Supplemental materials

Materials and Methods

Procedure for Sample Collection

Twenty-six ESCC patients, fourteen patients with ESCC after chemotherapy, eighteen patients with ESCC after immunotherapy and twenty-eight healthy volunteers were enrolled in this study. Blood, oral mucosal, saliva, urine, and fecal samples were collected once from the subjects. We used blood test tubes to collect the blood samples and urinary tubes to collect the urine samples and transferred the samples to sterile EP tubes. Oral mucosal, saliva, and fecal samples were collected using sterile sampling tubes. Oral mucosal and saliva samples were collected from subjects in the morning after they had brushed their teeth and gargled. We collected the middle part of the morning urine and the inside part of the middle feces. Samples were stored at −80 °C until analysis.

DNA Extraction

Total genomic DNA samples were extracted using the OMEGA Soil DNA Kit (M5635-02) (Omega Bio-Tek, Norcross, GA, USA), following the manufacturer's instructions, and stored at -20 °C prior to further analysis. The quantity and quality of extracted DNAs were measured using a NanoDrop NC2000 spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA) and agarose gel electrophoresis, respectively.

16S rRNA Gene Amplicon Sequencing

PCR amplification of the bacterial 16S rRNA genes V3–V4 region was performed using the forward primer 338F (5'-ACTCCTACGGGAGGCAGCA-3') and the reverse primer 806R (5'-GGACTACHVGGGTWTCTAAT-3'). Sample-specific 7-bp barcodes were incorporated into the primers for multiplex sequencing. The PCR components contained 5 μl of buffer (5×), 0.25 μl of Fast pfu DNA Polymerase (5U/μl), 2 μl (2.5 mM) of dNTPs, 1 μl (10 uM) of each Forward and Reverse primer, 1 μl of DNA Template, and 14.75 μl of ddH2O. Thermal cycling consisted of initial denaturation at 98 °C for 5 min, followed by 25 cycles consisting of denaturation at 98 °C for 30 s, annealing at 52°C for 30 s, and extension at 72 °C for 45 s, with a final extension of 5 min at 72 °C. PCR amplicons were purified with Vazyme VAHTSTM DNA Clean Beads (Vazyme, Nanjing, China) and quantified using the Quant-iT PicoGreen dsDNA Assay Kit (Invitrogen, Carlsbad, CA, USA). After the individual quantification step, amplicons were pooled in equal amounts, and pair-end 2×250 bp sequencing was performed using the Illlumina NovaSeq platform with NovaSeq 6000 SP Reagent Kit (500 cycles) at Shanghai Personal Biotechnology Co., Ltd (Shanghai, China).

Sequence Analysis

Microbiome bioinformatics were performed with QIIME2 2019.4 (Bolyen et al. 2018) with slight modification according to the official tutorials (https://docs.qiime2.org/2019.4/tutorials/). Briefly, raw sequence data were demultiplexed using the demux plugin following by primers cutting with cutadapt plugin (Martin, M., 2011). Sequences were then quality filtered, denoised, merged and chimera removed using the DADA2 plugin (Callahan et al. 2016). Non-singleton amplicon sequence variants (ASVs) were aligned with mafft (Katoh et al. 2002) and used to construct a phylogeny with fasttree2 (Price et al. 2010). Alpha-diversity metrics (Chao1 (Chao, 1984), Observed species, Shannon (Shannon, 1948a, b), Simpson (Simpson, 1949), Faith's PD (Faith, 1992), Pielou's evenness (Pielou, 1966) and Good's coverage (Good, 1953)), beta diversity metrics weighted UniFrac (Lozupone et al. 2007) was estimated using the diversity plugin with samples were rarefied to 22377 sequences per sample. Taxonomy was assigned to ASVs using the classify-sklearn naïve Bayes taxonomy classifier in feature-classifier plugin (Bokulich et al. 2018a) against the Greengenes Release 13.8 Database (DeSantis et al,2006).

Bioinformatics and Statistical Analysis

Sequence data analyses were mainly performed using QIIME2 and R packages (v3.2.0). ASV-level alpha diversity indices, such as Chao1 richness estimator, Observed species, Shannon diversity index, Simpson index, Faith's PD, Pielou's evenness and Good's coverage were calculated using the ASV table in QIIME2, and visualized as box plots. Beta diversity analysis was performed to investigate the structural variation of microbial communities across samples using UniFrac distance metrics (Lozupone and Knight 2005, Lozupone, Hamady et al. 2007) and visualized via principal coordinate analysis (PCoA).

Functional Prediction of the Microbiota

Microbial functions were predicted by PICRUSt2 (Phylogenetic investigation of communities by reconstruction of unobserved states) (Gavin M. Douglas, et al., preprint) upon KEGG (https://www.kegg.jp/) databases.

Accession numbers

Bacterial 16S rRNA gene sequencing data has been deposited in NCBI (BioProject ID: PRJNA626546).

Supplementary Figure Legends

Figure S1

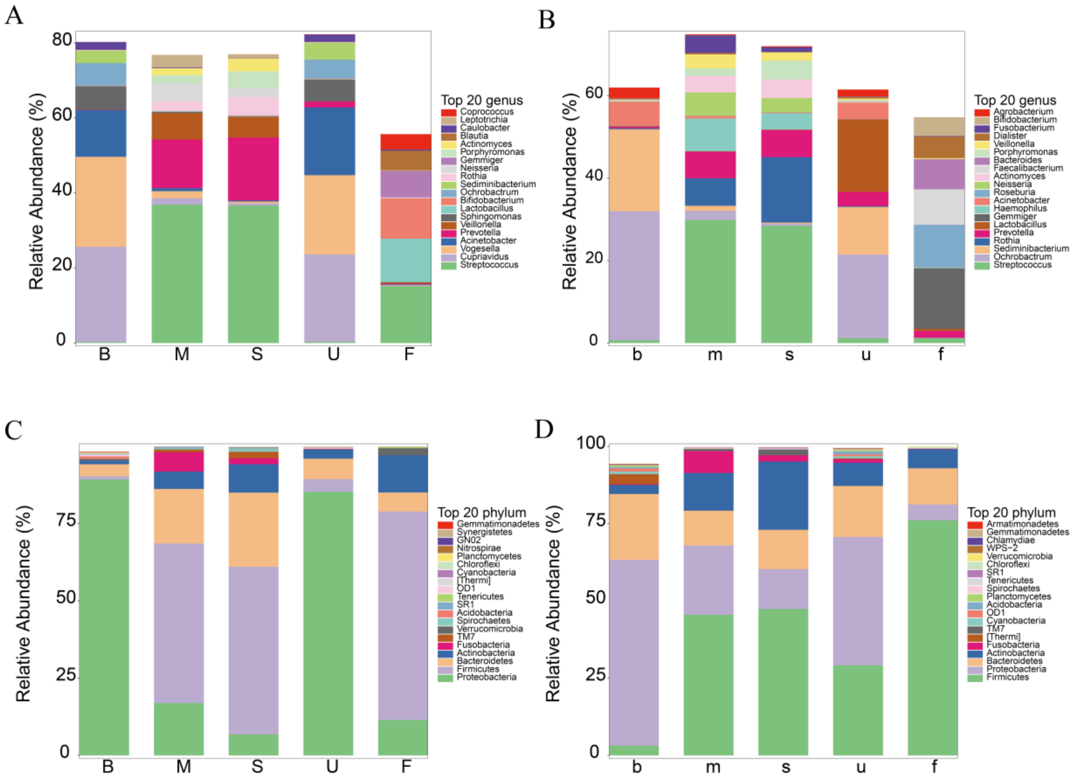

Figure S1. The microbial compositions of samples from ESCC patients and healthy subjects.

(A) The microbial composition of blood, oral mucosal, saliva, urine, and fecal samples at the genus level in ESCC patients. (B) The microbial composition of blood (b), oral mucosal, saliva, urine, and fecal samples at the genus level in healthy subjects. (C)The composition of microbiota in the blood, oral mucosa, saliva, urine, and feces of ESCC patients at the phylum level; the top 20 microbial types at the phylum level in ESCC patients are shown. (D) The composition of the microbiota in the blood, oral mucosa, saliva, urine, and feces of healthy subjects at the phylum level;

the top 20 microbial types at the phylum level in healthy subjects are shown. The number of biological replicates performed was as follows: in ESCC patients, BT (*n* =20), MT (*n*=24), ST (*n*=23), UT (*n*=21), FT (*n*=22); in healthy subjects, b (*n* =27), m (*n*=26), s (*n*=26), u (*n*=25), f (*n*=22).

Figure S2

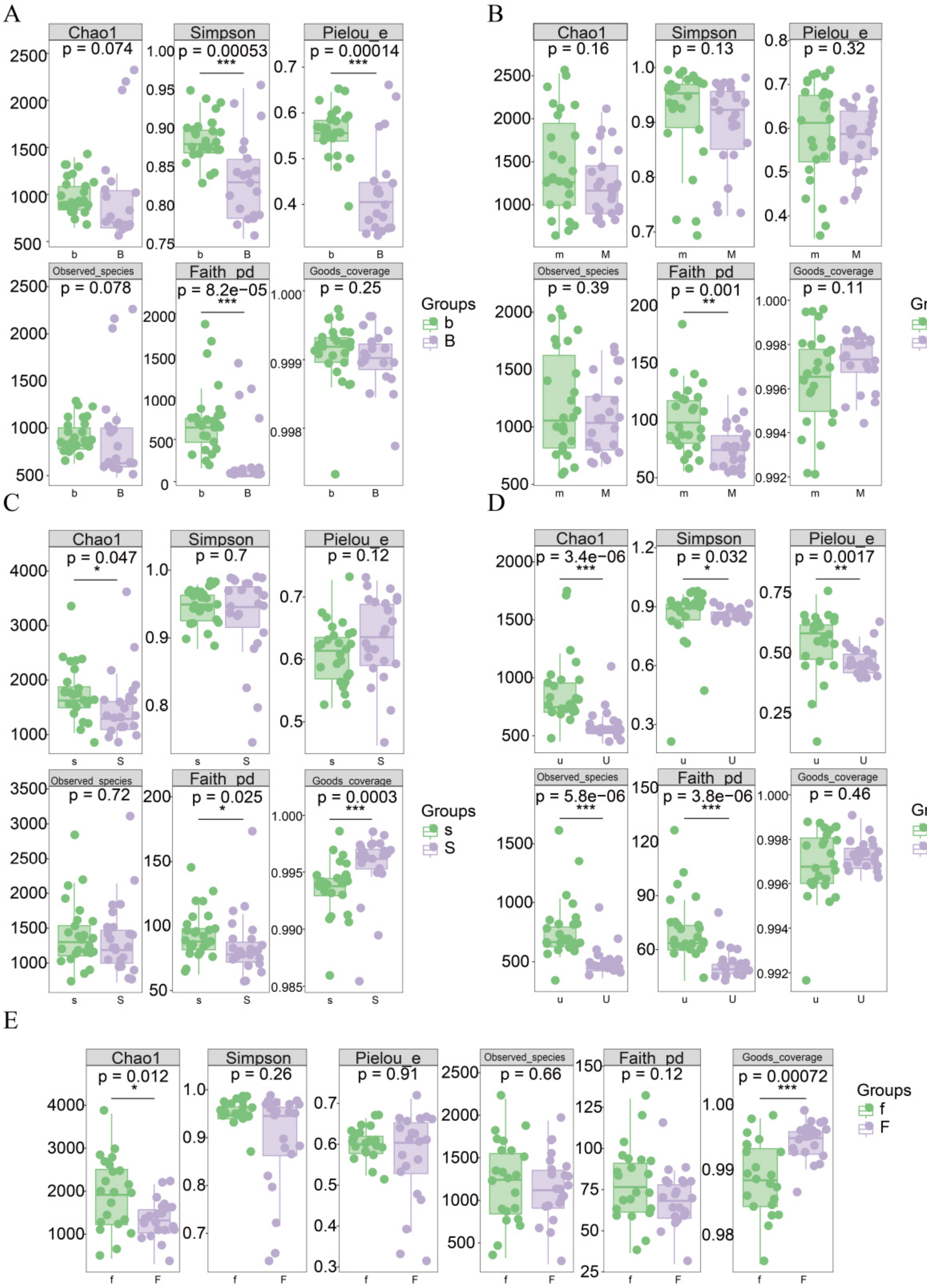

Figure S2. The microbial compositions of samples from ESCC patients and ESCC patients.

(A) In blood samples, the Simpson, Pielou, and Faith indexes were higher in healthy subjects than in ESCC patients. (B) In oral mucosal samples, the Faith index was higher in healthy subjects than in ESCC patients. (C) In saliva samples, the Chao1, Faith, and Good's coverage indexes were higher in healthy subjects than in ESCC patients. (D) In urine samples, the Chao1, Pielou, observed species, and Faith indexes were higher in healthy subjects than in ESCC patients. (E) In fecal samples, the Chao1 index was higher in healthy subjects than in ESCC patients, whereas the Good's coverage index was lower in healthy subjects than in ESCC patients. The number of biological replicates performed was as follows: in ESCC patients, B (*n* =20), M (*n*=24), S (*n*=23), U (*n*=21), F (*n*=22); in healthy subjects, b (*n* =27), m (*n*=26), s (*n*=26), u (*n*=25), f (*n*=22).

Figure S3

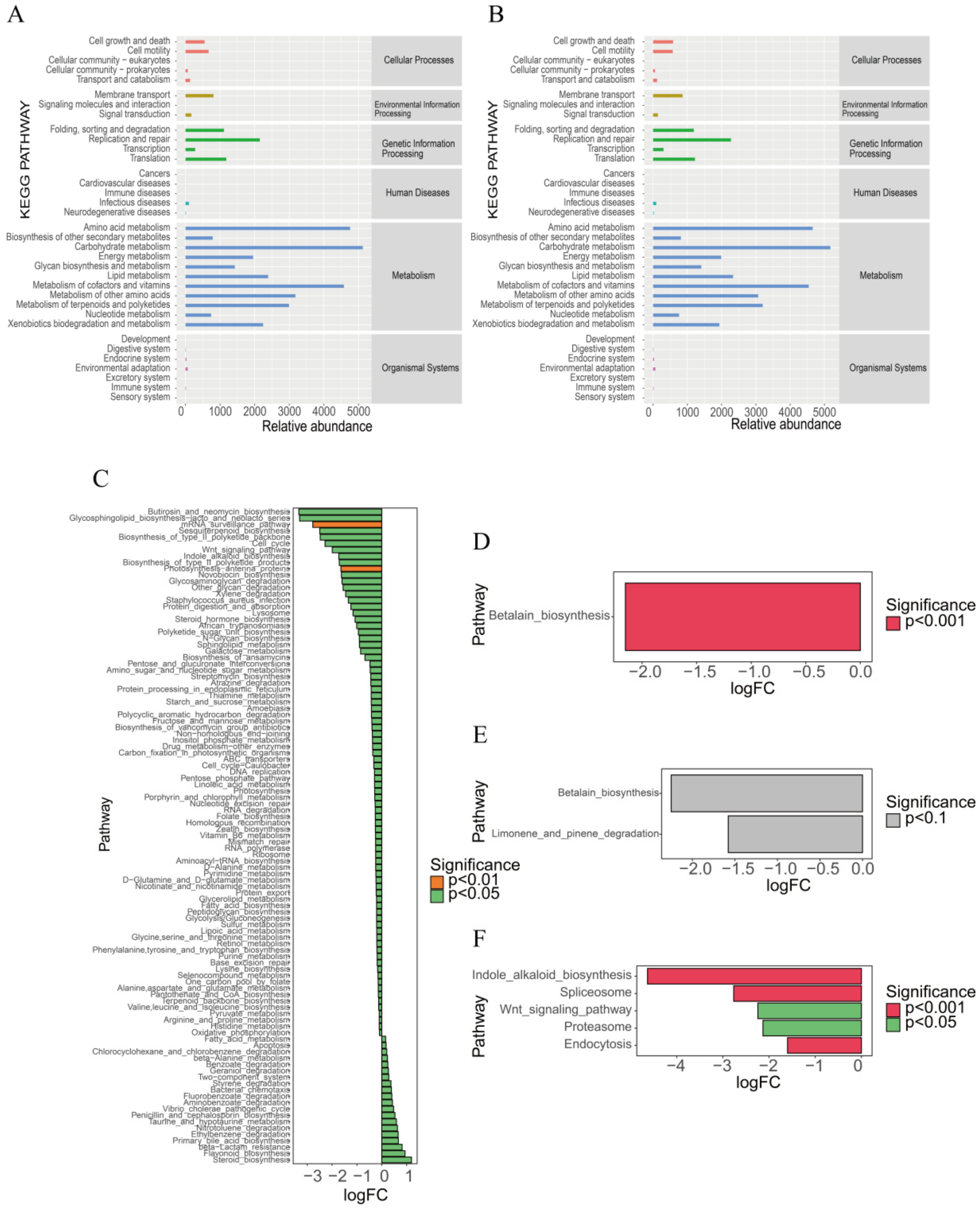

Figure S3. The predicted KEGG secondary functional pathways of samples from ESCC patients and healthy subjects are different.

(A) Abundance map of predicted KEGG secondary functional pathways in ESCC patients suggests that metabolic pathways accounted for the majority of pathways. (B) Abundance map of predicted KEGG secondary functional pathways in healthy subjects suggests that metabolic pathways accounted for the majority of pathways. (C) In blood samples, the metabolic pathways of microbes were significantly different between ESCC patients and healthy subjects. (D) In oral mucosal samples, only the betalain-biosynthesis metabolic pathway was upregulated in ESCC patients compared to healthy subjects. (E) In saliva samples, the betalain-biosynthesis and limonene-and-pinene-degradation metabolic pathways were upregulated in ESCC patients compared to healthy subjects. (F) In urine samples, the indole-alkaloid biosynthesis metabolic pathways was upregulated in ESCC patients compared to healthy subjects. The number of biological replicates performed was as follows: in ESCC patients, B (n =20), M (n=24), S (n=23), U (n=21), F (n=22); in healthy subjects, b (n =27), m (n=26), s (n=26), u (n=25), f (n=22).

Figure S4

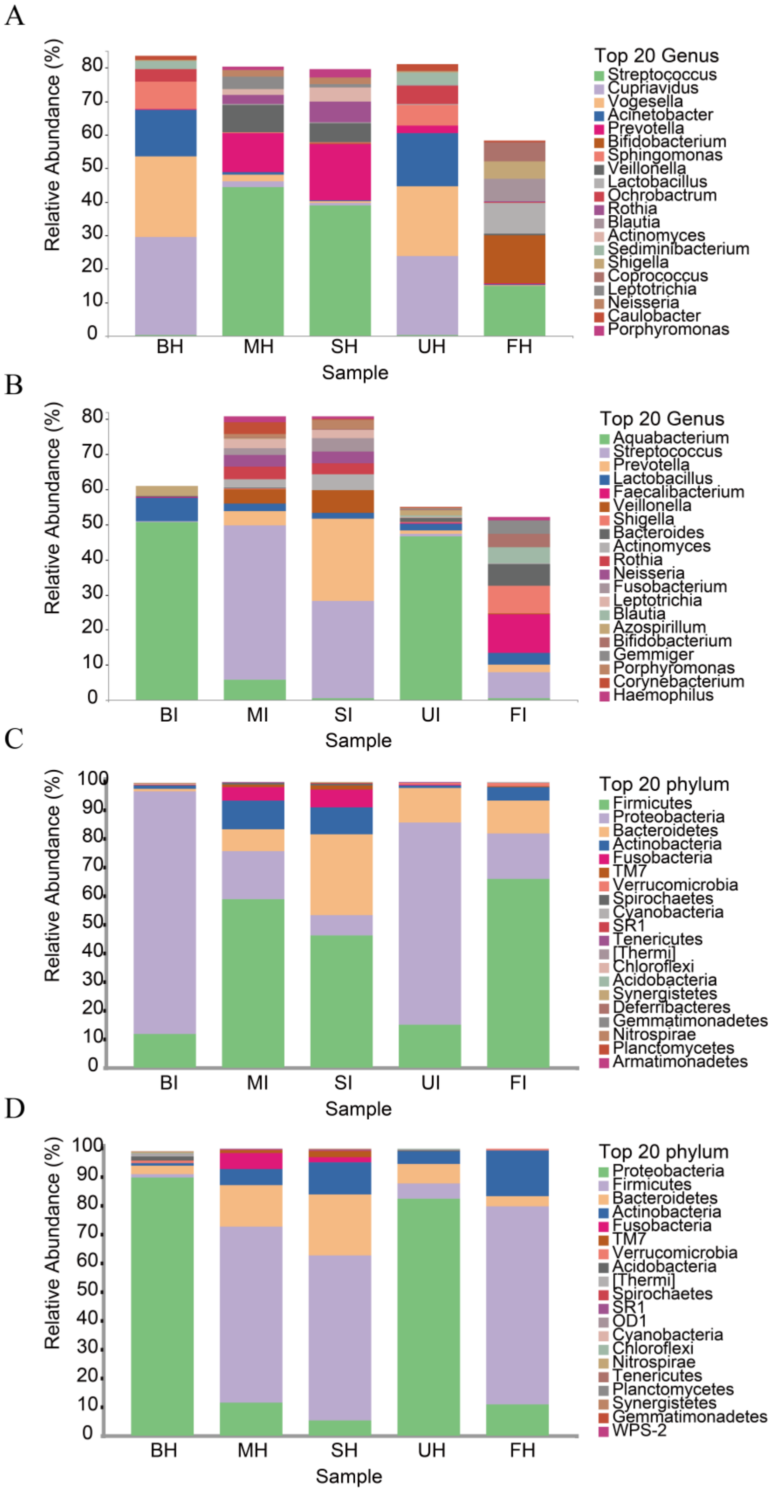

Figure S4. The microbial compositions of samples from ESCC patients after chemotherapy and ESCC patients after immunotherapy.

(A) The microbial composition of patients with ESCC after chemotherapy in blood, oral mucosal, saliva, urine, and fecal samples at the genus level. (B) The microbial composition of patients with ESCC after immunotherapy in blood, oral mucosal, saliva, urine, and fecal samples at the genus level. (C) The composition of the microbiota in the blood (BI), oral mucosa (MI), saliva (SI), urine (UI) and feces (FI) of patients with ESCC after immunotherapy at the phylum level; the top twenty kinds of microbes at the phylum level in patients with ESCC after immunotherapy. (D) The composition of the microbiota in the blood (BH), oral mucosa (MH), saliva (SH), urine (UH), and feces (FH) of patients with ESCC after chemotherapy at the phylum level; the top twenty kinds of microbes at the phylum level in patients with ESCC after chemotherapy. The number of biological replicates is as follows: in patients with ESCC after chemotherapy, BH(n =8), MH(n=14), SH(n=14), UH(n=13), FH(n=14); in patients with ESCC after immunotherapy, BI(n=27), MI(n=27), SI(n=27), UI(n=27), FI(n=22).

Figure S5

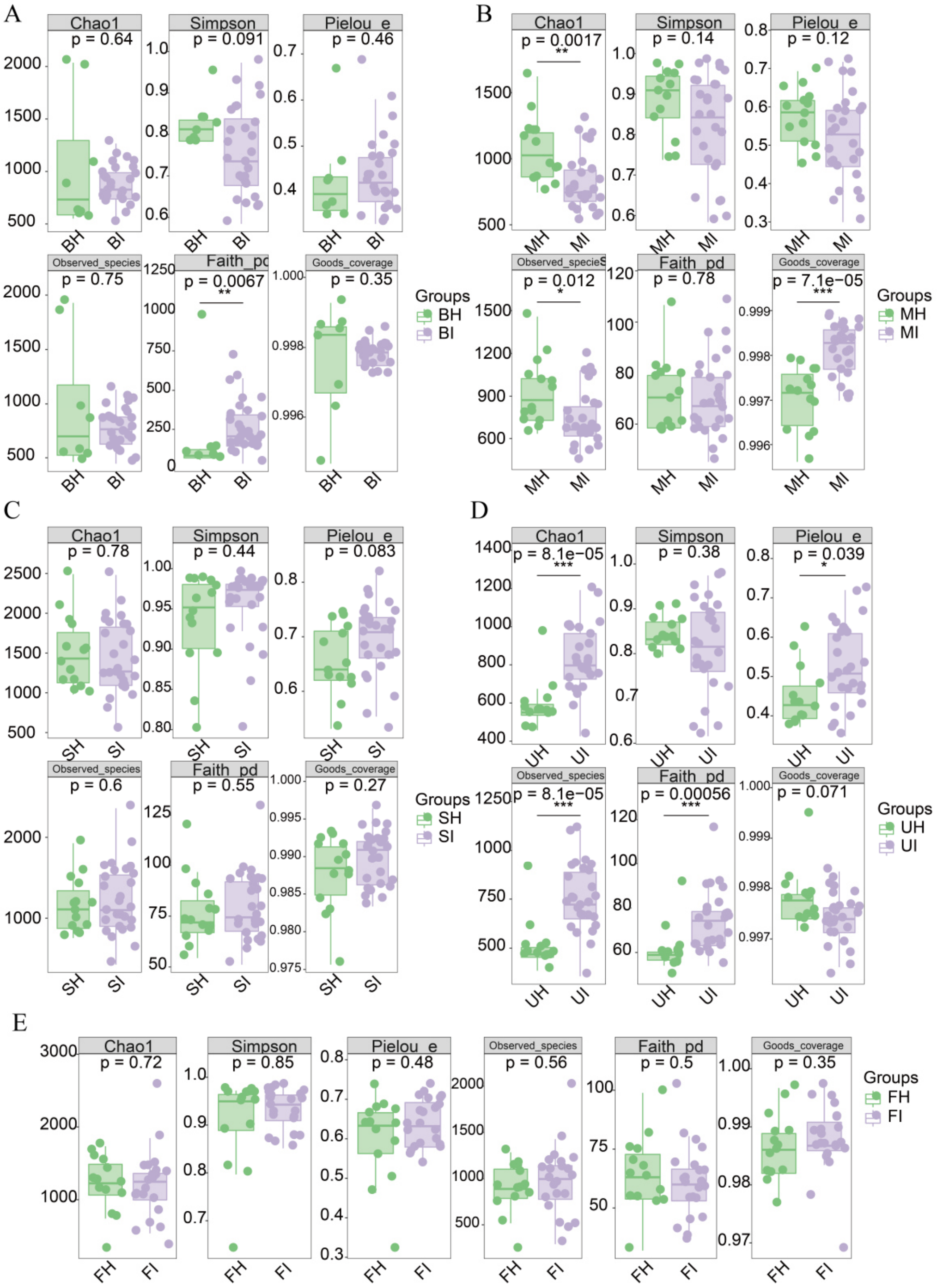

Figure S5. The microbial compositions of samples from ESCC patients after chemotherapy and ESCC patients after immunotherapy are highly different.

(A) In blood samples, the Faith index of patients with ESCC after immunotherapy was higher than those in samples from patients with ESCC after chemotherapy. (B) In oral mucosal samples, the Good’s coverage index of patients with ESCC after immunotherapy was higher than that of patients with ESCC after chemotherapy. The Chao1 and observed species indexes of patients with ESCC after immunotherapy was less than that of patients with ESCC after chemotherapy. (C) In saliva samples, there is no statistically significant difference in α diversity between patients with ESCC after immunotherapy and patients with ESCC after chemotherapy. (D) In urine samples, the Chao1, Pielou, observed species, and Faith indexes of patients with ESCC after immunotherapy were higher than those of patients with ESCC after chemotherapy. (E) In fecal samples, there is no statistically significant difference in α diversity between patients with ESCC after immunotherapy and patients with ESCC after chemotherapy. The number of biological replicates is as follows: in patients with ESCC after chemotherapy, BH(n =8), MH(n=14), SH(n=14), UH(n=13), FH(n=14); in patients with ESCC after immunotherapy, BI(n=27), MI(n=27), SI(n=27), UI(n=27), FI(n=22).

Figure S6

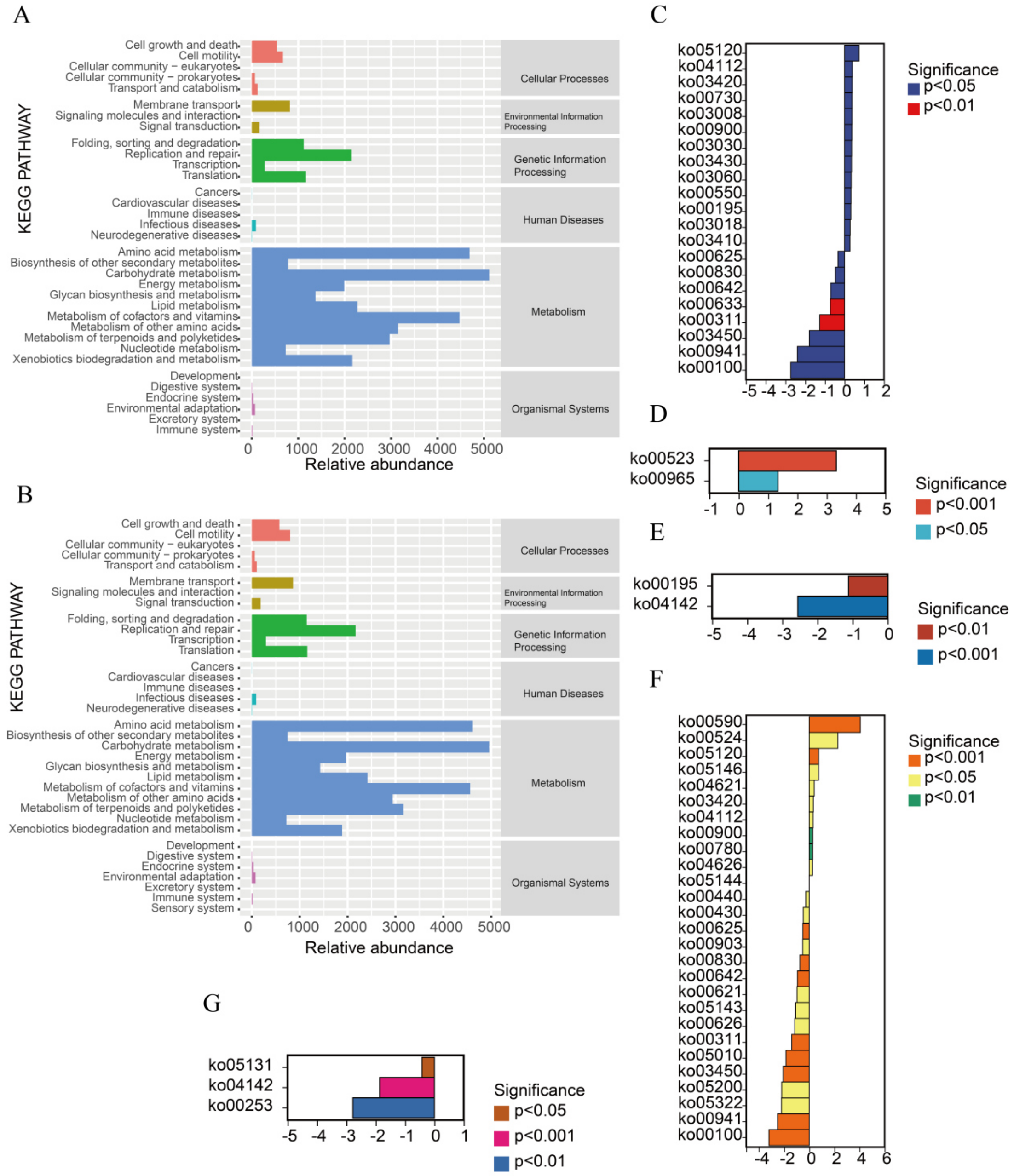

Figure S6. The predicted KEGG secondary functional pathways of samples from ESCC patients after chemotherapy and ESCC patients after immunotherapy are different.

(A) Abundance map of predicted KEGG secondary functional pathways in ESCC patients after chemotherapy suggests that metabolic pathways accounted for the majority of pathways. (B) Abundance map of predicted KEGG secondary functional pathways in ESCC patients after immunotherapy suggests that metabolic pathways accounted for the majority of pathways. (C) In blood samples, the metabolic pathways of microbes were significantly different between ESCC patients after chemotherapy and ESCC patients after immunotherapy. (D) In oral mucosal samples, the polyketide sugar unit biosynthesis and betalain biosynthesis metabolic pathway was underrepresented in patients with ESCC after immunotherapy compared with that in patients with ESCC after chemotherapy. (E) In saliva samples, the photosynthesis and lysosome metabolic pathways were overrepresented in patients with ESCC after immunotherapy. (F) In urine samples, the metabolic pathways of microbes were significantly different between ESCC patients after chemotherapy and ESCC patients after immunotherapy. (G) In fecal samples, the tetracycline biosynthesis, Lysosome, and shigellosis metabolic pathway was overrepresented in patients with ESCC after immunotherapy compared with that in patients with ESCC after chemotherapy. The number of biological replicates is as follows: in patients with ESCC after chemotherapy, BH(n =8), MH(n=14), SH(n=14), UH(n=13), FH(n=14); in patients with ESCC after immunotherapy, BI(n=27), MI(n=27), SI(n=27), UI(n=27), FI(n=22).

Table S1 Information of the samples from ESCC patients and healthy subjects.

NO.	ID	Type	Host	Regions	Longitude	Latitude
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5	a005	blood	healthy subjects	China:shijiazhuang	114.5090560000E	38.0496120000N
6	a006	blood	healthy subjects	China:shijiazhuang	114.5090560000E	38.0496120000N
7	a007	blood	healthy subjects	China:shijiazhuang	114.5090560000E	38.0496120000N
8	a008	blood	healthy subjects	China:shijiazhuang	114.5090560000E	38.0496120000N
9	a010	blood	healthy subjects	China:shijiazhuang	114.5090560000E	38.0496120000N
10	a011	blood	healthy subjects	China:shijiazhuang	114.5090560000E	38.0496120000N
11	a012	blood	healthy subjects	China:shijiazhuang	114.5090560000E	38.0496120000N
12	a013	blood	healthy subjects	China:shijiazhuang	114.5090560000E	38.0496120000N
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130	A04	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
131	A07	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
132	A08	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
133	A09	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
134	A10	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
135	A11	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
136	A12	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
137	A14	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
138	A19	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
139	A20	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
140	A21	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
141	A22	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
142	A23	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N

143	A25	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
144	A26	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
145	A27	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
146	A29	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
147	B01	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
148	B02	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
149	B03	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
150	B04	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
151	B05	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
152	B07	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
153	B09	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
154	B10	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
155	B11	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
156	B12	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
157	B13	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
158	B14	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
159	B15	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
160	B16	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
161	B18	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
162	B19	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
163	B20	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
164	B21	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
165	B22	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
166	B23	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
167	B24	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
168	B25	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
169	B26	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
170	B27	oral mucosa	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
171	C01	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
172	C02	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
173	C03	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
174	C04	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
175	C05	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
176	C07	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
177	C09	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
178	C10	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
179	C11	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
180	C12	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
181	C13	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
182	C14	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
183	C15	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
184	C16	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
185	C18	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
186	C19	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
187	C20	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
188	C21	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
189	C22	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
190	C23	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N

191	C24	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
192	C25	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
193	C26	saliva	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
194	D01	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
195	D02	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
196	D03	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
197	D04	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
198	D09	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
199	D10	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
200	D11	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
201	D12	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
202	D13	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
203	D14	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
204	D15	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
205	D16	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
206	D18	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
207	D19	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
208	D20	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
209	D21	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
210	D22	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
211	D23	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
212	D24	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
213	D25	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
214	D26	urine	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
215	E01	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
216	E02	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
217	E03	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
218	E04	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
219	E05	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
220	E07	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
221	E10	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
222	E11	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
223	E12	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
224	E13	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
225	E14	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
226	E15	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
227	E16	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
228	E18	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
229	E19	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
230	E20	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
231	E21	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
232	E22	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
233	E23	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
234	E24	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
235	E25	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
236	E26	feces	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N

Table S2 Information of the samples from ESCC patients after chemotherapy and ESCC patients after immunotherapy.

