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Lower airway microbiome and metabolomic profiles of recurrent wheezing in infants: a case-control study

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KEYWORDS
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Abstract
Objectives: To characterize the microbiome shifts and subsequent metabolite alterations associated with recurrent wheezing (RW) in infants.
Methods: A total of 33 subjects were enrolled in this study, including 18 infants diagnosed with RW, and 15 normal infants as controls. Bronchoalveolar lavage (BAL) fluid was collected from all the subjects. Bacterial DNA was then isolated and analyzed by 16S ribosomal RNA sequencing. In addition, the metabolomic profile of BAL fluid samples was analyzed with mass spectrometry using complementary chromatographic methods. Spearman's rank correlation analysis was conducted to explore associations between microbial taxa and metabolites.
Results: The study had 21 (63.6%) boys and 12 (36.4%) girls. The mean age was 26.8 ± 4.9 months. Haemophilus (P = 0.003) and Porphyromonas (P = 0.007) genera showed significant difference between the two groups. The metabolites of "starch and sucrose metabolism pathway" and "pentose phosphate pathway" showed significant correlations with the two bacterial genera. For starch and sucrose metabolism pathway, glucose-6-phosphate showed significant positive correlations with Haemophilus (r = 0.44 and P = 0.009) and Porphyromonas (r = 0.45 and P = 0.008). For pentose phosphate pathway, Sedoheptulose 7-phosphate, an intermediate in the pentose phosphate pathway, showed significantly positive correlations with Haemophilus (r = 0.42 and P = 0.02) and Porphyromonas (r = 0.43 and P = 0.01).
Conclusions: Our study provided new evidence that alteration in respiratory tract microbiome could be associated with RW in infants. By elucidating the microbiome and metabolite profile, we identified novel biomarkers potentially useful for personalized management of RW in infants. The future studies should validate the underlying mechanisms in longitudinal cohorts and explore interventions targeting metabolic-microbial crosstalk.

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Introduction

Recurrent wheezing (RW) in infants is defined as three or more episodes of wheezing within a period of 12 months, typically occurring in children aged <3 years.[1] It is a heterogeneous condition characterized by high-pitched expiratory breathing sounds because of narrowed or inflamed small airways. Epidemiologically, RW affects 5–10% of preschool-aged children globally, with higher prevalence in urbanized regions and low-income populations because of environmental exposures.[2,3] Unlike transient viral-induced wheezing, this condition persists beyond infancy and is strongly linked to subsequent development of asthma.[4] Longitudinal studies indicate that 30% of the affected children progress to asthma by adolescence, contributing to long-term pulmonary dysfunction and increased healthcare costs.[5] It is therefore important to elucidate the etiology of RW for risk stratification and early intervention.

Recent etiological studies have highlighted that RW in infants arises from the interplay of environmental triggers, genetic predisposition, and immune dysregulation.[6-8] Environmental factors, such as early-life viral infections, air pollution, and microbiome disruptions, may further modulate immune responses, particularly in genetically vulnerable individuals.[9,10] Despite extensive research, the etiology of RW in infants remains elusive. Multidisciplinary approaches integrating multi-omics and longitudinal cohorts are essential to unravel causal pathways and identify actionable therapeutic targets.

Bacterial diversity in the respiratory tract is critical for maintaining immune homeostasis, as commensal microbes regulate epithelial barrier integrity, and modulate inflammatory responses and prime adaptive immunity through metabolite-mediated signaling.[11] Disruption in microbial equilibrium is implicated in the pathogenesis of allergic diseases and asthma. Reduced diversity and dominance of proteobacterial taxa were reported to be implicated in airway inflammation and hyperreactivity.[12,13] Despite these advances, the composition and functional dynamics of the lower airway microbiome in infants with RW remain poorly understood. In this study, we addressed these gaps by characterizing the lower airway microbiome and metabolomics profile in infants with RW using 16S ribosomal RNA (rRNA) sequencing and untargeted metabolomics. We aimed to characterize the microbiome shifts and subsequent metabolite alterations associated with RW in infants.

Methods

Subjects

This is a prospective study approved by the Ethics Review Board of Children's Hospital of Soochow University (#2023CS038). We included 15 infants diagnosed with RW at our center between January 2018 and December 2022. Written informed consent was obtained from the guardians of all included participants. The following inclusion criteria were adopted: (1) diagnosed with wheezing by an experienced pediatric pulmonology physician; (2) aged between 12 and 36 months; (3) occurrence of wheezing for more than three times in the past year; and (4) no history of administration of inhaled corticosteroids or antibiotics in the past 2 weeks. In addition, 18 age-matched infants who underwent bronchoscopy because of aspiration of a foreign body were recruited as controls. Subjects with known diagnosis of lung disease, dysfunctional breathing, bronchopulmonary dysplasia, cystic fibrosis, or other acute illness were excluded from the study.

Collection of bronchoalveolar lavage (BAL) fluid

Bronchoalveolar lavage fluid was collected under sterile conditions via flexible bronchoscopy performed under general anesthesia to minimize contamination. By following standardized protocols, the bronchoscope was advanced to the subsegmental bronchus, and three aliquots of sterile saline (1–2 mL/kg per aliquot) were instilled and immediately aspirated, with the first aliquot discarded to reduce upper airway contamination. The retrieved BAL fluid was placed on ice and processed within 30 min to preserve microbial integrity. Samples were centrifuged (4°C, 10 min, 500 ×*g*) to pellet cellular debris, and the supernatant was aliquoted and stored at -80°C until further detection.

Bacterial DNA isolation and 16S rRNA sequencing

For microbiome profiling, DNA was extracted from the pellet using a validated microbial DNA isolation kit (Qiagen DNeasy PowerSoil Pro kit, Qiagen Inc., Hilden, Germany), incorporating mechanical lysis (bead-beating) to disrupt tough microbial cell walls. Extracted DNA underwent 16S rRNA gene amplification (V3–V4 hypervariable regions) via polymerase chain reaction (PCR), followed by high-throughput sequencing (Illumina MiSeq platforms).[11] Negative controls (sterile saline processed identically) were included to account for environmental or reagent contamination.

Paired-end reads were assigned to samples using unique barcodes, followed by truncation of barcode and primer sequences. The trimmed reads were merged with Fast Length Adjustment of Short Reads (FLASH, v1.2.7) to generate raw tags. Demultiplexing and subsequent processing were performed in Quantitative Insights into Microbial Ecology (QIIME) (V1.9.1), where sequence errors were corrected via Deficiency of Adenosine Deaminase 2 (DADA2). A phylogenetic tree was constructed to support phylogenetic diversity analyses. Taxonomic classification was conducted using the SILVA database. The alpha diversity index between groups was analyzed using the R software (Wilcoxon test). Beta diversity was evaluated using weighted and unweighted UniFrac distances, visualized through principal coordinates analysis (PCoA) to illustrate sample clustering. Finally, linear discriminant analysis (LDA) effect size (LEfSe) was applied to identify taxonomy exhibiting significant differences both statistically and biologically.

Metabolomics detection and analysis

For untargeted metabolomics analysis, thawed BAL supernatant was extracted using cold methanol acetonitrile

water. After centrifugation (14,000 ×*g*, 15 min, 4°C), the supernatant was analyzed via liquid chromatography tandem with mass spectrometry (LC-MS) using complementary chromatographic methods as reported previously. High-resolution mass spectrometry (HRMS) was performed in both positive and negative ion modes to maximize metabolite coverage. Raw data were processed using the XCMS software for peak detection, alignment, and noise reduction. Metabolites were annotated with spectral libraries (METLIN) and the functional pathways were annotated using Kyoto Encyclopedia of Genes and Genomes (KEGG).[14]

Statistical analysis

Statistical analysis was performed using the R software (v4.0.2). Characteristics of the study population were analyzed using the Chi-square test and *t*-test. Differences in bacterial diversity and relative abundance between the two groups were assessed by the Wilcoxon rank-sum test, with a false discovery rate (FDR) of 5%. Metabolomic data were log-transformed prior to analysis. Multivariate analyses were applied to illustrate differences in samples, including orthogonal partial least squares discriminant analysis (OPLS-DA). Spearman's rank correlation analysis was conducted to explore associations between microbial taxa and metabolites. All P values were two-tailed, and statistical significance was defined as $P < 0.05$. Specifically, for LEfSe analysis, LDA > 3.0 and $P < 0.05$ were considered as statistically significant. For metabolomics, differentially expressed metabolites were based on $P < 0.05$ from Student's *t*-test, and variable importance in projection (VIP) > 1 because of OPLS-DA.

Results

Characteristics of study population

A total of 33 subjects were enrolled in this study, including 18 infants with RW, and 15 infants as controls. There were 21 (63.6%) boys and 12 (36.4%) girls. The mean age was 26.8 ± 4.9 months. All children were from Han population. The baseline characteristics of each group are summarized in Table 1.

Table 1 The baseline characteristics of subjects.

	Recurrent wheezing (RW) group (n = 18)	Control group (n = 15)	P
Age (month)	25.3 ± 4.6	27.5 ± 5.7	0.22
Gender (M/F)	11/7	10/5	0.97
BMI (kg/m^2)	13.7 ± 2.1	14.1 ± 2.3	0.61
WBC counts (×10^9/L)	6.5 ± 3.5	5.7 ± 3.8	0.53
Neutrophils (%)	62.1 ± 18.6	71.3 ± 20.4	0.19
Eosinophils (%)	7.5 ± 3.1	3.2 ± 2.5	0.001

Note: BMI: body mass index; WBC: white blood cells.

Patients were found to have higher eosinophil count than the controls with statistical significance (P = 0.001). There was no significant difference in terms of age, gender, body mass index (BMI), and blood WBC and neutrophil counts between the two groups.

Diversity in lower airway microbiome

The characteristics of lower airway bacteria in the patients and the controls are shown in Figures 1A and 1B. The Chao1 (richness; P = 0.07) and Simpson (dominance; P = 0.08) indices showed no significant differences between the two groups, which indicated relatively similar bacterial richness and alpha diversity in both groups. The PCoA was performed using weighted UniFrace distance, and Analysis of Similarities (ANOSIM) was performed to evaluate differences between both groups. PCoA and ANOSIM results suggested significant differences in beta diversity between two groups (P = 0.023; Figures 1C and 1D).

Distribution of taxa at phylum and genus levels

The sequenced data were analyzed according to 35 phyla. The relative abundance of top 10 phyla is shown in Figure 2A. Proteobacteria, Firmicutes, Bacteroidetes, and Actinobacteria were the dominant phyla of bacteria in all samples. Bacteroidota (P = 0.008) and Fusobacteriota (P= 0.01) showed significant difference between the two groups. Figure 2B shows the relative abundance of top 20 genus between the two groups. Haemophilus (P = 0.003) and Porphyromonas (P = 0.007) genera showed significant differences between the two groups.

The LEfSe analysis was performed to identify differences in the composition of bacterial taxa between the two groups. With LDA scores > 3.0, differentially expressed bacteria were identified, some of which were highly abundant in RW infants. Notably, genera Haemophilus and Porphyromonas were significantly abundant in RW infants ($P < 0.05$; Figures 2C and 2D).

