostridium</i>	0.009	0.318
<i>Ruminiclostridium 6</i>	<i>Ruminococcaceae NK4A214 group</i>	0.024	0.277
<i>Ruminiclostridium 6</i>	<i>Ruminococcaceae UCG-005</i>	0.004	0.350
<i>Ruminiclostridium 6</i>	<i>Ruminococcaceae UCG-010</i>	<0.001	0.454
<i>Ruminiclostridium 6</i>	<i>Ruminococcaceae UCG-014</i>	0.010	0.313

<i>Ruminiclostridium</i> 6	<i>Escherichia Shigella</i>	0.021	0.283
<i>Ruminococcaceae</i> NK4A214 group	<i>Ruminococcaceae</i> UCG-002	0.001	0.414
<i>Ruminococcaceae</i> NK4A214 group	<i>Ruminococcaceae</i> UCG-005	<0.001	0.541
<i>Ruminococcaceae</i> NK4A214 group	<i>Ruminococcaceae</i> UCG-010	<0.001	0.420
<i>Ruminococcaceae</i> NK4A214 group	<i>Ruminococcaceae</i> UCG-014	0.022	0.282
<i>Ruminococcaceae</i> NK4A214 group	<i>Megamonas</i>	0.020	-0.286
<i>Ruminococcaceae</i> NK4A214 group	<i>Fusobacterium</i>	0.033	-0.263
<i>Ruminococcaceae</i> NK4A214 group	<i>Oxalobacter</i>	0.012	0.308
<i>Ruminococcaceae</i> UCG-002	<i>Ruminococcaceae</i> UCG-005	<0.001	0.668
<i>Ruminococcaceae</i> UCG-002	<i>Ruminococcaceae</i> UCG-010	0.008	0.322
<i>Ruminococcaceae</i> UCG-002	<i>Ruminococcaceae</i> UCG-014	0.017	0.292
<i>Ruminococcaceae</i> UCG-002	<i>Oxalobacter</i>	0.045	0.248
<i>Ruminococcaceae</i> UCG-005	<i>Ruminococcaceae</i> UCG-010	<0.001	0.542
<i>Ruminococcaceae</i> UCG-005	<i>Ruminococcaceae</i> UCG-014	<0.001	0.485
<i>Ruminococcaceae</i> UCG-005	<i>Oxalobacter</i>	0.015	0.299
<i>Ruminococcaceae</i> UCG-010	<i>Ruminococcaceae</i> UCG-014	<0.001	0.494
<i>Ruminococcaceae</i> UCG-010	<i>Thalassospira</i>	0.047	0.246
<i>Ruminococcaceae</i> UCG-010	<i>Oxalobacter</i>	<0.001	0.437
<i>Ruminococcaceae</i> UCG-014	<i>Thalassospira</i>	0.041	0.253
<i>Erysipelatoclostridium</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	<0.001	0.470
<i>Megamonas</i>	<i>Fusobacterium</i>	<0.001	0.427

Supplementary Table 6. Correlations between differential genera in type II colorectal adenoma (Type II VS. Type I)

Genus 1	Genus 2	P value	Correlation coefficient
<i>Actinomyces</i>	<i>Bacillus</i>	0.004	0.385
<i>Actinomyces</i>	<i>Lactococcus</i>	0.011	0.345
<i>Actinomyces</i>	<i>Lachnoclostridium</i>	0.004	0.388
<i>Actinomyces</i>	<i>Oribacterium</i>	<0.001	0.612
<i>Actinomyces</i>	<i>Erysipelatoclostridium</i>	0.027	0.300
<i>Actinomyces</i>	<i>Candidatus Saccharimonas</i>	0.001	0.439
<i>Adlercreutzia</i>	<i>Ruminococcaceae NK4A214 group</i>	0.006	0.368
<i>Adlercreutzia</i>	<i>Ruminococcaceae UCG-002</i>	0.026	0.302
<i>Adlercreutzia</i>	<i>Ruminococcaceae UCG-010</i>	0.001	0.441
<i>Adlercreutzia</i>	<i>Ruminococcaceae UCG-014</i>	0.025	0.304
<i>Adlercreutzia</i>	<i>Thalassospira</i>	0.006	0.372
<i>Copro bacter</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.037	0.284
<i>Bacillus</i>	<i>Lactococcus</i>	<0.001	0.660
<i>Bacillus</i>	<i>Lachnoclostridium</i>	<0.001	0.552
<i>Bacillus</i>	<i>Stomatobaculum</i>	0.023	0.310
<i>Bacillus</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.039	0.282
<i>Bacillus</i>	<i>Escherichia Shigella</i>	0.003	0.392
<i>Bacillus</i>	<i>Candidatus Saccharimonas</i>	0.001	0.452
<i>Enterococcus</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.007	0.362

<i>Enterococcus</i>	<i>Escherichia Shigella</i>	0.022	0.311
<i>Lactococcus</i>	<i>Oribacterium</i>	0.009	0.351
<i>Lactococcus</i>	<i>Stomatobaculum</i>	0.008	0.357
<i>Lactococcus</i>	<i>Escherichia Shigella</i>	0.007	0.365
<i>Lactococcus</i>	<i>Candidatus Saccharimonas</i>	0.034	0.289
<i>Christensenellaceae R-7 group</i>	<i>Coproccoccus 2</i>	0.001	0.453
<i>Christensenellaceae R-7 group</i>	<i>Stomatobaculum</i>	0.002	0.406
<i>Christensenellaceae R-7 group</i>	<i>Ruminiclostridium 6</i>	<0.001	0.484
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae NK4A214 group</i>	<0.001	0.482
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-002</i>	<0.001	0.546
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-005</i>	<0.001	0.626
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-010</i>	0.001	0.429
<i>Christensenellaceae R-7 group</i>	<i>Ruminococcaceae UCG-014</i>	0.041	0.279
<i>Christensenellaceae R-7 group</i>	<i>Thalassospira</i>	0.030	0.296
<i>Christensenellaceae R-7 group</i>	<i>Candidatus Saccharimonas</i>	0.024	0.306
<i>Eubacterium brachy group</i>	<i>Oribacterium</i>	0.010	0.349
<i>Eubacterium brachy group</i>	<i>Stomatobaculum</i>	0.002	0.418
<i>Eubacterium brachy group</i>	<i>Erysipelatoclostridium</i>	0.034	0.290
<i>Eubacterium brachy group</i>	<i>Megamonas</i>	0.043	-0.277
<i>Family XIII UCG-001</i>	<i>Ruminococcaceae NK4A214 group</i>	0.009	0.355
<i>Family XIII UCG-001</i>	<i>Ruminococcaceae UCG-002</i>	0.045	0.274

<i>Family XIII UCG-001</i>	<i>Ruminococcaceae UCG-005</i>	<0.001	0.519
<i>Coprococcus 2</i>	<i>Ruminiclostridium 6</i>	<0.001	0.611
<i>Coprococcus 2</i>	<i>Ruminococcaceae NK4A214 group</i>	0.010	0.346
<i>Coprococcus 2</i>	<i>Ruminococcaceae UCG-010</i>	0.029	0.298
<i>Coprococcus 2</i>	<i>Candidatus Saccharimonas</i>	0.029	0.297
<i>Lachnoclostridium</i>	<i>Oribacterium</i>	0.034	0.289
<i>Lachnoclostridium</i>	<i>Erysipelatoclostridium</i>	0.017	0.322
<i>Lachnoclostridium</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.002	0.411
<i>Lachnoclostridium</i>	<i>Fusobacterium</i>	0.037	0.284
<i>Lachnoclostridium</i>	<i>Escherichia Shigella</i>	<0.001	0.476
<i>Lachnoclostridium</i>	<i>Candidatus Saccharimonas</i>	0.008	0.356
<i>Oribacterium</i>	<i>Stomatobaculum</i>	0.007	0.365
<i>Stomatobaculum</i>	<i>Candidatus Saccharimonas</i>	0.002	0.417
<i>Tyzzrella 4</i>	<i>Ruminococcaceae UCG-002</i>	0.041	-0.279
<i>Tyzzrella 4</i>	<i>Fusobacterium</i>	0.026	0.303
<i>Ruminiclostridium 6</i>	<i>Ruminococcaceae NK4A214 group</i>	0.010	0.349
<i>Ruminiclostridium 6</i>	<i>Ruminococcaceae UCG-002</i>	0.011	0.343
<i>Ruminiclostridium 6</i>	<i>Ruminococcaceae UCG-005</i>	0.022	0.312
<i>Ruminiclostridium 6</i>	<i>Ruminococcaceae UCG-010</i>	<0.001	0.542
<i>Ruminiclostridium 6</i>	<i>Thalassospira</i>	<0.001	0.476
<i>Ruminococcaceae NK4A214 group</i>	<i>Ruminococcaceae UCG-002</i>	0.019	0.317

<i>Ruminococcaceae NK4A214 group</i>	<i>Ruminococcaceae UCG-005</i>	<0.001	0.464
<i>Ruminococcaceae NK4A214 group</i>	<i>Ruminococcaceae UCG-010</i>	0.028	0.300
<i>Ruminococcaceae NK4A214 group</i>	<i>Ruminococcaceae UCG-014</i>	0.037	0.284
<i>Ruminococcaceae UCG-002</i>	<i>Ruminococcaceae UCG-005</i>	<0.001	0.527
<i>Ruminococcaceae UCG-002</i>	<i>Ruminococcaceae UCG-010</i>	0.047	0.272
<i>Ruminococcaceae UCG-002</i>	<i>Ruminococcaceae UCG-014</i>	0.042	0.277
<i>Ruminococcaceae UCG-002</i>	<i>Erysipelatoclostridium</i>	0.049	-0.270
<i>Ruminococcaceae UCG-005</i>	<i>Erysipelatoclostridium</i>	0.041	-0.280
<i>Ruminococcaceae UCG-010</i>	<i>Ruminococcaceae UCG-014</i>	0.005	0.377
<i>Ruminococcaceae UCG-010</i>	<i>Thalassospira</i>	<0.001	0.588
<i>Ruminococcaceae UCG-010</i>	<i>Candidatus Saccharimonas</i>	0.044	0.275
<i>Ruminococcaceae UCG-014</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	0.027	-0.301
<i>Erysipelatoclostridium</i>	<i>Erysipelotrichaceae Incertae Sedis</i>	<0.001	0.558
<i>Erysipelatoclostridium</i>	<i>Megamonas</i>	0.048	-0.270
<i>Erysipelatoclostridium</i>	<i>Candidatus Saccharimonas</i>	0.036	0.287
<i>Megamonas</i>	<i>Escherichia Shigella</i>	0.015	-0.329

Supplementary Table 7. Correlations between plasma factors and differential genus (Type II VS. Type I)

Group	Plasma factor	Genus	P value	Correlation coefficient
CRC	Neutrophils	<i>Adlercreutzia</i>	0.030	-0.298
CRC	sTNFR-II	<i>Ruminococcaceae UCG-014</i>	0.046	-0.275
CRC	sTNFR-II	<i>Ruminococcaceae UCG-009</i>	0.014	-0.336
CRC	Endotoxin	<i>Ruminococcaceae NK4A214 group</i>	0.030	-0.298
CRC	Endotoxin	<i>Eubacterium coprostanoligenes group</i>	0.002	-0.410
Adenoma	Neutrophils	<i>Stomatobaculum</i>	0.011	0.343
Adenoma	sTNFR-II	<i>Tyzzarella 4</i>	0.009	0.353
Adenoma	Endotoxin	<i>Oxalobacter</i>	0.023	-0.310

Supplementary Table 8. Correlations between smoking and differential genus in type II colorectal cancer subgroup