NO.	ID	Type	Host	Regions	Longitude	Latitude
1	A01	blood	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
2	A02	blood	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
3	A03	blood	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
4	A04	blood	ESCC patients	China:shijiazhuang	114.5090560000E	38.0496120000N
5	A12	blood	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
6	A22	blood	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
7	A23	blood	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
8	A25	blood	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
9	B01	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
10	B02	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
11	B03	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
12	B04	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
13	B05	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
14	B12	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
15	B13	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
16	B15	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
17	B16	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
18	B18	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
19	B22	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
20	B23	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
21	B24	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
22	B25	oral mucosa	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
23	C01	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
24	C02	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
25	C03	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
26	C04	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
27	C05	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
28	C12	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
29	C13	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
30	C15	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
31	C16	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
32	C18	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
33	C22	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
34	C23	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
35	C24	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
36	C25	saliva	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
37	D01	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
38	D02	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
39	D03	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
40	D04	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
41	D12	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
42	D13	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
43	D15	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
44	D16	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
45	D18	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
46	D22	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
47	D23	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
48	D24	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
49	D25	urine	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
50	E01	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
51	E02	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
52	E03	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
53	E04	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
54	E05	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
55	E12	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
56	E13	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
57	E15	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N

58	E16	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
59	E18	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
60	E22	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
61	E23	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
62	E24	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
63	E25	feces	ESCC patients after chemotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
64	A0101	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
65	A0102	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
66	A0201	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
67	A0301	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
68	A0302	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
69	A0402	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
70	A0503	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
71	A0604	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
72	A0703	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
73	A0801	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
74	A0802	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
75	A0902	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
76	A1001	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
77	A1002	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
78	A1101	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
79	A1102	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
80	A1201	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
81	A1301	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
82	A1302	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
83	A1303	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
84	A1401	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
85	A1402	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
86	A1501	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
87	A1701	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
88	A1702	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
89	A1801	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
90	A1901	blood	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
91	B0101	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
92	B0102	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
93	B0201	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
94	B0301	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
95	B0302	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
96	B0402	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
97	B0503	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
98	B0604	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
99	B0703	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
100	B0801	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
101	B0802	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
102	B0902	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
103	B1001	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
104	B1002	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
105	B1101	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
106	B1102	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
107	B1201	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
108	B1301	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
109	B1302	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
110	B1303	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
111	B1401	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
112	B1402	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
113	B1501	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
114	B1701	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
115	B1702	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
116	B1801	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N

117	B1901	oral mucosa	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
118	C0101	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
119	C0102	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
120	C0201	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
121	C0301	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
122	C0302	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
123	C0402	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
124	C0503	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
125	C0604	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
126	C0703	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
127	C0801	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
128	C0802	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
129	C0902	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
130	C1001	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
131	C1002	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
132	C1101	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
133	C1102	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
134	C1201	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
135	C1301	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
136	C1302	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
137	C1303	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
138	C1401	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
139	C1402	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
140	C1501	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
141	C1701	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
142	C1702	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
143	C1801	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
144	C1901	saliva	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
145	D0101	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
146	D0102	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
147	D0201	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
148	D0301	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
149	D0302	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
150	D0402	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
151	D0503	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
152	D0604	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
153	D0703	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
154	D0801	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
155	D0802	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
156	D0902	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
157	D1001	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
158	D1002	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
159	D1101	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
160	D1102	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
161	D1201	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
162	D1301	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
163	D1302	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
164	D1303	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
165	D1401	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
166	D1402	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
167	D1501	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
168	D1701	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
169	D1702	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
170	D1801	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
171	D1901	urine	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
172	E0101	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
173	E0201	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
174	E0301	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
175	E0302	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N

176	E0402	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
177	E0503	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
178	E0604	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
179	E0703	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
180	E0801	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
181	E0802	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
182	E0902	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
183	E1101	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
184	E1102	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
185	E1301	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
186	E1302	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
187	E1303	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
188	E1401	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
189	E1402	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
190	E1501	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
191	E1701	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
192	E1702	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N
193	E1801	feces	ESCC patients after immunotherapy	China:shijiazhuang	114.5090560000E	38.0496120000N

Table S3 The composition and relative abundance of the microbiota of ESCC patients at the phylum level.

phylum	B	M	S	U	F
Proteobacteria	8.92E-01	0.169145865	0.067793998	0.852984375	0.114780697
Firmicutes	1.05E-02	0.516198059	0.54255418	4.09E-02	0.674163774
Bacteroidetes	3.88E-02	0.176517475	0.239500395	6.60E-02	0.061427223
Actinobacteria	1.21E-02	0.056236017	0.091951259	0.030253734	0.120983978
Fusobacteria	0.000300395	0.062691151	0.019245587	6.39E-04	5.48E-05
TM7	0.000240064	8.81E-03	2.13E-02	0.000180752	3.69E-04
Verrucomicrobia	0.004548654	4.19E-06	0.00E+00	0.000137658	2.21E-02
Spirochaetes	3.14E-05	0.002786087	0.007449482	4.79E-05	0
Acidobacteria	0.00836706	1.26E-05	2.62E-05	0.001298777	1.37E-05
SR1	6.28E-06	0.004523726	0.003390301	0	0
Tenericutes	7.54E-06	0.000295367	2.37E-03	4.31E-05	0.004088292
OD1	0.002991378	5.13E-05	2.40E-05	0.00206368	5.26E-05
[Thermi]	0.003973002	1.05E-05	6.56E-06	0.000694277	3.43E-06
Cyanobacteria	1.74E-03	1.67E-04	3.01E-04	0.001739284	6.99E-04
Chloroflexi	0.002195772	2.20E-05	6.56E-06	0.000511132	2.51E-05
Planctomycetes	0.001310927	5.24E-06	0	0.000809192	4.57E-06
Nitrospirae	1.81E-03	2.09E-06	4.37E-06	0.000137658	0
GN02	2.51E-06	6.78E-04	1.05E-03	3.59E-06	0
Synergistetes	6.28E-06	0.000569786	0.000719155	1.02E-04	5.37E-05
Gemmatimonadetes	8.72E-04	8.38E-06	5.46E-06	0.000128082	1.14E-05
others	0.017705689	0.001270498	0.002291896	0.001410101	0.001148333

Table S4 The composition and relative abundance of the microbiota of healthy subjects at the phylum level.

phylum	b	m	s	u	f
Firmicutes	0.031673547	0.454956436	0.473656428	2.91E-01	0.760956303
Proteobacteria	0.601297441	2.24E-01	0.129034005	0.415469308	0.051138934
Bacteroidetes	2.13E-01	0.112513197	0.127460042	0.164981147	1.17E-01
Actinobacteria	2.93E-02	0.122089426	0.220689295	7.53E-02	0.061206302
Fusobacteria	2.18E-03	7.04E-02	2.06E-02	0.011279473	0.001437379
[Thermi]	0.031914676	0.0002272	2.32E-05	0.002223116	1.14E-06
TM7	0.000830452	0.007052861	0.018517265	0.000630436	0.000474175
Cyanobacteria	0.008273796	5.14E-04	1.38E-04	0.006822181	0.001660184
OD1	9.85E-03	0.000535611	0.000195295	6.44E-03	9.14E-06
Acidobacteria	0.004313322	0.000244602	0.000280374	0.008879393	1.37E-05
Planctomycetes	0.004615897	3.14E-04	8.70E-05	0.003493037	9.14E-06
Spirochaetes	0.000177821	3.06E-03	2.06E-03	0.000322759	2.29E-06
Tenericutes	1.68E-05	4.90E-04	0.000949405	0.000555025	2.82E-03
SR1	3.35E-05	0.001048986	0.003358689	3.02E-06	0
Chloroflexi	0.001460739	8.12E-05	1.24E-04	0.001882258	3.43E-06
Verrucomicrobia	1.55E-04	4.83E-06	4.16E-05	8.54E-04	0.002478279
WPS-2	1.03E-03	6.48E-05	1.16E-05	1.07E-03	0
Chlamydiae	0.001176784	6.38E-05	6.77E-06	0.000930069	0
Gemmatimonadetes	0.0006517	5.22E-05	5.51E-05	0.001395606	1.14E-06
Armatimonadetes	0.001207507	7.44E-05	2.13E-05	8.49E-04	0
others	5.68E-02	0.001856271	0.002682891	5.21E-03	0.000711834

Table S5 The microbial composition and relative abundance in ESCC patients at the genus level.

genus	B	M	S	U	F
Streptococcus	2.00E-03	0.369	0.366	0.003	0.152
Cupriavidus	2.54E-01	0.017	0.006	2.33E-01	0.002
Vogesella	2.40E-01	0.019	0.005	0.212	0.001
Acinetobacter	0.125	0.008	0.003	1.81E-01	0.002
Prevotella	1.00E-03	0.13	0.168	0.016	0.002
Veillonella	0	0.071	0.055	0	0.003
Sphingomonas	0.062	3.00E-03	0.001	0.058	1.00E-03
Lactobacillus	1.00E-03	0.001	1.00E-03	0.001	0.116
Bifidobacterium	1.00E-03	0.001	0.002	0.002	0.107
Ochrobactrum	0.06	0.001	0	0.05	0.001
Sediminibacterium	3.30E-02	0	0	4.50E-02	0
Rothia	0.001	2.50E-02	0.049	0	0.002
Neisseria	1.00E-03	0.049	0.023	0	0
Gemmiger	0	0	0	0.001	0.071
Porphyromonas	0	2.10E-02	4.60E-02	1.00E-03	0
Actinomyces	0	0.019	0.034	0.001	0.001
Blautia	0	0	0	0	5.20E-02
Caulobacter	0.021	2.00E-03	0	2.00E-02	0.003
Leptotrichia	0	0.033	0.011	0.00E+00	0
Coprococcus	0	0	0	1.00E-03	4.10E-02
others	1.97E-01	0.232	0.23	0.177	0.443

Table S6 The microbial composition and relative abundance in healthy subjects at the genus level.

genus	b	m	s	u	f
Streptococcus	0.006599858	0.298271735	0.284027759	1.17E-02	0.011605294
Ochrobactrum	3.13E-01	0.02211959	0.004951022	0.20259816	0.000534732
Sediminibacterium	0.198826195	1.24E-02	0.002887854	0.115554774	0.000219377
Rothia	0.002305156	0.06647092	0.158749802	2.03E-03	0.000373627
Prevotella	4.02E-03	0.064532471	0.065676205	3.44E-02	0.016447594
Lactobacillus	0.000892829	0.000946505	0.000845957	1.76E-01	0.005145086
Gemmiger	4.97E-04	9.67E-05	0.000102482	2.43E-04	0.146619531
Haemophilus	7.67E-04	0.079447411	0.040158286	3.56E-04	0.001815577
Acinetobacter	0.057842091	0.006238809	0.001958752	0.040033181	7.90E-04
Roseburia	0.000313747	0.000118917	0.000132453	2.21E-04	0.103244501
Neisseria	1.35E-03	0.056774807	0.034370009	1.00E-03	8.68E-05
Actinomyces	1.65E-03	0.039848907	0.045016494	1.00E-03	0.000997482
Faecalibacterium	4.48E-04	7.35E-05	1.04E-04	0.000922025	0.084835078
Bacteroides	2.49E-04	1.37E-04	6.67E-05	0.000574129	0.073242353
Pseudomonas	0.025406056	0.004132136	0.022326487	1.95E-02	0.000193098
Granulicatella	7.75E-04	0.017978753	0.049998453	0.000584184	0.000513023
Porphyromonas	5.12E-04	0.018327771	0.045496997	2.70E-03	4.34E-05
Veillonella	1.46E-03	0.033899174	0.020224647	0.003419637	0.002258902
Dialister	2.48E-04	0.003550117	6.36E-04	0.003737369	5.20E-02
Fusobacterium	9.95E-04	0.042856646	1.19E-02	9.80E-04	0.0014111
others	3.82E-01	2.32E-01	2.10E-01	0.382551908	0.497646263

Table S7 The composition and relative abundance of the microbiota of patients with ESCC after chemotherapy at the phylum level.

phylum	BH	MH	SH	UH	FH
Proteobacteria	0.89872113	0.11445968	0.05347816	8.24E-01	0.10905826
Firmicutes	0.01217938	6.13E-01	0.57352834	0.05527243	0.68778012
Bacteroidetes	2.83E-02	0.14522097	0.21088135	0.06609879	3.63E-02
Actinobacteria	9.96E-03	0.05559513	0.11419516	4.46E-02	0.15835933
Fusobacteria	2.83E-04	5.69E-02	1.72E-02	0.00065679	0.00008887
TM7	0.00017676	0.00766364	1.89E-02	0.00017061	2.94E-04
Verrucomicrobia	0.00837005	0.0000052	0	0.00011595	0.00520793
Acidobacteria	0.01240171	1.32E-05	1.94E-05	0.00114854	0.00000532
[Thermi]	7.80E-03	0.00002045	0.00000774	8.27E-04	5.76E-06
Spirochaetes	0.00002372	0.00265073	0.00503112	0.00005778	0
SR1	0	3.04E-03	2.41E-03	0.00000171	0
OD1	0.00184542	4.43E-05	2.08E-05	0.00219202	2.67E-05
Cyanobacteria	1.36E-03	1.99E-04	0.00039866	0.00164666	4.03E-04
Chloroflexi	2.61E-03	0.00002741	0.00000551	5.58E-04	0.00001041
Nitrospirae	0.00268691	6.78E-06	1.80E-06	0.0001134	0
Tenericutes	6.63E-06	1.25E-04	5.62E-04	5.57E-05	0.00134156
Planctomycetes	1.18E-03	5.99E-06	1.80E-06	8.42E-04	0.00000173
Synergistetes	0.00001155	4.78E-04	7.71E-04	0.00012977	0.00004353
Gemmatimonadetes	0.00128394	5.64E-06	5.84E-06	0.00007445	0.00E+00
WPS-2	0.00035477	0	1.29E-06	2.31E-04	0
Others	1.04E-02	0.00097152	0.00263171	1.59E-03	0.00109163

Table S8 The composition and relative abundance of the microbiota of patients with ESCC after immunotherapy at the phylum level.

phylum	BI	MI	SI	UI	FI
Firmicutes	0.1169785	0.58864685	0.46263352	1.51E-01	0.65972155
Proteobacteria	0.84918865	1.67E-01	0.07010456	0.70626573	0.16043924
Bacteroidetes	7.95E-03	0.0775039	0.28233193	0.11911459	1.14E-01
Actinobacteria	1.12E-02	0.1006892	0.09404147	1.11E-02	0.04585261
Fusobacteria	9.57E-05	4.76E-02	6.37E-02	0.00076638	0.00030906
TM7	0.00042143	0.00759423	1.30E-02	0.00119244	2.07E-03
Verrucomicrobia	0.00034185	0.00015874	0.00003634	0.00461886	0.0141185
Spirochaetes	0.0000317	5.15E-03	5.92E-03	0.00051587	0
Cyanobacteria	1.74E-03	0.00167458	0.00048429	1.40E-03	2.05E-03
SR1	0.00000242	0.00058948	0.00289388	0.00008063	0
Tenericutes	0.00011645	1.02E-03	7.38E-04	0.00080342	0.00014438
[Thermi]	0.00221859	1.75E-04	4.59E-05	0.0002757	0.00E+00
Chloroflexi	1.58E-03	1.68E-04	0.00020982	0.0002193	9.31E-06
Acidobacteria	1.27E-03	0.00022672	0.00003615	3.60E-04	0.0000022
Synergistetes	0.00004434	3.51E-04	6.12E-04	0.00004784	0.00017336
Deferribacteres	2.39E-05	8.50E-07	0	1.03E-03	0
Gemmatimonadetes	5.27E-04	3.59E-05	6.63E-05	1.10E-04	0
Nitrospirae	0.00022602	4.71E-05	4.30E-06	0.00007776	0
Planctomycetes	0.00017729	1.39E-05	4.30E-06	0.00004713	0.00E+00
Armatimonadetes	0.00015412	0.0000041	1.21E-05	1.42E-05	0
Others	5.74E-03	0.00125981	0.00307294	8.61E-04	0.00117307

Table S9 The microbial composition and relative abundance in patients with ESCC after chemotherapy at the genus level.

genus	BH	MH	SH	UH	FH
Streptococcus	3.10E-03	0.44268297	0.39042395	0.00348121	0.14788195
Cupriavidus	2.92E-01	0.01746797	0.00544032	2.34E-01	0.00238184
Vogesella	2.41E-01	0.01998096	0.00472681	0.20770803	0.00179339
Acinetobacter	0.13930637	0.00865371	0.00245751	1.59E-01	0.00222943
Prevotella	1.23E-03	0.11569947	0.17063036	0.02151204	0.00185322
Bifidobacterium	0.0006853	0.00042165	0.00191307	0.00191986	0.14393672
Sphingomonas	0.08019013	3.16E-03	0.00099149	0.06101923	8.19E-04
Veillonella	2.48E-04	0.0809932	5.90E-02	0.00028651	0.00409751
Lactobacillus	9.05E-04	0.00134575	0.00151081	0.0014181	0.0928431
Ochrobactrum	0.03599393	0.00058897	0.00022628	0.05605626	0.00046262
Rothia	1.50E-03	0.02699778	0.06150667	2.39E-04	0.00225837
Blautia	0.00035965	3.81E-05	0.00000258	0.000475	0.06704001
Actinomyces	2.48E-04	0.01811327	0.04207715	0.00055116	0.00113784
Sediminibacterium	0.02234526	0.00046088	0.00008749	0.03835723	0.00028905
Shigella	0.00268907	7.82E-05	6.04E-05	2.29E-03	0.0521904
Coprococcus	0.00010088	0.00001235	0.00000467	0.00056517	0.05522923
Leptotrichia	0.0000157	0.035845	0.01041595	0.00012027	8.61E-06
Neisseria	0.00125822	2.04E-02	0.01800613	1.18E-04	0.00003192
Caulobacter	0.01244884	0.00013559	0.00025806	2.09E-02	0.00533113
Porphyromonas	0.00010537	0.00975543	0.02590996	6.19E-04	8.75E-05
Others	1.64E-01	0.19715956	0.20432089	0.18920767	0.41809682

Table S10 The microbial composition and relative abundance in patients with ESCC after immunotherapy at the genus level.

genus	BI	MI	SI	UI	FI
Aquabacterium	5.07E-01	0.056789	0.00416823	0.46558331	0.00474097
Streptococcus	2.57E-03	0.43950494	0.27934796	7.64E-03	0.07408401
Prevotella	6.21E-04	0.04287815	0.23289841	0.01004892	0.021987
Lactobacillus	0.06700159	0.02061227	0.0160053	1.86E-02	0.03350514
Faecalibacterium	8.71E-04	0.00052682	0.00004316	0.00216502	0.11085655
Veillonella	0.00004792	0.04073241	0.06521784	0.00109741	0.00201165
Shigella	0.00101927	1.04E-03	0.00013279	0.00268177	7.84E-02
Bacteroides	8.50E-04	0.002821	2.36E-04	0.01028405	0.06176823
Actinomyces	4.82E-05	0.02421858	0.04436134	0.00059567	0.00139323
Rothia	0.00003194	0.03466331	0.03204728	0.00018031	0.00095927
Neisseria	6.42E-05	0.0333567	0.03242865	5.29E-04	0.00005959
Fusobacterium	0.00004923	1.98E-02	0.03789468	0.0003822	0.00009396
Leptotrichia	3.67E-05	0.02758009	0.02497094	0.00037191	0.00001914
Blautia	0.00020824	0.00020916	0.00001115	0.00538972	0.04563537
Azospirillum	0.02823667	2.11E-03	3.03E-04	1.53E-02	0.00009918
Bifidobacterium	0.00052128	0.00128325	0.00240512	0.00174096	0.03900236
Gemmiger	0.0001137	0.0000812	0.00000374	0.00222532	3.61E-02
Porphyromonas	0.0000079	9.55E-03	0.02615063	2.09E-03	0.00018415
Corynebacterium	0.00014784	0.03294931	0.00159621	2.85E-03	0.00011777
Haemophilus	0.00005862	0.01746293	0.0085366	6.14E-04	9.51E-03
Others	3.90E-01	0.19187221	0.1912416	0.44958528	0.47952324

Table S11 The α diversity of blood samples between patients with ESCC and healthy subjects.

Sample	Chao1	Simpson	Shannon	Pielou e	Observed species	Faith pd	Goods coverage
b01	1163.19	0.888142	5.95487	0.590488	1085.9	1486.08	0.998902
B01	2074.7	0.821204	5.04359	0.459164	2025.8	113.127	0.998709
B02	2289.39	0.83674	4.6387	0.417074	2228.7	127.618	0.997695
b02	853.145	0.85791	5.1813	0.537347	799.2	725.365	0.999289
B03	1223.75	0.787406	3.48697	0.34236	1164.2	90.4314	0.998462
b03	1262.02	0.925179	6.56269	0.64081	1210.4	1632.66	0.999144
B04	647.055	0.778987	3.14933	0.34102	602.6	71.0349	0.999178
b04	900.432	0.865289	5.37996	0.555762	820.5	432.278	0.99914
b05	844.71	0.863991	5.29135	0.549544	791.6	744.819	0.999282
b06	993.29	0.886602	5.78927	0.587001	930.9	1110.36	0.999196
b07	1395.74	0.941014	6.64815	0.645632	1258.2	698.453	0.998635
B07	665.814	0.774117	3.00484	0.325097	605.9	60.3735	0.998907
B08	650.256	0.766895	3.06399	0.334164	575.7	58.3805	0.998945
b08	854.672	0.867672	5.11649	0.532819	777.5	508.094	0.999162
B09	529.357	0.752688	2.93115	0.329056	480.3	51.2561	0.999266
B10	677.97	0.774657	3.17025	0.342711	609.1	69.8059	0.998913
b10	850.08	0.86396	5.2878	0.549911	784.6	623.791	0.999226
B11	730.133	0.864157	4.1475	0.444387	645	57.2697	0.998676
b11	952.957	0.858899	5.26569	0.539387	868.5	757.781	0.999036
b12	1283.23	0.930084	6.34875	0.620822	1198	1835.25	0.998778
B12	627.176	0.804399	3.32599	0.365406	549.6	49.0632	0.998911
b13	1096.01	0.874065	5.49565	0.550431	1012.9	608.061	0.998912
b14	1053.87	0.820681	4.67798	0.474616	927	681.076	0.9986
B14	596.498	0.832593	3.56218	0.392786	537.1	48.6866	0.999005
b15	875.403	0.830838	4.80769	0.499551	789.1	606.524	0.999052
b16	828.682	0.875332	5.36873	0.559422	774.4	717.367	0.999352
b17	646.851	0.866787	5.22001	0.562106	624.5	279.583	0.999688
b18	702.756	0.898857	5.42786	0.577853	672.4	348.709	0.999573
B19	616.715	0.852714	4.00793	0.439194	558.6	50.2596	0.999045
b19	882.409	0.890027	5.42774	0.561026	817.3	641.834	0.99921
B20	2167.13	0.830609	4.7137	0.426352	2128.9	126.085	0.998451
b20	781.692	0.884019	5.14115	0.541824	718.4	285.742	0.999274
B21	1018.74	0.809671	3.7138	0.373335	987.5	90.2382	0.999111
b21	780.77	0.834081	4.72024	0.49642	728.4	207.778	0.999352
B22	643.23	0.779352	3.30851	0.358686	598	60.576	0.999215
b22	775.946	0.894159	5.54716	0.580576	752	828.072	0.999579
B23	646.296	0.83496	3.88583	0.419118	618	62.5151	0.999374
b23	881.311	0.899045	5.72287	0.589216	839.1	639.145	0.999361
b24	815.025	0.892247	5.76266	0.599336	784.2	823.868	0.999558
b25	1072.11	0.892716	5.72617	0.574836	997	158.205	0.999013
B25	985.575	0.947911	6.47093	0.653902	952.7	994.345	0.999454
B26	1104.06	0.874473	5.65209	0.563219	1049.4	1372.78	0.999116
b26	1185.08	0.917349	5.4448	0.540217	1081.6	500.415	0.99861
b27	897.157	0.866919	4.79935	0.493741	843.6	660.685	0.999189

B27	943.866	0.923992	6.1941	0.628652	924.8	1067.24	0.999582
b28	1283.5	0.846829	3.92716	0.389028	1093.6	336.238	0.997286
B29	797.79	0.907807	5.46293	0.569061	776	713.099	0.999582

Table S12 The α diversity of oral mucosal samples between patients with ESCC and healthy subjects.

Sample	Chao1	Simpson	Shannon	Pielou_e	Observed_species	Faith_pd	Goods_coverage
m01	1235.93	0.713302	3.6746	0.370051	975.6	83.4197	0.99651
M01	888.279	0.898906	5.62965	0.589483	749.7	53.0284	0.998217
m02	1767.28	0.981727	7.4603	0.711057	1440.1	130.196	0.995664
M02	741.749	0.773522	4.60158	0.491906	654.7	52.2548	0.998497
m03	2121.89	0.966452	7.19043	0.670783	1686.2	181.237	0.994349
M03	786.215	0.856532	5.08731	0.540145	684.3	50.2029	0.998358
M04	1162.3	0.965984	6.53622	0.651518	1047.2	75.8165	0.997354
m04	1241.56	0.941875	5.61446	0.565519	974.2	84.3505	0.996538
M05	1204.7	0.929957	5.91983	0.591636	1028.2	73.6678	0.99695
m05	2529.91	0.979391	7.36515	0.675241	1920.8	137.786	0.991971
m06	958.274	0.788914	4.16796	0.431775	805.2	116.475	0.99791
M07	1168.15	0.975578	6.55734	0.65421	1040.7	74.66	0.997263
m07	720.202	0.687653	3.75698	0.409191	580.7	139.143	0.998119
m08	1198.4	0.95802	6.02958	0.610796	936.9	73.946	0.996543
M09	1405.48	0.956343	6.59171	0.642175	1230.2	81.3307	0.996744
m09	2334.59	0.919588	6.05647	0.559304	1818.6	123.345	0.992025
M10	1231.64	0.957351	6.71582	0.664597	1101.4	73.9298	0.997119
m10	2140.05	0.989748	7.69668	0.715172	1736.6	108.438	0.99352
m11	1538.17	0.929768	5.76113	0.562902	1205	91.0875	0.995727
M11	863.992	0.834351	5.06636	0.523681	817.2	69.0912	0.998521
M12	898.191	0.943061	5.78601	0.60251	777.8	54.6666	0.99782
m13	1280.55	0.951376	6.52757	0.645162	1111.1	79.2413	0.997596
M13	1597.35	0.967159	7.18459	0.682537	1474.8	74.418	0.996744
m14	661.667	0.874512	4.61855	0.498211	617.5	67.9068	0.99913
M14	939.456	0.908656	5.67884	0.584849	837.5	55.8114	0.997995
M15	1029.25	0.938778	6.28829	0.63876	919.4	63.4803	0.997999
m15	1089.17	0.9276	5.35407	0.550355	848.3	104.89	0.997044
m16	1227.38	0.918692	5.168	0.521554	961.4	89.5362	0.996687
M16	935.242	0.730224	4.37221	0.452889	805.7	56.7918	0.997846
m17	1354.3	0.840931	4.76038	0.473946	1055.9	84.6553	0.996231
m18	2085.18	0.987743	7.72111	0.718197	1723	109.583	0.994319
M18	785.356	0.729186	4.01912	0.428501	666.1	57.3154	0.998073
M19	1346.93	0.742853	4.61108	0.450551	1204.6	90.0112	0.996908
m19	2006.31	0.975677	7.66996	0.702096	1943.4	119.307	0.996821
m20	1490.05	0.954936	6.33762	0.614227	1276.6	106.208	0.995982
M20	1833.39	0.963623	6.84035	0.641328	1624.7	95.715	0.99554
M21	1596.94	0.966736	6.57964	0.630907	1378.5	98.5173	0.995598
m21	763.185	0.96923	6.71452	0.705787	730.9	62.8448	0.999454
m22	605.248	0.881194	4.82693	0.528734	560	62.1107	0.999325
M22	813.707	0.886768	4.70696	0.496192	717.2	62.7598	0.998232
M23	1078.18	0.947025	6.1247	0.618349	958.7	74.4806	0.997978
m23	2465.71	0.972316	7.40391	0.675234	1998.9	115.653	0.993271
M24	1809.75	0.915774	5.88353	0.555077	1551.6	90.9245	0.995006
m24	963.926	0.716485	3.3327	0.34801	763.5	75.305	0.997491
M25	2079.41	0.834596	5.68244	0.530762	1670.7	122.492	0.994279

M26	1765.22	0.888935	5.62613	0.530736	1552.8	104.574	0.995232
m26	770.741	0.963569	6.89214	0.725837	721.8	55.2799	0.999358
M27	1182.64	0.931898	5.80705	0.578259	1054.5	85.4492	0.997294
m27	1743.84	0.969245	6.66456	0.6392	1376.2	82.0943	0.994721
m28	1223.17	0.964649	6.70402	0.667871	1051.3	117.691	0.997844

Table S13 The α diversity of saliva samples between patients with ESCC and healthy subjects.

Sample	Chao1	Simpson	Shannon	Pielou e	Observed species	Faith pd	Goods coverage
s01	1168.8	0.922171	5.68535	0.571951	982.5	81.5544	0.996691
S01	893.144	0.879401	5.64206	0.592351	736.7	54.6914	0.997261
S02	1010.1	0.792538	4.99756	0.5132	854	61.7052	0.99692
s02	1668.2	0.955024	6.5723	0.635799	1293.6	81.5304	0.993736
S03	1542.36	0.958029	6.46886	0.620715	1371.6	72.5824	0.995029
s03	1715.45	0.965749	6.88762	0.662206	1352.2	94.3207	0.994189
s04	1487.51	0.934635	5.62743	0.557796	1089	77.2487	0.993905
S04	1574.95	0.983865	7.38335	0.708273	1374.3	75.1091	0.994586
S05	1100.59	0.887177	5.77372	0.58792	904.3	66.7535	0.996536
s05	1145.94	0.883647	5.0884	0.522219	857.5	64.1845	0.995655
s06	796.114	0.916176	5.86302	0.621223	693.6	75.2262	0.998336
s07	1027.63	0.916853	5.19945	0.538773	803.8	62.3714	0.996251
S07	1636.12	0.964772	7.14755	0.686766	1358.3	78.4314	0.994674
s08	1559.45	0.959737	6.06076	0.592671	1197.9	85.5157	0.993773
S09	1262.69	0.903171	5.81704	0.580876	1034.2	71.6314	0.995521
s09	1580.77	0.960292	6.30614	0.61959	1158.5	86.247	0.99375
S10	1288.74	0.741016	4.71516	0.461744	1185.8	79.7548	0.996347
s10	1698.88	0.964222	6.50592	0.626373	1338.8	92.1129	0.993613
s11	2365.73	0.978083	7.37756	0.669967	2064.9	116.584	0.990829
S11	927.748	0.979929	6.81572	0.694482	900.2	82.6031	0.998284
S12	1425.21	0.983813	7.37695	0.713021	1301.6	80.3063	0.995928
S13	1756.06	0.821541	5.88488	0.549039	1685	87.4169	0.996204
s13	2285.86	0.957322	6.47215	0.602735	1707.9	104.538	0.990616
s14	1502.88	0.939608	6.2377	0.616152	1115.7	81.5033	0.994491
S14	800.569	0.945493	6.03605	0.635546	722.8	54.9811	0.997974
S15	1848.66	0.985545	7.84804	0.726366	1788.5	99.2775	0.996197
s15	1905.5	0.943355	6.44278	0.611427	1486.1	83.318	0.992734
S16	1085.4	0.941639	6.10812	0.612697	1002.4	68.2822	0.997167
s16	2142.46	0.918107	6.18355	0.582459	1569.8	98.7226	0.990971
s17	1790.84	0.939941	6.01682	0.567595	1552.7	93.2381	0.993052
S18	1247.4	0.965876	7.03234	0.689658	1173.7	77.903	0.997129
s18	1443.37	0.963167	6.25535	0.619219	1099.1	83.5547	0.994409
s19	1326.52	0.900803	5.22054	0.522884	1012.9	73.69	0.994444
S19	1561.85	0.94278	6.76792	0.643247	1469.9	94.3246	0.996155
s20	1504.42	0.962584	6.41609	0.63321	1122.7	76.093	0.994238
S20	1569.83	0.975366	7.08566	0.673559	1468.1	87.2643	0.995904
S21	1286.32	0.965505	7.04715	0.691103	1173.8	75.6115	0.99668
s21	2328.65	0.893681	5.9879	0.550555	1879.5	116.835	0.990345
S22	1079.63	0.93183	5.95905	0.598473	994	72.125	0.997232
s22	1737.58	0.944791	6.14034	0.587934	1393	105.129	0.993491
S23	1256.68	0.927917	6.20816	0.611131	1142.9	74.1	0.996614
s23	2301.88	0.97468	7.24084	0.654144	2148.6	124.272	0.992887
s24	1511.04	0.93877	5.67115	0.558614	1138	93.8273	0.993931
S24	2542.98	0.97556	7.25784	0.65608	2138.6	112.555	0.989184

S25	3562.1	0.982108	7.9284	0.684554	3065.4	170.982	0.985165
s26	1718.21	0.95385	6.6087	0.638047	1312.2	89.5146	0.993689
S26	2118.5	0.93042	6.12443	0.566515	1796.2	109.035	0.991576
s27	1572.04	0.978877	7.52986	0.727398	1306.8	95.3715	0.995477
s28	3297.81	0.972125	7.40792	0.64702	2796.3	142.741	0.985667

Table S14 The α diversity of urine samples between patients with ESCC and healthy subjects.