Characteristics of lower airway metabolomics

The OPLS-DA result suggested significant differences between the two groups (Figure 3A), with permutation test confirming OPLS-DA model (Figure 3B). Using Student's *t*-test ($P < 0.05$) and VIP > 1 because of OPLS-DA, we identified 256 significantly differentially expressed metabolites, which were predominantly lipids as shown in the heatmap (Figure 3C). Among all the differentially expressed metabolites, 50 were up-regulated and 206 were down-regulated (Figure 3D). Metabolic pathway analyses were then performed to reveal the relationship between differentially expressed metabolites and known metabolic pathways. In all, 20 pathways were significantly impacted in RW infants (Figure 3E). The pathway "glycine, serine and threonine metabolism" was the most significantly impacted in RW infants, followed by "pentose phosphate pathway (PPP)" and "starch and sucrose metabolism pathway" (Figure 3F).

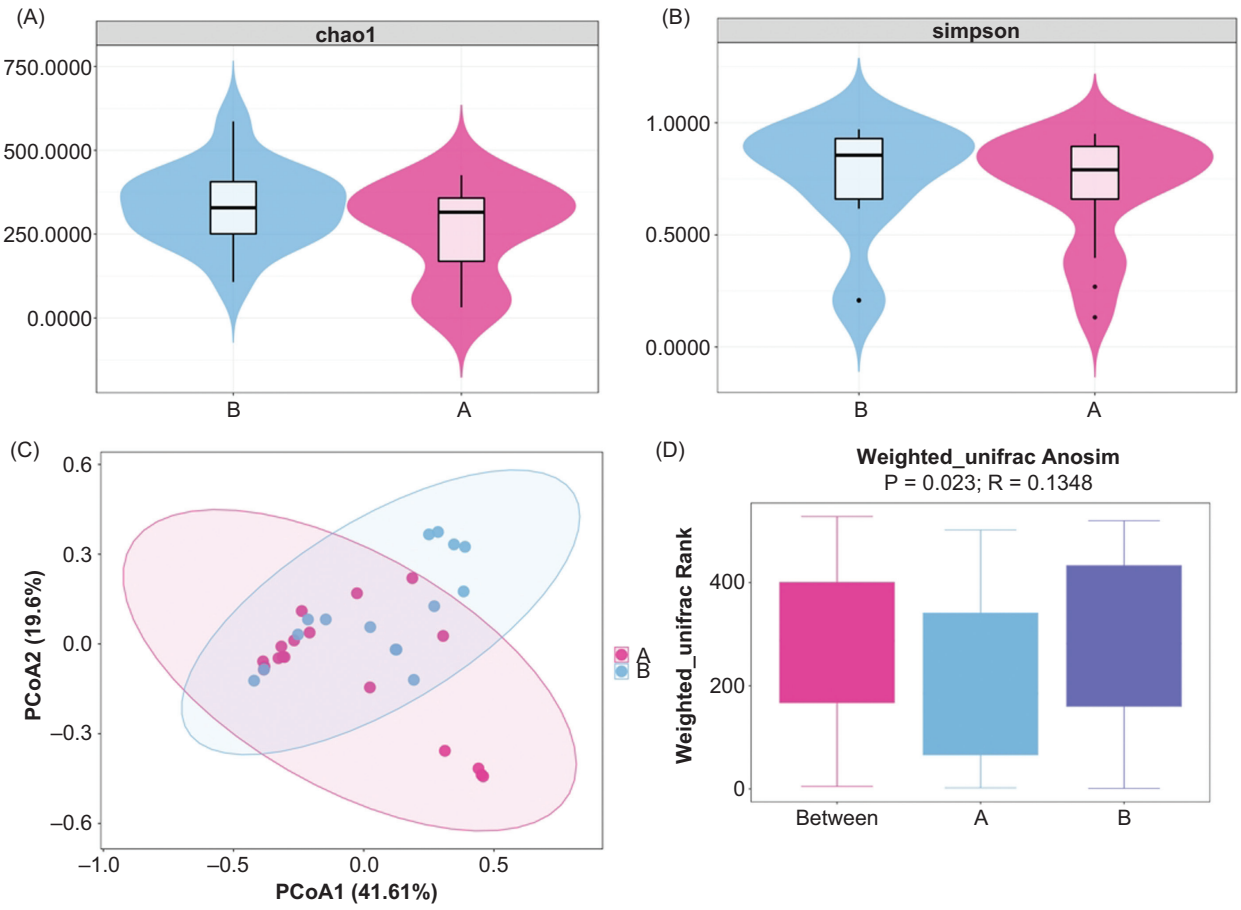

Figure 1 Characteristics of the lower airway microbiome. The (A) Chao1 (P = 0.07) and (B) Simpson (P = 0.08) indices indicated similar bacterial richness and alpha diversity in both groups (C) the PCoA plot based on unweighted UniFrac distance and (D) ANOSIM results based on weighted Unifrac showed significant difference in beta diversity between the two groups (P = 0.023).

Correlation between lower airway microbiome and metabolites

To investigate the relationship between altered microbiome and altered metabolites, we analyzed the correlations between altered genera and altered metabolites using the Spearman's rank correlation analysis. As summarized in Figure 4, we discovered that the metabolites of starch and sucrose metabolism pathway and PPP showed significant correlations, with the two microbes highly abundant in RW infants (Tables S1 and S2). For starch and sucrose metabolism pathway, glucose-6-phosphate (G6P) showed significantly positive correlations with Haemophilus (r = 0.44 and P = 0.009) and Porphyromonas (r = 0.45 and P = 0.008). For PPP, sedoheptulose 7-phosphate (S7P), an intermediate in the pentose phosphate pathway, showed significantly positive correlations with Haemophilus (r = 0.42 and P = 0.02) and Porphyromonas (r = 0.43 and P = 0.01).

Discussion

The pathological mechanism of RW in infants has not been fully elucidated. Recent studies have shown that the human lower airway microbiome could be an etiological factor of various diseases.[15-17] Variation of lower airway bacterial diversity is discovered as closely associated with respiratory diseases, such as asthma and cystic fibrosis.[18,19] Tang et al.[20] investigated the bronchial bacterial microbiome of infants with RW and reported significant differences in diversity in patients, compared to controls. In this study, for the first time, we combined 16S amplicon sequencing and untargeted metabolomics analysis to explore the association of lower airway microbiome with RW. We discovered that RW infants shared some alterations in lower airway microbes and microbiome-derived metabolites. Besides, in line with the findings of Tang et al.,[20] we confirmed that RW infants had significantly different lower airway microbiome diversity, which suggested that lower airway microbiome could be associated with the development of RW.

In the current study, we determined two microbes, Haemophilus and **Porphyromonas,** especially altered in RW infants. Haemophilus was reported to induce neutrophilic inflammation and exacerbate airway hyperreactivity.[21] Studies in Haemophilus-colonized murine models demonstrated enhanced airway remodeling driven by transforming growth factor-beta (TGF-ß) and matrix metalloproteinases, which could perpetuate wheezing episodes.[22] **Porphyromonas**, a genus traditionally linked to periodontal disease, has recently been implicated in

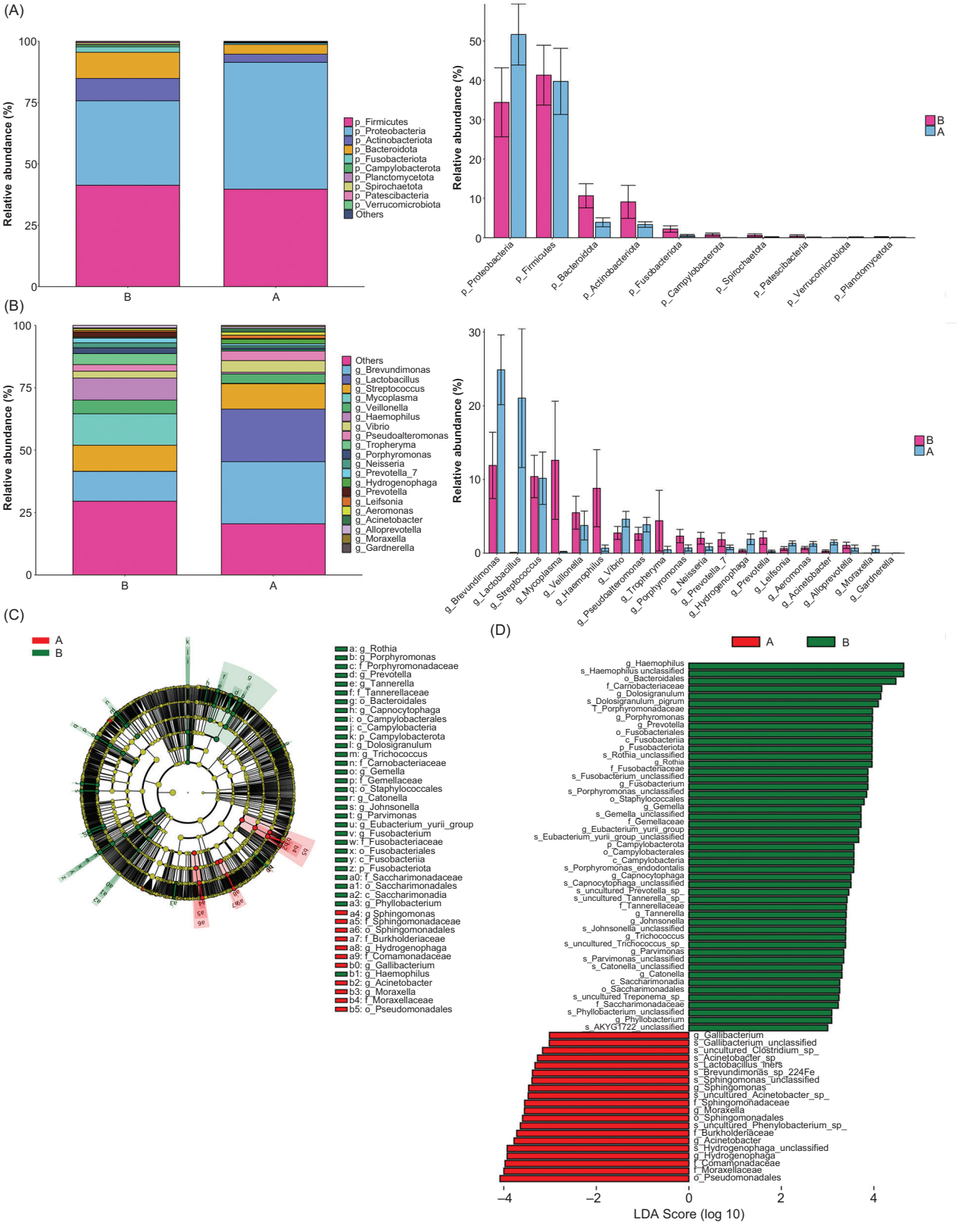

Figure 2 The distribution of taxa at phylum and genus levels. Composition of microbiome at (A) phylum level and (B) genus level. At phylum level, Bacteroidota (P = 0.008) and Fusobacteriota (P=0.01) showed significant difference between the two groups. At genus level, Haemophilus (P = 0.003) and Porphyromonas (P = 0.007) showed significant difference between the two groups. The height of bars represents relative abundance. (C) Bacterial taxa differentially abundant are visualized using a cladogram, with the size of each node indicating relative abundance; (D) with LDA scores > 3.0, the graph of LEfSe distinguishes the microbial communities of each group. Genera Haemophilus and Porphyromonas were significantly abundant in RW infants (P < 0.05).