Genus	P value	Correlation coefficient
<i>Ruminiclostridium 6</i>	0.818	-0.035
<i>Coprococcus 2</i>	0.916	0.016
<i>Eubacterium ruminantium group</i>	0.229	0.181
<i>Cloacibacillus</i>	0.496	0.103
<i>Christensenellaceae R7 group</i>	0.025	-0.331
<i>Ruminococcaceae UCG-014</i>	0.178	0.202
<i>Lachnospiraceae UCG-001</i>	0.493	0.104
<i>Adlercreutzia</i>	0.683	-0.062
<i>Lachnospiraceae UCG-005</i>	0.139	0.221
<i>Victivallis</i>	0.256	-0.171
<i>Oxalobacter</i>	0.882	0.023
<i>Ruminococcaceae UCG-002</i>	0.630	-0.073
<i>Hydrogenoanaerobacterium</i>	0.984	0.003
<i>Ruminococcaceae UCG-010</i>	0.273	-0.165
<i>Ruminococcaceae NK4A214 group</i>	0.839	0.031
<i>Porphyromonas</i>	0.266	-0.167
<i>Ruminococcus 1</i>	0.334	-0.146
<i>Peptococcus</i>	0.310	-0.153
<i>Prevotella 2</i>	0.842	0.030
<i>Eubacterium ventriosum group</i>	0.383	0.132
<i>Ruminococcaceae UCG-009</i>	0.302	-0.156
<i>Marvinbryantia</i>	0.218	0.185
<i>Lachnospiraceae NK4A136 group</i>	0.064	-0.275
<i>Pyramidobacter</i>	0.429	0.119
<i>Eubacterium coprostanoligenes group</i>	0.659	-0.067
<i>Ruminiclostridium 9</i>	0.350	-0.141
<i>Lachnoclostridium</i>	0.554	-0.090
<i>Eggerthella</i>	0.002	0.449
<i>Erysipelotrichaceae incertae sedis</i>	0.986	-0.003
<i>Escherichia Shigella</i>	0.551	0.09

Supplementary Table 9. Correlations between smoking and differential genus in type II colorectal adenoma subgroup

Genus	P value	Correlation coefficient
<i>Thalassospira</i>	0.958	-0.020
<i>Ruminococcaceae</i> UCG-010	0.958	-0.020
<i>Ruminococcaceae</i> UCG-014	0.349	-0.355
<i>Lactonifactor</i>	0.034	-0.704
<i>Christensenellaceae</i> R 7 group	0.944	0.028
<i>Coprococcus</i> 2	0.611	-0.197
<i>Coprobacter</i>	/	/
<i>Ruminiclostridium</i> 6	0.560	-0.225
<i>Ruminococcaceae</i> UCG-005	0.280	0.404
<i>Holdemanella</i>	0.351	-0.354
<i>Ruminococcaceae</i> UCG-002	0.403	0.319
<i>Family XIII</i> UCG-001	0.004	0.845
<i>Ruminococcaceae</i> NK4A214 group	0.479	0.272
<i>Oxalobacter</i>	0.947	-0.026
<i>Adlercreutzia</i>	0.252	-0.427
<i>Eubacterium brachy</i> group	0.699	-0.151
<i>Lactococcus</i>	0.481	0.271
<i>Bacillus</i>	0.925	0.037
<i>Lachnoclostridium</i>	0.836	0.081
<i>Erysipelotrichaceae</i> Incertae Sedis	0.733	-0.133
<i>Actinomyces</i>	0.134	0.539
<i>Tyzzarella</i> 4	0.947	-0.026
<i>Fusobacterium</i>	0.799	0.099
<i>Erysipelatoclostridium</i>	0.786	-0.106
<i>Megamonas</i>	0.179	0.491
<i>Escherichia Shigella</i>	0.531	0.242
<i>Oribacterium</i>	0.958	-0.021
<i>Candidatus Saccharimonas</i>	0.726	0.136
<i>Enterococcus</i>	0.710	-0.145
<i>Stomatobaculum</i>	0.731	-0.134

Supplementary Table 10. Correlations between smoking and differential genus in type I colorectal cancer subgroup

Genus	P value	Correlation coefficient
<i>Ruminiclostridium 6</i>	0.443	-0.094
<i>Coprococcus 2</i>	0.638	-0.058
<i>Eubacterium ruminantium group</i>	0.530	-0.077
<i>Cloacibacillus</i>	0.399	-0.103
<i>Christensenellaceae R7 group</i>	0.559	-0.072
<i>Ruminococcaceae UCG-014</i>	0.247	0.141
<i>Lachnospiraceae UCG-001</i>	0.586	-0.067
<i>Adlercreutzia</i>	0.355	0.113
<i>Lachnospiraceae UCG-005</i>	0.787	0.033
<i>Victivallis</i>	0.699	-0.047
<i>Oxalobacter</i>	0.585	0.067
<i>Ruminococcaceae UCG-002</i>	0.362	0.111
<i>Hydrogenoanaerobacterium</i>	0.538	0.075
<i>Ruminococcaceae UCG-010</i>	0.244	0.142
<i>Ruminococcaceae NK4A214 group</i>	0.388	-0.106
<i>Porphyromonas</i>	0.291	-0.129
<i>Ruminococcus 1</i>	0.839	0.025
<i>Peptococcus</i>	0.193	0.159
<i>Prevotella 2</i>	0.060	0.228
<i>Eubacterium ventriosum group</i>	0.322	0.121
<i>Ruminococcaceae UCG-009</i>	0.682	-0.05
<i>Marvinbryantia</i>	0.555	-0.072
<i>Lachnospiraceae NK4A136 group</i>	0.212	0.152
<i>Pyramidobacter</i>	0.254	-0.139
<i>Eubacterium coprostanoligenes group</i>	0.981	-0.003
<i>Ruminiclostridium 9</i>	0.592	0.066
<i>Lachnoclostridium</i>	0.939	0.009
<i>Eggerthella</i>	0.584	-0.067
<i>Erysipelotrichaceae incertae sedis</i>	0.508	-0.081
<i>Escherichia Shigella</i>	0.749	0.039

Supplementary Table 11. Correlations between smoking and differential genus in type I colorectal adenoma subgroup

Genus	P value	Correlation coefficient
<i>Thalassospira</i>	0.214	-0.155
<i>Ruminococcaceae</i> UCG-010	0.760	0.038
<i>Ruminococcaceae</i> UCG-014	0.233	-0.149
<i>Lactonifactor</i>	0.595	-0.067
<i>Christensenellaceae</i> R 7 group	0.595	0.067
<i>Coprococcus</i> 2	0.562	-0.073
<i>Coprobacter</i>	0.807	-0.031
<i>Ruminiclostridium</i> 6	0.801	-0.032
<i>Ruminococcaceae</i> UCG-005	0.385	-0.109
<i>Holdemanella</i>	0.864	-0.021
<i>Ruminococcaceae</i> UCG-002	0.320	0.124
<i>Family XIII</i> UCG-001	0.243	0.146
<i>Ruminococcaceae</i> NK4A214 group	0.711	-0.047
<i>Oxalobacter</i>	0.506	-0.083
<i>Adlercreutzia</i>	0.482	0.088
<i>Eubacterium brachy</i> group	0.462	-0.092
<i>Lactococcus</i>	0.524	0.080
<i>Bacillus</i>	0.403	-0.105
<i>Lachnoclostridium</i>	0.424	0.100
<i>Erysipelotrichaceae</i> Incertae Sedis	0.327	-0.122
<i>Actinomyces</i>	0.375	0.111
<i>Tyzzereella</i> 4	0.269	0.138
<i>Fusobacterium</i>	0.087	0.212
<i>Erysipelatoclostridium</i>	0.845	0.025
<i>Megamonas</i>	0.572	0.071
<i>Escherichia Shigella</i>	0.109	-0.199
<i>Oribacterium</i>	0.385	-0.109
<i>Candidatus Saccharimonas</i>	0.898	0.016
<i>Enterococcus</i>	0.412	-0.103
<i>Stomatobaculum</i>	0.469	-0.091

Supplementary Table 12. Potential microbiota markers that differentiate between the two subtypes of colorectal cancer by using linear support vector machine and logistic regression, respectively

Classifier	Threshold	AUC (mean±SD)	Biomarker	Coefficient
Linear support vector machine	0.2125	0.82±0.10	<i>Escherichia Shigella</i>	2.2751
			<i>Eubacterium coprostanoligenes group</i>	-0.2988
			<i>Lachnoclostridium</i>	0.7542
			<i>Lachnospiraceae NK4A136 group</i>	-0.3072
			<i>Porphyromonas</i>	-0.3290
			<i>Ruminococcaceae UCG-002</i>	-0.4211
Logistic regression	0.1698	0.84±0.10	<i>Escherichia Shigella</i>	1.0640
			<i>Eubacterium coprostanoligenes group</i>	-0.3273
			<i>Lachnoclostridium</i>	0.6098
			<i>Lachnospiraceae NK4A136 group</i>	-0.1934
			<i>Porphyromonas</i>	-0.3175
			<i>Prevotella 2</i>	-0.3235
			<i>Ruminococcaceae UCG-002</i>	-0.4762

Abbreviations: AUC, an area under the receiver operating characteristic curve; SD, standard deviation.

Supplementary Table 13. Potential microbiota markers that differentiate between the two subtypes of colorectal adenoma by using linear support vector machine and logistic regression, respectively

Classifier	Threshold	AUC (mean±SD)	Biomarker	Coefficient
Linear support vector machine	0.3459	0.86±0.11	<i>Escherichia Shigella</i>	2.3977
			<i>Fusobacterium</i>	1.3251
			<i>Lachnoclostridium</i>	1.3488
			<i>Megamonas</i>	2.4436
			<i>Ruminococcaceae UCG-002</i>	-0.5569
Logistic regression	0.2133	0.86±0.11	<i>Escherichia Shigella</i>	1.3873
			<i>Fusobacterium</i>	0.6964
			<i>Lachnoclostridium</i>	0.7799
			<i>Megamonas</i>	1.3853
			<i>Ruminococcaceae UCG-002</i>	-0.4091

Abbreviations: AUC, an area under the receiver operating characteristic curve; SD, standard deviation.

Supplementary Table 14. Detailed information on the dysregulated pathways in type II colorectal neoplasms (Type II VS. Type I)

Group	ko	Pathway	P value	FDR ^a	Log ₂ (Fold Change)
CRC	ko04975	Fat digestion and absorption	<0.001	<0.001	-1.226
CRC	ko04666	Fc gamma R-mediated phagocytosis	<0.001	<0.001	-1.068
CRC	ko00601	Glycosphingolipid biosynthesis - lacto and neolacto series	<0.001	<0.001	-0.634
CRC	ko04622	RIG-I-like receptor signaling pathway	<0.001	<0.001	0.641
CRC	ko05100	Bacterial invasion of epithelial cells	0.020	0.048	0.652
CRC	ko00984	Steroid degradation	0.002	0.007	0.705
CRC	ko04144	Endocytosis	0.006	0.017	0.745
CRC	ko04912	GnRH signaling pathway	0.006	0.017	0.745
CRC	ko00592	alpha-Linolenic acid metabolism	<0.001	<0.001	0.860
CRC	ko01053	Biosynthesis of siderophore group nonribosomal peptides	<0.001	<0.001	0.899
CRC	ko00232	Caffeine metabolism	<0.001	<0.001	1.040
CRC	ko05204	Chemical carcinogenesis	<0.001	<0.001	1.207
CRC	ko04725	Cholinergic synapse	0.017	0.044	1.232
CRC	ko04115	p53 signaling pathway	0.004	0.013	1.512
CRC	ko04610	Complement and coagulation cascades	0.002	0.007	1.734
adenoma	ko00513	N-Glycan biosynthesis	0.011	0.027	-6.779
adenoma	ko04975	Fat digestion and absorption	<0.001	<0.001	-2.843
adenoma	ko04666	Fc gamma R-mediated phagocytosis	<0.001	<0.001	-1.621
adenoma	ko00601	alpha-Linolenic acid metabolism	<0.001	<0.001	-0.815

adenoma	ko00943	Flavonoid biosynthesis	<0.001	<0.001	-0.651
adenoma	ko04115	p53 signaling pathway	0.021	0.045	0.587
adenoma	ko00440	beta-Alanine metabolism	<0.001	<0.001	0.688
adenoma	ko00364	Benzoate degradation	<0.001	<0.001	0.747
adenoma	ko03050	Proteasome	<0.001	<0.001	0.770
adenoma	ko00592	Arachidonic acid metabolism	0.002	0.006	0.886
adenoma	ko04144	Endocytosis	0.012	0.028	0.888
adenoma	ko04912	GnRH signaling pathway	0.012	0.028	0.888
adenoma	ko00633	Glyoxylate and dicarboxylate metabolism	<0.001	<0.001	0.925
adenoma	ko04622	RIG-I-like receptor signaling pathway	<0.001	<0.001	1.094
adenoma	ko00472	Cyanoamino acid metabolism	0.007	0.018	1.094
adenoma	ko00232	Caffeine metabolism	0.001	0.003	1.101
adenoma	ko05204	Chemical carcinogenesis	0.010	0.025	1.119
adenoma	ko04610	Complement and coagulation cascades	0.002	0.006	1.547
adenoma	ko00331	Arginine and proline metabolism	<0.001	<0.001	1.868

Abbreviations: CRC, colorectal cancer; FDR, false discovery rate.