Sample	Chao1	Simpson	Shannon	Pielou_e	Observed_species	Faith_pd	Goods_coverage
U01	524.01	0.828782	3.83052	0.438156	428.4	43.437	0.99731
u01	954.832	0.456144	2.64327	0.274546	791.2	71.8863	0.995038
u02	1209.68	0.697671	4.35254	0.434589	1035	85.89	0.995289
U02	667.83	0.807878	3.52602	0.384578	575.5	58.5118	0.996657
U03	523.176	0.811085	3.47385	0.390884	473.5	51.8989	0.99778
u03	785.567	0.890443	4.88129	0.524393	634.1	62.6107	0.996549
u04	1721.51	0.963962	7.92169	0.745122	1586.3	124.722	0.996066
U04	504.543	0.860175	3.96455	0.452591	433.5	48.1137	0.997602
u05	738.548	0.70792	3.2311	0.350804	592.5	61.4657	0.996204
u06	902.465	0.908097	5.79092	0.597717	825.1	73.5978	0.997587
u07	746.633	0.857689	5.29344	0.564312	666.5	61.5549	0.997821
u08	929.453	0.888014	5.15894	0.535616	793.4	71.7759	0.996451
U09	470.635	0.846042	3.78671	0.441344	382.8	43.7463	0.997356
U10	646.854	0.84159	3.97858	0.43976	529.1	59.1798	0.996433
u10	804.901	0.900102	6.07749	0.635738	754.7	69.6979	0.998386
U11	433.346	0.859114	3.96264	0.458608	399.1	43.9597	0.998281
u11	726.685	0.879739	4.15034	0.453144	571.8	61.6794	0.996008
U12	422.566	0.835673	3.62782	0.427303	359.6	41.1508	0.997828
U13	574.339	0.801256	3.40018	0.383323	468	50.4904	0.996677
u13	702.899	0.928323	4.95857	0.546418	539.3	59.8052	0.995953
U14	528.504	0.836938	3.79706	0.431942	442.9	47.4996	0.997177
u14	955.117	0.790902	4.19039	0.435649	786.3	73.3901	0.995237
U15	521.236	0.83888	3.83195	0.435487	445.5	49.0647	0.997258
u15	998.951	0.811213	4.6141	0.474459	846.3	94.5626	0.9958
u16	1683.39	0.914356	6.43303	0.620342	1323.6	101.095	0.991516
U16	533.595	0.835129	3.56241	0.40645	435	50.7965	0.996956
u17	705.626	0.83274	4.92883	0.529113	637.1	59.3996	0.998064
u18	1107.2	0.949698	6.30048	0.635647	963.4	87.5912	0.996018
U18	584.875	0.906708	4.68848	0.526947	476.9	49.7393	0.996825
U19	602.496	0.881155	4.43631	0.49563	494.9	52.6327	0.996627
u19	796.181	0.961046	6.10047	0.644663	705.8	69.9955	0.99724
u20	450.786	0.196966	0.991393	0.119409	315.8	42.6537	0.996757
U20	537.426	0.831961	3.668	0.418656	434	49.9389	0.996677
U21	517.444	0.887919	4.44415	0.509432	422.9	48.9618	0.997109
u21	659.123	0.913183	5.71817	0.617268	614.7	56.141	0.998426
U22	520.604	0.87324	4.22193	0.484481	420.1	48.8845	0.997089
u22	675.957	0.891067	5.55578	0.597982	626.4	58.7681	0.998266
U23	525.296	0.82533	3.51061	0.402759	420.7	44.5309	0.996878
u23	744.661	0.953882	6.05247	0.645119	667.2	63.5785	0.997637
U24	1069.92	0.899888	6.08375	0.616888	930.6	78.8169	0.996126
u24	709.208	0.89124	5.41881	0.582226	633.5	65.2421	0.997795
U25	522.867	0.875	5.08509	0.568742	491.5	46.7091	0.998942
u26	609.533	0.883237	5.47892	0.59965	563	60.767	0.998643
U26	739.442	0.858393	4.694	0.500302	667.4	60.8195	0.99763

u27	685.287	0.888856	5.58889	0.598338	648.4	55.9164	0.998595
u28	679.176	0.910658	5.72922	0.615661	632.9	58.5045	0.998442

Table S15 The α diversity of fecal samples between patients with ESCC and healthy subjects.

Sample	Chao1	Simpson	Shannon	Pielou e	Observed species	Faith pd	Goods coverage
F01	1555.88	0.963504	6.9058	0.653583	1516	71.9441	0.99598
f01	1903.09	0.963348	6.18494	0.605093	1194	71.4357	0.988731
F02	1031.53	0.954362	6.52912	0.655936	991.8	52.9157	0.997207
F03	1530.59	0.946591	6.48099	0.618274	1430.6	70.3085	0.994204
f03	3807.39	0.950503	6.80881	0.613379	2196	130.33	0.975546
F04	1291.13	0.96323	6.21843	0.603243	1268	77.1048	0.996993
f04	581.062	0.956153	5.40758	0.617762	431.7	41.9668	0.99736
F05	1183.5	0.813436	4.55636	0.456245	1014.6	57.2381	0.994618
f05	1657.26	0.936976	5.59247	0.557019	1052.9	67.1822	0.989891
f06	2403.86	0.980097	7.02455	0.663035	1546.3	91.1364	0.985033
f07	1263.33	0.943626	5.84803	0.602762	833.1	61.5716	0.993096
F07	1348.66	0.858928	5.81884	0.565352	1254.1	62.1011	0.995061
f08	1888.54	0.943857	6.15155	0.599721	1224.1	71.2048	0.988951
F10	1022.27	0.872212	5.31188	0.538494	932.1	54.5591	0.995924
f11	2082.79	0.939127	5.91531	0.572208	1294.2	83.8141	0.986894
F11	666.854	0.651752	2.97739	0.323978	584.2	47.4991	0.996995
F12	1202.4	0.969987	6.61861	0.655283	1097.8	67.8612	0.995162
F13	1025.27	0.962818	6.45782	0.659056	890.6	59.97	0.995575
f13	1161.94	0.925134	4.993	0.523781	740.7	57.2601	0.993323
F14	1784.81	0.981683	7.61962	0.711706	1670.6	78.5856	0.993284
f14	1929.73	0.969615	6.43527	0.624914	1258.9	82.4451	0.988101
f15	1207.89	0.86402	4.94406	0.506395	869.1	66.6824	0.993446
F15	1391.1	0.789973	4.74699	0.47015	1095.1	68.4133	0.992233
F16	1582.47	0.966864	6.80623	0.65377	1361.3	78.1236	0.991676
f16	430.647	0.937495	4.95007	0.594589	320.8	36.3997	0.997902
f17	2541.7	0.957012	6.35241	0.599375	1550.5	90.5099	0.984155
F18	1406.7	0.890479	5.32937	0.524848	1139.5	56.7501	0.992835
f18	2771.17	0.968693	6.64612	0.620083	1684.6	91.859	0.982607
f19	2618.48	0.974958	6.83849	0.639233	1661.3	86.3197	0.983894
F19	882.212	0.715243	3.6568	0.384467	729.9	62.2506	0.995719
F20	2132.1	0.948309	6.90166	0.6321	1935.7	86.5755	0.990128
F21	1105.91	0.940315	6.08189	0.619701	900.3	77.2247	0.994668
f21	2916.61	0.979745	7.1985	0.663707	1840.6	118.256	0.980949
f22	1031.5	0.940128	5.39214	0.574887	666.1	56.8819	0.994212
F22	1573.75	0.875957	5.75274	0.554587	1326.2	78.5345	0.992267
f23	2716.23	0.944179	6.11267	0.565878	1785.7	101.986	0.982531
F23	303.272	0.635691	2.44579	0.306875	250.8	29.7525	0.998649
F24	2161.63	0.962901	6.41754	0.599048	1678.5	113.802	0.986111
f24	2162.04	0.933073	6.05357	0.584478	1311.8	81.6146	0.987389
F25	836.375	0.944028	5.62359	0.603639	637.5	58.6778	0.995564
F26	1630.27	0.970841	6.67006	0.648805	1243.9	85.1992	0.990409
f26	2382.69	0.940617	6.19869	0.588778	1476.7	93.871	0.985562
f27	1371.38	0.947315	5.72	0.586647	861.5	61.2387	0.992263
f28	943.448	0.96436	6.06343	0.637739	728	58.8491	0.995233

Table S16 The P values of β diversity of blood samples.

	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
Blood	1	11.062935	11.062935	10.052582	0.1826	0.001
Residuals	45	49.522806	1.100507	NaN	0.8174	NaN
Total	46	60.585741	NaN	NaN	1	NaN

Table S17 The P values of β diversity of oral mucosal samples between patients with ESCC and healthy subjects.

	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
Mucosa	1	0.359153	0.359153	3.307025	0.064456	0.003
Residuals	48	5.212944	0.108603	NaN	0.935544	NaN
Total	49	5.572097	NaN	NaN	1	NaN

Table S18 The P values of β diversity of saliva samples between patients with ESCC and healthy subjects.

	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
Saliva	1	0.645291	0.645291	7.407429	0.136147	0.001
Residuals	47	4.094359	0.087114	NaN	0.863853	NaN
Total	48	4.73965	NaN	NaN	1	NaN

Table S19 The P values of β diversity of urine samples between patients with ESCC and healthy subjects.

	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
Urine	1	2.633799	2.633799	26.143152	0.372711	0.001
Residuals	44	4.432793	0.100745	NaN	0.627289	NaN
Total	45	7.066592	NaN	NaN	1	NaN

Table S20 The P values of β diversity of fecal samples between patients with ESCC and healthy subjects.

Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
Feces	1	0.781964	0.781964	6.887027	0.140876	0.001
Residuals	42	4.768744	0.113542	NaN	0.859124	NaN
Total	43	5.550707	NaN	NaN	1	NaN

Table S21 The α diversity of blood samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

Sample	Chao1	Simpson	Shannon	Pielou_e	Observed_species	Faith_pd	Goods_coverage
B0101	864.058	0.674335	3.82677	0.396772	800.5	235.109	0.997867
B0102	798.555	0.693011	3.75469	0.395413	721.9	292.202	0.997825
B01T	2035.58	0.82155	5.04135	0.461951	1928.4	120.15	0.996239
B0201	1072.12	0.775189	4.29059	0.4317	981.5	205.975	0.997196
B02T	1990.21	0.83485	4.54689	0.419364	1836	126.457	0.994671
B0301	733.216	0.627259	3.43516	0.366973	657.5	194.748	0.997992
B0302	724.799	0.688509	3.81843	0.4056	682.3	136.561	0.998508
B03T	1063.4	0.785556	3.43053	0.346655	952.9	90.8387	0.996855
B0402	1075.94	0.728488	4.32367	0.432197	1026.8	259.222	0.997993
B04T	590.298	0.778307	3.12421	0.34557	526.7	73.9538	0.99846
B0503	827.235	0.711093	4.02694	0.420629	762	185.116	0.998027
B0604	911.292	0.78967	4.58453	0.471881	840.7	576.253	0.997945
B0703	898.306	0.807942	4.64868	0.478417	841.5	330.419	0.9981
B0801	501.449	0.861813	4.15142	0.471656	446.3	32.9182	0.998397
B0802	582.091	0.623341	2.99321	0.336953	472.2	126.694	0.997996
B0902	696.513	0.735167	3.60613	0.392464	583.5	98.5966	0.997765
B1001	747.549	0.641838	3.30851	0.356959	616.8	131.734	0.997443
B1002	707.625	0.584329	3.0219	0.331256	557.5	87.1896	0.997477
B1101	652.99	0.691948	3.5763	0.394402	536.6	181.892	0.997856
B1102	741.03	0.634943	3.32476	0.359051	613.1	148.506	0.997644
B1201	764.849	0.803321	4.23817	0.455278	634.3	152.105	0.997471
B12T	550.834	0.803529	3.29818	0.372594	462.1	56.7839	0.998261
B1301	1016.53	0.910718	5.50852	0.558753	928.4	707.674	0.998035
B1302	1112.26	0.889035	5.16438	0.518056	1002.1	547.106	0.99736
B1303	925.31	0.860917	4.82535	0.497571	830.5	352.569	0.997879
B1401	1008.21	0.62024	3.35814	0.342367	896.8	312.646	0.997226
B1402	785.797	0.750486	3.45397	0.365099	704.5	169.602	0.997981
B1501	967.15	0.852511	4.8233	0.495894	847.2	382.343	0.997488
B1701	952.899	0.679422	3.81786	0.392002	854.8	433.288	0.997675
B1702	770.692	0.822746	4.01846	0.43013	649.2	139.016	0.997623
B1801	1265.8	0.97321	6.90882	0.681109	1131.1	436.853	0.99719
B1901	1147.47	0.924411	6.04049	0.6018	1050.9	217.857	0.997864
B22T	573.806	0.778648	3.28557	0.364998	512.6	67.4128	0.99857
B23T	605.55	0.834508	3.86103	0.423643	554.1	69.1471	0.998647
B25T	859.14	0.947721	6.43116	0.66201	840.2	960.866	0.999272

Table S22 The α diversity of oral mucosal samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

Sample	Chao1	Simpson	Shannon	Pielou e	Observed species	Faith pd	Goods coverage
M0101	546.249	0.628102	3.12453	0.349094	494.7	67.0502	0.998575
M0102	565.022	0.636604	2.68483	0.299455	500	60.4147	0.998385
M01T	912.127	0.901704	5.70081	0.594865	767.2	57.8367	0.997638
M0201	927.038	0.968405	6.61846	0.683578	821.5	67.4011	0.997751
M02T	785.913	0.773414	4.61499	0.492085	665.6	57.4443	0.997827
M0301	685.171	0.809932	4.98887	0.537617	621.5	57.729	0.99853
M0302	747.513	0.714055	4.12165	0.439707	663.4	57.5639	0.998291
M03T	833.653	0.855135	5.10488	0.539409	706.2	56.7308	0.997638
M0402	682.744	0.583582	3.28372	0.354347	616.1	68.5463	0.998311
M04T	1205.5	0.966276	6.56356	0.655631	1031.9	82.0066	0.996118
M0503	782.303	0.590902	3.53111	0.372401	715.1	65.4943	0.998074
M05T	1195.81	0.93144	5.98735	0.60086	999.3	77.9236	0.996223
M0604	763.868	0.731577	4.24927	0.453004	666.4	60.5612	0.998012
M0703	1129.69	0.979609	7.11663	0.709381	1047.1	94.8128	0.997447
M0801	704.152	0.882069	4.22269	0.448755	680.2	84.6495	0.998865
M0802	871.886	0.80042	4.36947	0.455133	776.3	78.6703	0.997545
M0902	715.696	0.720898	3.49434	0.373648	653.5	78.0645	0.998278
M1001	745.598	0.91588	5.54437	0.592824	653.7	60.9628	0.998057
M1002	616.204	0.842253	4.439	0.483675	579.1	57.0247	0.998615
M1101	823.68	0.883001	5.33989	0.5624	721.5	61.4499	0.997866
M1102	1197.33	0.968945	7.22911	0.717287	1081.2	82.1032	0.997055
M1201	698.658	0.891308	5.41648	0.584034	619.2	56.3071	0.998326
M12T	916.811	0.944222	5.84648	0.609221	774.3	60.1528	0.997146
M1301	671.763	0.841988	5.1389	0.553442	624	67.2323	0.998817
M1302	900.733	0.927679	5.71034	0.588776	831	88.05	0.99824
M1303	705.346	0.877302	4.9401	0.528189	653.9	73.243	0.998745
M13T	1623.22	0.968873	7.28384	0.693048	1458.1	79.2844	0.995614
M1401	1142.46	0.926116	6.02514	0.602941	1019	95.2486	0.997076
M1402	1292.85	0.951213	6.45155	0.631928	1183.9	107.793	0.996991
M1501	1174.51	0.960064	6.89618	0.685884	1063.4	77.2519	0.997228
M15T	1106.47	0.944087	6.38591	0.646099	944.8	71.8316	0.996958
M16T	944.927	0.737478	4.46039	0.462418	801.1	60.1006	0.997185
M1701	609.355	0.629671	3.77075	0.416141	534.2	53.1642	0.998564
M1702	594.069	0.798504	4.49047	0.496273	529.5	49.1744	0.998637
M1801	520.28	0.763654	4.15092	0.473324	436.5	45.2744	0.998683
M18T	744.53	0.739513	4.14207	0.445002	633.9	57.9754	0.997866
M1901	954.999	0.916529	5.66627	0.581605	856.6	70.7745	0.997629
M22T	845.585	0.888484	4.75298	0.501364	714.2	69.3149	0.997401
M23T	1151.15	0.947504	6.15849	0.619123	987.2	80.8117	0.9969
M24T	1196.23	0.916819	5.85036	0.576586	1133.5	78.9629	0.997266
M25T	1372.11	0.836472	5.6241	0.549655	1202.7	106.631	0.996267

Table S23 The α diversity of saliva samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

Sample	Chao1	Simpson	Shannon	Pielou_e	Observed_species	Faith_pd	Goods_coverage
S0101	525.752	0.973484	6.16202	0.704448	429.8	51.1416	0.996429
S0102	1178.39	0.960308	6.59461	0.660902	1008.7	78.491	0.990899
S01T	1002.97	0.891542	5.95923	0.619926	783	54.3786	0.992975
S0201	1712.83	0.981134	7.39746	0.707974	1397.7	94.6299	0.985065
S02T	979.736	0.798922	5.07985	0.531168	756.8	58.6768	0.992624
S0301	1228.96	0.982678	7.37904	0.742419	981.8	63.8156	0.991171
S0302	888.127	0.799934	5.02595	0.528025	733.4	57.7039	0.993846
S03T	1503.42	0.959676	6.58649	0.646453	1167.1	69.2068	0.987256
S0402	1116.9	0.960389	6.6209	0.678883	862.7	70.614	0.991508
S04T	1545.44	0.984605	7.48228	0.735345	1156.3	68.6937	0.987207
S0503	776.11	0.889219	5.42262	0.585115	616.4	60.98	0.994094
S05T	1046.35	0.891277	5.86862	0.608562	799.8	63.8044	0.992132
S0604	1960.19	0.981407	7.88247	0.739618	1615.2	91.9009	0.983337
S0703	1053.65	0.958781	6.47587	0.6656	848.9	65.4363	0.992218
S0801	1208.49	0.922424	6.16285	0.624197	937.9	69.6874	0.990337
S0802	1374.98	0.954664	6.87171	0.673737	1175.8	96.1288	0.98928
S0902	1033.66	0.856844	5.36153	0.553621	822.9	71.618	0.99199
S1001	1568.66	0.972291	7.63193	0.725203	1472.3	92.9367	0.990899
S1002	1069.17	0.951303	6.53066	0.661151	940.8	69.7177	0.992879
S1101	1823	0.979019	8.04609	0.758011	1568.1	86.0352	0.986663
S1102	2481.54	0.993165	9.1297	0.814887	2358.5	97.6943	0.986436
S1201	1170.2	0.979999	7.29598	0.730833	1012.1	74.4069	0.992014
S12T	1523.09	0.98416	7.43642	0.731471	1149.3	76.7512	0.987683
S1301	1890.31	0.976603	7.66363	0.72561	1511.4	89.4243	0.984101
S1302	1216.24	0.898768	6.22182	0.618581	1066.2	71.8786	0.991853
S1303	1737.16	0.923346	6.66294	0.640171	1358.8	86.7886	0.985341
S13T	1883.47	0.83182	6.00412	0.570426	1474.2	84.33	0.984063
S1401	2123.56	0.975085	7.81788	0.717505	1905.5	128.405	0.984349
S1402	1449.33	0.983517	7.65841	0.746241	1228.5	78.1489	0.989439
S1501	1851.72	0.983729	8.24929	0.772287	1642.5	92.294	0.9875
S15T	2067.66	0.985796	7.85817	0.74078	1560.8	96.6832	0.981925
S16T	1130.24	0.943865	6.18603	0.633293	872	66.3303	0.991295
S1701	1826.75	0.97382	7.57943	0.715219	1549.3	71.2	0.985957
S1702	1267.9	0.974723	7.3013	0.722744	1099.2	62.1801	0.991773
S1801	938.963	0.973581	6.83728	0.708374	804.6	61.5672	0.993929
S18T	1357.74	0.966178	7.04776	0.700632	1066.9	77.2537	0.989115
S1901	1933.8	0.984415	8.31464	0.781038	1602	91.8762	0.985579
S22T	1124.7	0.935262	6.07385	0.620685	882.7	71.5994	0.991281
S23T	1253.59	0.928449	6.1965	0.624045	975.3	72.1846	0.989859
S24T	1828.39	0.975512	7.1555	0.685062	1394.1	89.7382	0.982596
S25T	2492.14	0.981908	7.78671	0.713591	1926.9	119.033	0.97564

Table S24 The α diversity of urine samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

Sample	Chao1	Simpson	Shannon	Pielou_e	Observed_species	Faith_pd	Goods_coverage
U0101	822.177	0.796304	4.84093	0.507409	744.7	76.0458	0.997271
U0102	633.469	0.664033	3.58144	0.39195	563.2	62.4741	0.997595
U01T	536.004	0.82423	3.78545	0.42836	457.4	54.0774	0.997759
U0201	656.938	0.630353	3.41769	0.373303	570.2	61.0118	0.997586
U02T	674.476	0.803614	3.48161	0.377016	602.5	70.761	0.997437
U0301	775.708	0.849141	5.27376	0.55317	741.2	77.8309	0.998044
U0302	984.369	0.885788	6.01697	0.611856	912.7	78.951	0.997257
U03T	551.323	0.80721	3.42773	0.381866	503.7	61.8468	0.998176
U0402	796.892	0.87206	5.61052	0.591177	719.3	67.5214	0.997633
U04T	545.759	0.85837	3.9424	0.444341	468.7	58.6293	0.997876
U0503	1009.44	0.918674	6.34694	0.643131	935	90.9587	0.997171
U0604	947.073	0.970539	6.94939	0.710355	881	75.8386	0.997508
U0703	801.466	0.884247	5.89984	0.617725	750.1	75.2128	0.998165
U0801	816.753	0.761598	4.39544	0.464493	705.7	63.6879	0.996897
U0802	572.116	0.615694	3.27617	0.364814	505.1	58.8847	0.997882
U0902	756.705	0.728237	3.95954	0.4233	654.4	62.3938	0.997071
U1001	1161.98	0.89883	6.35739	0.630285	1087.3	89.4147	0.996684
U1002	731.757	0.769227	4.44694	0.474982	658.2	62.1078	0.997538
U1101	668.205	0.758956	4.257	0.46124	600.3	59.1479	0.997855
U1102	896.439	0.94652	6.417	0.659545	848.9	76.9843	0.997563
U1201	765.495	0.902081	5.75261	0.605818	721.9	70.7831	0.997991
U12T	457.25	0.832007	3.58047	0.4168	385.5	49.2826	0.998023
U1301	877.769	0.7835	4.84002	0.502237	796.2	74.2389	0.997078
U1302	718.594	0.866481	4.81642	0.516235	643.6	76.4012	0.997291
U1303	425.657	0.632106	2.95082	0.347996	357	53.9694	0.998331
U13T	611.273	0.792815	3.34156	0.371375	511.3	60.1548	0.997165
U1401	771.729	0.719722	3.91343	0.414916	690.7	74.1919	0.997327
U1402	995.098	0.820869	5.1924	0.528253	909.8	81.203	0.996788
U1501	671.523	0.767412	4.19963	0.455918	592.8	64.1808	0.997461
U15T	532.972	0.834395	3.78293	0.427315	462.4	58.0945	0.997801
U16T	565.411	0.83042	3.50481	0.394845	470	58.9235	0.997354
U1701	980.362	0.97432	7.08674	0.71965	921.3	88.0389	0.997367
U1702	1191.36	0.81532	4.74785	0.469694	1103.9	115.27	0.996263
U1801	993.21	0.924582	5.94059	0.60619	891.4	89.8106	0.996444
U18T	592.912	0.904404	4.64772	0.519347	494.3	59.4522	0.997395
U1901	739.999	0.769518	4.58612	0.49025	654.7	64.5687	0.997393
U22T	538.496	0.870514	4.19311	0.475568	451.1	59.8365	0.997531
U23T	550.372	0.820329	3.47037	0.393205	453.8	56.5509	0.997374
U24T	962.745	0.900331	6.08045	0.61919	903.9	90.7203	0.997844
U25T	463.436	0.873547	5.02043	0.570302	446.7	54.4735	0.999449

Table S25 The α diversity of fecal samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

Sample	Chao1	Simpson	Shannon	Pielou_e	Observed_species	Faith_pd	Goods_coverage
F0101	347.857	0.911699	4.54871	0.55576	291	37.2928	0.996942
F01T	1651.51	0.963963	6.89956	0.668113	1284.5	74.7085	0.980392
F0201	1031.3	0.950016	5.89379	0.615031	767	59.842	0.988307
F02T	1096.32	0.952019	6.44465	0.659305	876.2	53.7333	0.988728
F0301	646.731	0.922655	5.16158	0.578285	486.4	40.1476	0.993621
F0302	1231.55	0.977447	7.10688	0.712485	1006.3	58.0314	0.986642
F03T	1515.18	0.947191	6.43363	0.63527	1118.6	69.1746	0.981735
F0402	537.225	0.860376	4.69197	0.533248	445.4	35.8092	0.994906
F04T	1399.98	0.963213	6.1948	0.617112	1051.7	80.7688	0.981963
F0503	1474.54	0.951288	6.8833	0.671051	1224.1	61.2633	0.984882
F05T	1125.15	0.810056	4.48037	0.463102	817.4	56.5481	0.987156
F0604	1431.83	0.851477	5.66658	0.561345	1093.5	60.1149	0.983414
F0703	1119.55	0.915577	6.23579	0.631815	935.6	57.5231	0.98888
F0801	1033.9	0.963975	6.40501	0.66382	802.8	53.2631	0.989068
F0802	1307.62	0.959225	6.84508	0.679628	1076.3	53.426	0.986377
F0902	581.6	0.86672	5.12105	0.572499	492.9	44.0257	0.995053
F1101	1350.8	0.908399	6.27721	0.615815	1170.9	80.4749	0.986194
F1102	1294.69	0.873213	5.76674	0.57271	1074.4	77.8372	0.985787
F12T	1209.88	0.970078	6.60789	0.673392	899.5	66.7313	0.986355
F1301	1046.86	0.980572	7.06764	0.732248	804.6	64.7824	0.989377
F1302	1365.4	0.956674	6.75026	0.660281	1195.5	74.5105	0.986633
F1303	984.382	0.937108	6.20445	0.631922	902.9	52.9423	0.991387
F13T	1052.62	0.963864	6.52913	0.680298	774.8	62.5136	0.988884
F1401	1434.8	0.966756	7.1351	0.701604	1151.9	68.2045	0.984403
F1402	1261.67	0.972073	6.99152	0.703231	983.7	61.8434	0.986825
F1501	1305.68	0.971676	7.03017	0.695634	1102.2	64.8596	0.98636
F15T	1260.13	0.796907	4.85388	0.497122	869.6	63.5838	0.984976
F16T	764.725	0.971889	6.94695	0.730918	726.3	53.9344	0.99512
F1701	2555.74	0.948174	7.64034	0.696934	1995.9	101.528	0.968681
F1702	822.044	0.923405	5.57588	0.593032	676.8	44.797	0.991257
F1801	1845.4	0.872161	6.08992	0.581191	1426.6	67.0467	0.977791
F18T	1240.35	0.895853	5.44408	0.554293	905	51.7801	0.985724
F22T	1569.54	0.886435	5.94792	0.587209	1120	73.9484	0.98204
F23T	301.404	0.637687	2.47036	0.317006	221.8	31.9194	0.996683
F24T	1734.99	0.964055	6.4427	0.633725	1149.3	98.8527	0.976475
F25T	740.767	0.945839	5.69832	0.632336	516.2	52.3716	0.991826

Table S26 The P values of β diversity of blood samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

#	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
BB	1	1.909279	1.909279	18.932996	0.364566	0.001
Residuals	33	3.327852	0.100844	NaN	0.635434	NaN
Total	34	5.237131	NaN	NaN	1	NaN

Table S27 The P values of β diversity of oral mucosal samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

#	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
MHI	1	0.294665	0.294665	3.067735	0.072924	0.02
Residuals	39	3.746068	0.096053	NaN	0.927076	NaN
Total	40	4.040733	NaN	NaN	1	NaN

Table S28 The P values of β diversity of saliva samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

#	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
SHI	1	0.324377	0.324377	2.748456	0.065834	0.057
Residuals	39	4.602846	0.118022	NaN	0.934166	NaN
Total	40	4.927223	NaN	NaN	1	NaN

Table S29 The P values of β diversity of urine samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

#	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
UHI	1	2.404003	2.404003	33.594491	0.469233	0.001
Residuals	38	2.719258	0.071559	NaN	0.530767	NaN
Total	39	5.123261	NaN	NaN	1	NaN

Table S30 The P values of β diversity of fecal samples between patients with ESCC after chemotherapy and patients with ESCC after immunotherapy.

#	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
FHI	1	0.448258	0.448258	3.373972	0.090276	0.002
Residuals	34	4.517161	0.132858	NaN	0.909724	NaN
Total	35	4.965419	NaN	NaN	1	NaN

Table S31 The relative abundance of the predicted KEGG secondary functional pathways in ESCC patients.

Cellular Processes	Cell growth and death	551.604
Cellular Processes	Cell motility	668.122
Cellular Processes	Cellular community - eukaryotes	0.000176007
Cellular Processes	Cellular community - prokaryotes	65.7932
Cellular Processes	Transport and catabolism	130.138
Environmental Information Processing	Membrane transport	807.857
Environmental Information Processing	Signaling molecules and interaction	0.0017259
Environmental Information Processing	Signal transduction	168.537
Genetic Information Processing	Folding, sorting and degradation	1113.02
Genetic Information Processing	Replication and repair	2147.63
Genetic Information Processing	Transcription	278.431
Genetic Information Processing	Translation	1179.25
Human Diseases	Cancers	2.19485
Human Diseases	Cardiovascular diseases	0.633677
Human Diseases	Immune diseases	0.337001
Human Diseases	Infectious diseases	97.9539
Human Diseases	Neurodegenerative diseases	13.2197
Metabolism	Amino acid metabolism	4755.78
Metabolism	Biosynthesis of other secondary metabolites	786.2
Metabolism	Carbohydrate metabolism	5122.21
Metabolism	Energy metabolism	1953.05
Metabolism	Glycan biosynthesis and metabolism	1424.41
Metabolism	Lipid metabolism	2388.24
Metabolism	Metabolism of cofactors and vitamins	4576.83
Metabolism	Metabolism of other amino acids	3175.92
Metabolism	Metabolism of terpenoids and polyketides	2993.12
Metabolism	Nucleotide metabolism	740.285
Metabolism	Xenobiotics biodegradation and metabolism	2242.19
Organismal Systems	Development	0.000251733
Organismal Systems	Digestive system	10.2432
Organismal Systems	Endocrine system	29.4994
Organismal Systems	Environmental adaptation	64.8034
Organismal Systems	Excretory system	0.00171685
Organismal Systems	Immune system	16.294
Organismal Systems	Sensory system	4.80E-05

Table S32 The relative abundance of the predicted KEGG secondary functional pathways in healthy subjects.