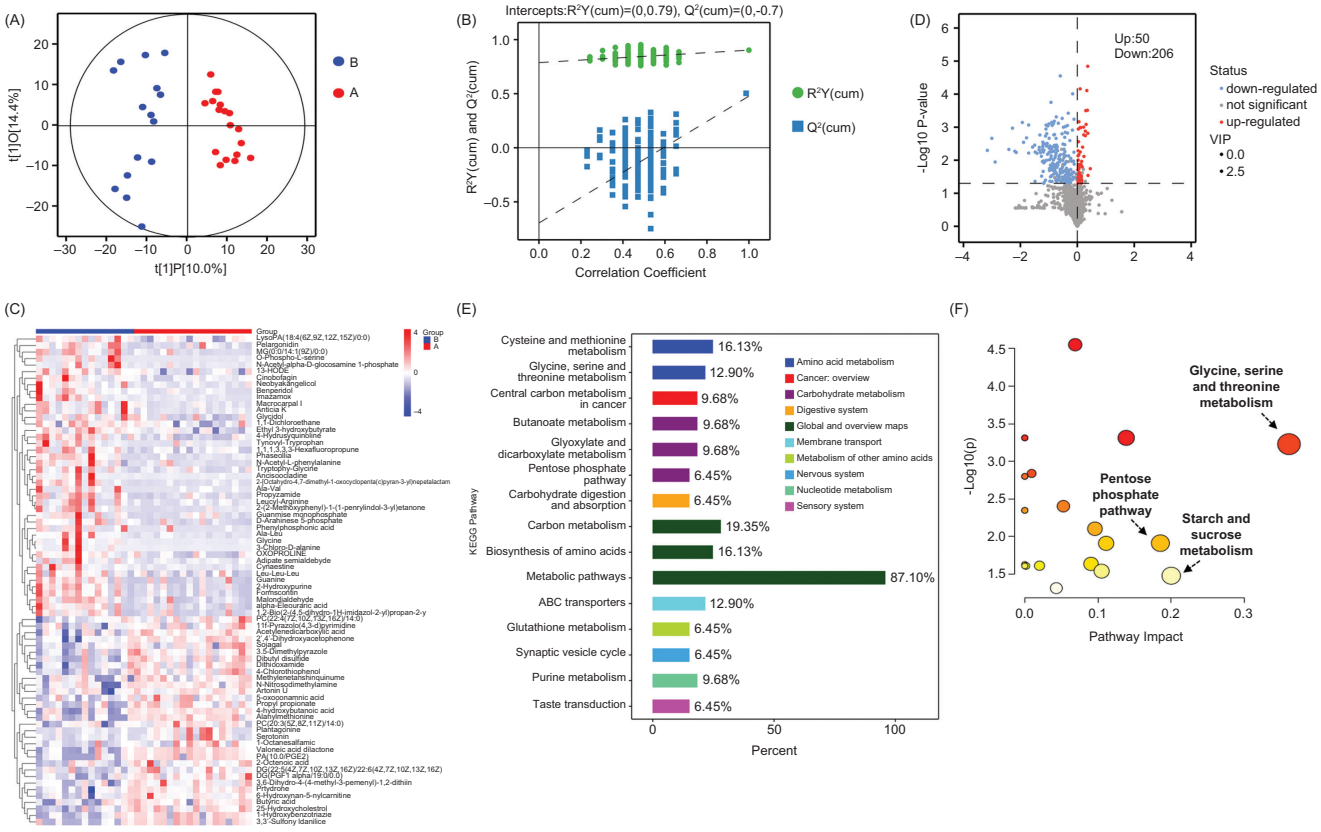

Figure 3 Characteristics of lower airway metabolomics. (A) The OPLS-DA results from all plasma metabolites demonstrated the discriminatory ability of metabolite profiles for both groups; (B) the OPLS-DA model was successfully confirmed with permutation test; (C) heatmap of significant metabolites which differed between the two groups: with higher concentrations, shown in red, and with lower concentrations, shown in blue; (D) volcano plots are displayed, with downregulated and upregulated metabolites shown in blue and red, respectively; (E) KEGG pathway analysis revealed a total of 20 pathways, which were significantly impacted in RW infants; (F) pathway impact represented relative importance of the identified metabolites in the pathway, with larger circles indicating more important pathway impact.

lung diseases. In allergic airways, *Porphyromonas gingivalis* exacerbates inflammation through activation of interleukin 6 (IL-6) and tumor necrosis factor-α (TNF-α).[23] These cytokines may promote neutrophilic infiltration and mucus hypersecretion, which are commonly featured in severe wheezing.[24] Taken together, the co-occurrence of these genera could be involved in RW through multiple mechanisms. The potential roles of these distinct microbes in the development of RW need to be further studied.

In addition to microbes, we further investigated the metabolomics profile of lower airway microbiome. We discovered that several pathways were significantly impacted in RW patients. The correlation analysis showed that two metabolites, G6P and S7P, were significantly associated with two microbes identified in microbiome sequencing. G6P and S7P belong to PPP and starch and sucrose metabolism pathway, respectively. G6P is critical for production of nicotinamide adenine dinucleotide phosphate (NADPH) and synthesis of ribose-5-phosphate. G6P-driven glycolysis in epithelial cells may reduce adenosine triphosphate (ATP) available for barrier maintenance.[25]

In murine asthma models, inhibition of glycolysis reduces airway hyperreactivity.[26] S7P is a precursor for ribose-5-phosphate, essential for nucleotide synthesis.[27] Excessive S7P could indicate dysregulated PPP activity.[28] In hypoxic or inflamed airways, rapid epithelial turnover may increase S7P demand to support DNA repair. Taken together, high G6P with Haemophilus dominance may signal Th17-high inflammation, warranting IL-17 inhibitors. Moreover, elevated S7P with *Porphyromonas* could indicate mucus hypersecretion, which may suggest anti-inflammation interventions.

The future studies should validate the convergence of G6P and S7P dysregulation with these microbes in longitudinal cohorts. Understanding the underlying mechanisms could pave the way for precision therapies tailored to individual microbial and metabolic profiles.

There were several limitations to this study, which need to be addressed. First, the sample size of the subjects was relatively small, which could limit the power to detect subtle but biologically relevant differences. Recruiting more subjects in the future, study can add to the statistical effectiveness. Second, it cannot be ruled out that the control subjects may have airway inflammation or microbiome disruption, which can potentially lead to selection bias. Third, the cross-sectional nature of the study limited mechanistic investigation. The causal relationship between metabolites and microbial taxa should be further

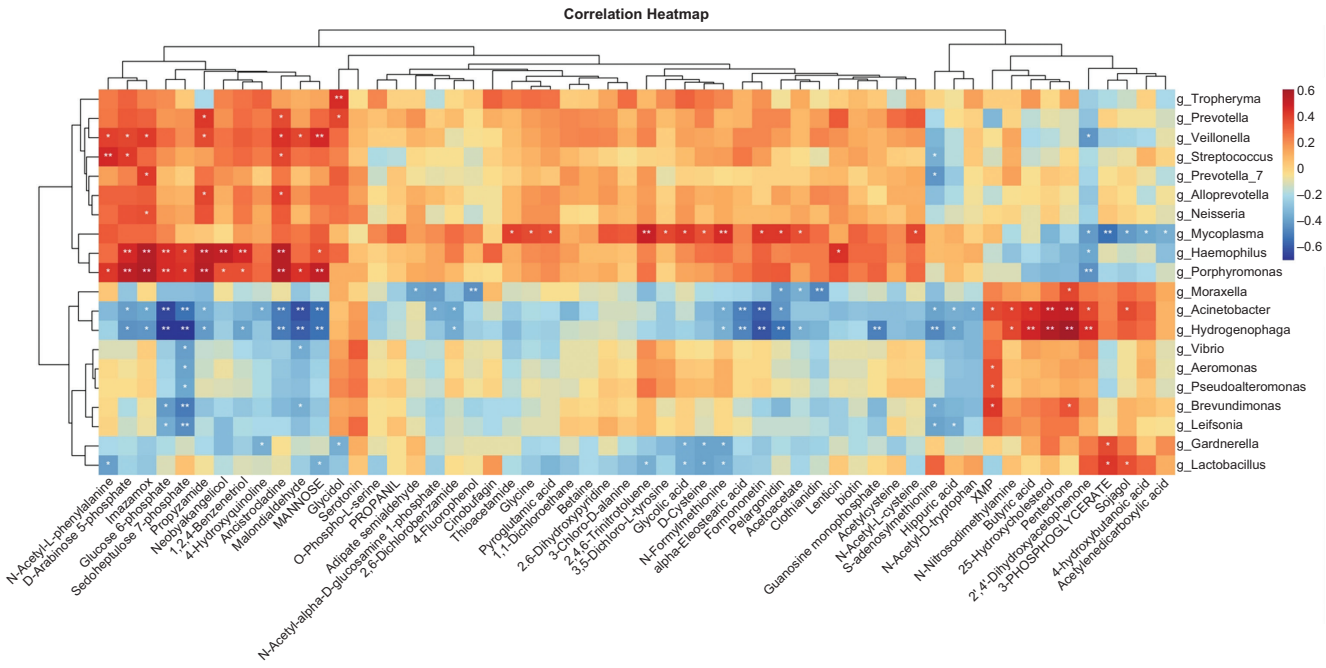

Figure 4 Spearman's rank correlation analysis for significantly altered metabolites and genera. The metabolites of starch and sucrose metabolism pathway and pentose phosphate pathway (PPP) showed significant correlations with the microbes highly abundant in RW infants. For starch and sucrose metabolism pathway, glucose-6-phosphate (G6P) showed significantly positive correlations with Haemophilus (r = 0.44 and P = 0.009) and Porphyromonas (r = 0.45 and P = 0.008). For PPP, sedoheptulose 7-phosphate (S7P) showed significantly positive correlations with Haemophilus (r = 0.42 and P = 0.02) and Porphyromonas (r = 0.43 and P = 0.01).

investigated by longitudinal study. Fourth, the taxonomic analysis of our study was limited to the genus level. In the future study, we plan to include shotgun metagenomics sequencing to further explore differences on species level, and if possible, find specific strains of bacteria.

Conclusions

Our study provided new evidence that alteration in the respiratory tract microbiome could be associated with RW in infants. By elucidating the microbiome and metabolite profile, we identified novel biomarkers potentially useful for personalized management of RW in infants. The future studies should validate the underlying mechanisms in longitudinal cohorts and explore interventions targeting metabolic-microbial crosstalk.