^a FDR refers to an adjusted P value corrected by a false discovery rate.

Supplementary Table 15. Detailed information on the dysregulated genes in type II colorectal neoplasms (Type II VS. Type I)

Group	KO	Gene	<i>P</i> value	FDR ^a	Log ₂ (Fold Change)
CRC	K04790	mbtC	<0.001	<0.001	-1.102
CRC	K16051	tesI	0.001	0.007	-0.940
CRC	K04782	pchB	<0.001	<0.001	-0.700
CRC	K03333	choD	<0.001	<0.001	-0.690
CRC	K04781	mbtI, irp9, ybtS	<0.001	<0.001	-0.676
CRC	K04792	mbtF	0.001	0.007	-0.389
CRC	K04784	irp2, HMWP2	0.010	0.038	-0.363
CRC	K04564	SOD2	0.005	0.022	0.224
CRC	K05296	E1.1.1.51	<0.001	<0.001	0.836
CRC	K16050	hsaD	<0.001	<0.001	0.847
CRC	K15982	kshA	0.001	0.007	0.886
CRC	K03781	katE, CAT, catB, srpA	<0.001	<0.001	0.927
CRC	K00412	CYTB, petB	<0.001	<0.001	0.958
CRC	K00863	DAK, TKFC	<0.001	<0.001	0.989
CRC	K16048	hsaB	0.006	0.025	1.204
CRC	K09483	quiC	0.005	0.022	1.217
CRC	K16047	hsaA	0.002	0.012	1.218
CRC	K01058	pIdA	<0.001	<0.001	1.227
CRC	K04097	HPGDS	<0.001	<0.001	1.243

CRC	K00413	CYC1, CYT1, petC	<0.001	<0.001	1.298
CRC	K08738	CYC	<0.001	<0.001	1.373
CRC	K00632	fadA, fadI	0.001	0.007	1.433
CRC	K00365	uaZ	<0.001	<0.001	1.437
CRC	K15983	kshB	<0.001	<0.001	1.463
CRC	K00492	tmuM	<0.001	<0.001	1.486
CRC	K00799	GST, gst	<0.001	<0.001	1.518
CRC	K01253	EPHX1	<0.001	<0.001	1.553
CRC	K15653	mxCG	<0.001	<0.001	1.555
CRC	K01851	pchA	0.009	0.035	1.579
CRC	K12238	pchD	0.005	0.022	1.588
CRC	K12241	pchG	0.006	0.025	1.609
CRC	K01115	PLD1_2	0.003	0.016	1.681
CRC	K04787	mbtA	0.001	0.007	1.682
CRC	K01014	SULT1A	0.001	0.007	1.708
CRC	K00355	NQO1	<0.001	<0.001	1.709
CRC	K13285	sipB, ipaB, bipB	0.004	0.020	1.743
CRC	K13287	sipD, ipaD, bipD	0.005	0.022	1.748
CRC	K13742	ipgB1	0.005	0.022	1.749
CRC	K13286	sipC, ipaC, bipC	0.005	0.022	1.750
CRC	K01252	entB, dhbB, vibB, mxCF	0.001	0.007	1.754

CRC	K00216	entA	0.001	0.007	1.758
CRC	K13741	sopE	0.005	0.022	1.760
CRC	K02362	entD	0.002	0.012	1.763
CRC	K12785	espG, virA	0.006	0.025	1.770
CRC	K13085	ipgD, sopB	0.005	0.022	1.774
CRC	K13284	sipA, ipaA	0.005	0.022	1.775
CRC	K13743	ipgB2	0.005	0.022	1.778
CRC	K04785	irp3, ybtU	0.003	0.016	1.781
CRC	K13739	sopD	0.006	0.025	1.781
CRC	K13740	sptP	0.006	0.025	1.783
CRC	K02552	menF	<0.001	<0.001	1.829
CRC	K00510	HMOX1	<0.001	<0.001	1.848
CRC	K15981	CYP125A	0.001	0.007	2.769
CRC	K16046	CYP142	0.013	0.048	3.982
CRC	K00622	nat	0.008	0.032	4.591
CRC	K11987	PTGS2, COX2	0.013	0.048	6.239
adenoma	K00729	ALG5	<0.001	<0.001	-2.688
adenoma	K04110	badA	<0.001	<0.001	-1.876
adenoma	K16173	acd	<0.001	<0.001	-1.862
adenoma	K15372	toa	<0.001	<0.001	-1.259
adenoma	K05350	bglB	<0.001	<0.001	-1.124

adenoma	K00232	ACOX1/3	0.011	0.045	-0.974
adenoma	K07151	STT3	<0.001	<0.001	-0.942
adenoma	K00284	GLU	<0.001	<0.001	-0.806
adenoma	K03420	psmR	<0.001	<0.001	-0.793
adenoma	K04115	bcrD	<0.001	<0.001	-0.772
adenoma	K01501	E3.5.5.1	0.002	0.010	-0.751
adenoma	K09251	patA	<0.001	<0.001	-0.751
adenoma	K07130	kynB	<0.001	<0.001	-0.750
adenoma	K09123	lhpI	<0.001	<0.001	-0.738
adenoma	K13527	mpa	0.003	0.014	-0.720
adenoma	K04114	bcrA	<0.001	<0.001	-0.620
adenoma	K01432	AFMID	<0.001	<0.001	-0.616
adenoma	K01607	pcaC	<0.001	<0.001	-0.561
adenoma	K01580	gadB, gadA, GAD	<0.001	<0.001	-0.527
adenoma	K03780	ttdB	0.002	0.010	-0.527
adenoma	K03779	ttdA	0.003	0.014	-0.506
adenoma	K07535	badH	0.001	0.005	-0.487
adenoma	K11263	bccA, pccA	<0.001	<0.001	-0.486
adenoma	K07250	gabT	0.001	0.005	-0.481
adenoma	K00074	paaH, hbd, fadB, mmgB	<0.001	<0.001	-0.435
adenoma	K01464	DPYS, dht, hydA	0.001	0.005	-0.386

adenoma	K05349	bglX	0.005	0.022	-0.353
adenoma	K00248	ACADS, bcd	<0.001	<0.001	-0.337
adenoma	K00274	MAO, aofH	0.007	0.030	-0.326
adenoma	K01091	gph	<0.001	<0.001	-0.321
adenoma	K01895	ACSS1_2, acs	0.006	0.026	-0.308
adenoma	K10536	aguA	0.008	0.034	-0.287
adenoma	K00721	DPM1	<0.001	<0.001	-0.274
adenoma	K04565	SOD1	0.007	0.030	-0.258
adenoma	K01915	glnA, GLUL	<0.001	<0.001	-0.230
adenoma	K00147	proA	0.001	0.005	-0.153
adenoma	K01424	ansA, ansB	0.001	0.005	0.186
adenoma	K01458	hutG	0.005	0.022	0.336
adenoma	K00819	rocD, OAT	0.002	0.010	0.422
adenoma	K01666	mhpE	0.005	0.022	0.528
adenoma	K05606	MCEE, epi	0.005	0.022	0.538
adenoma	K07248	aldA	<0.001	<0.001	0.561
adenoma	K01847	MUT	0.006	0.026	0.586
adenoma	K00865	glxK, garK	<0.001	<0.001	0.588
adenoma	K01485	codA	0.002	0.010	0.636
adenoma	K13821	putA	0.008	0.034	0.678
adenoma	K01821	praC, xylH	0.007	0.030	0.711

adenoma	K03781	katE, CAT, catB, srpA	0.002	0.010	0.725
adenoma	K00023	phbB	0.001	0.005	0.737
adenoma	K00217	E1.3.1.32	0.002	0.010	0.800
adenoma	K00123	fdoG, fdhF, fdwA	0.007	0.030	0.847
adenoma	K10220	ligJ	0.009	0.037	0.921
adenoma	K13051	ASRGL1, iaaA	<0.001	<0.001	0.926
adenoma	K01578	MLYCD	0.006	0.026	0.926
adenoma	K10221	ligI	<0.001	0.000	0.938
adenoma	K00015	gyaR, GOR1	<0.001	<0.001	0.939
adenoma	K00412	CYTB, petB	0.001	0.005	0.963
adenoma	K01617	dmpH, xylI, nahK	0.003	0.014	0.969
adenoma	K10217	dmpC, xylG, praB	0.005	0.022	1.020
adenoma	K01055	pcaD	0.005	0.022	1.074
adenoma	K03343	puo	0.010	0.041	1.103
adenoma	K08738	CYC	0.001	0.005	1.110
adenoma	K01816	hyi, gip	<0.001	<0.001	1.123
adenoma	K01014	SULT1A	0.001	0.005	1.153
adenoma	K14449	mch, mcd	0.007	0.030	1.171
adenoma	K05783	benD-xylL	0.007	0.030	1.176
adenoma	K08692	mtkB	0.006	0.026	1.208
adenoma	K00124	fdoH, fdsB	0.003	0.014	1.210

adenoma	K14067	mtkA	0.006	0.026	1.211
adenoma	K08691	mcl	0.006	0.026	1.229
adenoma	K14447	ecm	0.006	0.026	1.235
adenoma	K00126	fdsD	<0.001	<0.001	1.236
adenoma	K00588	E2.1.1.104	0.001	0.005	1.237
adenoma	K00824	dat	0.005	0.022	1.262
adenoma	K01031	pcaI	0.004	0.018	1.283
adenoma	K00492	tmuM	0.002	0.010	1.306
adenoma	K00090	ghrB	0.001	0.005	1.337
adenoma	K01032	pcaJ	0.004	0.018	1.338
adenoma	K00632	fadA, fadI	0.001	0.005	1.352
adenoma	K00446	dmpB, xylE	0.001	0.005	1.365
adenoma	K14446	ccr	0.001	0.005	1.376
adenoma	K04097	HPGDS	<0.001	<0.001	1.398
adenoma	K00316	spdH	0.008	0.034	1.403
adenoma	K01058	pIdA	<0.001	<0.001	1.411
adenoma	K00129	ALDH3	0.001	0.005	1.418
adenoma	K00355	NQO1	0.001	0.005	1.429
adenoma	K14727	pcaL	<0.001	<0.001	1.430
adenoma	K00365	uaZ	<0.001	<0.001	1.439
adenoma	K01253	EPHX1	<0.001	<0.001	1.460

adenoma	K01584	adiA	0.009	0.037	1.473
adenoma	K01577	oxc	0.001	0.005	1.476
adenoma	K02554	mhpD	0.002	0.010	1.513
adenoma	K00413	CYC1, CYT1, petC	<0.001	<0.001	1.517
adenoma	K00127	fdoI, fdsG	0.001	0.005	1.522
adenoma	K00799	GST, gst	<0.001	<0.001	1.533
adenoma	K01782	fadJ	<0.001	<0.001	1.541
adenoma	K00613	GATM	<0.001	<0.001	1.549
adenoma	K01638	aceB, glcB	0.002	0.010	1.564
adenoma	K00276	AOC3, AOC2, tynA	<0.001	<0.001	1.608
adenoma	K00448	pcaG	<0.001	<0.001	1.609
adenoma	K00137	prp	<0.001	<0.001	1.618
adenoma	K01682	acnB	<0.001	<0.001	1.639
adenoma	K00813	aspC	<0.001	<0.001	1.642
adenoma	K09471	puuB, ordL	<0.001	<0.001	1.648
adenoma	K09473	puuD	<0.001	<0.001	1.650
adenoma	K01115	PLD1_2	0.002	0.010	1.654
adenoma	K09470	puuA	<0.001	<0.001	1.658
adenoma	K01637	aceA	0.001	0.005	1.669
adenoma	K00840	astC	<0.001	<0.001	1.675
adenoma	K12972	ghrA	<0.001	<0.001	1.684