Cellular Processes	Cell growth and death	582.483
Cellular Processes	Cell motility	572.852
Cellular Processes	Cellular community - eukaryotes	0.000406683
Cellular Processes	Cellular community - prokaryotes	53.3131
Cellular Processes	Transport and catabolism	115.615
Environmental Information Processing	Membrane transport	860.8
Environmental Information Processing	Signaling molecules and interaction	0.00374587
Environmental Information Processing	Signal transduction	139.647
Genetic Information Processing	Folding, sorting and degradation	1189.19
Genetic Information Processing	Replication and repair	2273.91
Genetic Information Processing	Transcription	303.595
Genetic Information Processing	Translation	1222.52
Human Diseases	Cancers	2.4862
Human Diseases	Cardiovascular diseases	0.412136
Human Diseases	Immune diseases	0.50936
Human Diseases	Infectious diseases	92.4068
Human Diseases	Neurodegenerative diseases	18.5272
Metabolism	Amino acid metabolism	4659.12
Metabolism	Biosynthesis of other secondary metabo	809.97
Metabolism	Carbohydrate metabolism	5175.22
Metabolism	Energy metabolism	1988.25
Metabolism	Glycan biosynthesis and metabolism	1405.05
Metabolism	Lipid metabolism	2333.25
Metabolism	Metabolism of cofactors and vitamins	4543.2
Metabolism	Metabolism of other amino acids	3065.83
Metabolism	Metabolism of terpenoids and polyketid	3199.49
Metabolism	Nucleotide metabolism	756.877
Metabolism	Xenobiotics biodegradation and metabo	1934.2
Organismal Systems	Development	0.000504743
Organismal Systems	Digestive system	10.5432
Organismal Systems	Endocrine system	28.2686
Organismal Systems	Environmental adaptation	65.9993
Organismal Systems	Excretory system	0.00193252
Organismal Systems	Immune system	14.9874
Organismal Systems	Sensory system	5.78E-05

Table S33 The metabolic pathways of microbes in blood samples.

	logFC	se	pvalues	adjPvalues
Steroid_biosynthesis	1.197	0.4168	0.00409	0.01382
Flavonoid_biosynthesis	0.9377	0.327	0.004132	0.01382
beta-Lactam_resistance	0.8195	0.2574	0.001451	0.01162
Primary_bile_acid_biosynthesis	0.6691	0.2098	0.001424	0.01162
Ethylbenzene_degradation	0.6606	0.2262	0.003502	0.01332
Nitrotoluene_degradation	0.6316	0.2159	0.003447	0.01332
Hypertrophic_cardiomyopathy_(HCM)	0.6302	0.3475	0.0698	0.1119
Biosynthesis_of_siderophore_group_nonribosomal_peptides	0.6173	0.3143	0.04954	0.08431
Taurine_and_hypotaurine_metabolism	0.5909	0.1953	0.002478	0.01188
Huntingtons_disease	0.5519	0.747	0.46	0.525
Renin-angiotensin_system	0.5347	0.5695	0.3478	0.4244
Penicillin_and_cephalosporin_biosynthesis	0.532	0.2056	0.009658	0.02498
Vibrio_cholerae_pathogenic_cycle	0.4779	0.1816	0.008516	0.02263
Aminobenzoate_degradation	0.4309	0.1323	0.001125	0.01162
Fluorobenzoate_degradation	0.4054	0.1708	0.0176	0.03794
Bacterial_chemotaxis	0.3882	0.1513	0.01028	0.0258
Styrene_degradation	0.3698	0.1122	0.0009774	0.01162
Insulin_signaling_pathway	0.3144	0.1568	0.04501	0.07866
Two-component_system	0.2845	0.1051	0.006802	0.01885
Geraniol_degradation	0.2691	0.0985	0.00629	0.01769
Benzoate_degradation	0.2433	0.08551	0.004434	0.01427
Phosphonate_and_phosphinate_metabolism	0.2358	0.1074	0.0281	0.05191
beta-Alanine_metabolism	0.2303	0.09107	0.01144	0.02673
Epithelial_cell_signaling_in_Helicobacter_pylori_infection	0.2277	0.1407	0.1054	0.1538
Chlorocyclohexane_and_chlorobenzene_degradation	0.202	0.07272	0.005474	0.01602
Dioxin_degradation	0.1895	0.1095	0.08347	0.1285
Apoptosis	0.1744	0.07633	0.0223	0.04461
NOD-like_receptor_signaling_pathway	0.1571	0.1365	0.2497	0.3208
Fatty_acid_metabolism	0.1564	0.06119	0.01057	0.0258
Pathways_in_cancer	0.1483	0.3092	0.6315	0.6948
Bisphenol_degradation	0.1462	0.09394	0.1196	0.1669
Peroxisome	0.1426	0.07239	0.04881	0.0838
Biotin_metabolism	0.1371	0.08385	0.1021	0.15
Synthesis_and_degradation_of_ketone_bodies	0.1338	0.066	0.04258	0.07578
Nitrogen_metabolism	0.1233	0.06872	0.0727	0.1156
Limonene_and_pinene_degradation	0.1122	0.06771	0.09768	0.1458
Brassinosteroid_biosynthesis	0.1112	1.388	0.9361	0.966
Tyrosine_metabolism	0.1099	0.05762	0.05655	0.0954
Circadian_rhythm-plant	0.1036	0.1311	0.4292	0.5016
Cyanoamino_acid_metabolism	0.1013	0.06488	0.1185	0.1669
Butanoate_metabolism	0.09457	0.05197	0.0688	0.1112
Ubiquinone_and_other_terpenoid-quinone_biosynthesis	0.09224	0.07353	0.2097	0.2767
Malaria	0.08983	0.57	0.8748	0.9223
Toluene_degradation	0.083	0.05328	0.1193	0.1669
Glutathione_metabolism	0.08001	0.05208	0.1245	0.1718
Propanoate_metabolism	0.0782	0.05096	0.1249	0.1718
C5-Branched_dibasic_acid_metabolism	0.0777	0.06458	0.2289	0.3001
Ribosome_biogenesis_in_eukaryotes	0.07514	0.08476	0.3753	0.448
Flagellar_assembly	0.07359	0.09555	0.4412	0.5064
Bacterial_secretion_system	0.07204	0.04912	0.1425	0.1933
Metabolism_of_xenobiotics_by_cytochrome_P450	0.05229	0.06695	0.4348	0.5051
Tryptophan_metabolism	0.04927	0.0439	0.2617	0.3319

Glyoxylate_and_dicarboxylate_metabolism	0.04111	0.04647	0.3764	0.448
Phenylalanine_metabolism	0.03753	0.04477	0.4019	0.4725
Caprolactam_degradation	0.02923	0.06139	0.6339	0.6948
Glycerophospholipid_metabolism	0.0253	0.04577	0.5804	0.6472
Plant-pathogen_interaction	0.02446	0.05761	0.6712	0.7309
Riboflavin_metabolism	0.02352	0.05598	0.6744	0.7309
Valine,leucine_and_isoleucine_degradation	0.009995	0.03816	0.7934	0.8503
Lipopolysaccharide_biosynthesis	0.006637	0.07509	0.9296	0.9644
Phagosome	0.001722	0.09696	0.9858	1
Cell_cycle-yeast	0.001156	0.001025	0.2596	0.3313
Glycosaminoglycan_biosynthesis-chondroitin_sulfate	0	0.0005199	1	1
MAPK_signaling_pathway	0	0.0005199	1	1
Focal_adhesion	0	0.0005199	1	1
Amyotrophic_lateral_sclerosis_(ALS)	0	0.0005199	1	1
Cytokine-cytokine_receptor_interaction	-0.0002935	0.001502	0.8451	0.8959
Axon_guidance	-0.01121	0.007749	0.1479	0.1993
RNA_transport	-0.01945	0.1448	0.8931	0.9366
Shigellosis	-0.04408	0.1784	0.8049	0.8579
Carotenoid_biosynthesis	-0.04571	0.07122	0.521	0.5876
Ascorbate_and_aldarate_metabolism	-0.05059	0.05622	0.3682	0.4436
Methane_metabolism	-0.0566	0.05255	0.2814	0.3522
Carbon_fixation_pathways_in_prokaryotes	-0.06605	0.04178	0.114	0.1626
Citrate_cycle_(TCA_cycle)	-0.07271	0.03949	0.06562	0.1079
Dorso-ventral_axis_formation	-0.07743	1.189	0.9481	0.9731
Tropane,piperidine_and_pyridine_alkaloid_biosynthesis	-0.07944	0.04451	0.07431	0.1163
Biosynthesis_of_12-,14-_and_16-membered_macrolides	-0.08728	0.08237	0.2893	0.3588
Sulfur_relay_system	-0.0905	0.05486	0.09898	0.1466
Oxidative_phosphorylation	-0.09357	0.04137	0.02372	0.04601
Histidine_metabolism	-0.1013	0.04533	0.02545	0.04888
Arginine_and_proline_metabolism	-0.1015	0.04564	0.0262	0.04934
Pyruvate_metabolism	-0.1019	0.04458	0.02228	0.04461
Cysteine_and_methionine_metabolism	-0.1045	0.06061	0.08466	0.1293
Biosynthesis_of_unsaturated_fatty_acids	-0.1072	0.06654	0.1071	0.1538
Salivary_secretion	-0.1111	1.121	0.9211	0.9607
Lysine_degradation	-0.1138	0.05223	0.02929	0.05361
Chloroalkane_and_chloroalkene_degradation	-0.1226	0.07141	0.08597	0.1303
Valine,leucine_and_isoleucine_biosynthesis	-0.1247	0.05504	0.02347	0.046
Terpenoid_backbone_biosynthesis	-0.1252	0.0546	0.02179	0.0445
Pantothenate_and_CoA_biosynthesis	-0.1347	0.0542	0.01296	0.02958
Alanine,aspartate_and_glutamate_metabolism	-0.139	0.05307	0.008816	0.02311
One_carbon_pool_by_folate	-0.1432	0.06175	0.02036	0.04203
Selenocompound_metabolism	-0.1516	0.05415	0.005129	0.01531
Lysine_biosynthesis	-0.1676	0.05843	0.004119	0.01382
Glycosylphosphatidylinositol(GPI)-anchor_biosynthesis	-0.1762	0.09943	0.07645	0.1186
Phosphotransferase_system_(PTS)	-0.1785	0.1934	0.3559	0.4315
Base_excision_repair	-0.1849	0.06563	0.004836	0.01466
Purine_metabolism	-0.1853	0.06681	0.005533	0.01602
Phenylalanine,tyrosine_and_tryptophan_biosynthesis	-0.1933	0.06451	0.002739	0.01213
Retinol_metabolism	-0.1987	0.0836	0.01744	0.03794
Glycine,serine_and_threonine_metabolism	-0.2009	0.06739	0.002868	0.01233
Lipoic_acid_metabolism	-0.2016	0.06291	0.00135	0.01162
Sulfur_metabolism	-0.2059	0.07203	0.004252	0.01398
Glycolysis/Gluconeogenesis	-0.2081	0.06819	0.002278	0.01163
Peptidoglycan_biosynthesis	-0.2082	0.07178	0.003725	0.01375

Fatty_acid_biosynthesis	-0.2093	0.06699	0.001781	0.01163
Glycerolipid_metabolism	-0.2107	0.06766	0.001845	0.01163
Protein_export	-0.2248	0.07809	0.00399	0.01382
Nicotinate_and_nicotinamide_metabolism	-0.2267	0.07342	0.002021	0.01163
Clavulanic_acid_biosynthesis	-0.2293	0.1205	0.05706	0.09544
D-Glutamine_and_D-glutamate_metabolism	-0.2318	0.08161	0.004507	0.01427
Pyrimidine_metabolism	-0.2366	0.07952	0.002925	0.01233
Alzheimers_disease	-0.2438	NA	NA	NA
D-Alanine_metabolism	-0.2443	0.08611	0.004561	0.01427
Aminoacyl-tRNA_biosynthesis	-0.2444	0.08066	0.002441	0.01188
Ribosome	-0.2453	0.08317	0.00318	0.01269
RNA_polymerase	-0.2474	0.07556	0.001058	0.01162
Mismatch_repair	-0.2492	0.07737	0.001277	0.01162
Vitamin_B6_metabolism	-0.2507	0.08186	0.002192	0.01163
Zeatin_biosynthesis	-0.2569	0.08717	0.003204	0.01269
Homologous_recombination	-0.2583	0.08238	0.001715	0.01163
Folate_biosynthesis	-0.2589	0.08647	0.002751	0.01213
RNA_degradation	-0.2608	0.08256	0.001581	0.01163
Nucleotide_excision_repair	-0.2656	0.08647	0.002131	0.01163
Bile_secretion	-0.2756	0.205	0.1787	0.2374
Porphyrin_and_chlorophyll_metabolism	-0.2807	0.08526	0.0009928	0.01162
Photosynthesis	-0.2841	0.09431	0.002589	0.01196
alpha-Linolenic_acid_metabolism	-0.2895	0.4343	0.5051	0.573
Linoleic_acid_metabolism	-0.2902	0.1301	0.02575	0.04898
Pentose_phosphate_pathway	-0.2905	0.09412	0.002026	0.01163
DNA_replication	-0.2924	0.08594	0.0006665	0.01162
Secondary_bile_acid_biosynthesis	-0.3044	0.3495	0.3838	0.454
Cell_cycle-Caulobacter	-0.3208	0.1047	0.002177	0.01163
D-Arginine_and_D-ornithine_metabolism	-0.3209	0.1524	0.03521	0.06324
ABC_transporters	-0.3219	0.1272	0.01136	0.02673
Adipocytokine_signaling_pathway	-0.3253	0.4189	0.4375	0.5052
Various_types_of_N-glycan_biosynthesis	-0.3419	0.1864	0.06664	0.1086
Carbon_fixation_in_photosynthetic_organisms	-0.3633	0.1049	0.0005358	0.01162
ECM-receptor_interaction	-0.3665	1.234	0.7665	0.8262
Drug_metabolism-other_enzymes	-0.3691	0.1178	0.001726	0.01163
Inositol_phosphate_metabolism	-0.3737	0.1297	0.003949	0.01382
Non-homologous_end-joining	-0.379	0.1594	0.01746	0.03794
Biosynthesis_of_vancomycin_group_antibiotics	-0.3923	0.1214	0.001227	0.01162
Fructose_and_mannose_metabolism	-0.4012	0.1263	0.001498	0.01162
Polycyclic_aromatic_hydrocarbon_degradation	-0.4146	0.1772	0.01932	0.0403
Amoebiasis	-0.4152	0.1774	0.01927	0.0403
Starch_and_sucrose_metabolism	-0.4228	0.1309	0.001239	0.01162
Thiamine_metabolism	-0.4242	0.1261	0.0007652	0.01162
Protein_processing_in_endoplasmic_reticulum	-0.4242	0.1186	0.0003489	0.01162
Atrazine_degradation	-0.4423	0.1731	0.01064	0.0258
Streptomycin_biosynthesis	-0.4429	0.1306	0.0006969	0.01162
Amino_sugar_and_nucleotide_sugar_metabolism	-0.4627	0.1428	0.001197	0.01162
Pentose_and_glucuronate_interconversions	-0.4758	0.1557	0.002246	0.01163
Systemic_lupus_erythematosus	-0.5205	0.446	0.2432	0.3146
PPAR_signaling_pathway	-0.522	0.4461	0.2419	0.3146
Parkinsons_disease	-0.541	0.5558	0.3304	0.4057
Olfactory_transduction	-0.5856	0.9589	0.5414	0.6071
Vasopressin-regulated_water_reabsorption	-0.6147	1.22	0.6145	0.6812
Biosynthesis_of_ansamycins	-0.6745	0.2098	0.001304	0.01162

Tetracycline_biosynthesis	-0.6831	NA	NA	NA
Bacterial_invasion_of_epithelial_cells	-0.7081	0.6698	0.2904	0.3588
Meiosis-yeast	-0.8331	0.3903	0.03281	0.05949
Galactose_metabolism	-0.8528	0.2822	0.00251	0.01188
Isoflavonoid_biosynthesis	-0.8923	0.6518	0.171	0.2288
Sphingolipid_metabolism	-0.8979	0.3027	0.003017	0.01245
N-Glycan_biosynthesis	-0.9023	0.3188	0.004659	0.01435
Spliceosome	-0.9211	0.515	0.0737	0.1162
Polyketide_sugar_unit_biosynthesis	-0.9395	0.2942	0.001406	0.01162
African_trypanosomiasis	-1.008	0.3813	0.008175	0.02234
Steroid_hormone_biosynthesis	-1.075	0.422	0.01085	0.026
Lysosome	-1.157	0.3448	0.0007895	0.01162
Protein_digestion_and_absorption	-1.243	0.391	0.001482	0.01162
Phenylpropanoid_biosynthesis	-1.277	0.6468	0.04834	0.08373
Pathogenic_Escherichia_coli_infection	-1.325	0.7886	0.09287	0.1397
Staphylococcus_aureus_infection	-1.345	0.4906	0.006112	0.01744
Naphthalene_degradation	-1.352	0.9209	0.142	0.1933
Endocytosis	-1.38	NA	NA	NA
Other_types_of_O-glycan_biosynthesis	-1.389	1.257	0.2689	0.3388
Xylene_degradation	-1.452	0.6069	0.01676	0.03738
Betalain_biosynthesis	-1.48	0.9179	0.107	0.1538
Other_glycan_degradation	-1.556	0.4681	0.0008847	0.01162
Glycosaminoglycan_degradation	-1.6	0.6246	0.01043	0.0258
Novobiocin_biosynthesis	-1.625	0.7132	0.02271	0.04495
Photosynthesis-antenna_proteins	-1.644	0.4083	5.67E-05	0.007243
Vibrio_cholerae_infection	-1.673	0.8278	0.04321	0.07621
Biosynthesis_of_type_II_polyketide_products	-1.711	0.6633	0.009906	0.02529
Indole_alkaloid_biosynthesis	-1.731	0.522	0.0009114	0.01162
Proteasome	-1.857	0.8395	0.02692	0.05022
Neuroactive_ligand-receptor_interaction	-1.914	NA	NA	NA
Wnt_signaling_pathway	-1.992	0.8056	0.0134	0.03023
Arachidonic_acid_metabolism	-2.127	1.148	0.06389	0.1059
Cell_cycle	-2.284	0.9146	0.01253	0.02894
Biosynthesis_of_type_II_polyketide_backbone	-2.477	0.8546	0.003757	0.01375
Sesquiterpenoid_biosynthesis	-2.497	0.9479	0.008429	0.02263
Basal_transcription_factors	-2.707	NA	NA	NA
mRNA_surveillance_pathway	-2.776	0.7008	7.47E-05	0.007243
Glycosphingolipid_biosynthesis-lacto_and_neolacto_series	-3.308	1.408	0.01876	0.03999
Butirosin_and_neomycin_biosynthesis	-3.339	1.092	0.002235	0.01163

Table S34 The P values of the metabolic pathways of microbes in oral mucosal samples.

	logFC	se	pvalues	adjPvalues
Malaria	1.753	0.8444	0.03787	0.7461
Photosynthesis-antenna_proteins	0.9217	0.5687	0.1051	0.9933
Steroid_biosynthesis	0.7168	1.279	0.5751	1
Various_types_of_N-glycan_biosynthesis	0.4248	1.115	0.7032	1
Apoptosis	0.4139	0.7357	0.5737	1
Protein_digestion_and_absorption	0.3506	0.8941	0.6949	1
Nitrotoluene_degradation	0.2698	0.5331	0.6128	1
NOD-like_receptor_signaling_pathway	0.1728	0.6876	0.8016	1
Bacterial_invasion_of_epithelial_cells	0.1658	0.6793	0.8072	1
Endocytosis	0.1276	1.502	0.9323	1
Glycosaminoglycan_degradation	0.1276	0.4888	0.7941	1
Steroid_hormone_biosynthesis	0.1055	1.1	0.9236	1
Wnt_signaling_pathway	0.1002	1.592	0.9498	1
Penicillin_and_cephalosporin_biosynthesis	0.08479	0.6907	0.9023	1
Ethylbenzene_degradation	0.06694	0.2228	0.7638	1
Amoebiasis	0.06501	0.7905	0.9345	1
Lysosome	0.06284	0.4321	0.8844	1
Protein_processing_in_endoplasmic_reticulum	0.04513	0.6078	0.9408	1
beta-Alanine_metabolism	0.04139	0.2428	0.8647	1
Other_glycan_degradation	0.04036	0.4378	0.9265	1
Focal_adhesion	0.03765	0.05068	0.4576	1
beta-Lactam_resistance	0.02825	0.7795	0.9711	1
Geraniol_degradation	0.01604	0.9058	0.9859	1
Pathogenic_Escherichia_coli_infection	0.009717	0.009336	0.2979	1
Epithelial_cell_signaling_in_Helicobacter_pylori_infection	0.008096	0.3024	0.9786	1
Clavulanic_acid_biosynthesis	0	0.0001204	1	1
Novobiocin_biosynthesis	0	0.0001204	1	1
Glycosaminoglycan_biosynthesis-chondroitin_sulfate	0	0.0001204	1	1
alpha-Linolenic_acid_metabolism	0	0.0001204	1	1
Glycosphingolipid_biosynthesis-lacto_and_neolacto_series	0	0.0001204	1	1
Naphthalene_degradation	0	0.0001204	1	1
Brassinosteroid_biosynthesis	0	0.0001204	1	1
Phenylpropanoid_biosynthesis	0	0.0001204	1	1
PPAR_signaling_pathway	0	0.0001204	1	1
MAPK_signaling_pathway	0	0.0001204	1	1
Cytokine-cytokine_receptor_interaction	0	0.0001204	1	1
Cell_cycle	0	0.0001204	1	1
Axon_guidance	0	0.0001204	1	1
Circadian_rhythm-plant	0	0.0001204	1	1
Olfactory_transduction	0	0.0001204	1	1
Adipocytokine_signaling_pathway	0	0.0001204	1	1
Salivary_secretion	0	0.0001204	1	1
Bile_secretion	0	0.0001204	1	1
Parkinsons_disease	0	0.0001204	1	1
Amyotrophic_lateral_sclerosis_(ALS)	0	0.0001204	1	1
Huntingtons_disease	0	0.0001204	1	1
Sphingolipid_metabolism	-0.0009259	0.4276	0.9983	1
Dorso-ventral_axis_formation	-0.002574	0.005225	0.6223	1
Synthesis_and_degradation_of_ketone_bodies	-0.01311	0.2731	0.9617	1
N-Glycan_biosynthesis	-0.0134	0.6113	0.9825	1
Phagosome	-0.01721	0.01415	0.224	1
Flagellar_assembly	-0.01871	0.7083	0.9789	1

Aminobenzoate_degradation	-0.02114	0.181	0.907	1
Benzoate_degradation	-0.02136	0.2099	0.919	1
Taurine_and_hypotaurine_metabolism	-0.03729	0.1978	0.8504	1
Cell_cycle-yeast	-0.04274	0.06183	0.4895	1
Bacterial_chemotaxis	-0.04906	0.5583	0.93	1
Linoleic_acid_metabolism	-0.04932	0.5172	0.924	1
Lipopolysaccharide_biosynthesis	-0.04971	0.4883	0.9189	1
Zeatin_biosynthesis	-0.05935	0.2853	0.8352	1
Dioxin_degradation	-0.06422	0.4295	0.8811	1
Riboflavin_metabolism	-0.06993	0.3146	0.8241	1
Phosphonate_and_phosphinate_metabolism	-0.07382	0.2608	0.7771	1
Hypertrophic_cardiomyopathy_(HCM)	-0.07735	0.417	0.8528	1
Galactose_metabolism	-0.0787	0.369	0.8311	1
Carbon_fixation_pathways_in_prokaryotes	-0.0803	0.1706	0.6379	1
Tropane,piperidine_and_pyridine_alkaloid_biosynthesis	-0.08095	0.1892	0.6687	1
Fluorobenzoate_degradation	-0.08135	1.164	0.9443	1
Valine,leucine_and_isoleucine_degradation	-0.08535	0.1635	0.6017	1
ECM-receptor_interaction	-0.0871	0.1925	0.6509	1
Staphylococcus_aureus_infection	-0.08829	0.7855	0.9105	1
Folate_biosynthesis	-0.09208	0.2467	0.709	1
Biotin_metabolism	-0.0923	0.2744	0.7366	1
RNA_polymerase	-0.09313	0.2212	0.6737	1
Two-component_system	-0.09399	0.1403	0.5028	1
Flavonoid_biosynthesis	-0.09408	0.8486	0.9117	1
Peptidoglycan_biosynthesis	-0.09439	0.25	0.7057	1
Biosynthesis_of_12-,14-_and_16-membered_macrolides	-0.09463	0.03461	0.006251	0.2463
Propanoate_metabolism	-0.09682	0.1192	0.4167	1
Shigellosis	-0.09697	0.05362	0.07051	0.9633
Alanine,aspartate_and_glutamate_metabolism	-0.09769	0.1883	0.6038	1
Cysteine_and_methionine_metabolism	-0.0988	0.2245	0.6598	1
Primary_bile_acid_biosynthesis	-0.09959	0.6829	0.8841	1
Phenylalanine,tyrosine_and_tryptophan_biosynthesis	-0.09981	0.2201	0.6501	1
RNA_transport	-0.101	0.3392	0.766	1
One_carbon_pool_by_folate	-0.102	0.2319	0.6602	1
Vitamin_B6_metabolism	-0.1023	0.2182	0.6391	1
Pyrimidine_metabolism	-0.1037	0.2454	0.6727	1
Caprolactam_degradation	-0.1048	0.994	0.916	1
Pantothenate_and_CoA_biosynthesis	-0.1057	0.199	0.5951	1
Terpenoid_backbone_biosynthesis	-0.107	0.2209	0.6279	1
Streptomycin_biosynthesis	-0.1073	0.2266	0.6358	1
Butanoate_metabolism	-0.1078	0.1391	0.4383	1
Ascorbate_and_aldarate_metabolism	-0.1095	0.2388	0.6465	1
Lysine_degradation	-0.1096	0.1876	0.5589	1
Thiamine_metabolism	-0.1105	0.2631	0.6747	1
Porphyrin_and_chlorophyll_metabolism	-0.1121	0.3074	0.7154	1
Nicotinate_and_nicotinamide_metabolism	-0.1122	0.1963	0.5676	1
Fatty_acid_biosynthesis	-0.1122	0.215	0.6017	1
D-Arginine_and_D-ornithine_metabolism	-0.1132	0.7618	0.8819	1
Fatty_acid_metabolism	-0.1136	0.1429	0.4265	1
Drug_metabolism-other_enzymes	-0.117	0.278	0.6739	1
Cell_cycle-Caulobacter	-0.1178	0.2132	0.5806	1
Aminoacyl-tRNA_biosynthesis	-0.118	0.2351	0.6158	1
Ribosome	-0.118	0.2461	0.6317	1
D-Alanine_metabolism	-0.1189	0.2582	0.645	1

Mismatch_repair	-0.12	0.2359	0.6108	1
D-Glutamine_and_D-glutamate_metabolism	-0.1211	0.2453	0.6216	1
Photosynthesis	-0.1211	0.2416	0.6161	1
Tryptophan_metabolism	-0.1213	0.193	0.5296	1
C5-Branched_dibasic_acid_metabolism	-0.1215	0.1905	0.5236	1
Arginine_and_proline_metabolism	-0.1219	0.1187	0.3044	1
Lysine_biosynthesis	-0.1224	0.2129	0.5656	1
Phenylalanine_metabolism	-0.1236	0.3895	0.751	1
Glyoxylate_and_dicarboxylate_metabolism	-0.1238	0.1396	0.3751	1
Valine,leucine_and_isoleucine_biosynthesis	-0.1254	0.1902	0.5096	1
Retinol_metabolism	-0.1257	0.342	0.7133	1
Purine_metabolism	-0.1287	0.2224	0.5627	1
Homologous_recombination	-0.1291	0.2396	0.5901	1
Carbon_fixation_in_photosynthetic_organisms	-0.1315	0.2267	0.5618	1
Glutathione_metabolism	-0.1318	0.1432	0.3574	1
DNA_replication	-0.1321	0.2331	0.5711	1
Glycine,serine_and_threonine_metabolism	-0.1322	0.1729	0.4444	1
Biosynthesis_of_ansamycins	-0.1334	0.2663	0.6164	1
Nucleotide_excision_repair	-0.135	0.2346	0.5648	1
Bacterial_secretion_system	-0.1353	0.1575	0.3903	1
Vibrio_cholerae_pathogenic_cycle	-0.1385	0.2411	0.5657	1
Methane_metabolism	-0.1408	0.1881	0.4542	1
Protein_export	-0.1427	0.2238	0.5237	1
Oxidative_phosphorylation	-0.1429	0.1787	0.4241	1
Citrate_cycle_(TCA_cycle)	-0.144	0.2051	0.4828	1
Histidine_metabolism	-0.144	0.3115	0.6439	1
Selenocompound_metabolism	-0.1441	0.1688	0.3933	1
Amino_sugar_and_nucleotide_sugar_metabolism	-0.1469	0.2875	0.6095	1
Tyrosine_metabolism	-0.1477	0.1527	0.3334	1
Peroxisome	-0.1488	0.1594	0.3506	1
Indole_alkaloid_biosynthesis	-0.151	0.2204	0.4933	1
Base_excision_repair	-0.154	0.2216	0.487	1
Pentose_phosphate_pathway	-0.1545	0.2309	0.5033	1
Nitrogen_metabolism	-0.1559	0.1948	0.4235	1
Starch_and_sucrose_metabolism	-0.1588	0.2727	0.5604	1
Pyruvate_metabolism	-0.1616	0.1881	0.3902	1
Glycolysis/Gluconeogenesis	-0.163	0.2275	0.4736	1
Fructose_and_mannose_metabolism	-0.1647	0.2936	0.5749	1
Plant-pathogen_interaction	-0.1671	0.1818	0.3581	1
RNA_degradation	-0.1682	0.2028	0.4071	1
Glycerolipid_metabolism	-0.1703	0.1711	0.3195	1
Ubiquinone_and_other_terpenoid-quinone_biosynthesis	-0.1764	0.3264	0.5888	1
Lipoic_acid_metabolism	-0.1774	0.2536	0.4842	1
Chloroalkane_and_chloroalkene_degradation	-0.1791	0.1923	0.3517	1
Sulfur_metabolism	-0.1859	0.1852	0.3156	1
Biosynthesis_of_vancomycin_group_antibiotics	-0.1869	0.2627	0.4769	1
Ribosome_biogenesis_in_eukaryotes	-0.1896	0.2327	0.4151	1
Non-homologous_end-joining	-0.1897	1.21	0.8754	1
Glycerophospholipid_metabolism	-0.1923	0.197	0.3288	1
Biosynthesis_of_unsaturated_fatty_acids	-0.1971	0.1363	0.1482	1
Metabolism_of_xenobiotics_by_cytochrome_P450	-0.2	0.1561	0.2002	1
Styrene_degradation	-0.2016	0.7096	0.7763	1
Phosphotransferase_system_(PTS)	-0.2022	0.4289	0.6374	1
Insulin_signaling_pathway	-0.2053	0.2601	0.43	1

Toluene_degradation	-0.2078	0.346	0.5482	1
Basal_transcription_factors	-0.2232	0.1136	0.04951	0.8128
Biosynthesis_of_siderophore_group_nonribosomal_peptides	-0.2257	0.5385	0.6751	1
Pentose_and_glucuronate_interconversions	-0.2333	0.1327	0.07881	0.9633
Inositol_phosphate_metabolism	-0.239	0.1402	0.08817	0.965
ABC_transporters	-0.2413	0.1439	0.09358	0.9703
Sulfur_relay_system	-0.2586	0.197	0.1892	1
Xylene_degradation	-0.2598	0.5282	0.6228	1
Cyanoamino_acid_metabolism	-0.2744	NA	NA	NA
Carotenoid_biosynthesis	-0.2748	0.9207	0.7654	1
Renin-angiotensin_system	-0.3486	0.2758	0.2062	1
Chlorocyclohexane_and_chlorobenzene_degradation	-0.3647	0.5752	0.5261	1
Polycyclic_aromatic_hydrocarbon_degradation	-0.3809	0.8248	0.6442	1
Pathways_in_cancer	-0.3907	0.4909	0.4261	1
Butirosin_and_neomycin_biosynthesis	-0.4577	0.6014	0.4467	1
Secondary_bile_acid_biosynthesis	-0.543	0.6654	0.4145	1
Vibrio_cholerae_infection	-0.5475	1.463	0.7081	1
mRNA_surveillance_pathway	-0.5562	0.321	0.08313	0.9633
Bisphenol_degradation	-0.5934	0.4544	0.1916	1
Spliceosome	-0.5984	0.9937	0.5471	1
Limonene_and_pinene_degradation	-0.6059	0.2518	0.0161	0.3523
Other_types_of_O-glycan_biosynthesis	-0.6137	NA	NA	NA
Glycosylphosphatidylinositol(GPI)-anchor_biosynthesis	-0.619	0.524	0.2375	1
African_trypanosomiasis	-0.647	0.5226	0.2157	1
Systemic_lupus_erythematosus	-0.7014	1.552	0.6514	1
Meiosis-yeast	-0.7014	0.5456	0.1986	1
Atrazine_degradation	-0.7228	0.2805	0.00997	0.2806
Proteasome	-0.8316	0.787	0.2907	1
Isoflavonoid_biosynthesis	-0.949	1.018	0.351	1
Vasopressin-regulated_water_reabsorption	-1.163	0.6651	0.08047	0.9633
Biosynthesis_of_type_II_polyketide_products	-1.272	0.4195	0.00243	0.1197
Arachidonic_acid_metabolism	-1.281	0.7923	0.1059	0.9933
Polyketide_sugar_unit_biosynthesis	-1.995	1.05	0.05744	0.8704
Biosynthesis_of_type_II_polyketide_backbone	-2.064	0.6341	0.001135	0.07453
Betalain_biosynthesis	-2.153	0.3803	1.52E-08	2.99E-06
Neuroactive_ligand-receptor_interaction	-2.208	1.121	0.0489	0.8128
Alzheimers_disease	-2.468	0.9518	0.009521	0.2806
Sesquiterpenoid_biosynthesis	-2.471	0.7455	0.0009175	0.07453
Tetracycline_biosynthesis	-3.259	1.298	0.01207	0.2971

Table S35 The P values of metabolic pathways of microbes in saliva samples.

	logFC	se	pvalues	adjPvalues
Photosynthesis-antenna_proteins	1.228	0.9591	0.2006	1
Hypertrophic_cardiomyopathy_(HCM)	0.9039	0.4284	0.03486	0.8304
Steroid_hormone_biosynthesis	0.507	0.8925	0.57	1
Protein_digestion_and_absorption	0.4341	0.6935	0.5313	1
Fluorobenzoate_degradation	0.3966	0.3482	0.2547	1
Apoptosis	0.3965	0.589	0.5009	1
Amoebiasis	0.3726	0.6813	0.5844	1
D-Arginine_and_D-ornithine_metabolism	0.3173	0.8264	0.701	1
Nitrotoluene_degradation	0.3024	0.5046	0.549	1
Glycosaminoglycan_degradation	0.2576	0.3768	0.4943	1
Bacterial_invasion_of_epithelial_cells	0.2546	0.5824	0.6619	1
Various_types_of_N-glycan_biosynthesis	0.2356	0.1011	0.01983	0.5637
Protein_processing_in_endoplasmic_reticulum	0.2356	0.4471	0.5983	1
Other_glycan_degradation	0.2335	0.3353	0.4861	1
Sphingolipid_metabolism	0.1883	0.3506	0.5912	1
Vasopressin-regulated_water_reabsorption	0.1839	0.59	0.7552	1
Geraniol_degradation	0.1667	0.836	0.8419	1
Flagellar_assembly	0.1653	0.5428	0.7607	1
Lysosome	0.1639	0.1379	0.2346	1
NOD-like_receptor_signaling_pathway	0.1572	0.5141	0.7597	1
Steroid_biosynthesis	0.1532	1.093	0.8885	1
Flavonoid_biosynthesis	0.1381	0.8321	0.8682	1
Lipopolysaccharide_biosynthesis	0.1201	0.4651	0.7963	1
beta-Alanine_metabolism	0.113	0.2305	0.624	1
Epithelial_cell_signaling_in_Helicobacter_pylori_infection	0.07623	0.1967	0.6984	1
Tropane,piperidine_and_pyridine_alkaloid_biosynthesis	0.07249	0.207	0.7262	1
Renin-angiotensin_system	0.04929	0.1364	0.7178	1
Metabolism_of_xenobiotics_by_cytochrome_P450	0.03631	0.2291	0.8741	1
Zeatin_biosynthesis	0.03436	0.2342	0.8834	1
Bacterial_chemotaxis	0.02996	0.4731	0.9495	1
Benzoate_degradation	0.02527	0.2748	0.9267	1
Penicillin_and_cephalosporin_biosynthesis	0.01481	0.5326	0.9778	1
Galactose_metabolism	0.01105	0.2929	0.9699	1
RNA_polymerase	0.008966	0.1719	0.9584	1
Drug_metabolism-other_enzymes	0.004108	0.2274	0.9856	1
Folate_biosynthesis	0.0003215	0.1704	0.9985	1
Clavulanic_acid_biosynthesis	0	0.0001375	1	1
Novobiocin_biosynthesis	0	0.0001375	1	1
Biosynthesis_of_12-,14-_and_16-membered_macrolides	0	0.0001375	1	1
Butirosin_and_neomycin_biosynthesis	0	0.0001375	1	1
Arachidonic_acid_metabolism	0	0.0001375	1	1
alpha-Linolenic_acid_metabolism	0	0.0001375	1	1
Naphthalene_degradation	0	0.0001375	1	1
Brassinosteroid_biosynthesis	0	0.0001375	1	1
Phenylpropanoid_biosynthesis	0	0.0001375	1	1
PPAR_signaling_pathway	0	0.0001375	1	1
MAPK_signaling_pathway	0	0.0001375	1	1
Cytokine-cytokine_receptor_interaction	0	0.0001375	1	1
Cell_cycle	0	0.0001375	1	1
Axon_guidance	0	0.0001375	1	1
Circadian_rhythm-plant	0	0.0001375	1	1
Olfactory_transduction	0	0.0001375	1	1