Mandatory Disclosure on Use of Artificial Intelligence

The authors declare that no AI-assisted tools were used in the preparation of this manuscript. All references have been manually verified for accuracy and relevance.

Conflict of Interest

The authors had nothing to disclose regarding funding or any conflict of interest with respect to this manuscript.

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Author Contributions

All authors contributed equally to this study.

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Supplementary

Table S1

Data 1	Data 2	rho	p value	relation
g__Acinetobacter	1,1–Dichloroethane	−0.341	0.053	negtive
g__Lactobacillus	1,1–Dichloroethane	−0.282	0.111	negtive
g__Veillonella	1,1–Dichloroethane	0.211	0.238	positive
g__Prevotella	1,1–Dichloroethane	0.208	0.245	positive
g__Prevotella_7	1,1–Dichloroethane	0.191	0.286	positive
g__Haemophilus	1,1–Dichloroethane	0.157	0.383	positive
g__Alloprevotella	1,1–Dichloroethane	0.139	0.440	positive
g__Hydrogenophaga	1,1–Dichloroethane	−0.137	0.444	negtive
g__Gardnerella	1,1–Dichloroethane	−0.122	0.499	negtive
g__Pseudoalteromonas	1,1–Dichloroethane	−0.110	0.542	negtive
g__Mycoplasma	1,1–Dichloroethane	0.108	0.549	positive
g__Porphyromonas	1,1–Dichloroethane	0.104	0.565	positive
g__Aeromonas	1,1–Dichloroethane	−0.094	0.601	negtive
g__Vibrio	1,1–Dichloroethane	−0.091	0.613	negtive
g__Streptococcus	1,1–Dichloroethane	0.080	0.659	positive
g__Moraxella	1,1–Dichloroethane	−0.049	0.785	negtive
g__Leifsonia	1,1–Dichloroethane	0.043	0.812	positive
g__Neisseria	1,1–Dichloroethane	−0.025	0.890	negtive
g__Tropheryma	1,1–Dichloroethane	0.017	0.927	positive
g__Brevundimonas	1,1–Dichloroethane	−0.010	0.956	negtive
g__Haemophilus	1,2,4–Benzenetriol	0.458	0.007	positive
g__Hydrogenophaga	1,2,4–Benzenetriol	−0.390	0.026	negtive
g__Porphyromonas	1,2,4–Benzenetriol	0.351	0.045	positive
g__Acinetobacter	1,2,4–Benzenetriol	−0.323	0.068	negtive
g__Veillonella	1,2,4–Benzenetriol	0.321	0.069	positive
g__Streptococcus	1,2,4–Benzenetriol	0.291	0.100	positive
g__Brevundimonas	1,2,4–Benzenetriol	−0.276	0.120	negtive
g__Prevotella	1,2,4–Benzenetriol	0.274	0.123	positive
g__Alloprevotella	1,2,4–Benzenetriol	0.263	0.139	positive
g__Tropheryma	1,2,4–Benzenetriol	0.263	0.139	positive
g__Neisseria	1,2,4–Benzenetriol	0.255	0.151	positive
g__Gardnerella	1,2,4–Benzenetriol	−0.246	0.168	negtive
g__Vibrio	1,2,4–Benzenetriol	−0.203	0.257	negtive
g__Leifsonia	1,2,4–Benzenetriol	−0.198	0.269	negtive
g__Moraxella	1,2,4–Benzenetriol	−0.178	0.321	negtive
g__Mycoplasma	1,2,4–Benzenetriol	0.164	0.362	positive
g__Prevotella_7	1,2,4–Benzenetriol	0.151	0.402	positive
g__Aeromonas	1,2,4–Benzenetriol	−0.139	0.440	negtive
g__Pseudoalteromonas	1,2,4–Benzenetriol	−0.133	0.459	negtive
g__Lactobacillus	1,2,4–Benzenetriol	−0.118	0.512	negtive
g__Mycoplasma	2,4,6–Trinitrotoluene	0.483	0.004	positive
g__Lactobacillus	2,4,6–Trinitrotoluene	−0.350	0.047	negtive
g__Moraxella	2,4,6–Trinitrotoluene	−0.319	0.070	negtive
g__Porphyromonas	2,4,6–Trinitrotoluene	0.270	0.129	positive
g__Pseudoalteromonas	2,4,6–Trinitrotoluene	0.267	0.134	positive
g__Gardnerella	2,4,6–Trinitrotoluene	−0.259	0.146	negtive
g__Haemophilus	2,4,6–Trinitrotoluene	0.231	0.195	positive
g__Veillonella	2,4,6–Trinitrotoluene	0.228	0.203	positive
g__Hydrogenophaga	2,4,6–Trinitrotoluene	−0.226	0.205	negtive
g__Vibrio	2,4,6–Trinitrotoluene	0.205	0.252	positive
g__Prevotella	2,4,6–Trinitrotoluene	0.200	0.265	positive
g__Aeromonas	2,4,6–Trinitrotoluene	0.177	0.323	positive
g__Neisseria	2,4,6–Trinitrotoluene	0.173	0.334	positive
g__Prevotella_7	2,4,6–Trinitrotoluene	0.172	0.340	positive
g__Alloprevotella	2,4,6–Trinitrotoluene	0.166	0.355	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Acinetobacter	2,4,6–Trinitrotoluene	−0.161	0.370	negtive
g__Brevundimonas	2,4,6–Trinitrotoluene	0.085	0.636	positive
g__Tropheryma	2,4,6–Trinitrotoluene	0.081	0.652	positive
g__Leifsonia	2,4,6–Trinitrotoluene	0.079	0.662	positive
g__Streptococcus	2,4,6–Trinitrotoluene	−0.010	0.958	negtive
g__Porphyromonas	2’,4’–Dihydroxyacetophenone	−0.450	0.009	negtive
g__Hydrogenophaga	2’,4’–Dihydroxyacetophenone	0.448	0.010	positive
g__Veillonella	2’,4’–Dihydroxyacetophenone	−0.425	0.014	negtive
g__Mycoplasma	2’,4’–Dihydroxyacetophenone	−0.411	0.017	negtive
g__Acinetobacter	2’,4’–Dihydroxyacetophenone	0.386	0.027	positive
g__Haemophilus	2’,4’–Dihydroxyacetophenone	−0.374	0.032	negtive
g__Lactobacillus	2’,4’–Dihydroxyacetophenone	0.336	0.057	positive
g__Prevotella	2’,4’–Dihydroxyacetophenone	−0.282	0.112	negtive
g__Alloprevotella	2’,4’–Dihydroxyacetophenone	−0.271	0.127	negtive
g__Tropheryma	2’,4’–Dihydroxyacetophenone	−0.248	0.164	negtive
g__Neisseria	2’,4’–Dihydroxyacetophenone	−0.240	0.178	negtive
g__Gardnerella	2’,4’–Dihydroxyacetophenone	0.236	0.185	positive
g__Moraxella	2’,4’–Dihydroxyacetophenone	0.234	0.191	positive
g__Prevotella_7	2’,4’–Dihydroxyacetophenone	−0.226	0.206	negtive
g__Streptococcus	2’,4’–Dihydroxyacetophenone	−0.190	0.290	negtive
g__Vibrio	2’,4’–Dihydroxyacetophenone	0.189	0.292	positive
g__Brevundimonas	2’,4’–Dihydroxyacetophenone	0.171	0.339	positive
g__Aeromonas	2’,4’–Dihydroxyacetophenone	0.138	0.445	positive
g__Leifsonia	2’,4’–Dihydroxyacetophenone	0.098	0.589	positive
g__Pseudoalteromonas	2’,4’–Dihydroxyacetophenone	0.097	0.592	positive
g__Acinetobacter	2,6–Dichlorobenzamide	−0.373	0.033	negtive
g__Hydrogenophaga	2,6–Dichlorobenzamide	−0.371	0.034	negtive
g__Mycoplasma	2,6–Dichlorobenzamide	0.273	0.124	positive
g__Moraxella	2,6–Dichlorobenzamide	−0.271	0.127	negtive
g__Haemophilus	2,6–Dichlorobenzamide	0.236	0.186	positive
g__Brevundimonas	2,6–Dichlorobenzamide	−0.136	0.450	negtive
g__Leifsonia	2,6–Dichlorobenzamide	−0.130	0.471	negtive
g__Gardnerella	2,6–Dichlorobenzamide	−0.120	0.507	negtive
g__Veillonella	2,6–Dichlorobenzamide	−0.086	0.633	negtive
g__Prevotella_7	2,6–Dichlorobenzamide	−0.082	0.648	negtive
g__Porphyromonas	2,6–Dichlorobenzamide	0.081	0.655	positive
g__Prevotella	2,6–Dichlorobenzamide	0.067	0.710	positive
g__Streptococcus	2,6–Dichlorobenzamide	−0.056	0.755	negtive
g__Neisseria	2,6–Dichlorobenzamide	−0.042	0.816	negtive
g__Lactobacillus	2,6–Dichlorobenzamide	−0.038	0.834	negtive
g__Pseudoalteromonas	2,6–Dichlorobenzamide	0.026	0.885	positive
g__Aeromonas	2,6–Dichlorobenzamide	−0.022	0.901	negtive
g__Tropheryma	2,6–Dichlorobenzamide	−0.017	0.924	negtive
g__Vibrio	2,6–Dichlorobenzamide	0.016	0.928	positive
g__Alloprevotella	2,6–Dichlorobenzamide	0.010	0.954	positive
g__Mycoplasma	2,6–Dihydroxypyridine	0.338	0.055	positive
g__Lactobacillus	2,6–Dihydroxypyridine	−0.244	0.171	negtive
g__Veillonella	2,6–Dihydroxypyridine	0.209	0.242	positive
g__Prevotella	2,6–Dihydroxypyridine	0.186	0.299	positive
g__Alloprevotella	2,6–Dihydroxypyridine	0.172	0.339	positive
g__Prevotella_7	2,6–Dihydroxypyridine	0.156	0.386	positive
g__Tropheryma	2,6–Dihydroxypyridine	0.135	0.452	positive
g__Acinetobacter	2,6–Dihydroxypyridine	−0.132	0.462	negtive
g__Porphyromonas	2,6–Dihydroxypyridine	0.124	0.492	positive
g__Leifsonia	2,6–Dihydroxypyridine	0.113	0.530	positive
g__Hydrogenophaga	2,6–Dihydroxypyridine	−0.110	0.540	negtive
g__Moraxella	2,6–Dihydroxypyridine	−0.107	0.552	negtive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Neisseria	2,6−Dihydroxypyridine	0.094	0.604	positive
g__Gardnerella	2,6−Dihydroxypyridine	−0.086	0.634	negtive
g__Haemophilus	2,6−Dihydroxypyridine	0.063	0.726	positive
g__Pseudoalteromonas	2,6−Dihydroxypyridine	0.038	0.834	positive
g__Vibrio	2,6−Dihydroxypyridine	−0.018	0.919	negtive
g__Brevundimonas	2,6−Dihydroxypyridine	0.014	0.939	positive