adenoma	K01608	gcl	<0.001	<0.001	1.695
adenoma	K06447	astD	<0.001	<0.001	1.700
adenoma	K01484	astB	<0.001	<0.001	1.702
adenoma	K11472	glcE	<0.001	<0.001	1.716
adenoma	K05526	astE	<0.001	<0.001	1.719
adenoma	K00673	astA	<0.001	<0.001	1.720
adenoma	K01825	fadB	<0.001	<0.001	1.724
adenoma	K00822	E2.6.1.18	<0.001	<0.001	1.732
adenoma	K03464	catC	<0.001	<0.001	1.766
adenoma	K00449	pcaH	<0.001	<0.001	1.777
adenoma	K12256	spuC	0.001	0.005	1.819
adenoma	K00495	CYP71AN24	<0.001	<0.001	1.863
adenoma	K01849	mcmA2	<0.001	<0.001	1.913
adenoma	K01848	mcmA1	<0.001	<0.001	1.918
adenoma	K05784	benC-xylZ	<0.001	<0.001	1.930
adenoma	K05550	benB-xylY	<0.001	<0.001	1.931
adenoma	K11473	glcF	<0.001	<0.001	1.938
adenoma	K05549	benA-xylX	<0.001	<0.001	1.947
adenoma	K01075	E3.1.2.23	<0.001	<0.001	1.970
adenoma	K12252	aruH	<0.001	<0.001	2.067
adenoma	K07823	pcaF	<0.001	<0.001	2.071

adenoma	K10815	hcnB	<0.001	<0.001	2.078
adenoma	K12254	kauB	<0.001	<0.001	2.146
adenoma	K12255	gbuA	<0.001	<0.001	2.158
adenoma	K12253	aruI	<0.001	<0.001	2.184
adenoma	K10814	hcnA	<0.001	<0.001	2.194
adenoma	K10816	hcnC	<0.001	<0.001	2.196
adenoma	K00460	ALOX15	<0.001	<0.001	2.214
adenoma	K04835	mal	<0.001	<0.001	2.373
adenoma	K10219	ligC	<0.001	<0.001	2.384
adenoma	K01846	glmS	<0.001	<0.001	2.940

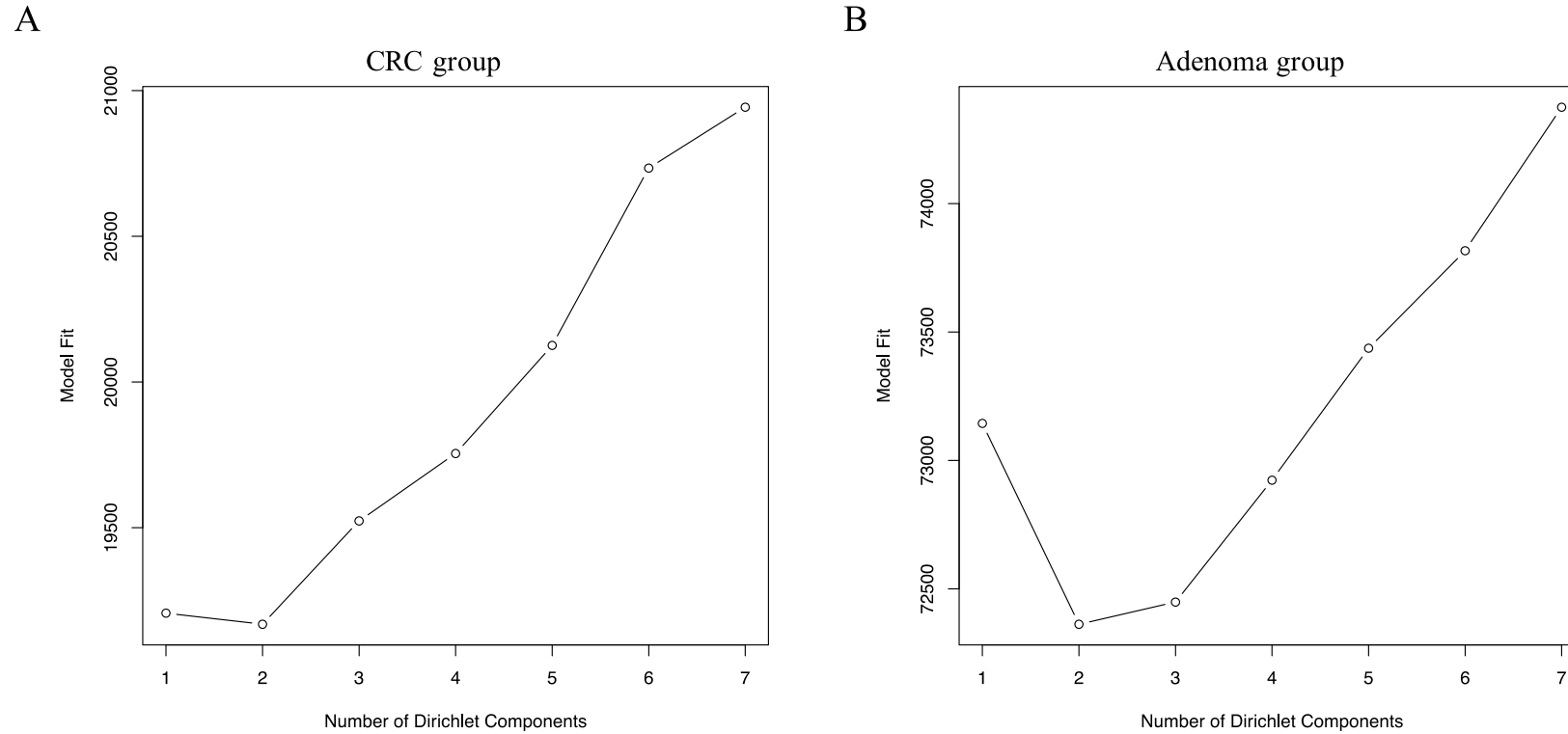
Abbreviations: CRC, colorectal cancer; FDR, false discovery rate.

^a FDR refers to an adjusted P value corrected by a false discovery rate.

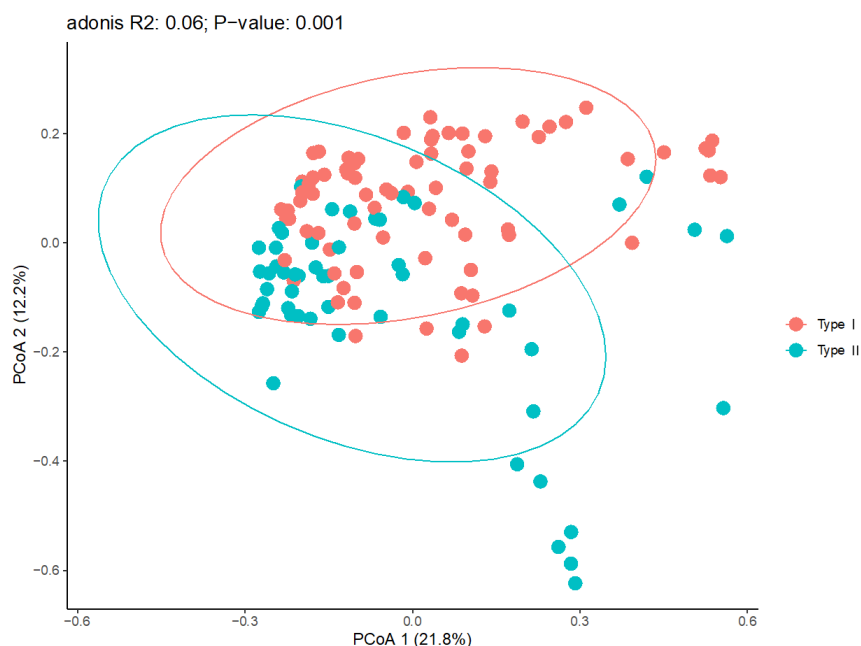
Supplementary Table 16. Correlations between differential genes and differential genus (Type II VS. Type I)

Group	KO gene (name)	Genus	P value	Correlation coefficient
CRC	K01115 (PLD1/2)	<i>Escherichia Shigella</i>	<0.001	0.718
Adenoma	K01115 (PLD1/2)	<i>Escherichia Shigella</i>	<0.001	0.88
Adenoma	K01115 (PLD1/2)	<i>Lachnoclostridium</i>	0.004	0.385
Adenoma	K01115 (PLD1/2)	<i>Lactococcus</i>	<0.001	0.477
Adenoma	K01115 (PLD1/2)	<i>Bacillus</i>	<0.001	0.492
Adenoma	K01115 (PLD1/2)	<i>Enterococcus</i>	0.004	0.387
Adenoma	K01115 (PLD1/2)	<i>Ruminococcaceae UCG-014</i>	0.008	-0.357
CRC	K08738 (CYC)	<i>Ruminiclostridium 9</i>	0.047	0.275
CRC	K08738 (CYC)	<i>Lachnoclostridium</i>	0.042	0.280
Adenoma	K08738 (CYC)	<i>Escherichia Shigella</i>	<0.001	0.520
Adenoma	K08738 (CYC)	<i>Erysipelotrichaceae Incertae Sedis</i>	0.008	0.359
Adenoma	K08738 (CYC)	<i>Lachnoclostridium</i>	<0.001	0.809
Adenoma	K08738 (CYC)	<i>Lactococcus</i>	0.019	0.317
Adenoma	K08738 (CYC)	<i>Bacillus</i>	<0.001	0.618
CRC	K11987 (PTGS2/COX2)	<i>Lachnospiraceae NK4A136 group</i>	0.031	-0.297

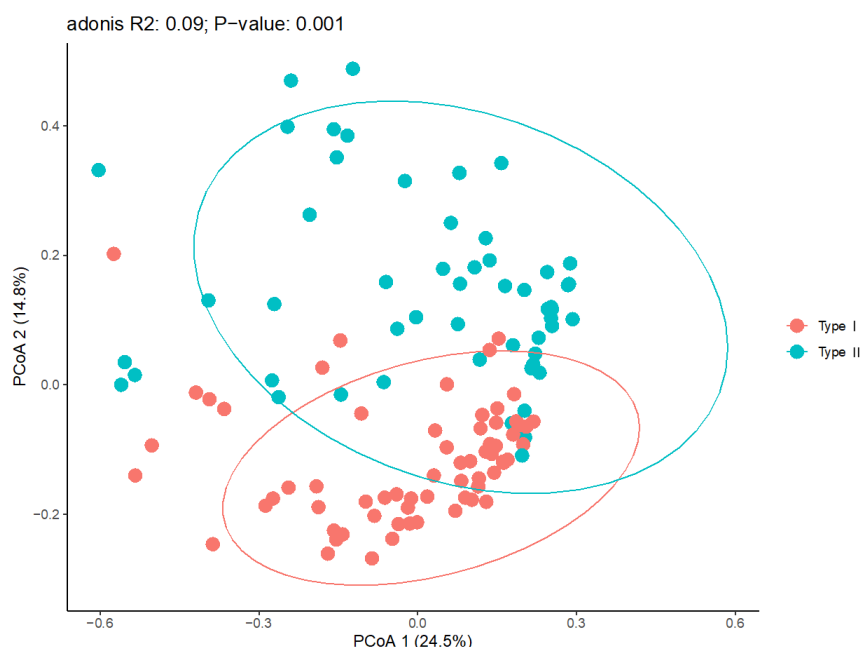
Supplementary Figure



Supplementary Figure 1. Fitting classification results of Dirichlet multinomial mixture model based on gut microbiota in each case group. (A) CRC group (n = 130). (B) Adenoma group (n = 120). According to Laplace goodness of fit as the ordinate, both of the optimal fit (Laplace minimum) is for abscissa value = 2 distinct Dirichlet components.