Adipocytokine_signaling_pathway	0	0.0001375	1	1
Salivary_secretion	0	0.0001375	1	1
Bile_secretion	0	0.0001375	1	1
Parkinsons_disease	0	0.0001375	1	1
Amyotrophic_lateral_sclerosis_(ALS)	0	0.0001375	1	1
Huntingtons_disease	0	0.0001375	1	1
Pathogenic_Escherichia_coli_infection	0	0.0001375	1	1
Wnt_signaling_pathway	-0.0009433	0.01827	0.9588	1
Glycosphingolipid_biosynthesis-lacto_and_neolacto_series	-0.001866	0.001537	0.2248	1
Vitamin_B6_metabolism	-0.004394	0.1448	0.9758	1
Taurine_and_hypotaurine_metabolism	-0.004601	0.1526	0.9759	1
Retinol_metabolism	-0.004842	0.331	0.9883	1
Glycosaminoglycan_biosynthesis-chondroitin_sulfate	-0.005089	0.006488	0.4328	1
Dorso-ventral_axis_formation	-0.00521	0.04957	0.9163	1
Streptomycin_biosynthesis	-0.005402	0.1543	0.9721	1
Neuroactive_ligand-receptor_interaction	-0.007023	0.003934	0.07421	0.9631
Peptidoglycan_biosynthesis	-0.0136	0.188	0.9424	1
Glyoxylate_and_dicarboxylate_metabolism	-0.01376	0.1275	0.914	1
Carbon_fixation_pathways_in_prokaryotes	-0.014	0.159	0.9298	1
mRNA_surveillance_pathway	-0.01747	0.04563	0.7019	1
Phagosome	-0.02251	0.02395	0.3472	1
Riboflavin_metabolism	-0.02363	0.2835	0.9336	1
Alanine,aspartate_and_glutamate_metabolism	-0.02421	0.1458	0.8681	1
Lysine_degradation	-0.02452	0.2431	0.9196	1
Caprolactam_degradation	-0.02528	1.037	0.9805	1
N-Glycan_biosynthesis	-0.02576	0.4007	0.9488	1
Malaria	-0.02665	0.01141	0.01949	0.5637
Shigellosis	-0.027	0.02599	0.2988	1
Pyrimidine_metabolism	-0.02998	0.1977	0.8794	1
Cysteine_and_methionine_metabolism	-0.03043	0.1687	0.8569	1
Carbon_fixation_in_photosynthetic_organisms	-0.0361	0.1976	0.855	1
Pantothenate_and_CoA_biosynthesis	-0.03755	0.1789	0.8338	1
Phenylalanine,tyrosine_and_tryptophan_biosynthesis	-0.03854	0.1756	0.8263	1
Thiamine_metabolism	-0.0405	0.1983	0.8382	1
Mismatch_repair	-0.04079	0.1781	0.8188	1
Biotin_metabolism	-0.04188	0.2691	0.8764	1
One_carbon_pool_by_folate	-0.04231	0.1669	0.7998	1
Nicotinate_and_nicotinamide_metabolism	-0.04291	0.1598	0.7883	1
RNA_transport	-0.04373	0.2377	0.854	1
Cell_cycle-Caulobacter	-0.0439	0.1603	0.7842	1
beta-Lactam_resistance	-0.04479	0.5765	0.9381	1
Synthesis_and_degradation_of_ketone_bodies	-0.04737	0.3251	0.8842	1
Phenylalanine_metabolism	-0.04788	0.2833	0.8658	1
Arginine_and_proline_metabolism	-0.04819	0.09369	0.607	1
Ribosome	-0.04922	0.2009	0.8065	1
D-Glutamine_and_D-glutamate_metabolism	-0.05002	0.2001	0.8026	1
Terpenoid_backbone_biosynthesis	-0.05176	0.1704	0.7614	1
Fatty_acid_biosynthesis	-0.05323	0.1675	0.7506	1
Linoleic_acid_metabolism	-0.05441	0.3625	0.8807	1
Photosynthesis	-0.05509	0.2145	0.7973	1
Homologous_recombination	-0.05582	0.1869	0.7652	1
Starch_and_sucrose_metabolism	-0.05586	0.1916	0.7706	1
Propanoate_metabolism	-0.05667	0.1103	0.6074	1
Amino_sugar_and_nucleotide_sugar_metabolism	-0.05758	0.2196	0.7932	1

Aminoacyl-tRNA_biosynthesis	-0.05814	0.1937	0.7641	1
DNA_replication	-0.05853	0.1875	0.755	1
ECM-receptor_interaction	-0.06177	0.06195	0.3187	1
Porphyrin_and_chlorophyll_metabolism	-0.06275	0.273	0.8182	1
Lysine_biosynthesis	-0.06318	0.1739	0.7163	1
Nucleotide_excision_repair	-0.06513	0.2013	0.7462	1
D-Alanine_metabolism	-0.06664	0.207	0.7475	1
Purine_metabolism	-0.07023	0.168	0.6759	1
Glycine,serine_and_threonine_metabolism	-0.07132	0.1127	0.5269	1
Biosynthesis_of_ansamycins	-0.07284	0.2314	0.7529	1
Valine,leucine_and_isoleucine_biosynthesis	-0.07346	0.1747	0.6741	1
Selenocompound_metabolism	-0.0747	0.1273	0.5575	1
Fatty_acid_metabolism	-0.07714	0.1384	0.5774	1
Valine,leucine_and_isoleucine_degradation	-0.07761	0.1463	0.5957	1
Basal_transcription_factors	-0.08255	0.0624	0.1858	1
Protein_export	-0.08525	0.1863	0.6472	1
Aminobenzoate_degradation	-0.08536	0.2441	0.7266	1
Staphylococcus_aureus_infection	-0.0855	0.5731	0.8814	1
Pentose_and_glucuronate_interconversions	-0.08633	0.1426	0.545	1
Butanoate_metabolism	-0.08656	0.1255	0.4903	1
Glycosylphosphatidylinositol(GPI)-anchor_biosynthesis	-0.09128	0.3945	0.817	1
Biosynthesis_of_vancomycin_group_antibiotics	-0.09293	0.1924	0.6291	1
Pentose_phosphate_pathway	-0.09624	0.1674	0.5653	1
Oxidative_phosphorylation	-0.09764	0.1486	0.5112	1
Histidine_metabolism	-0.09895	0.2491	0.6913	1
Citrate_cycle_(TCA_cycle)	-0.0994	0.1976	0.615	1
Two-component_system	-0.1006	0.1531	0.5108	1
Ascorbate_and_aldarate_metabolism	-0.1013	0.2474	0.6823	1
C5-Branched_dibasic_acid_metabolism	-0.1024	0.2053	0.618	1
Base_excision_repair	-0.1051	0.1716	0.5402	1
Vibrio_cholerae_pathogenic_cycle	-0.1064	0.1475	0.4706	1
Methane_metabolism	-0.1073	0.1601	0.5026	1
RNA_degradation	-0.111	0.163	0.4959	1
Bacterial_secretion_system	-0.1113	0.09902	0.2609	1
Glutathione_metabolism	-0.114	0.1044	0.275	1
Sulfur_metabolism	-0.1153	0.1207	0.3394	1
Glycerolipid_metabolism	-0.1158	0.1475	0.4326	1
Glycolysis/Gluconeogenesis	-0.116	0.1949	0.5516	1
Tyrosine_metabolism	-0.1168	0.1017	0.2506	1
Fructose_and_mannose_metabolism	-0.1168	0.2112	0.5801	1
Non-homologous_end-joining	-0.1189	1.087	0.9129	1
Peroxisome	-0.1191	0.1347	0.3766	1
Nitrogen_metabolism	-0.1193	0.1494	0.4246	1
Cell_cycle-yeast	-0.1214	0.09632	0.2074	1
Plant-pathogen_interaction	-0.1242	0.1537	0.4192	1
Pyruvate_metabolism	-0.1263	0.1575	0.4226	1
Dioxin_degradation	-0.1267	0.1487	0.3941	1
Chloroalkane_and_chloroalkene_degradation	-0.1353	0.2114	0.5222	1
Focal_adhesion	-0.1371	0.08653	0.113	1
Tryptophan_metabolism	-0.1396	0.2065	0.4989	1
Insulin_signaling_pathway	-0.1404	0.1956	0.473	1
Phosphonate_and_phosphinate_metabolism	-0.1423	0.2566	0.5792	1
Pathways_in_cancer	-0.1426	0.2932	0.6268	1
Glycerophospholipid_metabolism	-0.1507	0.144	0.2955	1

Biosynthesis_of_unsaturated_fatty_acids	-0.159	0.1153	0.1681	1
Inositol_phosphate_metabolism	-0.1596	0.1228	0.1939	1
Ribosome_biogenesis_in_eukaryotes	-0.1695	0.15	0.2583	1
Toluene_degradation	-0.1854	0.3039	0.5418	1
Spliceosome	-0.1874	0.6974	0.7882	1
Lipoic_acid_metabolism	-0.2019	0.2122	0.3414	1
Chlorocyclohexane_and_chlorobenzene_degradation	-0.2055	0.4584	0.6539	1
ABC_transporters	-0.207	0.1215	0.08856	1
Ubiquinone_and_other_terpenoid-quinone_biosynthesis	-0.2099	0.2908	0.4703	1
Carotenoid_biosynthesis	-0.217	0.96	0.8212	1
Isoflavonoid_biosynthesis	-0.236	0.4362	0.5885	1
Sulfur_relay_system	-0.2394	0.1356	0.07744	0.9631
Phosphotransferase_system_(PTS)	-0.2711	0.426	0.5246	1
Xylene_degradation	-0.2759	0.1986	0.1648	1
Sesquiterpenoid_biosynthesis	-0.2946	0.1451	0.0423	0.8304
Ethylbenzene_degradation	-0.3145	0.1629	0.05352	0.8304
Styrene_degradation	-0.3599	0.5002	0.4718	1
Polyketide_sugar_unit_biosynthesis	-0.36	0.8536	0.6732	1
Vibrio_cholerae_infection	-0.3735	1.526	0.8067	1
Alzheimers_disease	-0.4029	0.5491	0.4631	1
Biosynthesis_of_siderophore_group_nonribosomal_peptides	-0.4263	0.5551	0.4425	1
Endocytosis	-0.4519	1.675	0.7873	1
Tetracycline_biosynthesis	-0.4792	0.4612	0.2988	1
Systemic_lupus_erythematosus	-0.4826	1.462	0.7413	1
Indole_alkaloid_biosynthesis	-0.5251	0.2536	0.03842	0.8304
Biosynthesis_of_type_II_polyketide_backbone	-0.605	0.2398	0.01165	0.5637
Polycyclic_aromatic_hydrocarbon_degradation	-0.6598	0.788	0.4024	1
Meiosis-yeast	-0.6609	0.6649	0.3203	1
African_trypanosomiasis	-0.725	0.5743	0.2068	1
Proteasome	-0.7625	0.8315	0.3591	1
Primary_bile_acid_biosynthesis	-0.8599	0.5918	0.1462	1
Atrazine_degradation	-0.8638	0.4401	0.04965	0.8304
Cyanoamino_acid_metabolism	-0.9648	0.3596	0.007297	0.484
Secondary_bile_acid_biosynthesis	-1.137	0.5909	0.05425	0.8304
Bisphenol_degradation	-1.152	0.6515	0.0771	0.9631
Other_types_of_O-glycan_biosynthesis	-1.327	0.9907	0.1805	1
Biosynthesis_of_type_II_polyketide_products	-1.375	0.586	0.01892	0.5637
Limonene_and_pinene_degradation	-1.578	0.4778	0.0009543	0.09495
Betalain_biosynthesis	-2.249	0.6342	0.0003904	0.0777

Table S36 The P values of metabolic pathways of microbes in urine samples.

	logFC	se	pvalues	adjPvalues
Steroid_biosynthesis	1.38	0.5922	0.01976	0.19
Renin-angiotensin_system	1.301	0.5722	0.02302	0.19
Flavonoid_biosynthesis	1.112	0.5135	0.03033	0.19
Ethylbenzene_degradation	0.9097	0.3391	0.007307	0.1285
Malaria	0.8881	0.5728	0.121	0.2849
Penicillin_and_cephalosporin_biosynthesis	0.869	0.3528	0.01378	0.19
Amyotrophic_lateral_sclerosis_(ALS)	0.8614	0.8719	0.3232	0.5313
beta-Lactam_resistance	0.8519	0.3712	0.02173	0.19
Nitrotoluene_degradation	0.8502	0.4274	0.04667	0.2142
Fluorobenzoate_degradation	0.8104	0.4352	0.06258	0.2434
Hypertrophic_cardiomyopathy_(HCM)	0.7814	0.2712	0.003953	0.1084
Bacterial_chemotaxis	0.6461	0.4039	0.1097	0.27
Geraniol_degradation	0.6373	0.4055	0.1161	0.2796
Styrene_degradation	0.5503	0.2591	0.03364	0.19
beta-Alanine_metabolism	0.4905	0.3744	0.1901	0.3729
Aminobenzoate_degradation	0.4457	0.2343	0.05712	0.2339
Apoptosis	0.426	0.3987	0.2854	0.5027
Chlorocyclohexane_and_chlorobenzene_degradation	0.4096	0.2515	0.1033	0.2695
Phosphonate_and_phosphinate_metabolism	0.3935	0.2886	0.1726	0.3564
Limonene_and_pinene_degradation	0.3625	0.2084	0.08198	0.2489
Taurine_and_hypotaurine_metabolism	0.3554	0.2902	0.2208	0.4076
Caprolactam_degradation	0.3539	0.3964	0.372	0.5854
Biosynthesis_of_siderophore_group_nonribosomal_peptides	0.3375	0.503	0.5023	0.6973
Insulin_signaling_pathway	0.3302	0.3191	0.3007	0.5178
Benzoate_degradation	0.3287	0.1454	0.02375	0.19
Flagellar_assembly	0.3195	0.3928	0.4161	0.6241
Metabolism_of_xenobiotics_by_cytochrome_P450	0.317	0.3675	0.3885	0.6015
Bisphenol_degradation	0.316	0.3638	0.3851	0.6011
Arachidonic_acid_metabolism	0.3063	0.7543	0.6847	0.8481
Fatty_acid_metabolism	0.2952	0.1477	0.04556	0.2142
Two-component_system	0.2858	0.1555	0.06615	0.2434
C5-Branched_dibasic_acid_metabolism	0.2788	0.1776	0.1165	0.2796
Biotin_metabolism	0.2726	0.1929	0.1576	0.3346
Phenylalanine_metabolism	0.2678	0.2127	0.208	0.3878
Lipopolysaccharide_biosynthesis	0.2667	0.381	0.484	0.6832
Carotenoid_biosynthesis	0.2578	0.3865	0.5048	0.6973
Vibrio_cholerae_pathogenic_cycle	0.2515	0.2967	0.3967	0.6044
Peroxisome	0.2454	0.1123	0.02896	0.19
Tyrosine_metabolism	0.2056	0.09915	0.03812	0.1926
NOD-like_receptor_signaling_pathway	0.1981	0.456	0.6639	0.8334
Synthesis_and_degradation_of_ketone_bodies	0.1889	0.1492	0.2054	0.3866
Tryptophan_metabolism	0.1836	0.1245	0.1402	0.3131
Pathways_in_cancer	0.1794	0.5772	0.7559	0.8849
Shigellosis	0.1783	0.174	0.3056	0.5178
Glyoxylate_and_dicarboxylate_metabolism	0.1726	0.1281	0.1781	0.3637
Histidine_metabolism	0.1701	0.3275	0.6035	0.8016
Tropane,piperidine_and_pyridine_alkaloid_biosynthesis	0.1679	0.3615	0.6424	0.8222
Valine,leucine_and_isoleucine_degradation	0.1668	0.1313	0.204	0.3866
Ubiquinone_and_other_terpenoid-quinone_biosynthesis	0.158	0.2006	0.4309	0.6315
Epithelial_cell_signaling_in_Helicobacter_pylori_infection	0.1292	0.3796	0.7336	0.8749

Propanoate_metabolism	0.1073	0.1052	0.3074	0.5178
Butanoate_metabolism	0.106	0.1142	0.3532	0.5605
Lysine_degradation	0.09435	0.1936	0.6261	0.8177
Nitrogen_metabolism	0.0917	0.1279	0.4735	0.6735
Glutathione_metabolism	0.08685	0.1143	0.4472	0.6409
Pathogenic_Escherichia_coli_infection	0.06824	0.04163	0.1012	0.2695
Brassinosteroid_biosynthesis	0.05226	0.06605	0.4288	0.6315
Cyanoamino_acid_metabolism	0.01966	0.1631	0.904	0.9976
Riboflavin_metabolism	0.01866	0.1326	0.8881	0.9878
Dorso-ventral_axis_formation	0.007691	0.05049	0.8789	0.9878
Clavulanic_acid_biosynthesis	0	1.90E-05	1	1
Novobiocin_biosynthesis	0	1.90E-05	1	1
Glycosaminoglycan_biosynthesis-chondroitin_sulfate	0	1.90E-05	1	1
Phenylpropanoid_biosynthesis	0	1.90E-05	1	1
Cytokine-cytokine_receptor_interaction	0	1.90E-05	1	1
Cell_cycle	0	1.90E-05	1	1
Cell_cycle-yeast	0	1.90E-05	1	1
Axon_guidance	0	1.90E-05	1	1
Focal_adhesion	0	1.90E-05	1	1
Circadian_rhythm-plant	0	1.90E-05	1	1
Olfactory_transduction	0	1.90E-05	1	1
Adipocytokine_signaling_pathway	0	1.90E-05	1	1
Bile_secretion	0	1.90E-05	1	1
Huntingtons_disease	0	1.90E-05	1	1
Toluene_degradation	-0.002268	0.1802	0.99	1
MAPK_signaling_pathway	-0.008357	0.02302	0.7166	0.8639
Glycosylphosphatidylinositol(GPI)-anchor_biosynthesis	-0.00913	0.02546	0.7199	0.8639
Bacterial_secretion_system	-0.01857	0.1343	0.89	0.9878
Ascorbate_and_aldarate_metabolism	-0.02294	0.2838	0.9356	1
Arginine_and_proline_metabolism	-0.02867	0.1041	0.783	0.9111
Linoleic_acid_metabolism	-0.0299	0.3669	0.9351	1
Biosynthesis_of_unsaturated_fatty_acids	-0.03127	0.1338	0.8152	0.9373
Citrate_cycle_(TCA_cycle)	-0.04378	0.08473	0.6054	0.8016
Chloroalkane_and_chloroalkene_degradation	-0.04485	0.108	0.678	0.8453
Lipoic_acid_metabolism	-0.04948	0.2952	0.8669	0.9848
Plant-pathogen_interaction	-0.06286	0.1324	0.6349	0.8222
D-Arginine_and_D-ornithine_metabolism	-0.07084	0.397	0.8584	0.981
Carbon_fixation_pathways_in_prokaryotes	-0.08306	0.09796	0.3965	0.6044
Phenylalanine,tyrosine_and_tryptophan_biosynthesis	-0.08694	0.2002	0.6641	0.8334
Various_types_of_N-glycan_biosynthesis	-0.0874	0.1737	0.6147	0.8084
Porphyrin_and_chlorophyll_metabolism	-0.09197	0.2339	0.6942	0.8544
Polycyclic_aromatic_hydrocarbon_degradation	-0.107	0.4125	0.7954	0.9199
Salivary_secretion	-0.1084	0.1753	0.5364	0.7253
Other_types_of_O-glycan_biosynthesis	-0.1147	1.098	0.9168	1
Biosynthesis_of_12-,14-_and_16-membered_macrolides	-0.1173	0.2582	0.6497	0.8261
Primary_bile_acid_biosynthesis	-0.1193	0.8146	0.8836	0.9878
Valine,leucine_and_isoleucine_biosynthesis	-0.1195	0.1212	0.324	0.5313
Sulfur_metabolism	-0.1202	0.1548	0.4373	0.6361
Non-homologous_end-joining	-0.1333	0.4155	0.7484	0.8815
Oxidative_phosphorylation	-0.1345	0.1106	0.224	0.4096
Atrazine_degradation	-0.1532	0.4039	0.7046	0.8616
Glycerophospholipid_metabolism	-0.1533	0.2018	0.4473	0.6409

Sulfur_relay_system	-0.1553	0.1305	0.2342	0.4203
Glycine,serine_and_threonine_metabolism	-0.158	0.1206	0.1903	0.3729
Pyruvate_metabolism	-0.163	0.1662	0.3265	0.5313
Retinol_metabolism	-0.169	NA	NA	NA
Selenocompound_metabolism	-0.1693	0.1615	0.2943	0.5137
Ribosome_biogenesis_in_eukaryotes	-0.1696	0.2697	0.5294	0.7208
Fatty_acid_biosynthesis	-0.172	0.2058	0.4033	0.6098
Amoebiasis	-0.1861	0.3975	0.6397	0.8222
Pantothenate_and_CoA_biosynthesis	-0.1896	0.147	0.1972	0.3825
PPAR_signaling_pathway	-0.1941	0.5348	0.7166	0.8639
Cysteine_and_methionine_metabolism	-0.1986	0.193	0.3035	0.5178
Methane_metabolism	-0.2058	0.218	0.3452	0.557
Alzheimers_disease	-0.2109	0.1647	0.2003	0.3846
Folate_biosynthesis	-0.2233	0.1279	0.08079	0.2489
ECM-receptor_interaction	-0.238	0.1433	0.0966	0.2688
Vitamin_B6_metabolism	-0.258	0.1472	0.07955	0.2489
Alanine,aspartate_and_glutamate_metabolism	-0.2708	0.1756	0.123	0.2849
alpha-Linolenic_acid_metabolism	-0.2815	0.4869	0.5631	0.7561
One_carbon_pool_by_folate	-0.2988	0.2021	0.1392	0.3131
Dioxin_degradation	-0.303	0.4411	0.4922	0.6898
Nicotinate_and_nicotinamide_metabolism	-0.3076	0.1547	0.04685	0.2142
Glycerolipid_metabolism	-0.3192	0.1865	0.08704	0.2532
Protein_processing_in_endoplasmic_reticulum	-0.3214	0.4065	0.4292	0.6315
Lysine_biosynthesis	-0.327	0.2129	0.1247	0.2849
Terpenoid_backbone_biosynthesis	-0.329	0.2507	0.1895	0.3729
ABC_transporters	-0.3523	0.1303	0.006847	0.1285
Inositol_phosphate_metabolism	-0.3573	0.1582	0.02392	0.19
RNA_polymerase	-0.3661	0.1764	0.03797	0.1926
Purine_metabolism	-0.3924	0.2432	0.1067	0.2695
Base_excision_repair	-0.3968	0.2374	0.09459	0.2671
Glycosphingolipid_biosynthesis -lacto_and_neolacto_series	-0.4147	1.292	0.7483	0.8815
RNA_transport	-0.4171	0.4446	0.3481	0.557
Biosynthesis_of_vancomycin_group_antibiotics	-0.4221	0.3054	0.1669	0.3482
Protein_export	-0.4294	0.233	0.0654	0.2434
RNA_degradation	-0.4312	0.2247	0.05499	0.2339
Glycolysis/Gluconeogenesis	-0.4391	0.2849	0.1233	0.2849
Peptidoglycan_biosynthesis	-0.4436	0.2744	0.106	0.2695
Pentose_and_glucuronate_interconversions	-0.4553	0.2001	0.02286	0.19
Butirosin_and_neomycin_biosynthesis	-0.4611	0.7198	0.5219	0.7157
D-Alanine_metabolism	-0.4835	0.2874	0.09252	0.2651
Mismatch_repair	-0.4952	0.2726	0.06926	0.2434
Homologous_recombination	-0.4956	0.2741	0.07056	0.2434
Pyrimidine_metabolism	-0.4992	0.2883	0.08333	0.2489
D-Glutamine_and_D-glutamate_metabolism	-0.504	0.2904	0.08268	0.2489
Aminoacyl-tRNA_biosynthesis	-0.5041	0.2781	0.06987	0.2434
Cell_cycle-Caulobacter	-0.5052	0.2268	0.02592	0.19
DNA_replication	-0.5184	0.2726	0.05726	0.2339
Ribosome	-0.5202	0.2955	0.07837	0.2489
Carbon_fixation_in_photosynthetic_organisms	-0.5217	0.2355	0.02677	0.19
Streptomycin_biosynthesis	-0.522	0.245	0.03316	0.19
Thiamine_metabolism	-0.5394	0.2484	0.02992	0.19
Photosynthesis	-0.5404	0.2769	0.05092	0.2274

Nucleotide_excision_repair	-0.542	0.2867	0.05873	0.2349
Pentose_phosphate_pathway	-0.5431	0.2939	0.0646	0.2434
Zeatin_biosynthesis	-0.5519	0.307	0.07225	0.2434
Tetracycline_biosynthesis	-0.6127	0.4616	0.1844	0.3727
Drug_metabolism-other_enzymes	-0.6315	0.2946	0.03203	0.19
Systemic_lupus_erythematosus	-0.6703	0.56	0.2314	0.4191
Biosynthesis_of_ansamycins	-0.686	0.3606	0.05713	0.2339
Starch_and_sucrose_metabolism	-0.687	0.3257	0.0349	0.1915
Parkinsons_disease	-0.6899	0.4237	0.1035	0.2695
Bacterial_invasion_of_epithelial_cells	-0.7008	0.6093	0.2501	0.4446
Steroid_hormone_biosynthesis	-0.7154	0.5074	0.1586	0.3346
African_trypanosomiasis	-0.7401	0.4287	0.08428	0.2489
N-Glycan_biosynthesis	-0.7408	0.5185	0.1531	0.334
Amino_sugar_and_nucleotide_sugar_metabolism	-0.7474	0.3482	0.03182	0.19
Meiosis-yeast	-0.796	0.4822	0.09874	0.2695
Fructose_and_mannose_metabolism	-0.8094	0.4489	0.07139	0.2434
Phagosome	-0.8641	0.2856	0.002484	0.1012
Photosynthesis-antenna_proteins	-0.9252	NA	NA	NA
Sphingolipid_metabolism	-0.9842	0.4944	0.0465	0.2142
Protein_digestion_and_absorption	-1.001	0.6187	0.1057	0.2695
Isoflavonoid_biosynthesis	-1.11	0.6934	0.1093	0.27
Lysosome	-1.124	0.4764	0.01832	0.19
Secondary_bile_acid_biosynthesis	-1.137	1.136	0.3171	0.5293
Phosphotransferase_system_(PTS)	-1.177	0.8229	0.1527	0.334
Galactose_metabolism	-1.257	0.4969	0.01142	0.1828
Neuroactive_ligand-receptor_interaction	-1.283	NA	NA	NA
Basal_transcription_factors	-1.41	NA	NA	NA
Other_glycan_degradation	-1.424	0.5852	0.01492	0.19
Biosynthesis_of_type_II_polyketide_products	-1.654	0.7354	0.02453	0.19
Naphthalene_degradation	-1.66	1.174	1.57E-01	0.3346
Glycosaminoglycan_degradation	-1.723	0.8277	0.03739	0.1926
Vibrio_cholerae_infection	-1.732	0.7273	0.01726	0.19
Polyketide_sugar_unit_biosynthesis	-1.861	0.8631	0.03111	0.19
Vasopressin-regulated_water_reabsorption	-1.913	1.093	0.08019	0.2489
mRNA_surveillance_pathway	-1.941	0.7242	0.007361	0.1285
Staphylococcus_aureus_infection	-2.032	0.9486	0.03221	0.19
Xylene_degradation	-2.035	0.6768	0.002634	0.1012
Proteasome	-2.128	0.6336	0.0007835	0.07521
Betalain_biosynthesis	-2.667	0.9554	0.005249	0.126
Biosynthesis_of_type_II_polyketide_backbone	-3.04	1.054	0.003912	0.1084
Sesquiterpenoid_biosynthesis	-3.178	1.048	0.002427	0.1012
Indole_alkaloid_biosynthesis	-4.599	1.02	6.55E-06	1.26E-03

Table S37 The P values of metabolic pathways of microbes in fecal samples.

	logFC	se	pvalues	adjPvalues
Vasopressin-regulated_water_reabsorption	2.529	1.302	0.05206	0.9664
Biosynthesis_of_type_II_polyketide_products	2.013	0.6714	0.002714	0.5084
Staphylococcus_aureus_infection	1.51	1.109	0.1735	0.9794
Sesquiterpenoid_biosynthesis	1.484	1.038	0.1529	0.9664
Caprolactam_degradation	1.448	1.091	0.1844	0.9794
Neuroactive_ligand-receptor_interaction	1.309	2.13	0.5389	0.9794
Steroid_biosynthesis	1.23	1.295	0.3422	0.9794
Arachidonic_acid_metabolism	1.111	0.5435	0.04102	0.9664
Metabolism_of_xenobiotics_by_cytochrome_P450	1.098	0.6089	0.07145	0.9664
Isoflavonoid_biosynthesis	1.019	0.4179	0.01475	0.7358
Endocytosis	1.006	1.544	0.5146	0.9794
Polycyclic_aromatic_hydrocarbon_degradation	0.9534	0.4262	0.02529	0.8388
Ethylbenzene_degradation	0.925	0.5341	0.08327	0.9664
Bisphenol_degradation	0.8637	0.3666	0.01849	0.7358
African_trypanosomiasis	0.8399	1.09	0.4409	0.9794
Xylene_degradation	0.8075	0.2884	0.00511	0.5084
Vibrio_cholerae_infection	0.7078	0.7672	0.3563	0.9794
Parkinsons_disease	0.7005	0.529	0.1855	0.9794
Limonene_and_pinene_degradation	0.6554	0.4462	0.1419	0.9664
Alzheimers_disease	0.6292	0.8607	0.4648	0.9794
Photosynthesis-antenna_proteins	0.6194	0.4536	0.1721	0.9794
Carotenoid_biosynthesis	0.6023	1.014	0.5525	0.9794
Bacterial_invasion_of_epithelial_cells	0.5766	1.438	0.6886	1
Lipoic_acid_metabolism	0.5506	0.3875	0.1554	0.9664
Aminobenzoate_degradation	0.5381	0.3667	0.1423	0.9664
Non-homologous_end-joining	0.4863	0.7769	0.5313	0.9794
Biosynthesis_of_type_II_polyketide_backbone	0.4118	1.259	0.7436	1
Fluorobenzoate_degradation	0.3845	0.4679	0.4112	0.9794
Flavonoid_biosynthesis	0.3701	0.9791	0.7054	1
Styrene_degradation	0.3579	0.6392	0.5755	0.9794
Atrazine_degradation	0.3561	0.3449	0.302	0.9794
Phosphotransferase_system_(PTS)	0.3494	0.4959	0.4811	0.9794
Proteasome	0.3319	1.757	0.8502	1
Betalain_biosynthesis	0.3246	0.5697	0.5689	0.9794
Naphthalene_degradation	0.322	0.605	0.5946	0.9794
Ubiquinone_and_other_terpenoid-quinone_biosynthesis	0.3124	0.3917	0.4252	0.9794
Toluene_degradation	0.306	0.3517	0.3843	0.9794
Indole_alkaloid_biosynthesis	0.2938	0.1809	0.1044	0.9664
Geraniol_degradation	0.2809	0.7911	0.7225	1
Dioxin_degradation	0.2695	0.3948	0.4948	0.9794
Biosynthesis_of_siderophore_group_nonribosomal_peptides	0.2635	0.955	0.7826	1
Glutathione_metabolism	0.2475	0.2103	0.2392	0.9794
Meiosis-yeast	0.2281	0.8727	0.7938	1
Systemic_lupus_erythematosus	0.2072	0.5619	0.7123	1
Synthesis_and_degradation_of_ketone_bodies	0.1989	0.4076	0.6256	0.9803
Shigellosis	0.1768	0.414	0.6693	1
Tetracycline_biosynthesis	0.1452	1.221	0.9053	1
Ascorbate_and_aldarate_metabolism	0.1383	0.2966	0.6411	0.989
Tyrosine_metabolism	0.1234	0.1628	0.4483	0.9794
Taurine_and_hypotaurine_metabolism	0.08302	0.1532	0.5879	0.9794

Cyanoamino_acid_metabolism	0.0819	0.2604	0.7531	1
Phosphonate_and_phosphinate_metabolism	0.07456	0.1599	0.641	0.989
Chlorocyclohexane_and_chlorobenzene_degradation	0.06671	0.5409	0.9018	1
Benzoate_degradation	0.06184	0.2432	0.7993	1
Inositol_phosphate_metabolism	0.04214	0.1878	0.8224	1
Malaria	0.02819	0.01736	0.1044	0.9664
Fatty_acid_metabolism	0.02751	0.1752	0.8752	1
Polyketide_sugar_unit_biosynthesis	0.02325	1.165	0.9841	1
Pathogenic_Escherichia_coli_infection	0.02115	0.01302	0.1044	0.9664
Glycolysis/Gluconeogenesis	0.01312	0.1579	0.9338	1
Wnt_signaling_pathway	0.01134	0.004761	0.01722	0.7358
Butanoate_metabolism	0.009815	0.1095	0.9286	1
Chloroalkane_and_chloroalkene_degradation	0.004914	0.2003	0.9804	1
Valine,leucine_and_isoleucine_degradation	0.00453	0.1639	0.9779	1
Clavulanic_acid_biosynthesis	0	0.0001314	1	1
Novobiocin_biosynthesis	0	0.0001314	1	1
Various_types_of_N-glycan_biosynthesis	0	0.0001314	1	1
Butirosin_and_neomycin_biosynthesis	0	0.0001314	1	1
Glycosaminoglycan_biosynthesis-chondroitin_sulfate	0	0.0001314	1	1
Glycosylphosphatidylinositol(GPI)-anchor_biosynthesis	0	0.0001314	1	1
alpha-Linolenic_acid_metabolism	0	0.0001314	1	1
Brassinosteroid_biosynthesis	0	0.0001314	1	1
Phenylpropanoid_biosynthesis	0	0.0001314	1	1
PPAR_signaling_pathway	0	0.0001314	1	1
MAPK_signaling_pathway	0	0.0001314	1	1
Cytokine-cytokine_receptor_interaction	0	0.0001314	1	1
Cell_cycle	0	0.0001314	1	1
Cell_cycle-yeast	0	0.0001314	1	1
Dorso-ventral_axis_formation	0	0.0001314	1	1
Axon_guidance	0	0.0001314	1	1
Focal_adhesion	0	0.0001314	1	1
ECM-receptor_interaction	0	0.0001314	1	1
Circadian_rhythm-plant	0	0.0001314	1	1
Olfactory_transduction	0	0.0001314	1	1
Adipocytokine_signaling_pathway	0	0.0001314	1	1
Salivary_secretion	0	0.0001314	1	1
Bile_secretion	0	0.0001314	1	1
Amyotrophic_lateral_sclerosis_(ALS)	0	0.0001314	1	1
Huntingtons_disease	0	0.0001314	1	1
Pathways_in_cancer	0	0.0001314	1	1
Phagosome	-0.0003958	0.01887	0.9833	1
Biosynthesis_of_12-,14-_and_16-membered_macrolides	-0.003948	0.03216	0.9023	1
Glycosphingolipid_biosynthesis-lacto_and_neolacto_series	-0.01083	0.8824	0.9902	1
Peroxisome	-0.02177	0.2359	0.9265	1
Tryptophan_metabolism	-0.02252	0.1544	0.884	1
mRNA_surveillance_pathway	-0.02357	0.01902	0.2153	0.9794
Folate_biosynthesis	-0.02397	0.2128	0.9103	1
Ribosome_biogenesis_in_eukaryotes	-0.02605	0.2057	0.8992	1
Propanoate_metabolism	-0.03713	0.1299	0.775	1
D-Alanine_metabolism	-0.04403	0.1719	0.7979	1
Citrate_cycle_(TCA_cycle)	-0.04903	0.1431	0.7319	1
Fructose_and_mannose_metabolism	-0.05347	0.1791	0.7653	1
Biosynthesis_of_vancomycin_group_antibiotics	-0.05797	0.1976	0.7692	1