g__Aeromonas	2,6−Dihydroxypyridine	−0.011	0.950	negtive
g__Streptococcus	2,6−Dihydroxypyridine	−0.005	0.980	negtive
g__Hydrogenophaga	25−Hydroxycholesterol	0.565	0.001	positive
g__Acinetobacter	25−Hydroxycholesterol	0.507	0.003	positive
g__Mycoplasma	25−Hydroxycholesterol	−0.343	0.051	negtive
g__Porphyromonas	25−Hydroxycholesterol	−0.321	0.069	negtive
g__Haemophilus	25−Hydroxycholesterol	−0.274	0.122	negtive
g__Brevundimonas	25−Hydroxycholesterol	0.267	0.132	positive
g__Gardnerella	25−Hydroxycholesterol	0.266	0.135	positive
g__Leifsonia	25−Hydroxycholesterol	0.250	0.161	positive
g__Moraxella	25−Hydroxycholesterol	0.242	0.175	positive
g__Veillonella	25−Hydroxycholesterol	−0.176	0.327	negtive
g__Streptococcus	25−Hydroxycholesterol	−0.118	0.511	negtive
g__Vibrio	25−Hydroxycholesterol	0.117	0.517	positive
g__Aeromonas	25−Hydroxycholesterol	0.106	0.557	positive
g__Prevotella	25−Hydroxycholesterol	−0.087	0.631	negtive
g__Pseudoalteromonas	25−Hydroxycholesterol	0.084	0.642	positive
g__Lactobacillus	25−Hydroxycholesterol	0.072	0.690	positive
g__Prevotella_7	25−Hydroxycholesterol	0.048	0.790	positive
g__Tropheryma	25−Hydroxycholesterol	−0.019	0.916	negtive
g__Neisseria	25−Hydroxycholesterol	0.016	0.931	positive
g__Alloprevotella	25−Hydroxycholesterol	−0.005	0.976	negtive
g__Mycoplasma	3,5−Dichloro−L−tyrosine	0.390	0.025	positive
g__Gardnerella	3,5−Dichloro−L−tyrosine	−0.316	0.073	negtive
g__Hydrogenophaga	3,5−Dichloro−L−tyrosine	−0.266	0.135	negtive
g__Acinetobacter	3,5−Dichloro−L−tyrosine	−0.258	0.146	negtive
g__Lactobacillus	3,5−Dichloro−L−tyrosine	−0.232	0.193	negtive
g__Tropheryma	3,5−Dichloro−L−tyrosine	0.199	0.267	positive
g__Moraxella	3,5−Dichloro−L−tyrosine	−0.188	0.296	negtive
g__Pseudoalteromonas	3,5−Dichloro−L−tyrosine	0.178	0.321	positive
g__Aeromonas	3,5−Dichloro−L−tyrosine	0.157	0.384	positive
g__Prevotella_7	3,5−Dichloro−L−tyrosine	−0.091	0.614	negtive
g__Brevundimonas	3,5−Dichloro−L−tyrosine	−0.084	0.643	negtive
g__Vibrio	3,5−Dichloro−L−tyrosine	0.076	0.675	positive
g__Prevotella	3,5−Dichloro−L−tyrosine	0.074	0.681	positive
g__Haemophilus	3,5−Dichloro−L−tyrosine	0.074	0.681	positive
g__Leifsonia	3,5−Dichloro−L−tyrosine	−0.037	0.838	negtive
g__Neisseria	3,5−Dichloro−L−tyrosine	0.016	0.928	positive
g__Veillonella	3,5−Dichloro−L−tyrosine	0.014	0.938	positive
g__Alloprevotella	3,5−Dichloro−L−tyrosine	0.004	0.982	positive
g__Streptococcus	3,5−Dichloro−L−tyrosine	−0.004	0.983	negtive
g__Porphyromonas	3,5−Dichloro−L−tyrosine	0.003	0.988	positive
g__Mycoplasma	3−Chloro−D−alanine	0.329	0.061	positive
g__Lactobacillus	3−Chloro−D−alanine	−0.294	0.097	negtive
g__Tropheryma	3−Chloro−D−alanine	0.273	0.125	positive
g__Gardnerella	3−Chloro−D−alanine	−0.192	0.284	negtive
g__Hydrogenophaga	3−Chloro−D−alanine	−0.153	0.395	negtive
g__Moraxella	3−Chloro−D−alanine	−0.149	0.408	negtive
g__Acinetobacter	3−Chloro−D−alanine	−0.126	0.484	negtive
g__Veillonella	3−Chloro−D−alanine	0.104	0.566	positive
g__Alloprevotella	3−Chloro−D−alanine	0.087	0.632	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Vibrio	3-Chloro-D-alanine	−0.073	0.688	negtive
g__Neisseria	3-Chloro-D-alanine	0.066	0.714	positive
g__Prevotella	3-Chloro-D-alanine	0.066	0.715	positive
g__Haemophilus	3-Chloro-D-alanine	0.061	0.736	positive
g__Streptococcus	3-Chloro-D-alanine	−0.052	0.775	negtive
g__Leifsonia	3-Chloro-D-alanine	0.048	0.791	positive
g__Aeromonas	3-Chloro-D-alanine	−0.034	0.851	negtive
g__Porphyromonas	3-Chloro-D-alanine	0.032	0.861	positive
g__Prevotella_7	3-Chloro-D-alanine	0.019	0.917	positive
g__Brevundimonas	3-Chloro-D-alanine	−0.017	0.924	negtive
g__Pseudoalteromonas	3-Chloro-D-alanine	0.011	0.951	positive
g__Mycoplasma	3-PHOSPHOGLYCERATE	−0.542	0.001	negtive
g__Lactobacillus	3-PHOSPHOGLYCERATE	0.426	0.014	positive
g__Gardnerella	3-PHOSPHOGLYCERATE	0.375	0.031	positive
g__Veillonella	3-PHOSPHOGLYCERATE	−0.246	0.167	negtive
g__Hydrogenophaga	3-PHOSPHOGLYCERATE	0.236	0.185	positive
g__Acinetobacter	3-PHOSPHOGLYCERATE	0.231	0.195	positive
g__Pseudoalteromonas	3-PHOSPHOGLYCERATE	−0.227	0.203	negtive
g__Porphyromonas	3-PHOSPHOGLYCERATE	−0.225	0.209	negtive
g__Moraxella	3-PHOSPHOGLYCERATE	0.214	0.232	positive
g__Tropheryma	3-PHOSPHOGLYCERATE	−0.199	0.266	negtive
g__Vibrio	3-PHOSPHOGLYCERATE	−0.199	0.267	negtive
g__Aeromonas	3-PHOSPHOGLYCERATE	−0.187	0.298	negtive
g__Haemophilus	3-PHOSPHOGLYCERATE	−0.109	0.548	negtive
g__Streptococcus	3-PHOSPHOGLYCERATE	−0.101	0.576	negtive
g__Brevundimonas	3-PHOSPHOGLYCERATE	−0.077	0.670	negtive
g__Leifsonia	3-PHOSPHOGLYCERATE	−0.061	0.734	negtive
g__Prevotella_7	3-PHOSPHOGLYCERATE	−0.047	0.797	negtive
g__Neisseria	3-PHOSPHOGLYCERATE	0.046	0.801	positive
g__Prevotella	3-PHOSPHOGLYCERATE	0.006	0.972	positive
g__Alloprevotella	3-PHOSPHOGLYCERATE	0.003	0.986	positive
g__Moraxella	4-Fluorophenol	−0.448	0.009	negtive
g__Hydrogenophaga	4-Fluorophenol	−0.243	0.172	negtive
g__Brevundimonas	4-Fluorophenol	−0.231	0.196	negtive
g__Mycoplasma	4-Fluorophenol	0.230	0.198	positive
g__Acinetobacter	4-Fluorophenol	−0.226	0.205	negtive
g__Leifsonia	4-Fluorophenol	−0.172	0.337	negtive
g__Neisseria	4-Fluorophenol	−0.149	0.407	negtive
g__Streptococcus	4-Fluorophenol	−0.133	0.461	negtive
g__Aeromonas	4-Fluorophenol	−0.103	0.569	negtive
g__Vibrio	4-Fluorophenol	−0.095	0.599	negtive
g__Prevotella_7	4-Fluorophenol	−0.093	0.607	negtive
g__Gardnerella	4-Fluorophenol	−0.091	0.613	negtive
g__Haemophilus	4-Fluorophenol	0.078	0.668	positive
g__Alloprevotella	4-Fluorophenol	−0.069	0.703	negtive
g__Lactobacillus	4-Fluorophenol	−0.063	0.728	negtive
g__Pseudoalteromonas	4-Fluorophenol	−0.060	0.739	negtive
g__Veillonella	4-Fluorophenol	−0.044	0.806	negtive
g__Prevotella	4-Fluorophenol	−0.038	0.833	negtive
g__Porphyromonas	4-Fluorophenol	−0.028	0.877	negtive
g__Tropheryma	4-Fluorophenol	0.025	0.892	positive
g__Mycoplasma	4-hydroxybutanoic acid	−0.380	0.029	negtive
g__Acinetobacter	4-hydroxybutanoic acid	0.298	0.092	positive
g__Lactobacillus	4-hydroxybutanoic acid	0.291	0.100	positive
g__Hydrogenophaga	4-hydroxybutanoic acid	0.284	0.109	positive
g__Moraxella	4-hydroxybutanoic acid	0.242	0.176	positive
g__Porphyromonas	4-hydroxybutanoic acid	−0.204	0.254	negtive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Veillonella	4-hydroxybutanoic acid	−0.203	0.258	negtive
g__Alloprevotella	4-hydroxybutanoic acid	−0.179	0.319	negtive
g__Haemophilus	4-hydroxybutanoic acid	−0.113	0.531	negtive
g__Aeromonas	4-hydroxybutanoic acid	0.111	0.540	positive
g__Streptococcus	4-hydroxybutanoic acid	0.090	0.619	positive
g__Prevotella_7	4-hydroxybutanoic acid	−0.075	0.677	negtive
g__Vibrio	4-hydroxybutanoic acid	0.075	0.679	positive
g__Prevotella	4-hydroxybutanoic acid	−0.067	0.710	negtive
g__Brevundimonas	4-hydroxybutanoic acid	0.067	0.712	positive
g__Pseudoalteromonas	4-hydroxybutanoic acid	0.048	0.791	positive
g__Neisseria	4-hydroxybutanoic acid	−0.047	0.794	negtive
g__Leifsonia	4-hydroxybutanoic acid	−0.039	0.827	negtive
g__Gardnerella	4-hydroxybutanoic acid	0.027	0.884	positive
g__Tropheryma	4-hydroxybutanoic acid	0.005	0.977	positive
g__Acinetobacter	4-Hydroxyquinoline	−0.371	0.034	negtive
g__Gardnerella	4-Hydroxyquinoline	−0.355	0.042	negtive
g__Tropheryma	4-Hydroxyquinoline	0.301	0.089	positive
g__Porphyromonas	4-Hydroxyquinoline	0.298	0.093	positive
g__Veillonella	4-Hydroxyquinoline	0.286	0.107	positive
g__Hydrogenophaga	4-Hydroxyquinoline	−0.267	0.132	negtive
g__Haemophilus	4-Hydroxyquinoline	0.263	0.140	positive
g__Vibrio	4-Hydroxyquinoline	−0.255	0.151	negtive
g__Prevotella	4-Hydroxyquinoline	0.244	0.171	positive
g__Streptococcus	4-Hydroxyquinoline	0.240	0.179	positive
g__Brevundimonas	4-Hydroxyquinoline	−0.238	0.182	negtive