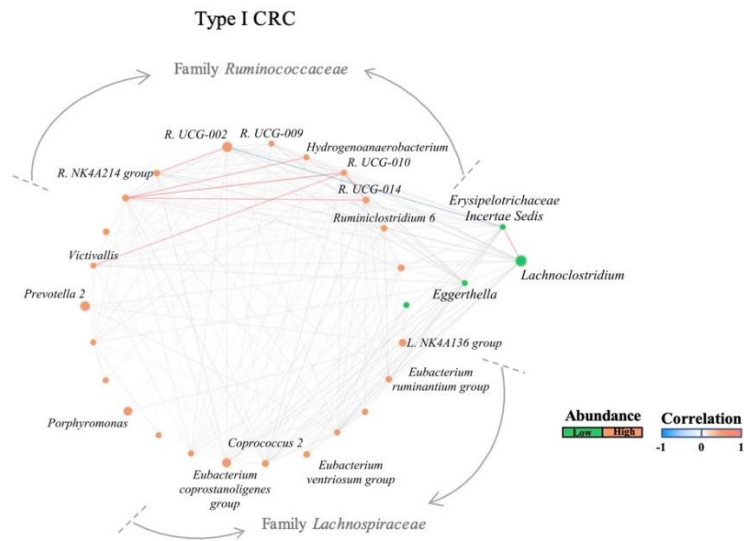


Supplementary Figure 2. Principal coordinate analysis (PCoA) plots based on Bray-Curtis distances depict the two distinct microbial community groups (type I and type II) in colorectal cancer samples. The plot displays PCoA 1 on the x-axis and PCoA 2 on the y-axis. In the plot, samples are represented by red (type I) and blue (type II) points, with surrounding ellipses illustrating the 95% confidence interval for each subtype.

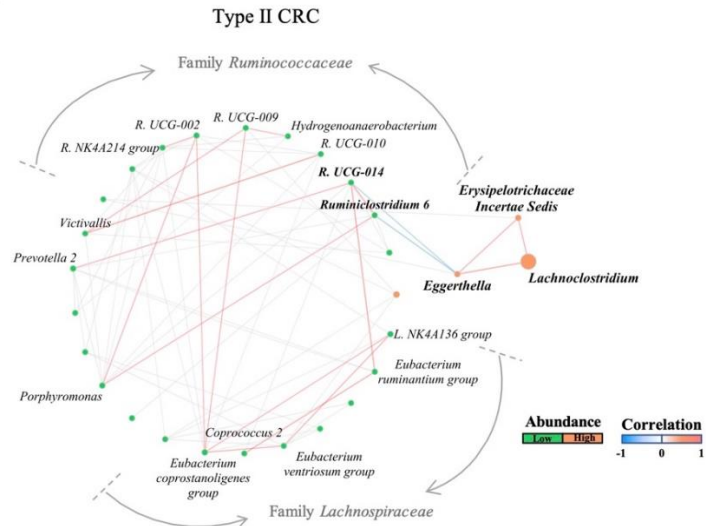


Supplementary Figure 3. Principal coordinate analysis (PCoA) plots based on Bray-Curtis distances depict the two distinct microbial community groups (type I and type II) in colorectal adenoma samples. The plot displays PCoA 1 on the x-axis and PCoA 2 on the y-axis. In the plot, samples are represented by red (type I) and blue (type II) points, with surrounding ellipses illustrating the 95% confidence interval for each subtype.