Retinol_metabolism	-0.05891	0.6624	0.9291	1
Base_excision_repair	-0.06132	0.1484	0.6794	1
Renin-angiotensin_system	-0.06155	0.1741	0.7237	1
Purine_metabolism	-0.06198	0.1559	0.6909	1
Vibrio_cholerae_pathogenic_cycle	-0.064	0.1505	0.6707	1
Penicillin_and_cephalosporin_biosynthesis	-0.06433	0.9234	0.9445	1
Pyruvate_metabolism	-0.06906	0.1411	0.6246	0.9803
Basal_transcription_factors	-0.07147	0.05767	0.2153	0.9794
Biosynthesis_of_unsaturated_fatty_acids	-0.07217	0.1325	0.5861	0.9794
Amino_sugar_and_nucleotide_sugar_metabolism	-0.07634	0.1556	0.6237	0.9803
DNA_replication	-0.08955	0.1673	0.5925	0.9794
beta-Lactam_resistance	-0.09033	0.5802	0.8763	1
Selenocompound_metabolism	-0.09047	0.146	0.5355	0.9794
Fatty_acid_biosynthesis	-0.09073	0.184	0.6219	0.9803
ABC_transporters	-0.09581	0.1829	0.6004	0.9794
Pyrimidine_metabolism	-0.09694	0.1658	0.5588	0.9794
Aminoacyl-tRNA_biosynthesis	-0.1	0.1865	0.5918	0.9794
Ribosome	-0.1024	0.1883	0.5864	0.9794
C5-Branched_dibasic_acid_metabolism	-0.1177	0.22	0.5928	0.9794
Glycine,serine_and_threonine_metabolism	-0.1181	0.1579	0.4544	0.9794
D-Glutamine_and_D-glutamate_metabolism	-0.1183	0.1907	0.5349	0.9794
Protein_export	-0.1196	0.1566	0.4452	0.9794
Mismatch_repair	-0.1253	0.1635	0.4433	0.9794
Homologous_recombination	-0.1262	0.1737	0.4676	0.9794
Galactose_metabolism	-0.127	0.1898	0.5036	0.9794
Glycerolipid_metabolism	-0.1292	0.163	0.4282	0.9794
Carbon_fixation_pathways_in_prokaryotes	-0.1311	0.1445	0.364	0.9794
Lysine_biosynthesis	-0.133	0.1918	0.4882	0.9794
Nucleotide_excision_repair	-0.1363	0.2102	0.5168	0.9794
Peptidoglycan_biosynthesis	-0.1397	0.1864	0.4533	0.9794
Cell_cycle-Caulobacter	-0.1401	0.1738	0.4201	0.9794
Cysteine_and_methionine_metabolism	-0.1408	0.1765	0.4249	0.9794
Nicotinate_and_nicotinamide_metabolism	-0.1431	0.2017	0.4779	0.9794
Streptomycin_biosynthesis	-0.1458	0.2057	0.4783	0.9794
One_carbon_pool_by_folate	-0.1471	0.1745	0.3991	0.9794
Glycerophospholipid_metabolism	-0.149	0.1307	0.2542	0.9794
Sulfur_metabolism	-0.1497	0.1355	0.2693	0.9794
RNA_degradation	-0.1501	0.1693	0.3753	0.9794
RNA_transport	-0.1534	0.1789	0.3913	0.9794
Vitamin_B6_metabolism	-0.1548	0.2232	0.4879	0.9794
Methane_metabolism	-0.1557	0.1642	0.3429	0.9794
Terpenoid_backbone_biosynthesis	-0.1562	0.1855	0.3997	0.9794
Bacterial_secretion_system	-0.157	0.1597	0.3256	0.9794
Valine,leucine_and_isoleucine_biosynthesis	-0.1594	0.2006	0.427	0.9794
Spliceosome	-0.1596	1.59	0.92	1
Drug_metabolism-other_enzymes	-0.1613	0.1686	0.3387	0.9794
Zeatin_biosynthesis	-0.1629	0.1941	0.4014	0.9794
Pantothenate_and_CoA_biosynthesis	-0.1666	0.1795	0.3532	0.9794
Pentose_phosphate_pathway	-0.1677	0.1737	0.3345	0.9794
Starch_and_sucrose_metabolism	-0.1736	0.1818	0.3395	0.9794
Lysine_degradation	-0.1778	0.2031	0.3813	0.9794
Two-component_system	-0.1819	0.1696	0.2836	0.9794
Oxidative_phosphorylation	-0.1821	0.1541	0.2372	0.9794

Phenylalanine_metabolism	-0.1917	0.1802	0.2874	0.9794
Carbon_fixation_in_photosynthetic_organisms	-0.1923	0.1733	0.2672	0.9794
Insulin_signaling_pathway	-0.2035	0.202	0.3138	0.9794
Nitrogen_metabolism	-0.2054	0.1281	0.1089	0.9664
Alanine,aspartate_and_glutamate_metabolism	-0.2155	0.192	0.2617	0.9794
Thiamine_metabolism	-0.2169	0.2226	0.3299	0.9794
Arginine_and_proline_metabolism	-0.2353	0.1633	0.1498	0.9664
Pentose_and_glucuronate_interconversions	-0.2424	0.1688	0.151	0.9664
Photosynthesis	-0.2429	0.2388	0.3091	0.9794
Sulfur_relay_system	-0.2518	0.1579	0.1107	0.9664
Phenylalanine,tyrosine_and_tryptophan_biosynthesis	-0.2527	0.2775	0.3625	0.9794
Linoleic_acid_metabolism	-0.2768	0.4769	0.5615	0.9794
Tropane,piperidine_and_pyridine_alkaloid_biosynthesis	-0.2891	0.249	0.2456	0.9794
Hypertrophic_cardiomyopathy_(HCM)	-0.3017	1.091	0.7822	1
beta-Alanine_metabolism	-0.3045	0.2076	0.1425	0.9664
Primary_bile_acid_biosynthesis	-0.3088	0.6042	0.6093	0.9803
Glyoxylate_and_dicarboxylate_metabolism	-0.3104	0.2002	0.1211	0.9664
Amoebiasis	-0.3164	0.7628	0.6783	1
Secondary_bile_acid_biosynthesis	-0.3248	0.6131	0.5962	0.9794
Nitrotoluene_degradation	-0.3252	0.4128	0.4308	0.9794
Biotin_metabolism	-0.34	0.1983	0.08635	0.9664
Histidine_metabolism	-0.3514	0.2796	0.2089	0.9794
Plant-pathogen_interaction	-0.3578	0.1969	0.06911	0.9664
Sphingolipid_metabolism	-0.3723	0.3579	0.2982	0.9794
RNA_polymerase	-0.388	0.2593	0.1345	0.9664
Epithelial_cell_signaling_in_Helicobacter_pylori_infection	-0.4071	0.297	0.1705	0.9794
Lysosome	-0.4173	0.7042	0.5535	0.9794
Protein_processing_in_endoplasmic_reticulum	-0.4552	0.3853	0.2374	0.9794
Riboflavin_metabolism	-0.4639	0.2221	0.03674	0.9664
Biosynthesis_of_ansamycins	-0.4728	0.3248	0.1456	0.9664
Other_glycan_degradation	-0.497	0.5345	0.3524	0.9794
Steroid_hormone_biosynthesis	-0.5044	1.155	0.6624	1
Lipopolysaccharide_biosynthesis	-0.5094	0.7809	0.5142	0.9794
Porphyrin_and_chlorophyll_metabolism	-0.5525	0.3107	0.0754	0.9664
D-Arginine_and_D-ornithine_metabolism	-0.5597	1.219	0.6462	0.9892
Glycosaminoglycan_degradation	-0.5724	0.9105	0.5296	0.9794
N-Glycan_biosynthesis	-0.6251	0.6671	0.3487	0.9794
Bacterial_chemotaxis	-0.6395	0.4076	0.1167	0.9664
NOD-like_receptor_signaling_pathway	-0.6633	0.3902	0.08917	0.9664
Flagellar_assembly	-0.7364	0.5053	0.145	0.9664
Other_types_of_O-glycan_biosynthesis	-0.8704	0.7966	0.2745	0.9794
Protein_digestion_and_absorption	-0.8739	1.248	0.4836	0.9794
Apoptosis	-0.9244	1.177	0.4324	0.9794

Table S38 The relative abundance of the predicted KEGG secondary functional pathways in ESCC patients after chemotherapy.

Level1	Level2	Abundance
Cellular Processes	Cell growth and death	542.54
Cellular Processes	Cell motility	678.58
Cellular Processes	Cellular community - eukaryotes	0
Cellular Processes	Cellular community - prokaryotes	65.63
Cellular Processes	Transport and catabolism	125.33
Environmental Information Processing	Membrane transport	819.16
Environmental Information Processing	Signal transduction	166.43
Environmental Information Processing	Signaling molecules and interaction	0.01
Genetic Information Processing	Folding, sorting and degradation	1117.38
Genetic Information Processing	Replication and repair	2141.27
Genetic Information Processing	Transcription	280.86
Genetic Information Processing	Translation	1160.96
Human Diseases	Cancers	3.43
Human Diseases	Cardiovascular diseases	0.86
Human Diseases	Immune diseases	0.31
Human Diseases	Infectious diseases	88.72
Human Diseases	Neurodegenerative diseases	9.69
Metabolism	Amino acid metabolism	4695.15
Metabolism	Biosynthesis of other secondary metabolites	783.53
Metabolism	Carbohydrate metabolism	5112.22
Metabolism	Energy metabolism	1990.94
Metabolism	Glycan biosynthesis and metabolism	1368.67
Metabolism	Lipid metabolism	2287.36
Metabolism	Metabolism of cofactors and vitamins	4473.13
Metabolism	Metabolism of other amino acids	3142.1
Metabolism	Metabolism of terpenoids and polyketides	2972
Metabolism	Nucleotide metabolism	729.1
Metabolism	Xenobiotics biodegradation and metabolism	2175.5
Organismal Systems	Development	0
Organismal Systems	Digestive system	10.49
Organismal Systems	Endocrine system	29.86
Organismal Systems	Environmental adaptation	69.17
Organismal Systems	Excretory system	0
Organismal Systems	Immune system	17.2
Organismal Systems	Nervous system	0
Organismal Systems	Sensory system	0

Table S39 The relative abundance of the predicted KEGG secondary functional pathways in ESCC patients after immunotherapy.

Level1	Level2	Abundance
Cellular Processes	Cell growth and death	574.47
Cellular Processes	Cell motility	796.97
Cellular Processes	Cellular community - eukaryotes	0
Cellular Processes	Cellular community - prokaryotes	60.34
Cellular Processes	Transport and catabolism	104.85
Environmental Information Processing	Membrane transport	863.86
Environmental Information Processing	Signal transduction	183.15
Environmental Information Processing	Signaling molecules and interaction	0.02
Genetic Information Processing	Folding, sorting and degradation	1145.07
Genetic Information Processing	Replication and repair	2166.84
Genetic Information Processing	Transcription	292.06
Genetic Information Processing	Translation	1156.62
Human Diseases	Cancers	3.35
Human Diseases	Cardiovascular diseases	0.48
Human Diseases	Immune diseases	0.32
Human Diseases	Infectious diseases	91.99
Human Diseases	Neurodegenerative diseases	10.09
Metabolism	Amino acid metabolism	4615.75
Metabolism	Biosynthesis of other secondary metabolites	746.01
Metabolism	Carbohydrate metabolism	4963.74
Metabolism	Energy metabolism	1971.1
Metabolism	Glycan biosynthesis and metabolism	1422.23
Metabolism	Lipid metabolism	2419.13
Metabolism	Metabolism of cofactors and vitamins	4550.37
Metabolism	Metabolism of other amino acids	2935.66
Metabolism	Metabolism of terpenoids and polyketides	3159.62
Metabolism	Nucleotide metabolism	722.14
Metabolism	Xenobiotics biodegradation and metabolism	1882.28
Organismal Systems	Development	0
Organismal Systems	Digestive system	9.2
Organismal Systems	Endocrine system	33.08
Organismal Systems	Environmental adaptation	77.65
Organismal Systems	Excretory system	0
Organismal Systems	Immune system	0
Organismal Systems	Nervous system	0
Organismal Systems	Sensory system	0

Table S40 The metabolic pathways of microbes in blood samples.

pathway	description	logFC	SE	Pvalues	adjPvalues
ko00196	Photosynthesis - antenna proteins	2.073	1.371	0.1305	0.4204
ko00622	Xylene degradation	1.249	0.6838	0.06779	0.2646
ko03015	mRNA surveillance pathway	1.249	1.102	0.2572	0.6045
ko03320	PPAR signaling pathway	1.005	0.577	0.08143	0.3061
ko00121	Secondary bile acid biosynthesis	0.994	1.162	0.3922	0.6867
ko00905	Brassinosteroid biosynthesis	0.8963	0.6904	0.1942	0.5553
ko04080	Neuroactive ligand-receptor interaction	0.852	1.293	0.5101	0.7845
ko05146	Amoebiasis	0.7473	0.3278	0.02263	0.1432
ko00590	Arachidonic acid metabolism	0.7418	0.8912	0.4052	0.6975
ko00531	Glycosaminoglycan degradation	0.7342	0.6459	0.2557	0.6045
ko05144	Malaria	0.7055	1.396	0.6133	0.8527
ko05100	Bacterial invasion of epithelial cells	0.6821	0.9882	0.4901	0.7611
ko05120	Epithelial cell signaling in Helicobacter pylori infection	0.6816	0.258	0.00825	0.1048
ko00791	Atrazine degradation	0.6556	0.3436	0.05637	0.2289
ko05150	Staphylococcus aureus infection	0.626	1.122	0.5769	0.8269
ko04144	Endocytosis	0.6131	0.8286	0.4594	0.7433
ko01056	Biosynthesis of type II polyketide backbone	0.5474	1.394	0.6946	0.9156
ko05200	Pathways in cancer	0.4842	0.4452	0.2768	0.6045
ko02060	Phosphotransferase system (PTS)	0.4492	0.512	0.3803	0.6848
ko00052	Galactose metabolism	0.4179	0.3782	0.2691	0.6045
ko00524	Butirosin and neomycin biosynthesis	0.3664	0.9583	0.7022	0.9157
ko04621	NOD-like receptor signaling pathway	0.3639	0.2574	0.1575	0.4772
ko04112	Cell cycle - Caulobacter	0.3634	0.1182	0.00211	0.07138
ko03420	Nucleotide excision repair	0.3585	0.1205	0.002918	0.07404
ko03008	Ribosome biogenesis in eukaryotes	0.3544	0.1268	0.005202	0.07543
ko00730	Thiamine metabolism	0.3518	0.1142	0.002061	0.07138
ko00900	Terpenoid backbone biosynthesis	0.3487	0.1084	0.001301	0.07138
ko03070	Bacterial secretion system	0.3383	0.1425	0.01759	0.1415
ko00943	Isoflavonoid biosynthesis	0.3373	0.9975	0.7353	0.9157
ko03030	DNA replication	0.3335	0.1302	0.01044	0.1076
ko03430	Mismatch repair	0.3255	0.1266	0.01014	0.1076
ko03060	Protein export	0.3093	0.108	0.004167	0.07543
ko04141	Protein processing in endoplasmic reticulum	0.3046	0.14	0.02963	0.1583
ko04626	Plant-pathogen interaction	0.3039	0.1296	0.01899	0.1415
ko00550	Peptidoglycan biosynthesis	0.3007	0.1067	0.004834	0.07543
ko03440	Homologous recombination	0.2975	0.1307	0.02282	0.1432
ko03010	Ribosome	0.297	0.1257	0.01817	0.1415
ko00072	Synthesis and degradation of ketone bodies	0.2931	0.1849	0.1129	0.3887
ko00908	Zeatin biosynthesis	0.2891	0.1315	0.02784	0.157
ko00195	Photosynthesis	0.2838	0.1083	0.008775	0.1048
ko00471	D-Glutamine and D-glutamate metabolism	0.2829	0.1165	0.01519	0.1341
ko00790	Folate biosynthesis	0.2766	0.1191	0.02021	0.1415
ko00780	Biotin metabolism	0.2708	0.1497	0.07051	0.2701
ko00970	Aminoacyl-tRNA biosynthesis	0.2657	0.1173	0.02352	0.1432
ko03018	RNA degradation	0.258	0.101	0.0106	0.1076
ko03410	Base excision repair	0.2501	0.1007	0.01297	0.1197
ko02040	Flagellar assembly	0.2399	0.2605	0.357	0.6673
ko00720	Carbon fixation pathways in prokaryotes	0.2359	0.1012	0.0198	0.1415
ko00281	Geraniol degradation	0.235	0.328	0.4735	0.751
ko00920	Sulfur metabolism	0.2335	0.1106	0.03471	0.1678
ko00230	Purine metabolism	0.2334	0.1081	0.03083	0.1605
ko00540	Lipopolysaccharide biosynthesis	0.2316	0.2935	0.43	0.7213
ko01055	Biosynthesis of vancomycin group antibiotics	0.2296	0.1494	0.1245	0.4144
ko00240	Pyrimidine metabolism	0.2276	0.1327	0.0864	0.3132
ko00670	One carbon pool by folate	0.2271	0.1006	0.02399	0.1432
ko00623	Toluene degradation	0.2219	0.1018	0.02924	0.1583
ko00626	Naphthalene degradation	0.2188	0.6229	0.7254	0.9157
ko00630	Glyoxylate and dicarboxylate metabolism	0.2107	0.193	0.275	0.6045
ko05010	Alzheimer's disease	0.2086	0.6082	0.7316	0.9157
ko00300	Lysine biosynthesis	0.2044	0.1013	0.04365	0.1969
ko04910	Insulin signaling pathway	0.2033	0.1299	0.1176	0.3978
ko03013	RNA transport	0.2027	0.2207	0.3583	0.6673
ko00785	Lipoic acid metabolism	0.1984	0.181	0.2729	0.6045
ko00523	Polyketide sugar unit biosynthesis	0.1961	0.1604	0.2215	0.5793
ko01051	Biosynthesis of ansamycins	0.1953	0.1589	0.2191	0.5793
ko00710	Carbon fixation in photosynthetic organisms	0.1933	0.1051	0.06581	0.2619

ko00270	Cysteine and methionine metabolism	0.1884	0.0906	0.03761	0.1735
ko04122	Sulfur relay system	0.1869	0.09605	0.05165	0.2184
ko00520	Amino sugar and nucleotide sugar metabolism	0.1824	0.2114	0.3881	0.6867
ko00750	Vitamin B6 metabolism	0.1778	0.1032	0.08475	0.3128
ko00620	Pyruvate metabolism	0.1776	0.08406	0.03458	0.1678
ko02020	Two-component system	0.1774	0.1432	0.2153	0.5793
ko03020	RNA polymerase	0.1771	0.09264	0.0559	0.2289
ko00310	Lysine degradation	0.1748	0.2115	0.4084	0.6975
ko00253	Tetracycline biosynthesis	0.1739	0.0877	0.04739	0.2092
ko00190	Oxidative phosphorylation	0.1692	0.1116	0.1293	0.4204
ko00030	Pentose phosphate pathway	0.1624	0.1331	0.2226	0.5793
ko04113	Meiosis - yeast	0.1538	0.5319	0.7725	0.939
ko04210	Apoptosis	0.1534	0.3513	0.6623	0.8904
ko00650	Butanoate metabolism	0.1489	0.1251	0.2339	0.6009
ko00380	Tryptophan metabolism	0.1474	0.1922	0.4432	0.7315
ko00860	Porphyrin and chlorophyll metabolism	0.1452	0.2108	0.4912	0.7611
ko00500	Starch and sucrose metabolism	0.1413	0.2352	0.5481	0.8181
ko00473	D-Alanine metabolism	0.1412	0.1511	0.3499	0.6673
ko00770	Pantothenate and CoA biosynthesis	0.1381	0.08716	0.113	0.3887
ko00600	Sphingolipid metabolism	0.1374	0.5466	0.8016	0.9629
ko00760	Nicotinate and nicotinamide metabolism	0.13	0.0867	0.1336	0.4239
ko00130	Ubiquinone and other terpenoid-quinone biosynthesis	0.1295	0.1258	0.3032	0.6344
ko00740	Riboflavin metabolism	0.1288	0.134	0.3365	0.6647
ko03050	Proteasome	0.127	1.171	0.9136	1
ko00561	Glycerolipid metabolism	0.1228	0.1168	0.2931	0.6262
ko00400	Phenylalanine, tyrosine and tryptophan biosynthesis	0.119	0.1441	0.4089	0.6975
ko02010	ABC transporters	0.1177	0.1274	0.3557	0.6673
ko04614	Renin-angiotensin system	0.1157	0.2369	0.6251	0.8574
ko00061	Fatty acid biosynthesis	0.1148	0.08301	0.1665	0.4971
ko00901	Indole alkaloid biosynthesis	0.1121	0.1415	0.4284	0.7213
ko00521	Streptomycin biosynthesis	0.1119	0.1106	0.3115	0.6425
ko00020	Citrate cycle (TCA cycle)	0.09882	0.09089	0.2769	0.6045
ko02030	Bacterial chemotaxis	0.09859	0.2715	0.7165	0.9157
ko00511	Other glycan degradation	0.09781	0.5302	0.8536	1
ko00480	Glutathione metabolism	0.09168	0.1255	0.465	0.7433
ko00010	Glycolysis / Gluconeogenesis	0.0916	0.1328	0.4903	0.7611
ko00051	Fructose and mannose metabolism	0.09153	0.2852	0.7482	0.9237
ko00280	Valine, leucine and isoleucine degradation	0.09037	0.2009	0.6529	0.8836
ko00450	Selenocompound metabolism	0.08927	0.09366	0.3405	0.6647
ko00680	Methane metabolism	0.08919	0.08134	0.2728	0.6045
ko00071	Fatty acid metabolism	0.07369	0.1854	0.691	0.9156
ko01040	Biosynthesis of unsaturated fatty acids	0.07265	0.1277	0.5694	0.8269
ko00564	Glycerophospholipid metabolism	0.07158	0.0928	0.4405	0.7315
ko00340	Histidine metabolism	0.06667	0.1792	0.7099	0.9157
ko00910	Nitrogen metabolism	0.05721	0.1111	0.6067	0.8494
ko00363	Bisphenol degradation	0.05521	0.1841	0.7642	0.9346
ko00640	Propanoate metabolism	0.04934	0.1048	0.6379	0.8691
ko00250	Alanine, aspartate and glutamate metabolism	0.0422	0.08076	0.6013	0.8477
ko00643	Styrene degradation	0.03761	0.2745	0.891	1
ko00290	Valine, leucine and isoleucine biosynthesis	0.03294	0.09222	0.721	0.9157
ko04976	Bile secretion	0.02248	0.01806	0.2132	0.5793
ko00522	Biosynthesis of 12-, 14- and 16-membered macrolides	0.01191	0.005344	0.02582	0.1497
ko00260	Glycine, serine and threonine metabolism	0.01109	0.08883	0.9007	1
ko00053	Ascorbate and aldarate metabolism	0.01027	0.1126	0.9273	1
ko00360	Phenylalanine metabolism	0.009907	0.2316	0.9659	1
ko04712	Circadian rhythm - plant	0.002458	0.001975	0.2132	0.5793
ko04520	Adherens junction	0.002229	0.0024	0.353	0.6673
ko04340	Hedgehog signaling pathway	0.001558	0.002466	0.5274	0.7989
ko00601	Glycosphingolipid biosynthesis - lacto and neolacto series	0.0001271	0.001538	0.9342	1
ko00331	Clavulanic acid biosynthesis	0	4.767E-07	1	1
ko00513	Various types of N-glycan biosynthesis	0	4.767E-07	1	1
ko00532	Glycosaminoglycan biosynthesis - chondroitin sulfate	0	4.767E-07	1	1
ko00592	alpha-Linolenic acid metabolism	0	4.767E-07	1	1
ko00940	Phenylpropanoid biosynthesis	0	4.767E-07	1	1
ko04010	MAPK signaling pathway	0	4.767E-07	1	1
ko04020	Calcium signaling pathway	0	4.767E-07	1	1
ko04060	Cytokine-cytokine receptor interaction	0	4.767E-07	1	1
ko04110	Cell cycle	0	4.767E-07	1	1

ko04510	Focal adhesion	0	4.767E-07	1	1
ko04722	Neurotrophin signaling pathway	0	4.767E-07	1	1
ko04920	Adipocytokine signaling pathway	0	4.767E-07	1	1
ko04970	Salivary secretion	0	4.767E-07	1	1
ko05142	Chagas disease (American trypanosomiasis)	0	4.767E-07	1	1
ko05145	Toxoplasmosis	0	4.767E-07	1	1
ko05160	Hepatitis C	0	4.767E-07	1	1
ko05412	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	0	4.767E-07	1	1
ko04145	Phagosome	-0.00004441	0.0004935	0.9283	1
ko00563	Glycosylphosphatidylinositol(GPI) -anchor biosynthesis	-0.0001598	0.000587	0.7855	0.9491
ko04740	Olfactory transduction	-0.00034	0.003538	0.9234	1
ko04962	Vasopressin-regulated water reabsorption	-0.0008293	0.0007749	0.2845	0.6144
ko04810	Regulation of actin cytoskeleton	-0.002652	0.001656	0.1092	0.3887
ko00514	Other types of O-glycan biosynthesis	-0.003517	0.001676	0.03584	0.1692
ko00362	Benzoate degradation	-0.005376	0.1584	0.9729	1
ko04310	Wnt signaling pathway	-0.014	0.007174	0.05103	0.2184
ko03022	Basal transcription factors	-0.01791	0.01985	0.367	0.6772
ko00040	Pentose and glucuronate interconversions	-0.0304	0.1249	0.8077	0.9645
ko00364	Fluorobenzoate degradation	-0.03328	0.3161	0.9162	1
ko05014	Amyotrophic lateral sclerosis (ALS)	-0.03864	0.402	0.9234	1
ko00906	Carotenoid biosynthesis	-0.0496	0.2457	0.84	0.9972
ko04146	Peroxisome	-0.05919	0.1472	0.6876	0.9156
ko00960	Tropane, piperidine and pyridine alkaloid biosynthesis	-0.0605	0.1726	0.726	0.9157
ko00591	Linoleic acid metabolism	-0.06496	0.1896	0.7319	0.9157
ko00562	Inositol phosphate metabolism	-0.07363	0.1325	0.5784	0.8269
ko00401	Novobiocin biosynthesis	-0.07871	0.7042	0.911	1
ko00460	Cyanoamino acid metabolism	-0.08469	0.09495	0.3724	0.6811
ko00361	Chlorocyclohexane and chlorobenzene degradation	-0.08789	0.1499	0.5578	0.8245
ko05111	Vibrio cholerae pathogenic cycle	-0.08998	0.1461	0.5379	0.8088
ko00350	Tyrosine metabolism	-0.1036	0.1057	0.3267	0.6565
ko00330	Arginine and proline metabolism	-0.1077	0.09212	0.2425	0.6045
ko00965	Betalain biosynthesis	-0.1122	0.6377	0.8603	1
ko00627	Aminobenzoate degradation	-0.1209	0.1886	0.5216	0.7962
ko00930	Caprolactam degradation	-0.1336	0.236	0.5714	0.8269
ko00660	C5-Branched dibasic acid metabolism	-0.136	0.1418	0.3375	0.6647
ko00410	beta-Alanine metabolism	-0.1401	0.2407	0.5605	0.8245
ko00909	Sesquiterpenoid biosynthesis	-0.1427	1.337	0.915	1
ko00980	Metabolism of xenobiotics by cytochrome P450	-0.1847	0.1629	0.2571	0.6045
ko00440	Phosphonate and phosphinate metabolism	-0.1906	0.1432	0.1832	0.539
ko00140	Steroid hormone biosynthesis	-0.2009	0.6326	0.7508	0.9237
ko00983	Drug metabolism - other enzymes	-0.2545	0.2574	0.3227	0.655
ko00472	D-Arginine and D-ornithine metabolism	-0.265	0.3026	0.3812	0.6848
ko00903	Limonene and pinene degradation	-0.2701	0.2353	0.2511	0.6045
ko00625	Chloroalkane and chloroalkene degradation	-0.3137	0.111	0.004707	0.07543
ko00120	Primary bile acid biosynthesis	-0.3434	0.4649	0.4602	0.7433
ko00430	Taurine and hypotaurine metabolism	-0.3548	0.1673	0.03397	0.1678
ko05012	Parkinson's disease	-0.3831	0.4479	0.3924	0.6867
ko00624	Polycyclic aromatic hydrocarbon degradation	-0.3848	0.3724	0.3013	0.6344
ko00830	Retinol metabolism	-0.425	0.1513	0.004964	0.07543
ko05016	Huntington's disease	-0.4388	0.2986	0.1417	0.4357
ko04320	Dorso-ventral axis formation	-0.5246	1.066	0.6228	0.8574
ko05143	African trypanosomiasis	-0.5667	0.4967	0.2539	0.6045
ko05110	Vibrio cholerae infection	-0.5783	1.103	0.6001	0.8477
ko00621	Dioxin degradation	-0.6239	0.4733	0.1874	0.5435
ko00642	Ethylbenzene degradation	-0.6305	0.2527	0.01258	0.1197
ko05322	Systemic lupus erythematosus	-0.6603	0.8989	0.4626	0.7433
ko04142	Lysosome	-0.6648	NaN	NaN	NaN
ko00633	Nitrotoluene degradation	-0.6771	0.1983	0.0006392	0.06488
ko04974	Protein digestion and absorption	-0.6953	0.6225	0.264	0.6045
ko00510	N-Glycan biosynthesis	-0.847	0.6597	0.1992	0.5616
ko05410	Hypertrophic cardiomyopathy (HCM)	-0.9069	NaN	NaN	NaN
ko05130	Pathogenic Escherichia coli infection	-0.9287	0.9212	0.3134	0.6425
ko05131	Shigellosis	-1.046	0.4565	0.02198	0.1432
ko03040	Spliceosome	-1.078	NaN	NaN	NaN
ko04512	ECM-receptor interaction	-1.096	0.9949	0.2707	0.6045
ko01053	Biosynthesis of siderophore group nonribosomal peptides	-1.109	0.7472	0.1376	0.4298
ko01057	Biosynthesis of type II polyketide products	-1.141	NaN	NaN	NaN
ko00311	Penicillin and cephalosporin biosynthesis	-1.189	0.3096	0.0001229	0.02494

ko00312	beta-Lactam resistance	-1.576	0.6781	0.02015	0.1415
ko03450	Non-homologous end-joining	-1.705	0.5652	0.002556	0.07404
ko04075	Plant hormone signal transduction	-1.943	0.7386	0.008529	0.1048
ko00941	Flavonoid biosynthesis	-2.283	0.7389	0.002002	0.07138
ko00100	Steroid biosynthesis	-2.587	0.9194	0.004891	0.07543

Table S41 The P values of the metabolic pathways of microbes in oral mucosal samples.