g__Leifsonia	4-Hydroxyquinoline	−0.206	0.250	negtive
g__Aeromonas	4-Hydroxyquinoline	−0.192	0.285	negtive
g__Pseudoalteromonas	4-Hydroxyquinoline	−0.191	0.288	negtive
g__Alloprevotella	4-Hydroxyquinoline	0.188	0.296	positive
g__Moraxella	4-Hydroxyquinoline	−0.161	0.371	negtive
g__Mycoplasma	4-Hydroxyquinoline	0.133	0.460	positive
g__Lactobacillus	4-Hydroxyquinoline	−0.126	0.483	negtive
g__Neisseria	4-Hydroxyquinoline	0.117	0.518	positive
g__Prevotella_7	4-Hydroxyquinoline	0.017	0.925	positive
g__Mycoplasma	Acetoacetate	0.352	0.045	positive
g__Moraxella	Acetoacetate	−0.350	0.046	negtive
g__Hydrogenophaga	Acetoacetate	−0.350	0.047	negtive
g__Acinetobacter	Acetoacetate	−0.278	0.118	negtive
g__Gardnerella	Acetoacetate	−0.244	0.171	negtive
g__Haemophilus	Acetoacetate	0.234	0.190	positive
g__Lactobacillus	Acetoacetate	−0.219	0.219	negtive
g__Brevundimonas	Acetoacetate	−0.188	0.294	negtive
g__Vibrio	Acetoacetate	−0.163	0.365	negtive
g__Leifsonia	Acetoacetate	−0.160	0.375	negtive
g__Porphyromonas	Acetoacetate	0.142	0.429	positive
g__Neisseria	Acetoacetate	0.137	0.448	positive
g__Aeromonas	Acetoacetate	−0.136	0.449	negtive
g__Tropheryma	Acetoacetate	0.117	0.517	positive
g__Alloprevotella	Acetoacetate	0.100	0.581	positive
g__Pseudoalteromonas	Acetoacetate	−0.094	0.605	negtive
g__Veillonella	Acetoacetate	0.082	0.648	positive
g__Prevotella	Acetoacetate	0.080	0.657	positive
g__Streptococcus	Acetoacetate	−0.043	0.811	negtive
g__Prevotella_7	Acetoacetate	0.004	0.984	positive
g__Acinetobacter	Acetylcysteine	−0.298	0.092	negtive
g__Hydrogenophaga	Acetylcysteine	−0.297	0.093	negtive
g__Prevotella	Acetylcysteine	0.274	0.124	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Gardnerella	Acetylcysteine	−0.256	0.151	negtive
g__Moraxella	Acetylcysteine	−0.247	0.167	negtive
g__Mycoplasma	Acetylcysteine	0.196	0.275	positive
g__Haemophilus	Acetylcysteine	0.189	0.293	positive
g__Tropheryma	Acetylcysteine	−0.159	0.376	negtive
g__Veillonella	Acetylcysteine	0.145	0.420	positive
g__Porphyromonas	Acetylcysteine	0.123	0.497	positive
g__Alloprevotella	Acetylcysteine	0.110	0.544	positive
g__Brevundimonas	Acetylcysteine	−0.104	0.565	negtive
g__Prevotella_7	Acetylcysteine	0.090	0.618	positive
g__Pseudoalteromonas	Acetylcysteine	0.050	0.783	positive
g__Neisseria	Acetylcysteine	0.047	0.794	positive
g__Lactobacillus	Acetylcysteine	0.046	0.798	positive
g__Vibrio	Acetylcysteine	0.015	0.932	positive
g__Leifsonia	Acetylcysteine	−0.015	0.935	negtive
g__Streptococcus	Acetylcysteine	0.012	0.948	positive
g__Aeromonas	Acetylcysteine	−0.002	0.993	negtive
g__Mycoplasma	Acetylenedicarboxylic acid	−0.351	0.045	negtive
g__Haemophilus	Acetylenedicarboxylic acid	−0.300	0.090	negtive
g__Tropheryma	Acetylenedicarboxylic acid	−0.213	0.235	negtive
g__Gardnerella	Acetylenedicarboxylic acid	0.203	0.258	positive
g__Prevotella_7	Acetylenedicarboxylic acid	−0.176	0.328	negtive
g__Porphyromonas	Acetylenedicarboxylic acid	−0.135	0.454	negtive
g__Prevotella	Acetylenedicarboxylic acid	−0.123	0.497	negtive
g__Moraxella	Acetylenedicarboxylic acid	0.121	0.501	positive
g__Pseudoalteromonas	Acetylenedicarboxylic acid	−0.112	0.536	negtive
g__Lactobacillus	Acetylenedicarboxylic acid	0.110	0.540	positive
g__Neisseria	Acetylenedicarboxylic acid	−0.101	0.574	negtive
g__Vibrio	Acetylenedicarboxylic acid	−0.097	0.590	negtive
g__Hydrogenophaga	Acetylenedicarboxylic acid	0.094	0.603	positive
g__Veillonella	Acetylenedicarboxylic acid	−0.089	0.624	negtive
g__Acinetobacter	Acetylenedicarboxylic acid	0.088	0.624	positive
g__Aeromonas	Acetylenedicarboxylic acid	−0.084	0.642	negtive
g__Alloprevotella	Acetylenedicarboxylic acid	−0.059	0.744	negtive
g__Leifsonia	Acetylenedicarboxylic acid	−0.053	0.769	negtive
g__Brevundimonas	Acetylenedicarboxylic acid	0.035	0.848	positive
g__Streptococcus	Acetylenedicarboxylic acid	−0.006	0.973	negtive
g__Moraxella	Adipate semialdehyde	−0.394	0.023	negtive
g__Prevotella	Adipate semialdehyde	0.186	0.301	positive
g__Vibrio	Adipate semialdehyde	−0.179	0.318	negtive
g__Brevundimonas	Adipate semialdehyde	−0.164	0.360	negtive
g__Mycoplasma	Adipate semialdehyde	0.159	0.377	positive
g__Neisseria	Adipate semialdehyde	0.153	0.395	positive
g__Aeromonas	Adipate semialdehyde	−0.138	0.445	negtive
g__Porphyromonas	Adipate semialdehyde	0.122	0.499	positive
g__Pseudoalteromonas	Adipate semialdehyde	−0.110	0.542	negtive
g__Alloprevotella	Adipate semialdehyde	0.106	0.559	positive
g__Hydrogenophaga	Adipate semialdehyde	−0.098	0.585	negtive
g__Leifsonia	Adipate semialdehyde	−0.095	0.598	negtive
g__Veillonella	Adipate semialdehyde	0.092	0.609	positive
g__Acinetobacter	Adipate semialdehyde	−0.084	0.643	negtive
g__Gardnerella	Adipate semialdehyde	0.082	0.650	positive
g__Haemophilus	Adipate semialdehyde	0.064	0.725	positive
g__Prevotella_7	Adipate semialdehyde	−0.062	0.732	negtive
g__Lactobacillus	Adipate semialdehyde	0.047	0.793	positive
g__Streptococcus	Adipate semialdehyde	−0.027	0.882	negtive
g__Tropheryma	Adipate semialdehyde	0.002	0.990	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Acinetobacter	alpha-Eleostearic acid	−0.496	0.004	negtive
g__Hydrogenophaga	alpha-Eleostearic acid	−0.489	0.004	negtive
g__Lactobacillus	alpha-Eleostearic acid	−0.262	0.141	negtive
g__Streptococcus	alpha-Eleostearic acid	0.255	0.152	positive
g__Porphyromonas	alpha-Eleostearic acid	0.253	0.155	positive
g__Mycoplasma	alpha-Eleostearic acid	0.232	0.194	positive
g__Moraxella	alpha-Eleostearic acid	−0.218	0.223	negtive
g__Veillonella	alpha-Eleostearic acid	0.217	0.225	positive
g__Gardnerella	alpha-Eleostearic acid	−0.204	0.255	negtive
g__Haemophilus	alpha-Eleostearic acid	0.199	0.268	positive
g__Brevundimonas	alpha-Eleostearic acid	−0.161	0.369	negtive
g__Prevotella	alpha-Eleostearic acid	0.100	0.581	positive
g__Tropheryma	alpha-Eleostearic acid	0.094	0.603	positive
g__Alloprevotella	alpha-Eleostearic acid	0.077	0.668	positive
g__Neisseria	alpha-Eleostearic acid	0.067	0.710	positive
g__Leifsonia	alpha-Eleostearic acid	−0.065	0.718	negtive
g__Vibrio	alpha-Eleostearic acid	−0.053	0.768	negtive
g__Aeromonas	alpha-Eleostearic acid	−0.022	0.903	negtive
g__Pseudoalteromonas	alpha-Eleostearic acid	−0.019	0.917	negtive
g__Prevotella_7	alpha-Eleostearic acid	−0.019	0.918	negtive
g__Porphyromonas	Ancistrocladine	0.542	0.001	positive
g__Haemophilus	Ancistrocladine	0.538	0.001	positive
g__Hydrogenophaga	Ancistrocladine	−0.515	0.002	negtive
g__Acinetobacter	Ancistrocladine	−0.509	0.003	negtive
g__Veillonella	Ancistrocladine	0.432	0.012	positive
g__Alloprevotella	Ancistrocladine	0.398	0.022	positive
g__Streptococcus	Ancistrocladine	0.379	0.030	positive
g__Prevotella	Ancistrocladine	0.365	0.037	positive
g__Neisseria	Ancistrocladine	0.328	0.062	positive
g__Brevundimonas	Ancistrocladine	−0.319	0.071	negtive
g__Mycoplasma	Ancistrocladine	0.286	0.107	positive
g__Pseudoalteromonas	Ancistrocladine	−0.284	0.110	negtive
g__Aeromonas	Ancistrocladine	−0.277	0.119	negtive
g__Prevotella_7	Ancistrocladine	0.250	0.161	positive
g__Vibrio	Ancistrocladine	−0.244	0.171	negtive
g__Leifsonia	Ancistrocladine	−0.209	0.243	negtive
g__Tropheryma	Ancistrocladine	0.149	0.407	positive
g__Lactobacillus	Ancistrocladine	−0.095	0.598	negtive
g__Moraxella	Ancistrocladine	−0.071	0.695	negtive
g__Gardnerella	Ancistrocladine	−0.048	0.789	negtive
g__Veillonella	Betaine	0.231	0.196	positive
g__Gardnerella	Betaine	−0.209	0.243	negtive
g__Lactobacillus	Betaine	−0.208	0.245	negtive
g__Prevotella	Betaine	0.206	0.251	positive
g__Acinetobacter	Betaine	−0.201	0.260	negtive
g__Mycoplasma	Betaine	0.150	0.405	positive
g__Hydrogenophaga	Betaine	−0.130	0.470	negtive