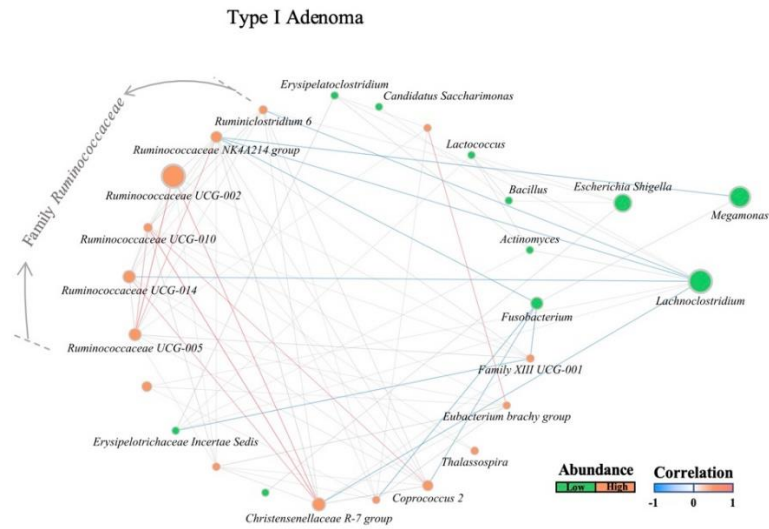
A



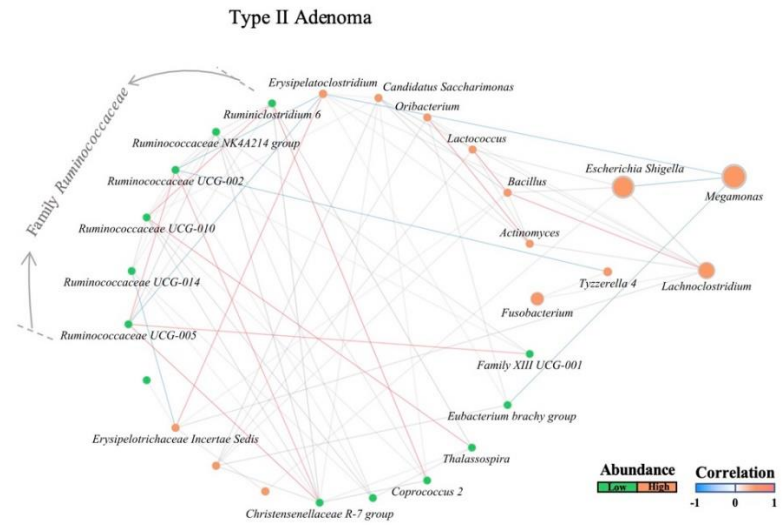
B



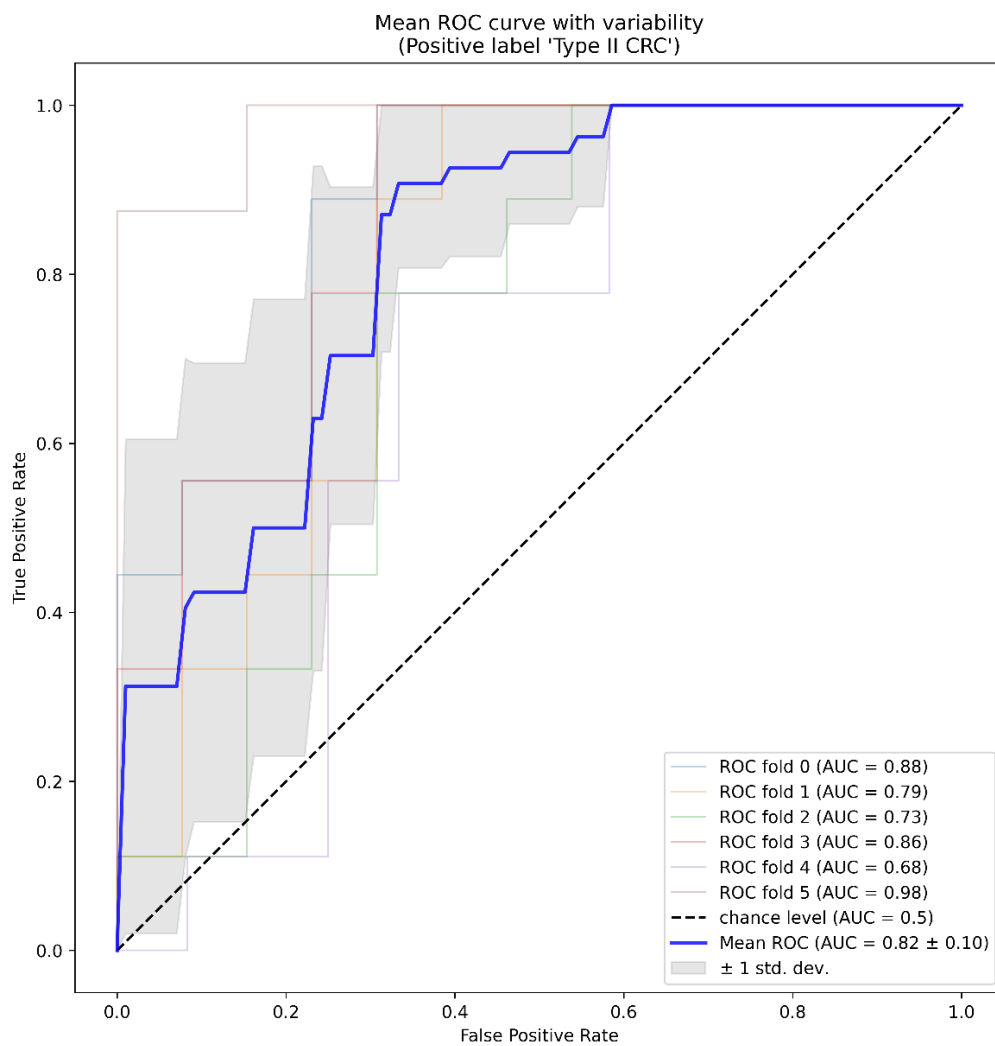
C



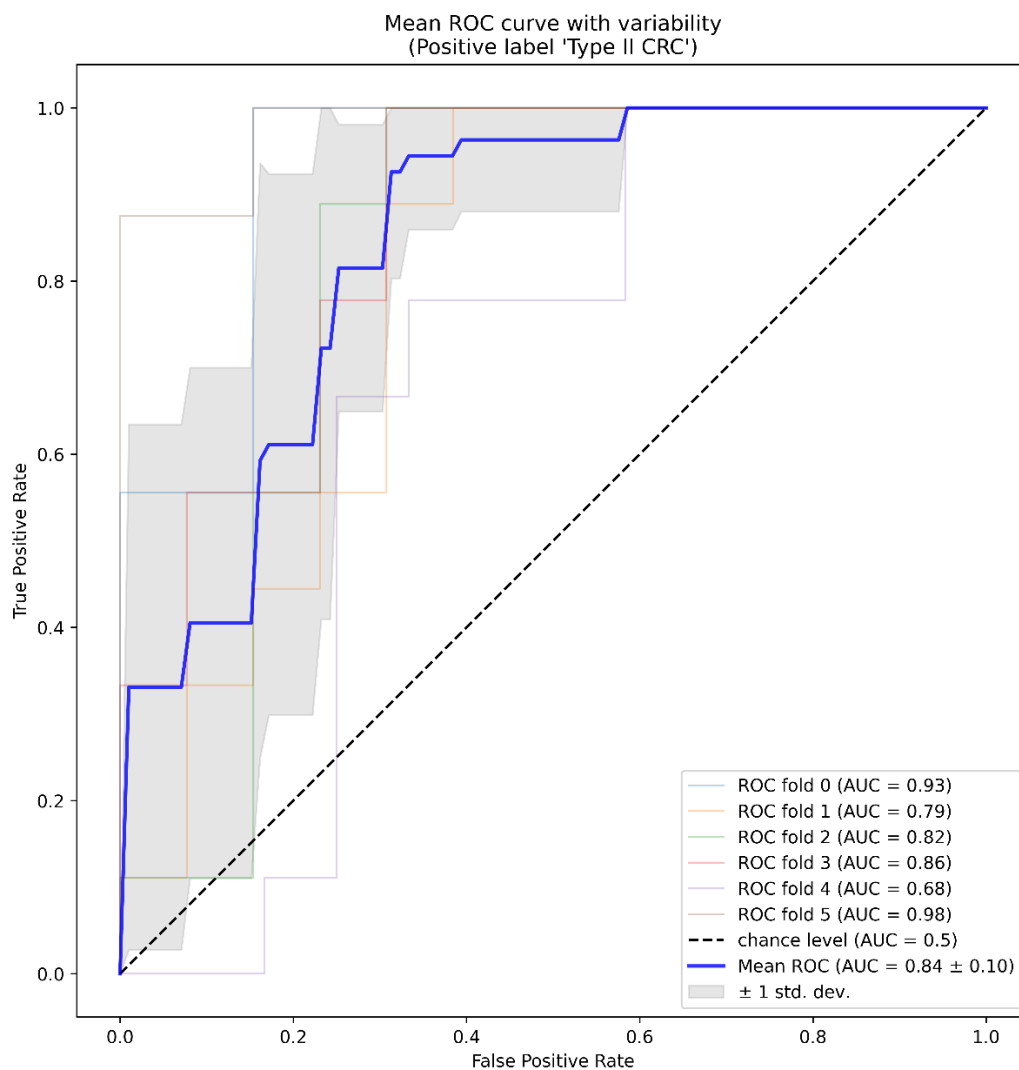
D



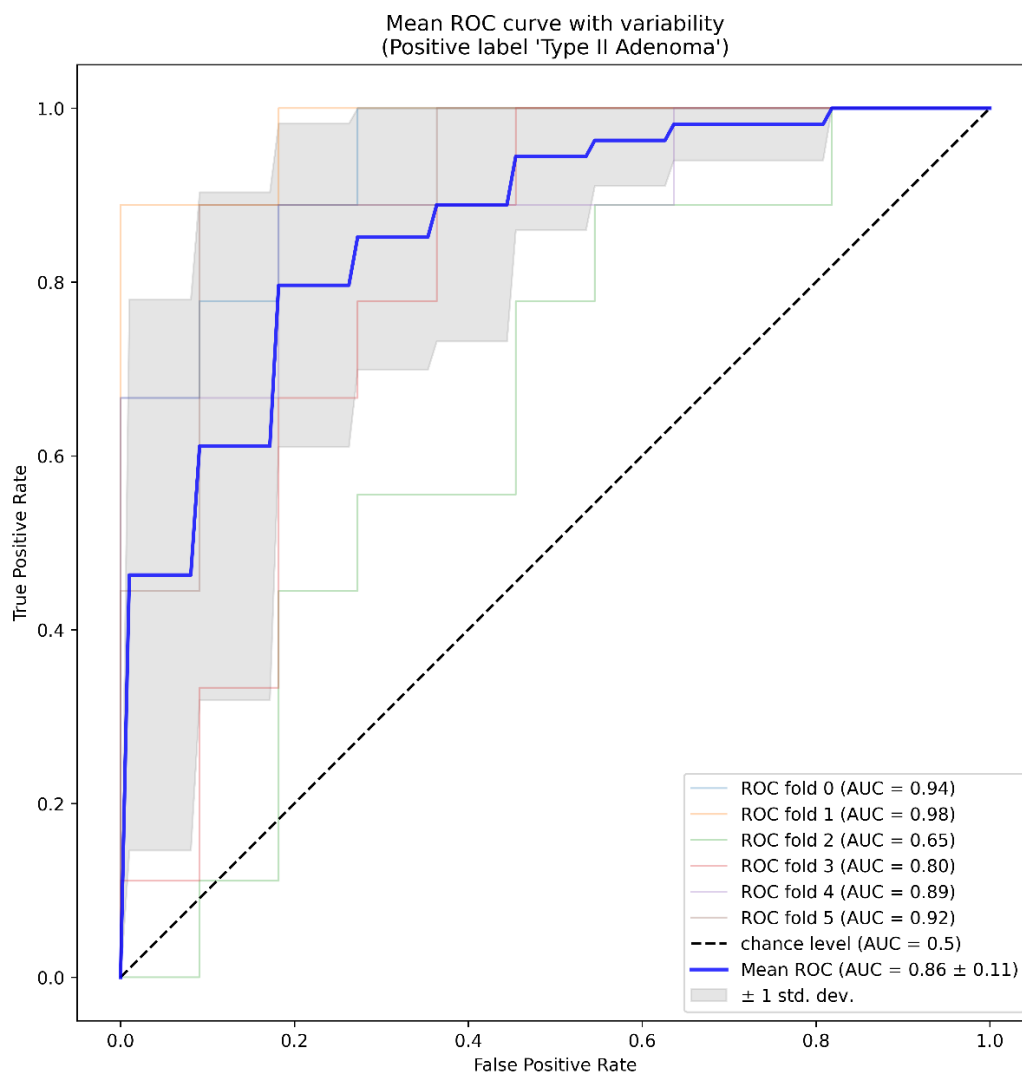
Supplementary Figure 4. Microbial interaction networks among top 30 differential genera between type I and type II enterotypes within CRC or adenoma groups. Correlations were measured by Spearman's correlation analysis ($P < 0.05$). Node sizes are proportional to the abundance of genera, with orange representing elevated abundance and green representing decreased abundance by comparing subgroups within CRC or adenoma groups. (A) Type I CRC and (B) type II CRC. Edge color depths are proportional to correlation coefficients, with orange representing positive correlations greater than 0.4, blue representing negative correlations less than -0.45, and gray representing the rest. (C) Type I adenoma and (D) type II adenoma. Edge color depths are proportional to correlation coefficients, with orange representing positive correlations greater than 0.5, blue representing all significant negative correlations, and gray representing the rest.



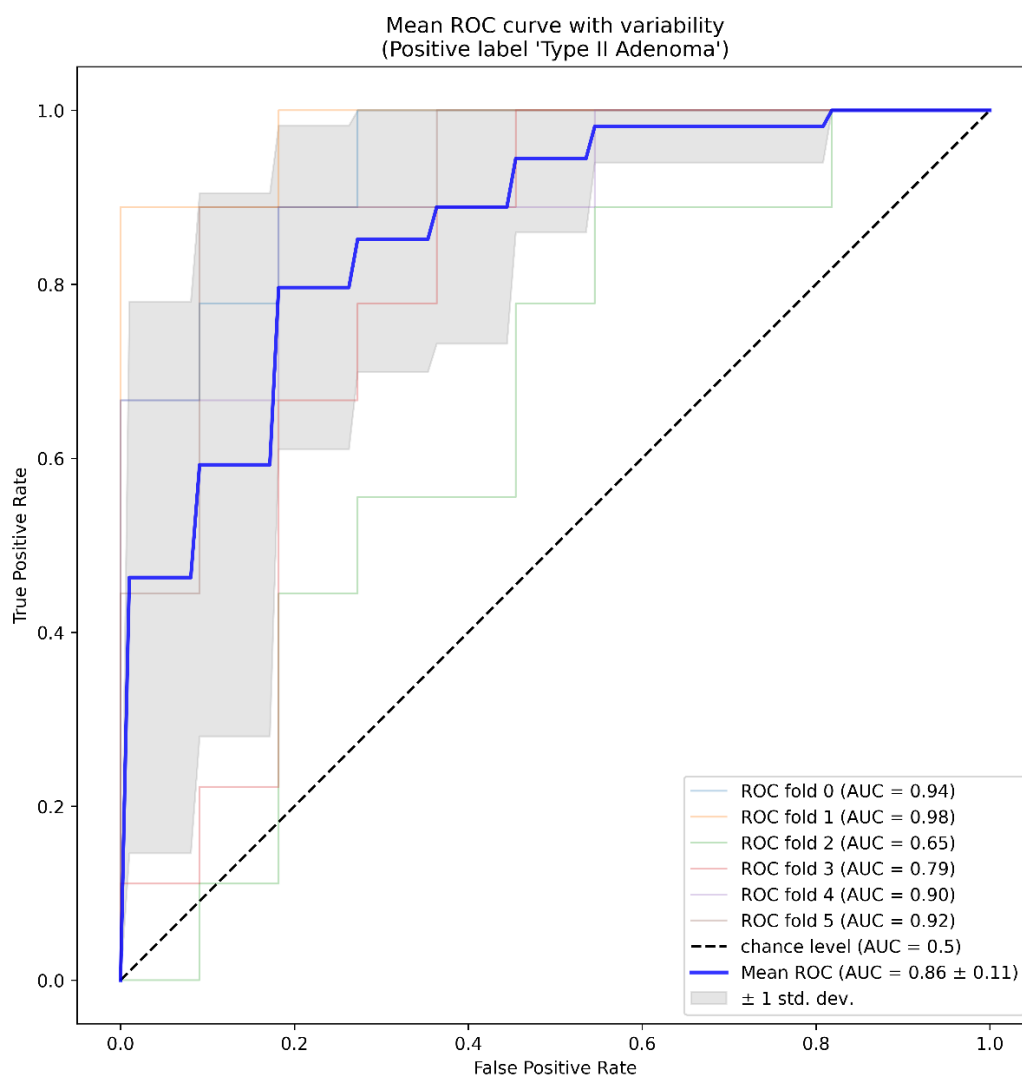
Supplementary Figure 5. Performance of the linear support vector machine classifier using AUC was evaluated using 5 randomized 5-fold cross-validation in CRC group. AUC, an area under the receiver operating characteristic curve; CRC, colorectal cancer; ROC, receiver operating characteristic.



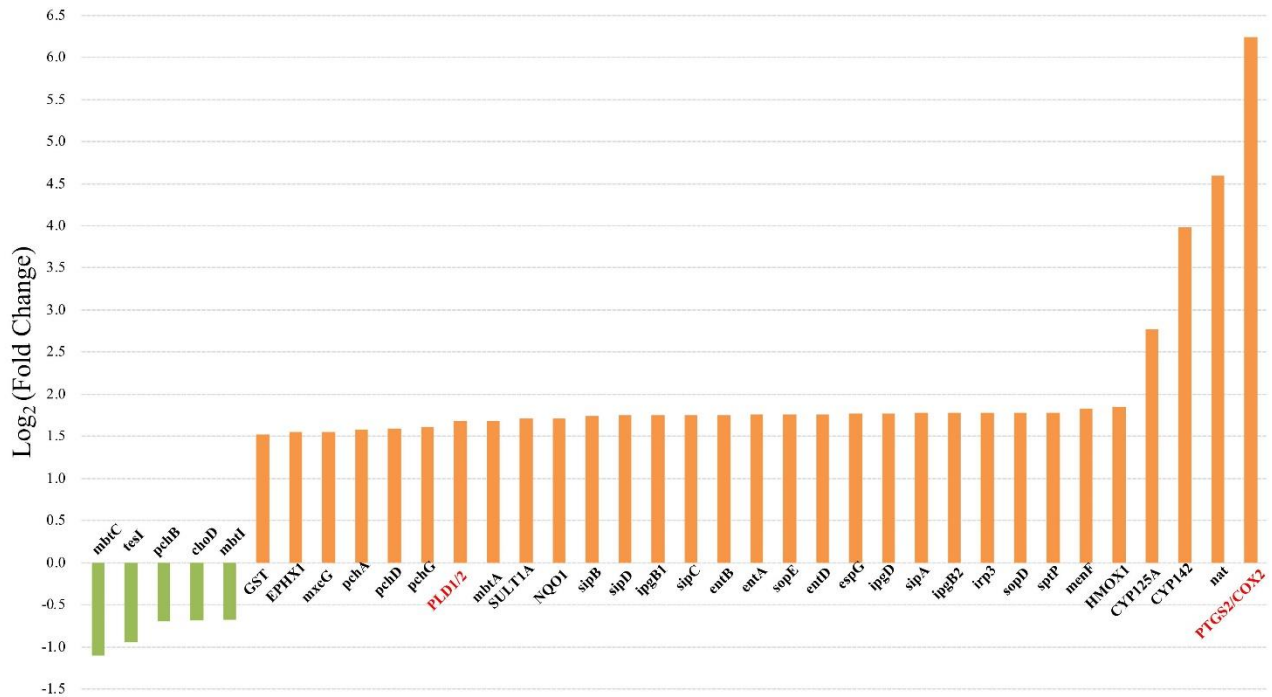
Supplementary Figure 6. Performance of the logistic regression classifier using AUC was evaluated using 5 randomized 5-fold cross-validation in CRC group. AUC, an area under the receiver operating characteristic curve; CRC, colorectal cancer; ROC, receiver operating characteristic.