pathway	description	logFC	SE	Pvalues	adjPvalues
ko00523	Polyketide sugar unit biosynthesis	3.328	0.6564	3.993E-07	0.00008145
ko00909	Sesquiterpenoid biosynthesis	2.219	0.9052	0.01423	0.4148
ko01056	Biosynthesis of type II polyketide backbone	2.192	0.8857	0.01333	0.4148
ko00791	Atrazine degradation	1.633	0.6244	0.008933	0.4148
ko00590	Arachidonic acid metabolism	1.42	0.5054	0.00495	0.3366
ko05130	Pathogenic Escherichia coli infection	1.39	0.6826	0.04167	0.9444
ko00965	Betalain biosynthesis	1.34	0.3537	0.000152	0.01551
ko00513	Various types of N-glycan biosynthesis	1.232	0.6884	0.07354	1
ko00943	Isoflavonoid biosynthesis	1.135	1.122	0.3115	1
ko00903	Limonene and pinene degradation	1.067	0.4214	0.01133	0.4148
ko00196	Photosynthesis - antenna proteins	1.059	0.8936	0.2358	1
ko00121	Secondary bile acid biosynthesis	0.856	0.8509	0.3144	1
ko00281	Geraniol degradation	0.6707	0.8656	0.4384	1
ko00364	Fluorobenzoate degradation	0.6054	1.06	0.5679	1
ko00906	Carotenoid biosynthesis	0.5971	0.6534	0.3608	1
ko00930	Caprolactam degradation	0.5887	0.8797	0.5034	1
ko00120	Primary bile acid biosynthesis	0.582	0.7168	0.4168	1
ko00643	Styrene degradation	0.5049	0.5608	0.3679	1
ko00401	Novobiocin biosynthesis	0.5024	0.3871	0.1944	1
ko05200	Pathways in cancer	0.4816	0.257	0.0609	1
ko00524	Butirosin and neomycin biosynthesis	0.4461	0.3606	0.216	1
ko01057	Biosynthesis of type II polyketide products	0.4129	0.5769	0.4742	1
ko05146	Amoebiasis	0.3227	0.6871	0.6387	1
ko00361	Chlorocyclohexane and chlorobenzene degradation	0.2972	0.6652	0.655	1
ko02040	Flagellar assembly	0.2637	0.7094	0.7102	1
ko00380	Tryptophan metabolism	0.2592	0.3183	0.4155	1
ko05100	Bacterial invasion of epithelial cells	0.2339	0.6279	0.7095	1
ko05322	Systemic lupus erythematosus	0.2251	1.754	0.8978	1
ko00072	Synthesis and degradation of ketone bodies	0.2206	0.3909	0.5724	1
ko00310	Lysine degradation	0.2203	0.3388	0.5155	1
ko05012	Parkinson's disease	0.1829	0.1983	0.3562	1
ko05143	African trypanosomiasis	0.1791	0.6919	0.7958	1
ko00622	Xylene degradation	0.1643	0.4746	0.7292	1
ko00280	Valine, leucine and isoleucine degradation	0.1547	0.2322	0.5052	1
ko02030	Bacterial chemotaxis	0.1509	0.4709	0.7487	1
ko04113	Meiosis - yeast	0.1475	0.5255	0.7789	1
ko00071	Fatty acid metabolism	0.1339	0.2547	0.5989	1
ko02020	Two-component system	0.1331	0.1651	0.4203	1
ko00980	Metabolism of xenobiotics by cytochrome P450	0.1245	0.37	0.7365	1
ko01040	Biosynthesis of unsaturated fatty acids	0.1241	0.1311	0.3439	1
ko03050	Proteasome	0.1226	0.9449	0.8968	1
ko05010	Alzheimer's disease	0.1163	0.1653	0.4817	1
ko03040	Spliceosome	0.1152	1.366	0.9328	1
ko00630	Glyoxylate and dicarboxylate metabolism	0.1061	0.1946	0.5855	1
ko00627	Aminobenzoate degradation	0.1043	0.2307	0.651	1
ko00362	Benzoate degradation	0.09806	0.3104	0.7521	1
ko00360	Phenylalanine metabolism	0.0927	0.2918	0.7507	1
ko00785	Lipoic acid metabolism	0.09104	0.2472	0.7126	1
ko04614	Renin-angiotensin system	0.07843	0.06256	0.21	1
ko00480	Glutathione metabolism	0.07729	0.1232	0.5305	1
ko04122	Sulfur relay system	0.07695	0.1608	0.6322	1
ko00363	Bisphenol degradation	0.0744	0.3245	0.8187	1
ko00624	Polycyclic aromatic hydrocarbon degradation	0.0718	0.8651	0.9338	1
ko00623	Toluene degradation	0.06618	0.1926	0.7312	1
ko00562	Inositol phosphate metabolism	0.06132	0.1666	0.7128	1
ko01055	Biosynthesis of vancomycin group antibiotics	0.05442	0.2906	0.8515	1
ko00650	Butanoate metabolism	0.0499	0.08474	0.556	1

ko05150	Staphylococcus aureus infection	0.04834	0.68	0.9433	1
ko04512	ECM-receptor interaction	0.04482	0.05804	0.44	1
ko00563	Glycosylphosphatidylinositol(GPI) -anchor biosynthesis	0.04231	0.6994	0.9518	1
ko03008	Ribosome biogenesis in eukaryotes	0.04181	0.1865	0.8226	1
ko00640	Propanoate metabolism	0.03697	0.08234	0.6534	1
ko03070	Bacterial secretion system	0.03618	0.1111	0.7447	1
ko00460	Cyanoamino acid metabolism	0.03617	0.1593	0.8203	1
ko02060	Phosphotransferase system (PTS)	0.03138	0.4163	0.9399	1
ko00350	Tyrosine metabolism	0.02924	0.1191	0.806	1
ko02010	ABC transporters	0.02729	0.1261	0.8287	1
ko00190	Oxidative phosphorylation	0.01615	0.1203	0.8932	1
ko00620	Pyruvate metabolism	0.01351	0.1512	0.9288	1
ko03013	RNA transport	0.008358	0.3273	0.9796	1
ko00040	Pentose and glucuronate interconversions	0.00809	0.166	0.9611	1
ko03015	mRNA surveillance pathway	0.006161	0.004036	0.1269	1
ko03022	Basal transcription factors	0.005885	0.007589	0.4381	1
ko05160	Hepatitis C	0.003633	0.003561	0.3077	1
ko00920	Sulfur metabolism	0.002751	0.1955	0.9888	1
ko04320	Dorso-ventral axis formation	0.001619	0.001118	0.1477	1
ko04075	Plant hormone signal transduction	0.0005501	0.0008638	0.5242	1
ko00522	Biosynthesis of 12-, 14- and 16-membered macrolides	0.0004238	0.0005287	0.4228	1
ko04970	Salivary secretion	0.0003794	0.0005458	0.487	1
ko00601	Glycosphingolipid biosynthesis - lacto and neolacto series	0.000378	0.0003809	0.3209	1
ko04626	Plant-pathogen interaction	0.0003446	0.1177	0.9977	1
ko04520	Adherens junction	0.0003132	0.000267	0.2407	1
ko04962	Vasopressin-regulated water reabsorption	0.0002567	0.0002801	0.3593	1
ko04145	Phagosome	0.0001042	0.0001354	0.4415	1
ko05144	Malaria	0.00005062	0.0001182	0.6685	1
ko00331	Clavulanic acid biosynthesis	0	0.00008475	1	1
ko00532	Glycosaminoglycan biosynthesis - chondroitin sulfate	0	0.00008475	1	1
ko00592	alpha-Linolenic acid metabolism	0	0.00008475	1	1
ko00626	Naphthalene degradation	0	0.00008475	1	1
ko00901	Indole alkaloid biosynthesis	0	0.00008475	1	1
ko00905	Brassinosteroid biosynthesis	0	0.00008475	1	1
ko00940	Phenylpropanoid biosynthesis	0	0.00008475	1	1
ko03320	PPAR signaling pathway	0	0.00008475	1	1
ko04010	MAPK signaling pathway	0	0.00008475	1	1
ko04020	Calcium signaling pathway	0	0.00008475	1	1
ko04060	Cytokine-cytokine receptor interaction	0	0.00008475	1	1
ko04110	Cell cycle	0	0.00008475	1	1
ko04340	Hedgehog signaling pathway	0	0.00008475	1	1
ko04510	Focal adhesion	0	0.00008475	1	1
ko04712	Circadian rhythm - plant	0	0.00008475	1	1
ko04722	Neurotrophin signaling pathway	0	0.00008475	1	1
ko04740	Olfactory transduction	0	0.00008475	1	1
ko04810	Regulation of actin cytoskeleton	0	0.00008475	1	1
ko04920	Adipocytokine signaling pathway	0	0.00008475	1	1
ko04976	Bile secretion	0	0.00008475	1	1
ko05014	Amyotrophic lateral sclerosis (ALS)	0	0.00008475	1	1
ko05016	Huntington's disease	0	0.00008475	1	1
ko05142	Chagas disease (American trypanosomiasis)	0	0.00008475	1	1
ko05145	Toxoplasmosis	0	0.00008475	1	1
ko05412	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	0	0.00008475	1	1
ko04310	Wnt signaling pathway	-0.0001197	0.00009762	0.2201	1
ko00780	Biotin metabolism	-0.001208	0.2012	0.9952	1
ko00521	Streptomycin biosynthesis	-0.002321	0.2609	0.9929	1
ko04141	Protein processing in endoplasmic reticulum	-0.006751	0.4095	0.9868	1
ko05131	Shigellosis	-0.006868	0.003023	0.02309	0.5887
ko04146	Peroxisome	-0.00771	0.147	0.9582	1

ko04910	Insulin signaling pathway	-0.009737	0.2353	0.967	1
ko00625	Chloroalkane and chloroalkene degradation	-0.01102	0.1894	0.9536	1
ko03018	RNA degradation	-0.01188	0.1988	0.9523	1
ko00010	Glycolysis / Gluconeogenesis	-0.01755	0.2252	0.9379	1
ko00900	Terpenoid backbone biosynthesis	-0.01945	0.1852	0.9164	1
ko00720	Carbon fixation pathways in prokaryotes	-0.02014	0.139	0.8848	1
ko00591	Linoleic acid metabolism	-0.0211	0.3274	0.9486	1
ko00061	Fatty acid biosynthesis	-0.02152	0.1713	0.9	1
ko00230	Purine metabolism	-0.02324	0.2191	0.9155	1
ko00300	Lysine biosynthesis	-0.02382	0.2092	0.9093	1
ko03410	Base excision repair	-0.0239	0.2038	0.9067	1
ko03060	Protein export	-0.02432	0.229	0.9154	1
ko03420	Nucleotide excision repair	-0.02568	0.2295	0.9109	1
ko00500	Starch and sucrose metabolism	-0.02688	0.298	0.9281	1
ko04112	Cell cycle - Caulobacter	-0.02755	0.2074	0.8943	1
ko00561	Glycerolipid metabolism	-0.0278	0.1801	0.8774	1
ko03030	DNA replication	-0.02912	0.2302	0.8994	1
ko00564	Glycerophospholipid metabolism	-0.03051	0.1663	0.8544	1
ko00030	Pentose phosphate pathway	-0.03107	0.2442	0.8988	1
ko00450	Selenocompound metabolism	-0.0312	0.1878	0.8681	1
ko00290	Valine, leucine and isoleucine biosynthesis	-0.03505	0.1859	0.8504	1
ko00052	Galactose metabolism	-0.03685	0.4019	0.9269	1
ko00340	Histidine metabolism	-0.03805	0.2406	0.8743	1
ko00410	beta-Alanine metabolism	-0.03841	0.2683	0.8862	1
ko00760	Nicotinate and nicotinamide metabolism	-0.03989	0.188	0.832	1
ko04144	Endocytosis	-0.04101	1.567	0.9791	1
ko00020	Citrate cycle (TCA cycle)	-0.04207	0.1644	0.798	1
ko00680	Methane metabolism	-0.04288	0.1891	0.8206	1
ko00260	Glycine, serine and threonine metabolism	-0.04307	0.1795	0.8104	1
ko03440	Homologous recombination	-0.04384	0.2413	0.8558	1
ko00730	Thiamine metabolism	-0.04512	0.2077	0.828	1
ko00970	Aminoacyl-tRNA biosynthesis	-0.04569	0.2405	0.8493	1
ko03430	Mismatch repair	-0.04617	0.2338	0.8434	1
ko00550	Peptidoglycan biosynthesis	-0.04648	0.2324	0.8415	1
ko00130	Ubiquinone and other terpenoid-quinone biosynthesis	-0.04684	0.2085	0.8223	1
ko00471	D-Glutamine and D-glutamate metabolism	-0.04721	0.2518	0.8513	1
ko03010	Ribosome	-0.0478	0.2506	0.8487	1
ko00400	Phenylalanine, tyrosine and tryptophan biosynthesis	-0.04799	0.2325	0.8365	1
ko03020	RNA polymerase	-0.0489	0.2143	0.8195	1
ko00770	Pantothenate and CoA biosynthesis	-0.04922	0.1878	0.7932	1
ko00250	Alanine, aspartate and glutamate metabolism	-0.05285	0.1959	0.7874	1
ko00473	D-Alanine metabolism	-0.05461	0.2651	0.8368	1
ko00520	Amino sugar and nucleotide sugar metabolism	-0.05491	0.3123	0.8604	1
ko05111	Vibrio cholerae pathogenic cycle	-0.05763	0.1919	0.764	1
ko00660	C5-Branched dibasic acid metabolism	-0.05958	0.1562	0.7028	1
ko00240	Pyrimidine metabolism	-0.06077	0.2479	0.8063	1
ko00330	Arginine and proline metabolism	-0.06276	0.1381	0.6496	1
ko00750	Vitamin B6 metabolism	-0.06326	0.2005	0.7523	1
ko00670	One carbon pool by folate	-0.06519	0.2346	0.7811	1
ko00051	Fructose and mannose metabolism	-0.07394	0.3195	0.817	1
ko00910	Nitrogen metabolism	-0.07494	0.1453	0.606	1
ko00830	Retinol metabolism	-0.07596	0.3055	0.8036	1
ko00430	Taurine and hypotaurine metabolism	-0.08095	0.1719	0.6377	1
ko00790	Folate biosynthesis	-0.08214	0.2385	0.7306	1
ko00621	Dioxin degradation	-0.08613	0.3752	0.8185	1
ko00710	Carbon fixation in photosynthetic organisms	-0.08867	0.2399	0.7117	1
ko00270	Cysteine and methionine metabolism	-0.09114	0.2239	0.684	1
ko00253	Tetracycline biosynthesis	-0.09921	0.7168	0.8899	1
ko01053	Biosynthesis of siderophore group nonribosomal peptides	-0.1017	0.6742	0.8801	1

ko01051	Biosynthesis of ansamycins	-0.1028	0.3652	0.7784	1
ko00860	Porphyrin and chlorophyll metabolism	-0.1044	0.304	0.7313	1
ko00960	Tropane, piperidine and pyridine alkaloid biosynthesis	-0.107	0.2459	0.6635	1
ko00908	Zeatin biosynthesis	-0.1142	0.2953	0.6989	1
ko05110	Vibrio cholerae infection	-0.115	1.27	0.9278	1
ko00440	Phosphonate and phosphinate metabolism	-0.1158	0.2187	0.5964	1
ko05120	Epithelial cell signaling in Helicobacter pylori infection	-0.122	0.2261	0.5895	1
ko00642	Ethylbenzene degradation	-0.1285	0.1967	0.5136	1
ko00983	Drug metabolism - other enzymes	-0.1342	0.331	0.6852	1
ko00053	Ascorbate and aldarate metabolism	-0.1403	0.2385	0.5563	1
ko05410	Hypertrophic cardiomyopathy (HCM)	-0.1471	NaN	NaN	NaN
ko00740	Riboflavin metabolism	-0.15	0.2386	0.5296	1
ko00311	Penicillin and cephalosporin biosynthesis	-0.1516	0.5803	0.794	1
ko00540	Lipopolysaccharide biosynthesis	-0.1578	0.3023	0.6016	1
ko04621	NOD-like receptor signaling pathway	-0.1581	0.4472	0.7238	1
ko04080	Neuroactive ligand-receptor interaction	-0.1658	0.6296	0.7923	1
ko00312	beta-Lactam resistance	-0.1702	0.6399	0.7902	1
ko04210	Apoptosis	-0.2316	0.5745	0.6869	1
ko00514	Other types of O-glycan biosynthesis	-0.236	0.4939	0.6328	1
ko00195	Photosynthesis	-0.2643	NaN	NaN	NaN
ko00510	N-Glycan biosynthesis	-0.2742	0.6278	0.6623	1
ko00941	Flavonoid biosynthesis	-0.2764	0.7783	0.7225	1
ko00633	Nitrotoluene degradation	-0.2848	0.4188	0.4964	1
ko00511	Other glycan degradation	-0.2941	0.575	0.609	1
ko00140	Steroid hormone biosynthesis	-0.3084	0.7958	0.6983	1
ko00600	Sphingolipid metabolism	-0.3129	0.5356	0.5591	1
ko00472	D-Arginine and D-ornithine metabolism	-0.3444	0.5471	0.529	1
ko00531	Glycosaminoglycan degradation	-0.4133	0.6545	0.5277	1
ko04974	Protein digestion and absorption	-0.4991	0.803	0.5343	1
ko03450	Non-homologous end-joining	-0.6892	1.023	0.5007	1
ko00100	Steroid biosynthesis	-0.7846	1.079	0.4673	1
ko04142	Lysosome	-1.827	NaN	NaN	NaN

Table S42 The P values of metabolic pathways of microbes in saliva samples.

pathway	description	logFC	SE	Pvalues	adjPvalues
ko00523	Polyketide sugar unit biosynthesis	1.495	0.7463	0.0451	0.7743
ko00965	Betalain biosynthesis	1.152	0.9842	0.2418	1
ko05110	Vibrio cholerae infection	0.6513	1.561	0.6765	1
ko05160	Hepatitis C	0.6099	0.8039	0.448	1
ko05322	Systemic lupus erythematosus	0.5994	1.348	0.6566	1
ko05130	Pathogenic Escherichia coli infection	0.5167	0.4382	0.2384	1
ko00941	Flavonoid biosynthesis	0.4997	0.8428	0.5532	1
ko00196	Photosynthesis - antenna proteins	0.4586	1.052	0.6627	1
ko00121	Secondary bile acid biosynthesis	0.3517	0.8264	0.6704	1
ko03040	Spliceosome	0.3154	0.9557	0.7414	1
ko00140	Steroid hormone biosynthesis	0.2822	0.8178	0.73	1
ko04621	NOD-like receptor signaling pathway	0.2746	0.4759	0.564	1
ko00626	Naphthalene degradation	0.268	0.3185	0.4001	1
ko04210	Apoptosis	0.2514	0.4961	0.6123	1
ko00540	Lipopolysaccharide biosynthesis	0.243	0.336	0.4695	1
ko05146	Amoebiasis	0.2214	0.66	0.7373	1
ko00903	Limonene and pinene degradation	0.2102	0.4796	0.6613	1
ko04974	Protein digestion and absorption	0.2077	0.7221	0.7737	1
ko04141	Protein processing in endoplasmic reticulum	0.1782	0.3934	0.6506	1
ko00120	Primary bile acid biosynthesis	0.1344	0.796	0.8659	1
ko00513	Various types of N-glycan biosynthesis	0.1176	0.4583	0.7976	1
ko00643	Styrene degradation	0.1104	0.4991	0.825	1
ko00960	Tropane, piperidine and pyridine alkaloid biosynthesis	0.1087	0.23	0.6364	1
ko00510	N-Glycan biosynthesis	0.09385	0.2965	0.7516	1
ko01051	Biosynthesis of ansamycins	0.09064	0.223	0.6844	1
ko00600	Sphingolipid metabolism	0.08884	0.3296	0.7875	1
ko00531	Glycosaminoglycan degradation	0.08643	0.4063	0.8316	1
ko00340	Histidine metabolism	0.0827	0.1465	0.5725	1
ko05120	Epithelial cell signaling in Helicobacter pylori infection	0.07348	0.2169	0.7348	1
ko00401	Novobiocin biosynthesis	0.07275	0.2206	0.7416	1
ko00591	Linoleic acid metabolism	0.06919	0.3392	0.8384	1
ko00740	Riboflavin metabolism	0.06599	0.196	0.7364	1
ko00943	Isoflavonoid biosynthesis	0.06522	0.5099	0.8982	1
ko03020	RNA polymerase	0.06416	0.185	0.7288	1
ko00053	Ascorbate and aldarate metabolism	0.0586	0.1787	0.743	1
ko00623	Toluene degradation	0.05832	0.1617	0.7183	1
ko00410	beta-Alanine metabolism	0.05111	0.1823	0.7792	1
ko05010	Alzheimer's disease	0.04801	0.1456	0.7416	1
ko00780	Biotin metabolism	0.04753	0.2165	0.8263	1
ko00511	Other glycan degradation	0.04621	0.3218	0.8858	1
ko00908	Zeatin biosynthesis	0.04298	0.192	0.8228	1
ko00130	Ubiquinone and other terpenoid-quinone biosynthesis	0.03956	0.1966	0.8405	1
ko00360	Phenylalanine metabolism	0.0387	0.155	0.8029	1
ko00750	Vitamin B6 metabolism	0.03687	0.1569	0.8142	1
ko05200	Pathways in cancer	0.03043	0.09229	0.7416	1
ko01055	Biosynthesis of vancomycin group antibiotics	0.02983	0.1458	0.8379	1
ko05111	Vibrio cholerae pathogenic cycle	0.02762	0.1531	0.8568	1
ko00760	Nicotinate and nicotinamide metabolism	0.02615	0.139	0.8508	1
ko01056	Biosynthesis of type II polyketide backbone	0.02446	0.08358	0.7698	1
ko00020	Citrate cycle (TCA cycle)	0.02296	0.1326	0.8626	1
ko00710	Carbon fixation in photosynthetic organisms	0.0172	0.1418	0.9035	1
ko00720	Carbon fixation pathways in prokaryotes	0.01673	0.1207	0.8897	1
ko00920	Sulfur metabolism	0.01551	0.1059	0.8836	1
ko00514	Other types of O-glycan biosynthesis	0.01497	1.399	0.9915	1
ko00730	Thiamine metabolism	0.01311	0.1366	0.9236	1
ko00900	Terpenoid backbone biosynthesis	0.01256	0.1199	0.9165	1
ko00670	One carbon pool by folate	0.009103	0.1176	0.9383	1

ko00909	Sesquiterpenoid biosynthesis	0.007496	0.02846	0.7922	1
ko00521	Streptomycin biosynthesis	0.006873	0.13	0.9578	1
ko00250	Alanine, aspartate and glutamate metabolism	0.00586	0.1149	0.9593	1
ko00910	Nitrogen metabolism	0.005786	0.1109	0.9584	1
ko04614	Renin-angiotensin system	0.005705	0.01289	0.658	1
ko00790	Folate biosynthesis	0.00549	0.1257	0.9652	1
ko04976	Bile secretion	0.005278	0.01601	0.7416	1
ko00860	Porphyrin and chlorophyll metabolism	0.004866	0.1905	0.9796	1
ko03015	mRNA surveillance pathway	0.003943	0.01196	0.7416	1
ko04810	Regulation of actin cytoskeleton	0.002358	0.00373	0.5273	1
ko04626	Plant-pathogen interaction	0.002196	0.1162	0.9849	1
ko04512	ECM-receptor interaction	0.002044	0.006198	0.7416	1
ko04110	Cell cycle	0.001541	0.002612	0.5552	1
ko04320	Dorso-ventral axis formation	0.0009632	0.001192	0.4189	1
ko00522	Biosynthesis of 12-, 14- and 16-membered macrolides	0.0008944	0.002713	0.7416	1
ko04340	Hedgehog signaling pathway	0.0003836	0.001163	0.7416	1
ko04712	Circadian rhythm - plant	0.0003036	0.0009207	0.7416	1
ko00532	Glycosaminoglycan biosynthesis - chondroitin sulfate	0.0001965	0.0002634	0.4556	1
ko04510	Focal adhesion	0.0001075	0.001544	0.9445	1
ko00601	Glycosphingolipid biosynthesis - lacto and neolacto series	0.00004385	0.00006032	0.4672	1
ko00331	Clavulanic acid biosynthesis	0	1.971E-07	1	1
ko00592	alpha-Linolenic acid metabolism	0	1.971E-07	1	1
ko00901	Indole alkaloid biosynthesis	0	1.971E-07	1	1
ko00905	Brassinosteroid biosynthesis	0	1.971E-07	1	1
ko00940	Phenylpropanoid biosynthesis	0	1.971E-07	1	1
ko03022	Basal transcription factors	0	1.971E-07	1	1
ko03320	PPAR signaling pathway	0	1.971E-07	1	1
ko04010	MAPK signaling pathway	0	1.971E-07	1	1
ko04020	Calcium signaling pathway	0	1.971E-07	1	1
ko04060	Cytokine-cytokine receptor interaction	0	1.971E-07	1	1
ko04145	Phagosome	0	1.971E-07	1	1
ko04520	Adherens junction	0	1.971E-07	1	1
ko04722	Neurotrophin signaling pathway	0	1.971E-07	1	1
ko04740	Olfactory transduction	0	1.971E-07	1	1
ko04920	Adipocytokine signaling pathway	0	1.971E-07	1	1
ko04970	Salivary secretion	0	1.971E-07	1	1
ko05012	Parkinson's disease	0	1.971E-07	1	1
ko05014	Amyotrophic lateral sclerosis (ALS)	0	1.971E-07	1	1
ko05016	Huntington's disease	0	1.971E-07	1	1
ko05144	Malaria	0	1.971E-07	1	1
ko05145	Toxoplasmosis	0	1.971E-07	1	1
ko05412	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	0	1.971E-07	1	1
ko04075	Plant hormone signal transduction	-0.00003768	0.00002963	0.2034	1
ko00190	Oxidative phosphorylation	-0.000213	0.1075	0.9984	1
ko04310	Wnt signaling pathway	-0.0002292	0.0001076	0.03315	0.683
ko01057	Biosynthesis of type II polyketide products	-0.0012	0.0305	0.9686	1
ko04112	Cell cycle - Caulobacter	-0.002436	0.1111	0.9825	1
ko03430	Mismatch repair	-0.003493	0.1119	0.9751	1
ko03420	Nucleotide excision repair	-0.005514	0.1177	0.9626	1
ko03018	RNA degradation	-0.006291	0.101	0.9503	1
ko00983	Drug metabolism - other enzymes	-0.007168	0.1473	0.9612	1
ko00471	D-Glutamine and D-glutamate metabolism	-0.007264	0.1153	0.9497	1
ko00270	Cysteine and methionine metabolism	-0.007441	0.1134	0.9477	1
ko00630	Glyoxylate and dicarboxylate metabolism	-0.008473	0.1208	0.9441	1
ko00550	Peptidoglycan biosynthesis	-0.01121	0.1138	0.9215	1
ko03440	Homologous recombination	-0.01156	0.111	0.9171	1
ko00500	Starch and sucrose metabolism	-0.01453	0.1329	0.9129	1
ko00564	Glycerophospholipid metabolism	-0.01563	0.1047	0.8813	1
ko05142	Chagas disease (American trypanosomiasis)	-0.01573	0.09463	0.868	1

ko00330	Arginine and proline metabolism	-0.01694	0.08915	0.8493	1
ko03010	Ribosome	-0.01757	0.1116	0.875	1
ko00240	Pyrimidine metabolism	-0.01947	0.1088	0.8579	1
ko00350	Tyrosine metabolism	-0.02055	0.1125	0.855	1
ko00260	Glycine, serine and threonine metabolism	-0.02064	0.09371	0.8257	1
ko03410	Base excision repair	-0.02092	0.09138	0.8189	1
ko00450	Selenocompound metabolism	-0.02117	0.08949	0.813	1
ko05131	Shigellosis	-0.02152	0.008351	0.009955	0.5127
ko00970	Aminoacyl-tRNA biosynthesis	-0.02156	0.1034	0.8348	1
ko03030	DNA replication	-0.02199	0.1029	0.8307	1
ko04146	Peroxisome	-0.02506	0.1247	0.8408	1
ko00230	Purine metabolism	-0.02674	0.09687	0.7825	1
ko00300	Lysine biosynthesis	-0.02752	0.09287	0.767	1
ko00680	Methane metabolism	-0.02818	0.09212	0.7597	1
ko00633	Nitrotoluene degradation	-0.0283	0.3882	0.9419	1
ko03070	Bacterial secretion system	-0.03152	0.07975	0.6927	1
ko00040	Pentose and glucuronate interconversions	-0.03574	0.1816	0.8439	1
ko00472	D-Arginine and D-ornithine metabolism	-0.0363	0.677	0.9572	1
ko03008	Ribosome biogenesis in eukaryotes	-0.03878	0.1071	0.7173	1
ko00785	Lipoic acid metabolism	-0.03926	0.1855	0.8324	1
ko00473	D-Alanine metabolism	-0.04152	0.1072	0.6984	1
ko00562	Inositol phosphate metabolism	-0.04348	0.1631	0.7897	1
ko00770	Pantothenate and CoA biosynthesis	-0.04412	0.1002	0.6598	1
ko02010	ABC transporters	-0.04498	0.1091	0.68	1
ko00030	Pentose phosphate pathway	-0.04561	0.1017	0.6537	1
ko03060	Protein export	-0.04845	0.09222	0.5993	1
ko00620	Pyruvate metabolism	-0.04857	0.08842	0.5828	1
ko00310	Lysine degradation	-0.0486	0.1775	0.7842	1
ko00480	Glutathione metabolism	-0.05181	0.09921	0.6015	1
ko00520	Amino sugar and nucleotide sugar metabolism	-0.05325	0.1104	0.6297	1
ko00010	Glycolysis / Gluconeogenesis	-0.05502	0.09597	0.5664	1
ko00051	Fructose and mannose metabolism	-0.05767	0.1273	0.6505	1
ko00561	Glycerolipid metabolism	-0.05769	0.1028	0.5746	1
ko00627	Aminobenzoate degradation	-0.06153	0.2401	0.7978	1
ko00590	Arachidonic acid metabolism	-0.06573	0.3094	0.8317	1
ko00061	Fatty acid biosynthesis	-0.06575	0.116	0.571	1
ko00071	Fatty acid metabolism	-0.06704	0.1453	0.6445	1
ko00640	Propanoate metabolism	-0.06748	0.07854	0.3902	1
ko00650	Butanoate metabolism	-0.06853	0.09212	0.4569	1
ko00400	Phenylalanine, tyrosine and tryptophan biosynthesis	-0.07321	0.1131	0.5173	1
ko03013	RNA transport	-0.0739	0.19	0.6974	1
ko00642	Ethylbenzene degradation	-0.07446	0.3179	0.8148	1
ko01053	Biosynthesis of siderophore group nonribosomal peptides	-0.0762	0.2863	0.7901	1
ko00380	Tryptophan metabolism	-0.07624	0.2105	0.7172	1
ko04910	Insulin signaling pathway	-0.07673	0.1509	0.6112	1
ko00290	Valine, leucine and isoleucine biosynthesis	-0.07813	0.1071	0.4659	1
ko00430	Taurine and hypotaurine metabolism	-0.09381	0.08257	0.2559	1
ko00052	Galactose metabolism	-0.09419	0.1378	0.4943	1
ko00906	Carotenoid biosynthesis	-0.09703	0.8695	0.9111	1
ko00280	Valine, leucine and isoleucine degradation	-0.1001	0.1372	0.4659	1
ko00363	Bisphenol degradation	-0.1004	0.3715	0.7869	1
ko01040	Biosynthesis of unsaturated fatty acids	-0.1145	0.1308	0.3811	1
ko04122	Sulfur relay system	-0.1176	0.1538	0.4446	1
ko00660	C5-Branched dibasic acid metabolism	-0.1181	0.1505	0.4328	1
ko00362	Benzoate degradation	-0.132	0.2803	0.6378	1
ko02040	Flagellar assembly	-0.1401	0.4462	0.7536	1
ko02020	Two-component system	-0.1458	0.1619	0.3676	1
ko02030	Bacterial chemotaxis	-0.1553	0.3331	0.641	1
ko02060	Phosphotransferase system (PTS)	-0.1683	0.2783	0.5453	1

ko00072	Synthesis and degradation of ketone bodies	-0.1928	0.324	0.5519	1
ko00625	Chloroalkane and chloroalkene degradation	-0.2044	0.2882	0.4782	1
ko00440	Phosphonate and phosphinate metabolism	-0.215	0.2411	0.3725	1
ko00281	Geraniol degradation	-0.2231	0.7155	0.7551	1
ko00524	Butirosin and neomycin biosynthesis	-0.2437	0.3297	0.4598	1
ko05100	Bacterial invasion of epithelial cells	-0.2675	0.474	0.5724	1
ko00830	Retinol metabolism	-0.2736	0.3511	0.4359	1
ko00563	Glycosylphosphatidylinositol(GPI)-anchor biosynthesis	-0.2985	0.4918	0.5439	1
ko04962	Vasopressin-regulated water reabsorption	-0.3094	1.007	0.7586	1
ko00621	Dioxin degradation	-0.3559	0.2013	0.07703	1
ko04113	Meiosis - yeast	-0.3675	0.619	0.5527	1
ko04144	Endocytosis	-0.3755	1.005	0.7085	1
ko05150	Staphylococcus aureus infection	-0.3888	0.5032	0.4397	1
ko00361	Chlorocyclohexane and chlorobenzene degradation	-0.3901	0.6899	0.5717	1
ko05143	African trypanosomiasis	-0.409	0.2576	0.1124	1
ko00930	Caprolactam degradation	-0.4204	0.9421	0.6555	1
ko03050	Proteasome	-0.4744	0.7402	0.5216	1
ko00311	Penicillin and cephalosporin biosynthesis	-0.5242	0.5658	0.3542	1
ko04080	Neuroactive ligand-receptor interaction	-0.5287	0.9383	0.5731	1
ko00312	beta-Lactam resistance	-0.5452	0.2554	0.0328	0.683
ko00791	Atrazine degradation	-0.6426	0.6747	0.3409	1
ko00980	Metabolism of xenobiotics by cytochrome P450	-0.6787	0.3255	0.03705	0.6938
ko00622	Xylene degradation	-0.7035	0.3172	0.0266	0.683
ko00624	Polycyclic aromatic hydrocarbon degradation	-0.8614	NaN	NaN	NaN
ko05410	Hypertrophic cardiomyopathy (HCM)	-0.9607	0.4362	0.02763	0.683
ko00460	Cyanoamino acid metabolism	-1.015	0.4163	0.01479	0.6093
ko03450	Non-homologous end-joining	-1.039	0.9843	0.2911	1
ko00195	Photosynthesis	-1.111	0.2813	0.00007832	0.008067
ko00253	Tetracycline biosynthesis	-1.183	0.4486	0.008382	0.5127
ko00364	Fluorobenzoate degradation	-1.218	0.5535	0.02778	0.683
ko00100	Steroid biosynthesis	-1.39	0.9496	0.1433	1
ko04142	Lysosome	-2.56	0.2906	0	0

Table S43 The P values of metabolic pathways of microbes in urine samples.