g__Moraxella	Betaine	−0.122	0.500	negtive
g__Alloprevotella	Betaine	0.119	0.509	positive
g__Prevotella_7	Betaine	0.116	0.520	positive
g__Vibrio	Betaine	−0.092	0.611	negtive
g__Porphyromonas	Betaine	0.091	0.616	positive
g__Aeromonas	Betaine	−0.090	0.617	negtive
g__Haemophilus	Betaine	0.070	0.699	positive
g__Pseudoalteromonas	Betaine	−0.055	0.759	negtive
g__Streptococcus	Betaine	0.045	0.803	positive
g__Tropheryma	Betaine	0.034	0.851	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Neisseria	Betaine	−0.033	0.853	negtive
g__Leifsonia	Betaine	0.030	0.870	positive
g__Brevundimonas	Betaine	−0.028	0.875	negtive
g__Mycoplasma	biotin	0.302	0.087	positive
g__Acinetobacter	biotin	−0.293	0.098	negtive
g__Haemophilus	biotin	0.292	0.099	positive
g__Porphyromonas	biotin	0.239	0.181	positive
g__Hydrogenophaga	biotin	−0.209	0.243	negtive
g__Gardnerella	biotin	−0.191	0.287	negtive
g__Leifsonia	biotin	−0.189	0.291	negtive
g__Moraxella	biotin	−0.157	0.383	negtive
g__Streptococcus	biotin	0.144	0.424	positive
g__Veillonella	biotin	0.127	0.481	positive
g__Brevundimonas	biotin	−0.123	0.493	negtive
g__Neisseria	biotin	0.119	0.509	positive
g__Aeromonas	biotin	−0.115	0.523	negtive
g__Prevotella	biotin	0.108	0.548	positive
g__Pseudoalteromonas	biotin	−0.093	0.605	negtive
g__Vibrio	biotin	−0.092	0.609	negtive
g__Lactobacillus	biotin	−0.088	0.627	negtive
g__Tropheryma	biotin	0.072	0.689	positive
g__Alloprevotella	biotin	0.052	0.775	positive
g__Prevotella_7	biotin	−0.005	0.976	negtive
g__Hydrogenophaga	Butyric acid	0.469	0.006	positive
g__Acinetobacter	Butyric acid	0.440	0.011	positive
g__Porphyromonas	Butyric acid	−0.294	0.096	negtive
g__Brevundimonas	Butyric acid	0.225	0.207	positive
g__Haemophilus	Butyric acid	−0.205	0.254	negtive
g__Veillonella	Butyric acid	−0.204	0.256	negtive
g__Tropheryma	Butyric acid	0.178	0.322	positive
g__Prevotella	Butyric acid	−0.169	0.346	negtive
g__Leifsonia	Butyric acid	0.168	0.350	positive
g__Streptococcus	Butyric acid	−0.159	0.377	negtive
g__Vibrio	Butyric acid	0.141	0.434	positive
g__Moraxella	Butyric acid	0.117	0.516	positive
g__Gardnerella	Butyric acid	0.106	0.559	positive
g__Pseudoalteromonas	Butyric acid	0.095	0.598	positive
g__Neisseria	Butyric acid	−0.090	0.617	negtive
g__Mycoplasma	Butyric acid	−0.084	0.644	negtive
g__Aeromonas	Butyric acid	0.066	0.716	positive
g__Prevotella_7	Butyric acid	−0.053	0.771	negtive
g__Alloprevotella	Butyric acid	−0.034	0.849	negtive
g__Lactobacillus	Butyric acid	−0.030	0.869	negtive
g__Haemophilus	Cinobufagin	0.309	0.080	positive
g__Tropheryma	Cinobufagin	0.308	0.081	positive
g__Hydrogenophaga	Cinobufagin	−0.220	0.217	negtive
g__Brevundimonas	Cinobufagin	−0.214	0.231	negtive
g__Leifsonia	Cinobufagin	−0.204	0.256	negtive
g__Lactobacillus	Cinobufagin	0.175	0.328	positive
g__Acinetobacter	Cinobufagin	−0.123	0.493	negtive
g__Prevotella	Cinobufagin	0.103	0.569	positive
g__Gardnerella	Cinobufagin	−0.095	0.597	negtive
g__Vibrio	Cinobufagin	−0.073	0.687	negtive
g__Moraxella	Cinobufagin	0.069	0.702	positive
g__Alloprevotella	Cinobufagin	−0.069	0.703	negtive
g__Neisseria	Cinobufagin	−0.058	0.750	negtive
g__Prevotella_7	Cinobufagin	−0.040	0.826	negtive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Veillonella	Cinobufagin	−0.031	0.864	negtive
g__Porphyromonas	Cinobufagin	−0.031	0.866	negtive
g__Aeromonas	Cinobufagin	−0.019	0.917	negtive
g__Mycoplasma	Cinobufagin	−0.009	0.959	negtive
g__Pseudoalteromonas	Cinobufagin	−0.005	0.976	negtive
g__Streptococcus	Cinobufagin	0.002	0.991	positive
g__Moraxella	Clothianidin	−0.466	0.006	negtive
g__Hydrogenophaga	Clothianidin	−0.340	0.054	negtive
g__Mycoplasma	Clothianidin	0.281	0.113	positive
g__Acinetobacter	Clothianidin	−0.279	0.116	negtive
g__Brevundimonas	Clothianidin	−0.267	0.133	negtive
g__Aeromonas	Clothianidin	−0.253	0.155	negtive
g__Porphyromonas	Clothianidin	0.243	0.173	positive
g__Haemophilus	Clothianidin	0.236	0.185	positive
g__Gardnerella	Clothianidin	−0.232	0.193	negtive
g__Veillonella	Clothianidin	0.225	0.208	positive
g__Vibrio	Clothianidin	−0.219	0.222	negtive
g__Alloprevotella	Clothianidin	0.207	0.247	positive
g__Leifsonia	Clothianidin	−0.185	0.302	negtive
g__Pseudoalteromonas	Clothianidin	−0.173	0.335	negtive
g__Prevotella	Clothianidin	0.155	0.390	positive
g__Lactobacillus	Clothianidin	−0.148	0.409	negtive
g__Streptococcus	Clothianidin	−0.084	0.641	negtive
g__Neisseria	Clothianidin	0.072	0.691	positive
g__Prevotella_7	Clothianidin	0.069	0.705	positive
g__Tropheryma	Clothianidin	−0.065	0.721	negtive
g__Porphyromonas	D−Arabinose 5−phosphate	0.524	0.002	positive
g__Haemophilus	D−Arabinose 5−phosphate	0.465	0.006	positive
g__Hydrogenophaga	D−Arabinose 5−phosphate	−0.445	0.010	negtive
g__Acinetobacter	D−Arabinose 5−phosphate	−0.408	0.019	negtive
g__Streptococcus	D−Arabinose 5−phosphate	0.405	0.020	positive
g__Veillonella	D−Arabinose 5−phosphate	0.387	0.026	positive
g__Neisseria	D−Arabinose 5−phosphate	0.338	0.055	positive
g__Prevotella	D−Arabinose 5−phosphate	0.331	0.060	positive
g__Tropheryma	D−Arabinose 5−phosphate	0.310	0.079	positive
g__Alloprevotella	D−Arabinose 5−phosphate	0.303	0.086	positive
g__Mycoplasma	D−Arabinose 5−phosphate	0.286	0.107	positive
g__Moraxella	D−Arabinose 5−phosphate	−0.273	0.124	negtive
g__Prevotella_7	D−Arabinose 5−phosphate	0.231	0.195	positive
g__Lactobacillus	D−Arabinose 5−phosphate	−0.229	0.200	negtive
g__Brevundimonas	D−Arabinose 5−phosphate	−0.197	0.271	negtive
g__Gardnerella	D−Arabinose 5−phosphate	−0.196	0.275	negtive
g__Leifsonia	D−Arabinose 5−phosphate	−0.142	0.432	negtive
g__Vibrio	D−Arabinose 5−phosphate	−0.115	0.523	negtive
g__Aeromonas	D−Arabinose 5−phosphate	−0.066	0.717	negtive
g__Pseudoalteromonas	D−Arabinose 5−phosphate	−0.039	0.831	negtive
g__Lactobacillus	D−Cysteine	−0.390	0.025	negtive
g__Gardnerella	D−Cysteine	−0.389	0.025	negtive
g__Mycoplasma	D−Cysteine	0.351	0.045	positive
g__Acinetobacter	D−Cysteine	−0.307	0.082	negtive
g__Hydrogenophaga	D−Cysteine	−0.286	0.106	negtive
g__Haemophilus	D−Cysteine	0.268	0.132	positive
g__Tropheryma	D−Cysteine	0.248	0.163	positive
g__Prevotella	D−Cysteine	0.228	0.203	positive
g__Moraxella	D−Cysteine	−0.194	0.280	negtive
g__Porphyromonas	D−Cysteine	0.149	0.406	positive
g__Streptococcus	D−Cysteine	0.144	0.423	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Veillonella	D-Cysteine	0.135	0.454	positive
g__Leifsonia	D-Cysteine	−0.121	0.504	negtive
g__Brevundimonas	D-Cysteine	−0.106	0.555	negtive
g__Alloprevotella	D-Cysteine	0.101	0.575	positive
g__Pseudoalteromonas	D-Cysteine	0.063	0.728	positive
g__Neisseria	D-Cysteine	0.055	0.760	positive
g__Vibrio	D-Cysteine	−0.046	0.799	negtive
g__Aeromonas	D-Cysteine	0.032	0.860	positive
g__Prevotella_7	D-Cysteine	−0.013	0.943	negtive
g__Hydrogenophaga	Formononetin	−0.611	0.000	negtive
g__Acinetobacter	Formononetin	−0.593	0.000	negtive
g__Mycoplasma	Formononetin	0.419	0.015	positive
g__Porphyromonas	Formononetin	0.313	0.076	positive
g__Haemophilus	Formononetin	0.309	0.081	positive
g__Gardnerella	Formononetin	−0.273	0.124	negtive
g__Moraxella	Formononetin	−0.269	0.130	negtive
g__Lactobacillus	Formononetin	−0.246	0.167	negtive
g__Brevundimonas	Formononetin	−0.232	0.193	negtive
g__Prevotella	Formononetin	0.214	0.233	positive
g__Veillonella	Formononetin	0.207	0.248	positive
g__Tropheryma	Formononetin	0.185	0.304	positive
g__Streptococcus	Formononetin	0.164	0.360	positive
g__Leifsonia	Formononetin	−0.149	0.407	negtive
g__Neisseria	Formononetin	0.073	0.686	positive
g__Vibrio	Formononetin	−0.023	0.901	negtive
g__Aeromonas	Formononetin	−0.022	0.905	negtive
g__Prevotella_7	Formononetin	0.004	0.982	positive
g__Alloprevotella	Formononetin	0.003	0.985	positive