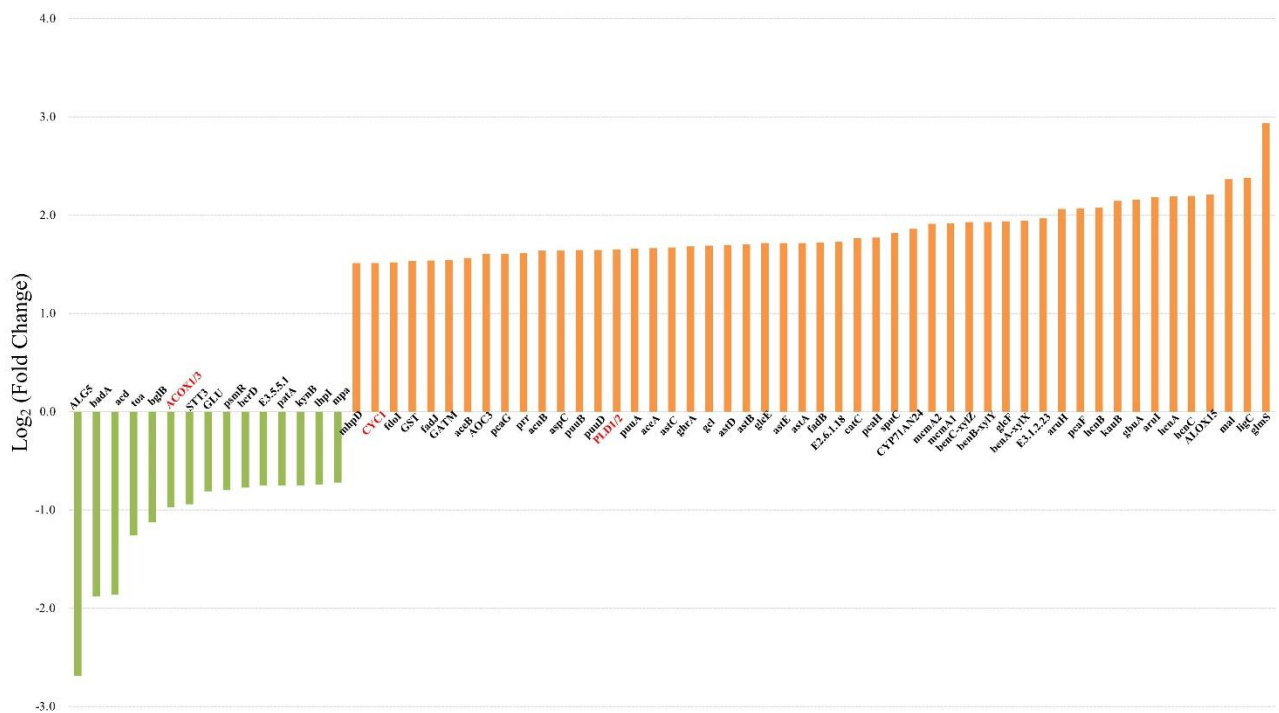
Supplementary Figure 7. Performance of the linear support vector machine classifier using AUC was evaluated using 5 randomized 5-fold cross-validation in colorectal adenoma group. AUC, an area under the receiver operating characteristic curve; ROC, receiver operating characteristic.



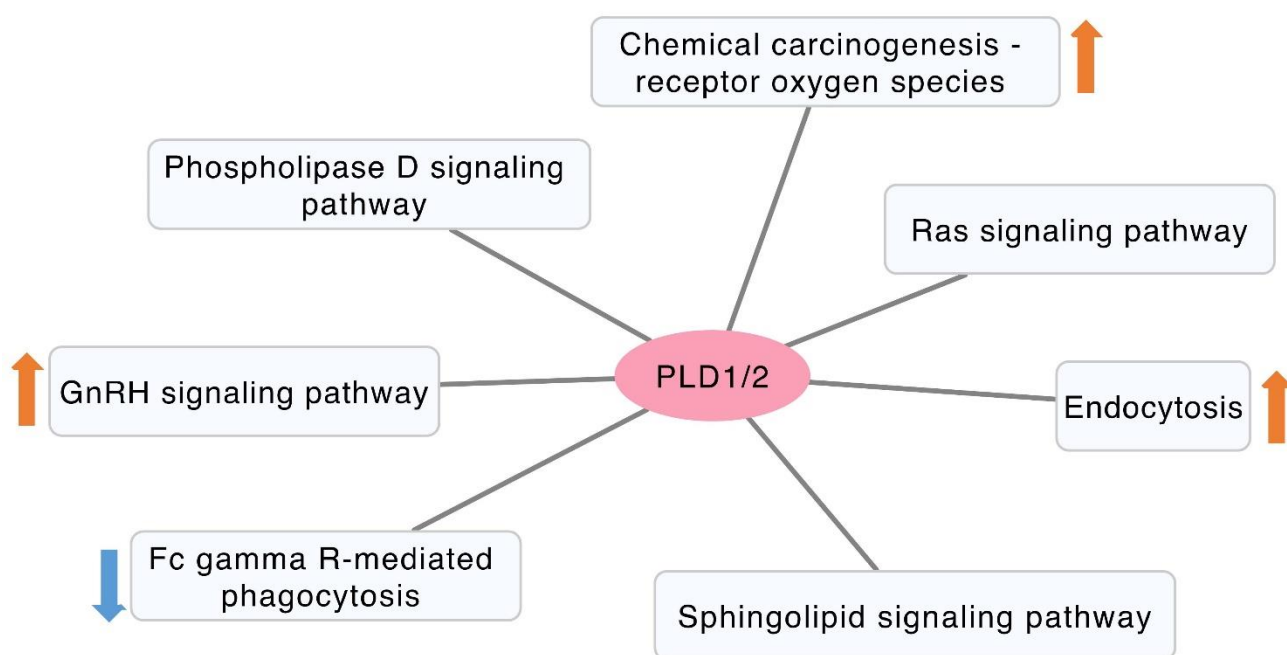
Supplementary Figure 8. Performance of the logistic regression classifier using AUC was evaluated using 5 randomized 5-fold cross-validation in colorectal adenoma group. AUC, an area under the receiver operating characteristic curve; ROC, receiver operating characteristic.



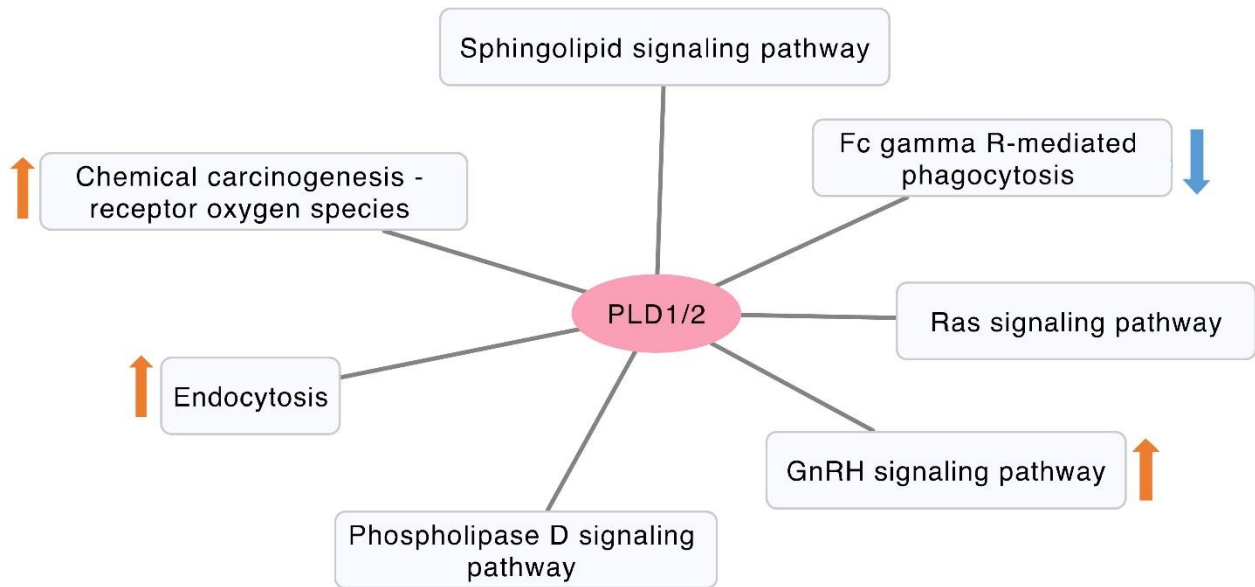
Supplementary Figure 9. Differential genes in type II CRC subtype relative to type I subtype based on Tax4FUN functional analysis (FDR adjusted $p < 0.05$, $FC > 1.5$). Genes that are significantly associated with differential pathways are highlighted in red. CRC, colorectal cancer; FDR, false discovery rate; FC, fold change.



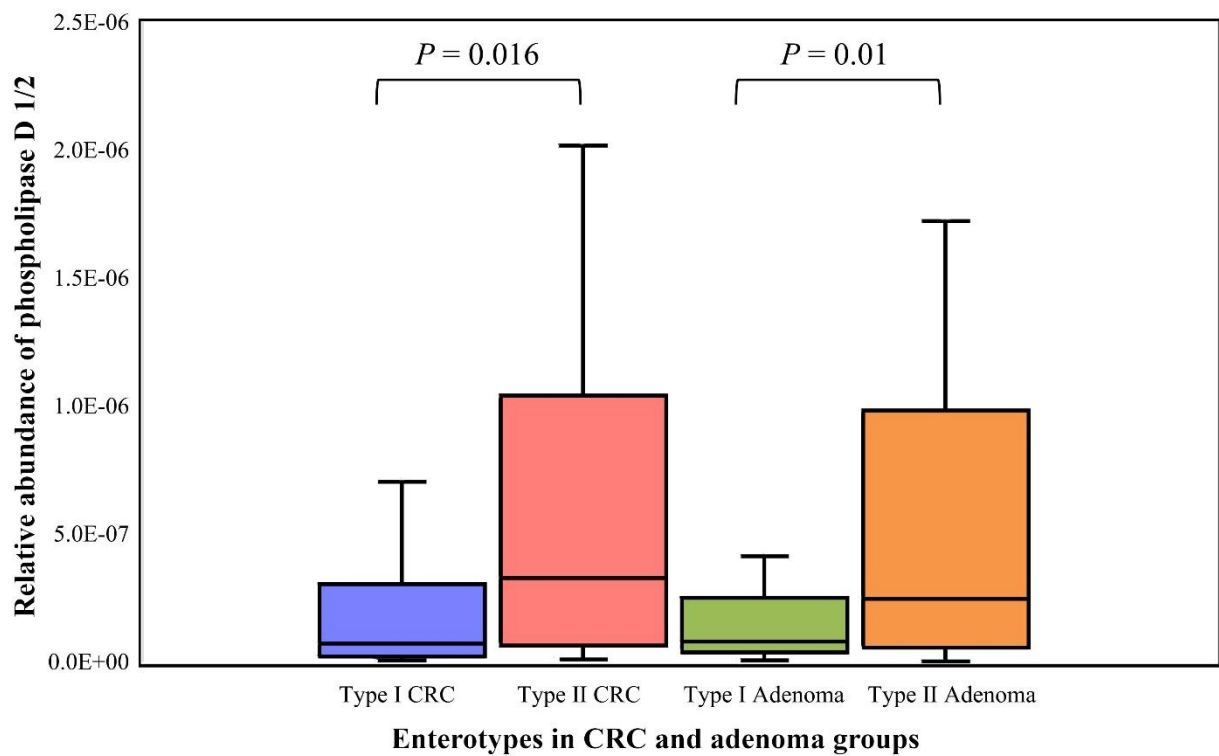
Supplementary Figure 10. Differential genes in type II colorectal adenoma subtype relative to type I subtype based on Tax4FUN functional analysis (FDR adjusted $p < 0.05$, $FC > 1.5$). Genes that are significantly associated with differential pathways are highlighted in red. FDR, false discovery rate; FC, fold change.