pathway	description	logFC	SE	Pvalues	adjPvalues
ko00590	Arachidonic acid metabolism	4.066	0.5256	1.021E-14	2.084E-12
ko00524	Butirosin and neomycin biosynthesis	2.268	0.6993	0.001181	0.01811
ko00196	Photosynthesis - antenna proteins	1.258	0.5065	0.013	0.07575
ko05012	Parkinson's disease	1.21	0.7573	0.1101	0.2994
ko00531	Glycosaminoglycan degradation	1.09	0.846	0.1978	0.4434
ko00523	Polyketide sugar unit biosynthesis	1.007	0.4456	0.02381	0.1049
ko00514	Other types of O-glycan biosynthesis	0.9669	1.19	0.4165	0.7507
ko03015	mRNA surveillance pathway	0.9025	0.6471	0.1631	0.399
ko00121	Secondary bile acid biosynthesis	0.8371	1.075	0.436	0.7638
ko00622	Xylene degradation	0.7938	0.5274	0.1323	0.3445
ko05120	Epithelial cell signaling in Helicobacter pylori infection	0.7505	0.1205	4.713E-10	3.205E-08
ko05146	Amoebiasis	0.7442	0.2492	0.002828	0.03393
ko04075	Plant hormone signal transduction	0.6712	1.4	0.6316	0.927
ko00791	Atrazine degradation	0.6065	0.2678	0.02355	0.1049
ko00943	Isoflavonoid biosynthesis	0.4544	0.643	0.4798	0.8076
ko04621	NOD-like receptor signaling pathway	0.3972	0.1364	0.003584	0.03539
ko00052	Galactose metabolism	0.396	0.4039	0.3269	0.6233
ko03050	Proteasome	0.3632	0.9187	0.6926	0.9611
ko04141	Protein processing in endoplasmic reticulum	0.3368	0.134	0.01196	0.07408
ko04144	Endocytosis	0.3356	0.5787	0.5619	0.8751
ko03420	Nucleotide excision repair	0.3237	0.1119	0.003807	0.03539
ko04112	Cell cycle - Caulobacter	0.2981	0.1025	0.003638	0.03539
ko05100	Bacterial invasion of epithelial cells	0.2968	0.9883	0.7639	0.9863
ko01055	Biosynthesis of vancomycin group antibiotics	0.2963	0.1592	0.06277	0.2065
ko00600	Sphingolipid metabolism	0.2881	0.6784	0.6711	0.9573
ko02040	Flagellar assembly	0.2798	0.1265	0.02699	0.1147
ko01051	Biosynthesis of ansamycins	0.277	0.247	0.262	0.5399
ko00900	Terpenoid backbone biosynthesis	0.2752	0.07586	0.0002861	0.005305
ko00908	Zeatin biosynthesis	0.2729	0.1389	0.04952	0.1747
ko00780	Biotin metabolism	0.2714	0.07693	0.0004189	0.007121
ko03070	Bacterial secretion system	0.2669	0.1062	0.01198	0.07408
ko03430	Mismatch repair	0.2635	0.1056	0.01259	0.07552
ko03008	Ribosome biogenesis in eukaryotes	0.2581	0.1016	0.01107	0.07287
ko04626	Plant-pathogen interaction	0.2575	0.08782	0.003365	0.03539
ko00511	Other glycan degradation	0.2567	0.7621	0.7362	0.9858
ko00730	Thiamine metabolism	0.2464	0.1313	0.06064	0.2028
ko03030	DNA replication	0.2427	0.1071	0.02341	0.1049
ko03060	Protein export	0.2427	0.09449	0.01023	0.06954
ko00550	Peptidoglycan biosynthesis	0.2416	0.0993	0.01497	0.08482
ko03440	Homologous recombination	0.2321	0.1117	0.03776	0.1481
ko03010	Ribosome	0.2281	0.1158	0.04892	0.1747
ko00195	Photosynthesis	0.225	0.1252	0.07236	0.2237
ko04910	Insulin signaling pathway	0.218	0.1272	0.08649	0.2557
ko03020	RNA polymerase	0.209	0.129	0.1052	0.294
ko00540	Lipopolysaccharide biosynthesis	0.203	0.161	0.2074	0.4587
ko00970	Aminoacyl-tRNA biosynthesis	0.2024	0.1113	0.06909	0.2202
ko02060	Phosphotransferase system (PTS)	0.2009	0.3556	0.572	0.8841
ko00471	D-Glutamine and D-glutamate metabolism	0.1959	0.1138	0.08529	0.2557
ko00790	Folate biosynthesis	0.1942	0.08944	0.02993	0.1246
ko03013	RNA transport	0.1932	0.1736	0.2659	0.5424
ko03410	Base excision repair	0.19	0.07988	0.01741	0.09086
ko03018	RNA degradation	0.1882	0.09595	0.0498	0.1747
ko00670	One carbon pool by folate	0.1794	0.08704	0.03926	0.1511
ko04113	Meiosis - yeast	0.1702	0.3483	0.6251	0.924
ko00240	Pyrimidine metabolism	0.1689	0.1182	0.1532	0.3857
ko00500	Starch and sucrose metabolism	0.1573	0.2702	0.5605	0.8751
ko00300	Lysine biosynthesis	0.1564	0.08833	0.07652	0.233

ko00230	Purine metabolism	0.1562	0.08633	0.0703	0.2206
ko00710	Carbon fixation in photosynthetic organisms	0.1557	0.1291	0.2278	0.487
ko00520	Amino sugar and nucleotide sugar metabolism	0.1488	0.217	0.4931	0.8177
ko00072	Synthesis and degradation of ketone bodies	0.1482	0.2113	0.483	0.8076
ko00630	Glyoxylate and dicarboxylate metabolism	0.1419	0.1316	0.2809	0.5618
ko00521	Streptomycin biosynthesis	0.1353	0.1674	0.4192	0.7507
ko00720	Carbon fixation pathways in prokaryotes	0.1312	0.08035	0.1025	0.2904
ko00860	Porphyrin and chlorophyll metabolism	0.1293	0.1103	0.2411	0.507
ko00750	Vitamin B6 metabolism	0.1273	0.09329	0.1723	0.4088
ko00920	Sulfur metabolism	0.1239	0.08965	0.1668	0.4003
ko00270	Cysteine and methionine metabolism	0.1186	0.0853	0.1643	0.399
ko00030	Pentose phosphate pathway	0.1169	0.146	0.4232	0.7507
ko00400	Phenylalanine, tyrosine and tryptophan biosynthesis	0.114	0.08758	0.193	0.4374
ko00281	Geraniol degradation	0.105	0.2586	0.6847	0.9611
ko00740	Riboflavin metabolism	0.09833	0.08178	0.2292	0.487
ko00965	Betalain biosynthesis	0.09778	0.85	0.9084	1
ko00770	Pantothenate and CoA biosynthesis	0.09614	0.07329	0.1896	0.4345
ko00190	Oxidative phosphorylation	0.08803	0.08438	0.2968	0.5823
ko02020	Two-component system	0.08694	0.131	0.5069	0.8255
ko00051	Fructose and mannose metabolism	0.08661	0.271	0.7493	0.9858
ko02030	Bacterial chemotaxis	0.08496	0.1581	0.5911	0.8999
ko03040	Spliceosome	0.07982	0.4712	0.8655	1
ko04614	Renin-angiotensin system	0.07876	0.1105	0.476	0.8076
ko04122	Sulfur relay system	0.07248	0.08715	0.4056	0.7507
ko00785	Lipoic acid metabolism	0.07242	0.1472	0.6226	0.924
ko00620	Pyruvate metabolism	0.07082	0.07668	0.3557	0.6719
ko00680	Methane metabolism	0.06702	0.08643	0.4381	0.7638
ko04210	Apoptosis	0.05438	0.1602	0.7342	0.9858
ko00760	Nicotinate and nicotinamide metabolism	0.05404	0.08915	0.5444	0.8676
ko02010	ABC transporters	0.05394	0.1066	0.6129	0.9193
ko00561	Glycerolipid metabolism	0.05278	0.1184	0.6556	0.9486
ko00623	Toluene degradation	0.04706	0.1246	0.7055	0.9686
ko00650	Butanoate metabolism	0.0369	0.1177	0.7538	0.9858
ko00340	Histidine metabolism	0.03388	0.08115	0.6763	0.9581
ko00310	Lysine degradation	0.0195	0.1764	0.912	1
ko05150	Staphylococcus aureus infection	0.01415	0.8251	0.9863	1
ko00290	Valine, leucine and isoleucine biosynthesis	0.01206	0.0812	0.8819	1
ko00061	Fatty acid biosynthesis	0.00915	0.08518	0.9145	1
ko04512	ECM-receptor interaction	0.006811	0.01286	0.5963	0.9011
ko00250	Alanine, aspartate and glutamate metabolism	0.006254	0.09671	0.9484	1
ko00450	Selenocompound metabolism	0.002868	0.07896	0.971	1
ko00473	D-Alanine metabolism	0.002372	0.116	0.9837	1
ko00363	Bisphenol degradation	0.001784	0.1149	0.9876	1
ko00253	Tetracycline biosynthesis	0.001182	0.3134	0.997	1
ko00522	Biosynthesis of 12-, 14- and 16-membered macrolides	0.0004808	0.0008161	0.5557	0.8751
ko00130	Ubiquinone and other terpenoid-quinone biosynthesis	0.0004157	0.1269	0.9974	1
ko04970	Salivary secretion	0.000366	0.001522	0.8099	1
ko05160	Hepatitis C	0.00001747	0.000112	0.876	1
ko00331	Clavulanic acid biosynthesis	0	0.0000896	1	1
ko00532	Glycosaminoglycan biosynthesis - chondroitin sulfate	0	0.0000896	1	1
ko00592	alpha-Linolenic acid metabolism	0	0.0000896	1	1
ko00901	Indole alkaloid biosynthesis	0	0.0000896	1	1
ko00940	Phenylpropanoid biosynthesis	0	0.0000896	1	1
ko03320	PPAR signaling pathway	0	0.0000896	1	1
ko04010	MAPK signaling pathway	0	0.0000896	1	1
ko04020	Calcium signaling pathway	0	0.0000896	1	1
ko04060	Cytokine-cytokine receptor interaction	0	0.0000896	1	1
ko04110	Cell cycle	0	0.0000896	1	1
ko04145	Phagosome	0	0.0000896	1	1

ko04340	Hedgehog signaling pathway	0	0.0000896	1	1
ko04510	Focal adhesion	0	0.0000896	1	1
ko04712	Circadian rhythm - plant	0	0.0000896	1	1
ko04722	Neurotrophin signaling pathway	0	0.0000896	1	1
ko04740	Olfactory transduction	0	0.0000896	1	1
ko04920	Adipocytokine signaling pathway	0	0.0000896	1	1
ko04976	Bile secretion	0	0.0000896	1	1
ko05016	Huntington's disease	0	0.0000896	1	1
ko05142	Chagas disease (American trypanosomiasis)	0	0.0000896	1	1
ko05145	Toxoplasmosis	0	0.0000896	1	1
ko05412	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	0	0.0000896	1	1
ko04520	Adherens junction	-0.0001273	0.0001267	0.3151	0.6064
ko00563	Glycosylphosphatidylinositol(GPI)-anchor biosynthesis	-0.0004987	0.0004673	0.2859	0.5662
ko04320	Dorso-ventral axis formation	-0.0006016	0.002375	0.8	1
ko04962	Vasopressin-regulated water reabsorption	-0.0007725	0.000333	0.02034	0.09878
ko04310	Wnt signaling pathway	-0.001128	0.0006101	0.06443	0.2086
ko04080	Neuroactive ligand-receptor interaction	-0.001239	0.000523	0.01782	0.09086
ko05144	Malaria	-0.001634	0.0005117	0.001401	0.01906
ko00513	Various types of N-glycan biosynthesis	-0.003198	0.01056	0.762	0.9863
ko04810	Regulation of actin cytoskeleton	-0.00503	0.001947	0.009795	0.0689
ko00380	Tryptophan metabolism	-0.008279	0.1771	0.9627	1
ko00020	Citrate cycle (TCA cycle)	-0.01378	0.08321	0.8685	1
ko00010	Glycolysis / Gluconeogenesis	-0.01846	0.1055	0.8611	1
ko00564	Glycerophospholipid metabolism	-0.02275	0.07175	0.7512	0.9858
ko00910	Nitrogen metabolism	-0.02467	0.07337	0.7366	0.9858
ko00040	Pentose and glucuronate interconversions	-0.02864	0.195	0.8833	1
ko00280	Valine, leucine and isoleucine degradation	-0.05405	0.168	0.7476	0.9858
ko00480	Glutathione metabolism	-0.05411	0.1442	0.7075	0.9686
ko00260	Glycine, serine and threonine metabolism	-0.0545	0.0834	0.5135	0.8255
ko01040	Biosynthesis of unsaturated fatty acids	-0.05973	0.1098	0.5863	0.8993
ko00643	Styrene degradation	-0.0606	0.2351	0.7966	1
ko00460	Cyanoamino acid metabolism	-0.0691	0.1047	0.5091	0.8255
ko00071	Fatty acid metabolism	-0.07323	0.1706	0.6678	0.9573
ko00401	Novobiocin biosynthesis	-0.08484	0.5448	0.8763	1
ko00640	Propanoate metabolism	-0.09032	0.1116	0.4184	0.7507
ko00360	Phenylalanine metabolism	-0.09893	0.1516	0.5139	0.8255
ko00591	Linoleic acid metabolism	-0.1028	0.1416	0.4681	0.8076
ko00510	N-Glycan biosynthesis	-0.1103	0.5939	0.8527	1
ko00053	Ascorbate and aldarate metabolism	-0.1166	0.1149	0.3105	0.6033
ko00960	Tropane, piperidine and pyridine alkaloid biosynthesis	-0.1199	0.08285	0.1477	0.3767
ko04974	Protein digestion and absorption	-0.1398	0.644	0.8281	1
ko00660	C5-Branched dibasic acid metabolism	-0.1626	0.08251	0.04882	0.1747
ko05111	Vibrio cholerae pathogenic cycle	-0.1632	0.1428	0.2532	0.527
ko04146	Peroxisome	-0.1764	0.104	0.08986	0.2619
ko00330	Arginine and proline metabolism	-0.1828	0.07048	0.009521	0.0689
ko00120	Primary bile acid biosynthesis	-0.1951	0.4291	0.6493	0.9461
ko00562	Inositol phosphate metabolism	-0.2025	0.1072	0.05885	0.2001
ko00362	Benzoate degradation	-0.2057	0.1872	0.2719	0.5493
ko00364	Fluorobenzoate degradation	-0.2086	0.2592	0.4211	0.7507
ko00983	Drug metabolism - other enzymes	-0.2126	0.3001	0.4787	0.8076
ko05130	Pathogenic Escherichia coli infection	-0.2148	1.239	0.8624	1
ko00410	beta-Alanine metabolism	-0.2475	0.1478	0.0941	0.2704
ko00361	Chlorocyclohexane and chlorobenzene degradation	-0.2545	0.1791	0.1552	0.386
ko00440	Phosphonate and phosphinate metabolism	-0.2773	0.09884	0.005018	0.04095
ko00906	Carotenoid biosynthesis	-0.2884	0.1922	0.1334	0.3445
ko00350	Tyrosine metabolism	-0.2934	0.1215	0.01578	0.08701
ko05014	Amyotrophic lateral sclerosis (ALS)	-0.3314	0.2515	0.1876	0.4345
ko00627	Aminobenzoate degradation	-0.332	0.2076	0.1098	0.2994
ko00980	Metabolism of xenobiotics by cytochrome P450	-0.3954	0.1853	0.03288	0.1315

ko05110	Vibrio cholerae infection	-0.404	1.009	0.6888	0.9611
ko00930	Caprolactam degradation	-0.4054	0.2073	0.05052	0.1747
ko00140	Steroid hormone biosynthesis	-0.4164	0.4924	0.3977	0.7444
ko01057	Biosynthesis of type II polyketide products	-0.418	NaN	NaN	NaN
ko00430	Taurine and hypotaurine metabolism	-0.4677	0.1667	0.005019	0.04095
ko00625	Chloroalkane and chloroalkene degradation	-0.5031	0.0834	1.612E-09	7.756E-08
ko00903	Limonene and pinene degradation	-0.5136	0.1794	0.004197	0.03722
ko00633	Nitrotoluene degradation	-0.5986	0.2568	0.01977	0.09837
ko00472	D-Arginine and D-ornithine metabolism	-0.6842	0.3023	0.02363	0.1049
ko00830	Retinol metabolism	-0.733	0.1036	1.521E-12	1.552E-10
ko00905	Brassinosteroid biosynthesis	-0.7894	0.6374	0.2155	0.4678
ko00624	Polycyclic aromatic hydrocarbon degradation	-0.8233	0.3451	0.01704	0.09086
ko00642	Ethylbenzene degradation	-0.936	0.2189	0.00001901	0.0004309
ko00621	Dioxin degradation	-0.9742	0.3017	0.001243	0.01811
ko05410	Hypertrophic cardiomyopathy (HCM)	-0.9753	0.4326	0.02416	0.1049
ko01056	Biosynthesis of type II polyketide backbone	-0.9891	0.7405	0.1817	0.426
ko00909	Sesquiterpenoid biosynthesis	-1.01	NaN	NaN	NaN
ko00312	beta-Lactam resistance	-1.049	0.8355	0.2091	0.4587
ko05143	African trypanosomiasis	-1.082	0.3971	0.006419	0.0485
ko00626	Naphthalene degradation	-1.146	0.4177	0.006093	0.04781
ko04142	Lysosome	-1.232	NaN	NaN	NaN
ko01053	Biosynthesis of siderophore group nonribosomal peptides	-1.243	0.7852	0.1133	0.3042
ko00311	Penicillin and cephalosporin biosynthesis	-1.388	0.2726	3.567E-07	0.00001213
ko00601	Glycosphingolipid biosynthesis - lacto and neolacto series	-1.817	1.19	0.1269	0.3361
ko05010	Alzheimer's disease	-1.847	0.4512	0.0000425	0.0008669
ko03450	Non-homologous end-joining	-2.063	0.3435	1.901E-09	7.756E-08
ko05200	Pathways in cancer	-2.188	0.7563	0.003817	0.03539
ko05131	Shigellosis	-2.19	1.08	0.04254	0.1607
ko05322	Systemic lupus erythematosus	-2.206	0.7301	0.002521	0.03215
ko00941	Flavonoid biosynthesis	-2.516	0.5265	0.000001755	0.00005115
ko03022	Basal transcription factors	-2.805	1.301	0.03109	0.1268
ko00100	Steroid biosynthesis	-3.202	0.7154	0.000007626	0.0001945

Table S44 The P values of metabolic pathways of microbes in fecal samples.

pathway	description	logFC	SE	Pvalues	adjPvalues
ko00601	Glycosphingolipid biosynthesis - lacto and neolacto series	1.221	0.9458	0.1967	1
ko00514	Other types of O-glycan biosynthesis	0.7555	1.629	0.6428	1
ko04210	Apoptosis	0.5229	1.061	0.6222	1
ko00540	Lipopolysaccharide biosynthesis	0.4795	0.6794	0.4803	1
ko00140	Steroid hormone biosynthesis	0.4656	0.9587	0.6272	1
ko00626	Naphthalene degradation	0.4346	0.3763	0.2481	1
ko00281	Geraniol degradation	0.323	0.9256	0.7271	1
ko01053	Biosynthesis of siderophore group nonribosomal peptides	0.2753	1.222	0.8218	1
ko00590	Arachidonic acid metabolism	0.2752	0.2573	0.2849	1
ko03015	mRNA surveillance pathway	0.2641	0.9671	0.7848	1
ko00830	Retinol metabolism	0.2505	0.59	0.6712	1
ko05130	Pathogenic Escherichia coli infection	0.2103	2.07	0.9191	1
ko03040	Spliceosome	0.1912	0.6944	0.7831	1
ko00311	Penicillin and cephalosporin biosynthesis	0.1888	0.5682	0.7396	1
ko04621	NOD-like receptor signaling pathway	0.1709	0.398	0.6678	1
ko04075	Plant hormone signal transduction	0.1595	1.244	0.898	1
ko00310	Lysine degradation	0.158	0.2524	0.5314	1
ko00630	Glyoxylate and dicarboxylate metabolism	0.1481	0.2247	0.5097	1
ko00531	Glycosaminoglycan degradation	0.1334	0.9496	0.8883	1
ko04974	Protein digestion and absorption	0.1191	1.557	0.939	1
ko00361	Chlorocyclohexane and chlorobenzene degradation	0.119	0.2875	0.679	1
ko02040	Flagellar assembly	0.1081	0.5148	0.8337	1
ko04141	Protein processing in endoplasmic reticulum	0.1011	0.4208	0.8102	1
ko00524	Butirosin and neomycin biosynthesis	0.09086	0.3129	0.7716	1
ko00511	Other glycan degradation	0.08955	0.5003	0.8579	1
ko00040	Pentose and glucuronate interconversions	0.08902	0.204	0.6626	1
ko01051	Biosynthesis of ansamycins	0.07145	0.3128	0.8194	1
ko00960	Tropane, piperidine and pyridine alkaloid biosynthesis	0.07063	0.21	0.7366	1
ko00740	Riboflavin metabolism	0.06741	0.2412	0.7799	1
ko05142	Chagas disease (American trypanosomiasis)	0.05757	0.07931	0.4679	1
ko00053	Ascorbate and aldarate metabolism	0.04055	0.3323	0.9029	1
ko00633	Nitrotoluene degradation	0.03649	0.4159	0.9301	1
ko00910	Nitrogen metabolism	0.03513	0.1645	0.8309	1
ko00360	Phenylalanine metabolism	0.03281	0.2006	0.8701	1
ko02020	Two-component system	0.03095	0.2189	0.8875	1
ko00472	D-Arginine and D-ornithine metabolism	0.02963	1.298	0.9818	1
ko05100	Bacterial invasion of epithelial cells	0.0289	1.325	0.9826	1
ko00410	beta-Alanine metabolism	0.02823	0.2237	0.8996	1
ko03070	Bacterial secretion system	0.02368	0.1877	0.8996	1
ko00860	Porphyrin and chlorophyll metabolism	0.0223	0.3132	0.9432	1
ko02030	Bacterial chemotaxis	0.01446	0.3301	0.9651	1
ko00130	Ubiquinone and other terpenoid-quinone biosynthesis	0.01263	0.5439	0.9815	1
ko00600	Sphingolipid metabolism	0.006966	0.3603	0.9846	1
ko04626	Plant-pathogen interaction	0.006049	0.1446	0.9666	1
ko05412	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	0.001218	0.001562	0.4356	1
ko04970	Salivary secretion	0.000174	0.001095	0.8738	1
ko04110	Cell cycle	0.0001282	0.000137	0.3491	1
ko04510	Focal adhesion	0.00004288	0.00009741	0.6598	1
ko00331	Clavulanic acid biosynthesis	0	0.00008951	1	1
ko00401	Novobiocin biosynthesis	0	0.00008951	1	1
ko00513	Various types of N-glycan biosynthesis	0	0.00008951	1	1
ko00522	Biosynthesis of 12-, 14- and 16-membered macrolides	0	0.00008951	1	1
ko00532	Glycosaminoglycan biosynthesis - chondroitin sulfate	0	0.00008951	1	1
ko00563	Glycosylphosphatidylinositol(GPI)-anchor biosynthesis	0	0.00008951	1	1
ko00592	alpha-Linolenic acid metabolism	0	0.00008951	1	1
ko00901	Indole alkaloid biosynthesis	0	0.00008951	1	1
ko00905	Brassinosteroid biosynthesis	0	0.00008951	1	1
ko00909	Sesquiterpenoid biosynthesis	0	0.00008951	1	1

ko00940	Phenylpropanoid biosynthesis	0	0.00008951	1	1
ko01056	Biosynthesis of type II polyketide backbone	0	0.00008951	1	1
ko03022	Basal transcription factors	0	0.00008951	1	1
ko03320	PPAR signaling pathway	0	0.00008951	1	1
ko04010	MAPK signaling pathway	0	0.00008951	1	1
ko04020	Calcium signaling pathway	0	0.00008951	1	1
ko04060	Cytokine-cytokine receptor interaction	0	0.00008951	1	1
ko04145	Phagosome	0	0.00008951	1	1
ko04320	Dorso-ventral axis formation	0	0.00008951	1	1
ko04340	Hedgehog signaling pathway	0	0.00008951	1	1
ko04520	Adherens junction	0	0.00008951	1	1
ko04614	Renin-angiotensin system	0	0.00008951	1	1
ko04712	Circadian rhythm - plant	0	0.00008951	1	1
ko04722	Neurotrophin signaling pathway	0	0.00008951	1	1
ko04740	Olfactory transduction	0	0.00008951	1	1
ko04810	Regulation of actin cytoskeleton	0	0.00008951	1	1
ko04920	Adipocytokine signaling pathway	0	0.00008951	1	1
ko04976	Bile secretion	0	0.00008951	1	1
ko05014	Amyotrophic lateral sclerosis (ALS)	0	0.00008951	1	1
ko05016	Huntington's disease	0	0.00008951	1	1
ko05145	Toxoplasmosis	0	0.00008951	1	1
ko05160	Hepatitis C	0	0.00008951	1	1
ko05200	Pathways in cancer	0	0.00008951	1	1
ko04080	Neuroactive ligand-receptor interaction	-0.00000994	0.00009006	0.9121	1
ko05144	Malaria	-0.0002935	0.0001532	0.05545	1
ko04512	ECM-receptor interaction	-0.0004874	0.0004888	0.3186	1
ko01057	Biosynthesis of type II polyketide products	-0.005863	0.001884	0.001861	0.09444
ko05120	Epithelial cell signaling in Helicobacter pylori infection	-0.006149	0.3183	0.9846	1
ko00190	Oxidative phosphorylation	-0.01907	0.1906	0.9203	1
ko05111	Vibrio cholerae pathogenic cycle	-0.02522	0.2114	0.905	1
ko03020	RNA polymerase	-0.02926	0.3596	0.9351	1
ko00380	Tryptophan metabolism	-0.0293	0.1812	0.8715	1
ko00920	Sulfur metabolism	-0.03067	0.143	0.8303	1
ko02010	ABC transporters	-0.03743	0.1966	0.849	1
ko00460	Cyanoamino acid metabolism	-0.03966	0.5091	0.9379	1
ko00340	Histidine metabolism	-0.04201	0.3516	0.9049	1
ko00564	Glycerophospholipid metabolism	-0.04335	0.1276	0.7341	1
ko00780	Biotin metabolism	-0.04468	0.2139	0.8346	1
ko04910	Insulin signaling pathway	-0.04475	0.2347	0.8488	1
ko04122	Sulfur relay system	-0.04691	0.1553	0.7625	1
ko00330	Arginine and proline metabolism	-0.04825	0.1558	0.7569	1
ko00020	Citrate cycle (TCA cycle)	-0.05002	0.1364	0.7139	1
ko03013	RNA transport	-0.06034	0.1859	0.7455	1
ko00791	Atrazine degradation	-0.06126	0.7176	0.932	1
ko00510	N-Glycan biosynthesis	-0.06253	0.7013	0.929	1
ko00750	Vitamin B6 metabolism	-0.06564	0.1806	0.7162	1
ko00280	Valine, leucine and isoleucine degradation	-0.06572	0.149	0.6591	1
ko00121	Secondary bile acid biosynthesis	-0.06838	0.7614	0.9284	1
ko00500	Starch and sucrose metabolism	-0.06939	0.2019	0.7311	1
ko00561	Glycerolipid metabolism	-0.07406	0.1651	0.6538	1
ko00250	Alanine, aspartate and glutamate metabolism	-0.07509	0.2435	0.7578	1
ko00523	Polyketide sugar unit biosynthesis	-0.07763	0.3039	0.7984	1
ko00030	Pentose phosphate pathway	-0.08136	0.2088	0.6968	1
ko00120	Primary bile acid biosynthesis	-0.08202	0.7563	0.9136	1
ko00710	Carbon fixation in photosynthetic organisms	-0.08326	0.184	0.6509	1
ko00720	Carbon fixation pathways in prokaryotes	-0.0834	0.1501	0.5784	1
ko00260	Glycine, serine and threonine metabolism	-0.08633	0.1549	0.5773	1
ko00052	Galactose metabolism	-0.08656	0.1801	0.6307	1
ko00520	Amino sugar and nucleotide sugar metabolism	-0.09043	0.1852	0.6254	1

ko00680	Methane metabolism	-0.09107	0.1858	0.624	1
ko00051	Fructose and mannose metabolism	-0.09252	0.1807	0.6088	1
ko00270	Cysteine and methionine metabolism	-0.09386	0.2119	0.6578	1
ko00071	Fatty acid metabolism	-0.09676	0.1711	0.5718	1
ko00473	D-Alanine metabolism	-0.09866	0.2119	0.6415	1
ko00650	Butanoate metabolism	-0.1067	0.1114	0.3383	1
ko00640	Propanoate metabolism	-0.1081	0.1204	0.3695	1
ko00521	Streptomycin biosynthesis	-0.1085	0.2969	0.7147	1
ko00450	Selenocompound metabolism	-0.1097	0.1467	0.4547	1
ko03018	RNA degradation	-0.111	0.2061	0.5902	1
ko03440	Homologous recombination	-0.1147	0.2271	0.6135	1
ko00620	Pyruvate metabolism	-0.1149	0.1529	0.4525	1
ko00550	Peptidoglycan biosynthesis	-0.1158	0.2612	0.6576	1
ko00643	Styrene degradation	-0.1189	0.7368	0.8718	1
ko01040	Biosynthesis of unsaturated fatty acids	-0.1193	0.1452	0.4114	1
ko00290	Valine, leucine and isoleucine biosynthesis	-0.1222	0.2315	0.5975	1
ko03430	Mismatch repair	-0.123	0.2089	0.5559	1
ko00908	Zeatin biosynthesis	-0.123	0.274	0.6534	1
ko00240	Pyrimidine metabolism	-0.1237	0.2206	0.575	1
ko00900	Terpenoid backbone biosynthesis	-0.1258	0.2216	0.5703	1
ko00300	Lysine biosynthesis	-0.126	0.2508	0.6154	1
ko00770	Pantothenate and CoA biosynthesis	-0.1265	0.1935	0.5133	1
ko00670	One carbon pool by folate	-0.1279	0.2302	0.5786	1
ko03410	Base excision repair	-0.1299	0.1751	0.4581	1
ko00760	Nicotinate and nicotinamide metabolism	-0.1344	0.2051	0.5122	1
ko00660	C5-Branched dibasic acid metabolism	-0.139	0.2045	0.4967	1
ko00350	Tyrosine metabolism	-0.1404	0.171	0.4116	1
ko00061	Fatty acid biosynthesis	-0.142	0.2567	0.5802	1
ko00400	Phenylalanine, tyrosine and tryptophan biosynthesis	-0.1436	0.2379	0.5459	1
ko00230	Purine metabolism	-0.1455	0.1766	0.4098	1
ko04112	Cell cycle - Caulobacter	-0.1464	0.2426	0.5463	1
ko01055	Biosynthesis of vancomycin group antibiotics	-0.1472	0.267	0.5815	1
ko03030	DNA replication	-0.1483	0.2108	0.4817	1
ko03060	Protein export	-0.1586	0.2045	0.4382	1
ko00010	Glycolysis / Gluconeogenesis	-0.1621	0.1451	0.264	1
ko00471	D-Glutamine and D-glutamate metabolism	-0.1635	0.2614	0.5317	1
ko03010	Ribosome	-0.1642	0.2561	0.5214	1
ko00430	Taurine and hypotaurine metabolism	-0.165	0.185	0.3723	1
ko04146	Peroxisome	-0.1653	0.1934	0.3928	1
ko03420	Nucleotide excision repair	-0.1658	0.2727	0.5433	1
ko00970	Aminoacyl-tRNA biosynthesis	-0.171	0.2473	0.4893	1
ko00625	Chloroalkane and chloroalkene degradation	-0.1715	0.264	0.5159	1
ko00362	Benzoate degradation	-0.1743	0.2533	0.4912	1
ko00790	Folate biosynthesis	-0.1746	0.1937	0.3673	1
ko00562	Inositol phosphate metabolism	-0.1778	0.2277	0.4348	1
ko02060	Phosphotransferase system (PTS)	-0.1819	0.4295	0.672	1
ko00730	Thiamine metabolism	-0.1928	0.2247	0.3908	1
ko03008	Ribosome biogenesis in eukaryotes	-0.2009	0.2294	0.381	1
ko00480	Glutathione metabolism	-0.2047	0.2888	0.4784	1
ko00440	Phosphonate and phosphinate metabolism	-0.2097	0.192	0.2746	1
ko05410	Hypertrophic cardiomyopathy (HCM)	-0.2396	NaN	NaN	NaN
ko00903	Limonene and pinene degradation	-0.2431	0.5739	0.6719	1
ko00072	Synthesis and degradation of ketone bodies	-0.2482	0.5718	0.6643	1
ko00312	beta-Lactam resistance	-0.2536	0.5048	0.6155	1
ko00621	Dioxin degradation	-0.2551	0.28	0.3622	1
ko00785	Lipoic acid metabolism	-0.2615	0.4482	0.5595	1
ko00627	Aminobenzoate degradation	-0.2763	0.3981	0.4877	1
ko00930	Caprolactam degradation	-0.2932	1.131	0.7955	1
ko00941	Flavonoid biosynthesis	-0.3008	0.8421	0.7209	1

ko05322	Systemic lupus erythematosus	-0.3163	0.6725	0.6381	1
ko05010	Alzheimer's disease	-0.3225	0.1367	0.01828	0.7421
ko00591	Linoleic acid metabolism	-0.3508	0.5472	0.5215	1
ko00624	Polycyclic aromatic hydrocarbon degradation	-0.3715	0.6338	0.5578	1
ko05146	Amoebiasis	-0.4203	0.8903	0.6368	1
ko05131	Shigellosis	-0.4228	0.124	0.0006487	0.04389
ko00364	Fluorobenzoate degradation	-0.4265	0.7305	0.5593	1
ko00983	Drug metabolism - other enzymes	-0.4478	NaN	NaN	NaN
ko00906	Carotenoid biosynthesis	-0.4983	1.154	0.666	1
ko00965	Betalain biosynthesis	-0.6255	1.751	0.721	1
ko00623	Toluene degradation	-0.6442	0.3453	0.06213	1
ko04144	Endocytosis	-0.6907	1.728	0.6894	1
ko04310	Wnt signaling pathway	-0.6969	1.388	0.6157	1
ko05110	Vibrio cholerae infection	-0.7063	0.5858	0.228	1
ko00980	Metabolism of xenobiotics by cytochrome P450	-0.7227	0.5043	0.1518	1
ko05143	African trypanosomiasis	-0.7376	1.134	0.5153	1
ko04113	Meiosis - yeast	-0.7782	NaN	NaN	NaN
ko00622	Xylene degradation	-0.8059	0.3699	0.02936	0.9934
ko03450	Non-homologous end-joining	-0.8399	1.11	0.4494	1
ko05150	Staphylococcus aureus infection	-0.8961	0.9637	0.3525	1
ko00363	Bisphenol degradation	-1.013	0.489	0.03829	1
ko00943	Isoflavonoid biosynthesis	-1.121	0.647	0.08317	1
ko05012	Parkinson's disease	-1.123	1.009	0.266	1
ko00100	Steroid biosynthesis	-1.222	1.826	0.5035	1
ko03050	Proteasome	-1.308	1.788	0.4646	1
ko04962	Vasopressin-regulated water reabsorption	-1.38	1.3	0.2885	1
ko00196	Photosynthesis - antenna proteins	-1.641	0.8937	0.06632	1
ko00642	Ethylbenzene degradation	-1.784	0.9623	0.06368	1
ko00195	Photosynthesis	-1.785	NaN	NaN	NaN
ko04142	Lysosome	-1.861	0.2934	2.243E-10	4.553E-08
ko00253	Tetracycline biosynthesis	-2.776	0.639	0.00001394	0.001414