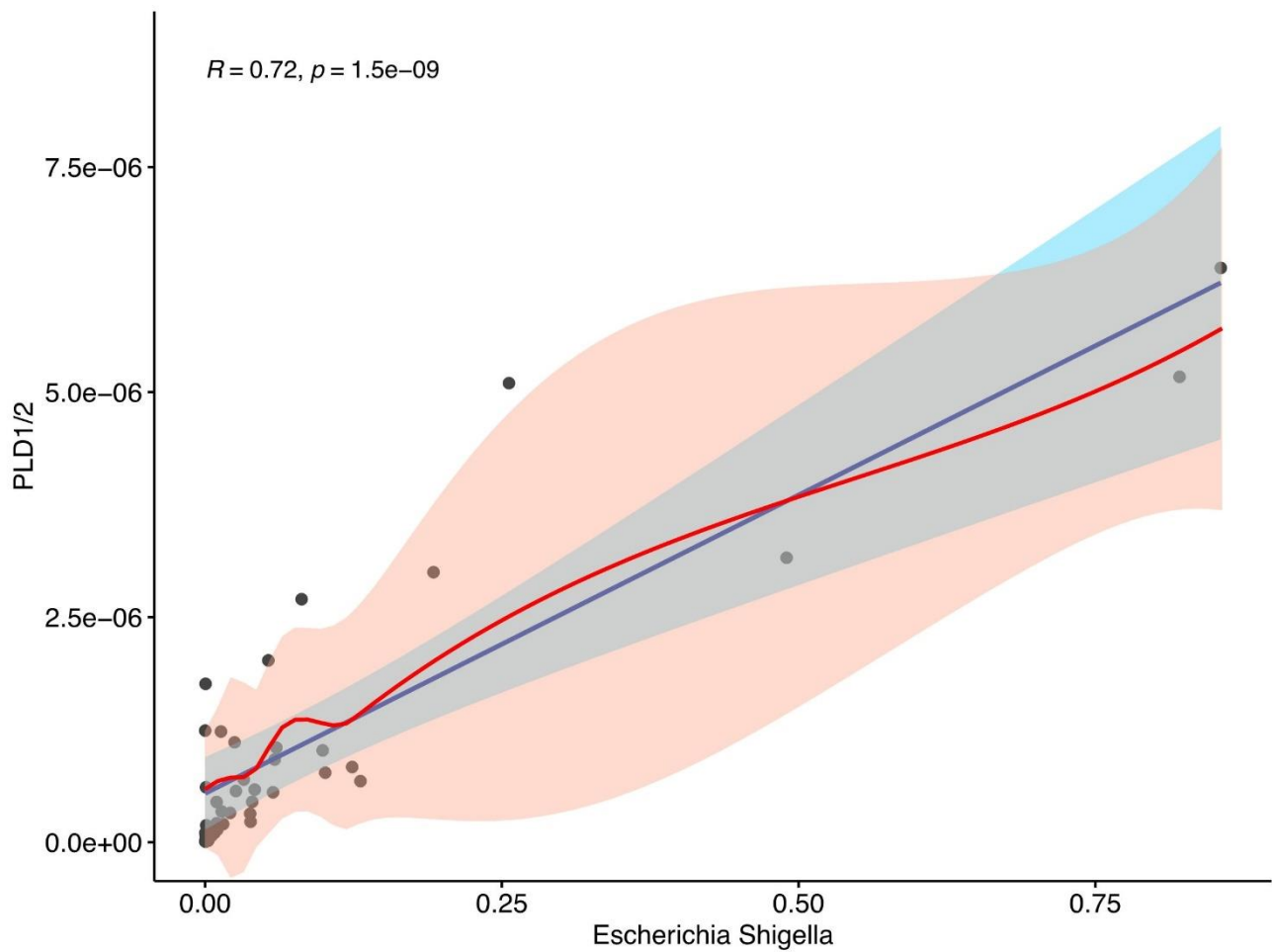
Supplementary Figure 11. The pathways involving phospholipase D 1/2 (PLD 1/2) in type II CRC subtype. The orange arrows indicate a significant increase, and the blue arrow indicates a significant decrease (FDR adjusted $p < 0.05$, $FC > 1.5$). CRC, colorectal cancer; FDR, false discovery rate; FC, fold change.



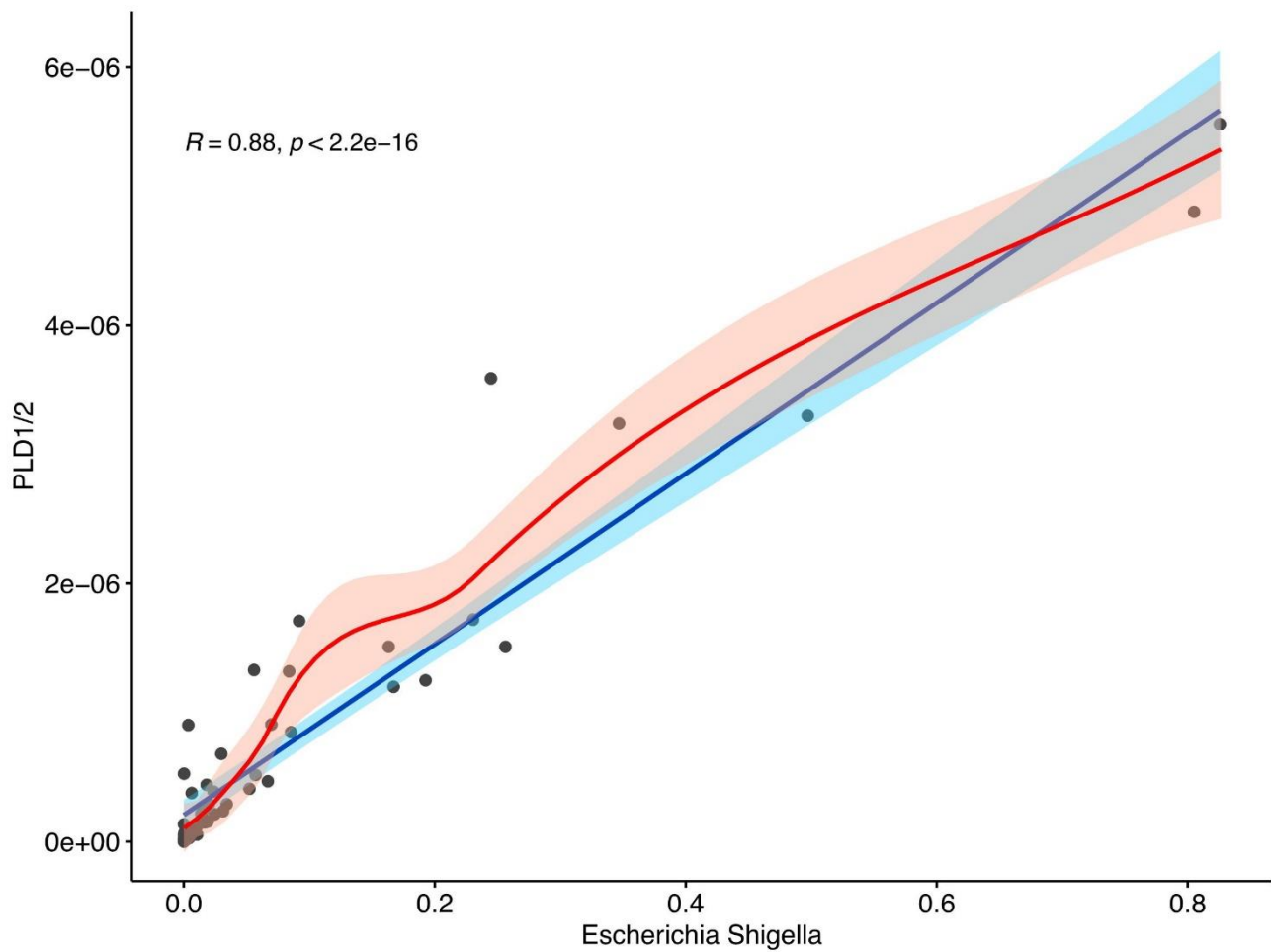
Supplementary Figure 12. The pathways involving phospholipase D 1/2 (PLD 1/2) in type II colorectal adenoma subtype. The orange arrows indicate a significant increase, and the blue arrow indicates a significant decrease (FDR adjusted $p < 0.05$, $FC > 1.5$). FDR, false discovery rate; FC, fold change.



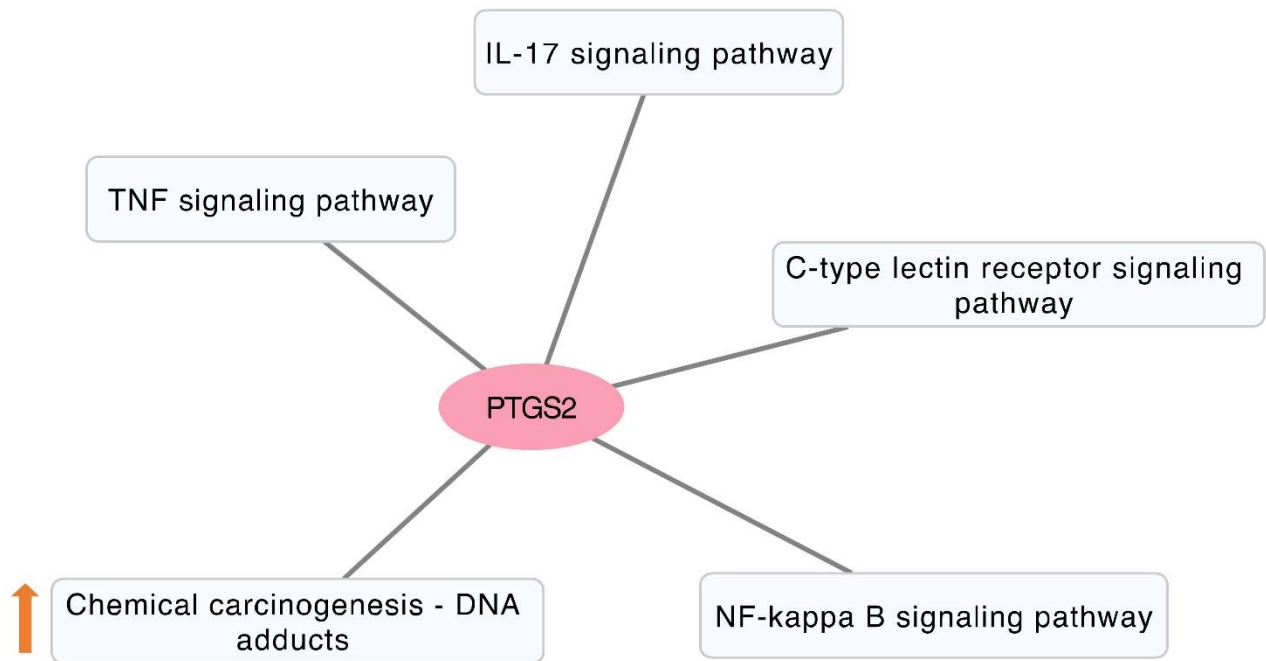
Supplementary Figure 13. The relative abundance of phospholipase D 1/2 (PLD 1/2) in different subtypes. The boxplots show the relative abundance of PLD 1/2 in type I and type II subtypes of CRC and adenoma groups. PLD 1/2 was significantly more abundant in type II subtypes than in type I subtypes in both groups (Mann-Whitney U test, all $P < 0.05$).



Supplementary Figure 14. Spearman's correlation analysis between the relative abundance of *Escherichia Shigella* and phospholipase D 1/2 (PLD 1/2) within type II colorectal cancer. The scatter plot shows the data points in black, the linear model fit and its 95% confidence interval in blue, and the locally weighted regression fit and its 95% confidence interval in red. The correlation coefficient R and the P value are also shown.



Supplementary Figure 15. Spearman's correlation analysis between the relative abundance of *Escherichia Shigella* and phospholipase D 1/2 (PLD 1/2) within type II colorectal adenoma. The scatter plot shows the data points in black, the linear model fit and its 95% confidence interval in blue, and the locally weighted regression fit and its 95% confidence interval in red. The correlation coefficient R and the P value are also shown.



Supplementary Figure 16. The pathways involving prostaglandin-endoperoxide synthase 2 (PTGS2) in type II CRC subtype. The orange arrow indicates a significant increase (FDR adjusted $p < 0.05$, $FC > 1.5$). CRC, colorectal cancer; FDR, false discovery rate; FC, fold change.