g__Pseudoalteromonas	Formononetin	−0.002	0.993	negtive
g__Hydrogenophaga	Glucose 6-phosphate	−0.741	0.000	negtive
g__Acinetobacter	Glucose 6-phosphate	−0.650	0.000	negtive
g__Porphyromonas	Glucose 6-phosphate	0.452	0.008	positive
g__Haemophilus	Glucose 6-phosphate	0.443	0.010	positive
g__Brevundimonas	Glucose 6-phosphate	−0.414	0.017	negtive
g__Leifsonia	Glucose 6-phosphate	−0.361	0.039	negtive
g__Moraxella	Glucose 6-phosphate	−0.294	0.097	negtive
g__Veillonella	Glucose 6-phosphate	0.289	0.103	positive
g__Vibrio	Glucose 6-phosphate	−0.247	0.166	negtive
g__Mycoplasma	Glucose 6-phosphate	0.218	0.222	positive
g__Aeromonas	Glucose 6-phosphate	−0.217	0.224	negtive
g__Pseudoalteromonas	Glucose 6-phosphate	−0.208	0.245	negtive
g__Tropheryma	Glucose 6-phosphate	0.200	0.265	positive
g__Gardnerella	Glucose 6-phosphate	−0.192	0.286	negtive
g__Streptococcus	Glucose 6-phosphate	0.182	0.310	positive
g__Prevotella	Glucose 6-phosphate	0.173	0.334	positive
g__Neisseria	Glucose 6-phosphate	0.166	0.357	positive
g__Lactobacillus	Glucose 6-phosphate	−0.118	0.513	negtive
g__Alloprevotella	Glucose 6-phosphate	0.107	0.555	positive
g__Prevotella_7	Glucose 6-phosphate	0.073	0.687	positive
g__Tropheryma	Glycidol	0.452	0.008	positive
g__Prevotella	Glycidol	0.379	0.029	positive
g__Gardnerella	Glycidol	−0.357	0.041	negtive
g__Prevotella_7	Glycidol	0.317	0.072	positive
g__Haemophilus	Glycidol	0.292	0.099	positive
g__Veillonella	Glycidol	0.284	0.109	positive
g__Alloprevotella	Glycidol	0.282	0.112	positive
g__Lactobacillus	Glycidol	−0.277	0.119	negtive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Neisseria	Glycidol	0.266	0.134	positive
g__Streptococcus	Glycidol	0.229	0.200	positive
g__Pseudoalteromonas	Glycidol	0.212	0.237	positive
g__Aeromonas	Glycidol	0.186	0.299	positive
g__Leifsonia	Glycidol	0.163	0.364	positive
g__Vibrio	Glycidol	0.147	0.415	positive
g__Brevundimonas	Glycidol	0.132	0.461	positive
g__Moraxella	Glycidol	0.113	0.533	positive
g__Porphyromonas	Glycidol	0.110	0.544	positive
g__Hydrogenophaga	Glycidol	0.081	0.652	positive
g__Mycoplasma	Glycidol	0.074	0.683	positive
g__Acinetobacter	Glycidol	0.054	0.764	positive
g__Mycoplasma	Glycine	0.375	0.031	positive
g__Tropheryma	Glycine	0.281	0.114	positive
g__Lactobacillus	Glycine	−0.265	0.135	negtive
g__Hydrogenophaga	Glycine	−0.235	0.187	negtive
g__Gardnerella	Glycine	−0.220	0.219	negtive
g__Haemophilus	Glycine	0.204	0.255	positive
g__Vibrio	Glycine	−0.197	0.272	negtive
g__Acinetobacter	Glycine	−0.193	0.282	negtive
g__Neisseria	Glycine	0.182	0.309	positive
g__Alloprevotella	Glycine	0.175	0.330	positive
g__Porphyromonas	Glycine	0.166	0.355	positive
g__Prevotella	Glycine	0.164	0.361	positive
g__Brevundimonas	Glycine	−0.140	0.434	negtive
g__Veillonella	Glycine	0.140	0.436	positive
g__Moraxella	Glycine	−0.119	0.508	negtive
g__Aeromonas	Glycine	−0.111	0.539	negtive
g__Leifsonia	Glycine	−0.107	0.553	negtive
g__Streptococcus	Glycine	0.100	0.581	positive
g__Pseudoalteromonas	Glycine	−0.081	0.656	negtive
g__Prevotella_7	Glycine	0.063	0.728	positive
g__Mycoplasma	Glycolic acid	0.427	0.013	positive
g__Lactobacillus	Glycolic acid	−0.365	0.038	negtive
g__Gardnerella	Glycolic acid	−0.364	0.037	negtive
g__Tropheryma	Glycolic acid	0.305	0.084	positive
g__Hydrogenophaga	Glycolic acid	−0.240	0.178	negtive
g__Haemophilus	Glycolic acid	0.203	0.257	positive
g__Neisseria	Glycolic acid	0.179	0.320	positive
g__Acinetobacter	Glycolic acid	−0.161	0.369	negtive
g__Alloprevotella	Glycolic acid	0.156	0.385	positive
g__Veillonella	Glycolic acid	0.144	0.426	positive
g__Porphyromonas	Glycolic acid	0.137	0.449	positive
g__Prevotella	Glycolic acid	0.134	0.456	positive
g__Moraxella	Glycolic acid	−0.106	0.557	negtive
g__Pseudoalteromonas	Glycolic acid	0.077	0.672	positive
g__Streptococcus	Glycolic acid	0.067	0.712	positive
g__Aeromonas	Glycolic acid	0.037	0.836	positive
g__Vibrio	Glycolic acid	−0.037	0.836	negtive
g__Leifsonia	Glycolic acid	0.007	0.971	positive
g__Prevotella_7	Glycolic acid	0.002	0.991	positive
g__Brevundimonas	Glycolic acid	−0.002	0.992	negtive
g__Hydrogenophaga	Guanosine monophosphate	−0.502	0.003	negtive
g__Brevundimonas	Guanosine monophosphate	−0.324	0.066	negtive
g__Porphyromonas	Guanosine monophosphate	0.309	0.080	positive
g__Acinetobacter	Guanosine monophosphate	−0.301	0.089	negtive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Haemophilus	Guanosine monophosphate	0.289	0.103	positive
g__Leifsonia	Guanosine monophosphate	−0.278	0.117	negtive
g__Mycoplasma	Guanosine monophosphate	0.255	0.152	positive
g__Prevotella	Guanosine monophosphate	0.150	0.406	positive
g__Gardnerella	Guanosine monophosphate	−0.149	0.408	negtive
g__Moraxella	Guanosine monophosphate	−0.134	0.458	negtive
g__Vibrio	Guanosine monophosphate	−0.108	0.549	negtive
g__Veillonella	Guanosine monophosphate	0.098	0.586	positive
g__Streptococcus	Guanosine monophosphate	0.088	0.625	positive
g__Prevotella_7	Guanosine monophosphate	0.066	0.714	positive
g__Neisseria	Guanosine monophosphate	0.065	0.721	positive
g__Aeromonas	Guanosine monophosphate	−0.047	0.796	negtive
g__Pseudoalteromonas	Guanosine monophosphate	−0.045	0.802	negtive
g__Alloprevotella	Guanosine monophosphate	−0.040	0.825	negtive
g__Tropheryma	Guanosine monophosphate	0.027	0.881	positive
g__Lactobacillus	Guanosine monophosphate	−0.026	0.887	negtive
g__Hydrogenophaga	Hippuric acid	−0.386	0.027	negtive
g__Leifsonia	Hippuric acid	−0.370	0.034	negtive
g__Acinetobacter	Hippuric acid	−0.352	0.045	negtive
g__Brevundimonas	Hippuric acid	−0.344	0.051	negtive
g__Vibrio	Hippuric acid	−0.304	0.086	negtive
g__Pseudoalteromonas	Hippuric acid	−0.299	0.092	negtive
g__Aeromonas	Hippuric acid	−0.292	0.099	negtive
g__Prevotella_7	Hippuric acid	−0.266	0.135	negtive
g__Alloprevotella	Hippuric acid	−0.188	0.294	negtive
g__Veillonella	Hippuric acid	−0.183	0.308	negtive
g__Streptococcus	Hippuric acid	−0.182	0.311	negtive
g__Gardnerella	Hippuric acid	−0.147	0.415	negtive
g__Moraxella	Hippuric acid	−0.131	0.469	negtive
g__Neisseria	Hippuric acid	−0.117	0.517	negtive
g__Mycoplasma	Hippuric acid	0.110	0.543	positive
g__Haemophilus	Hippuric acid	0.083	0.647	positive
g__Lactobacillus	Hippuric acid	0.081	0.653	positive
g__Porphyromonas	Hippuric acid	0.073	0.687	positive
g__Tropheryma	Hippuric acid	−0.068	0.705	negtive
g__Prevotella	Hippuric acid	−0.033	0.855	negtive
g__Porphyromonas	Imazamox	0.568	0.001	positive
g__Haemophilus	Imazamox	0.558	0.001	positive
g__Hydrogenophaga	Imazamox	−0.430	0.013	negtive
g__Veillonella	Imazamox	0.415	0.016	positive
g__Prevotella_7	Imazamox	0.413	0.017	positive
g__Acinetobacter	Imazamox	−0.374	0.033	negtive
g__Neisseria	Imazamox	0.362	0.038	positive
g__Alloprevotella	Imazamox	0.311	0.078	positive
g__Prevotella	Imazamox	0.299	0.091	positive
g__Streptococcus	Imazamox	0.296	0.094	positive
g__Mycoplasma	Imazamox	0.287	0.106	positive
g__Lactobacillus	Imazamox	−0.269	0.130	negtive
g__Gardnerella	Imazamox	−0.256	0.151	negtive
g__Tropheryma	Imazamox	0.227	0.205	positive
g__Leifsonia	Imazamox	−0.075	0.677	negtive
g__Brevundimonas	Imazamox	−0.058	0.746	negtive
g__Moraxella	Imazamox	−0.020	0.914	negtive
g__Vibrio	Imazamox	0.019	0.917	positive
g__Aeromonas	Imazamox	−0.016	0.931	negtive
g__Pseudoalteromonas	Imazamox	0.007	0.968	positive
g__Haemophilus	Lenticin	0.442	0.010	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Porphyromonas	Lenticin	0.336	0.056	positive
g__Prevotella	Lenticin	0.327	0.063	positive
g__Acinetobacter	Lenticin	−0.314	0.075	negtive
g__Brevundimonas	Lenticin	−0.252	0.157	negtive
g__Leifsonia	Lenticin	−0.249	0.162	negtive
g__Hydrogenophaga	Lenticin	−0.235	0.187	negtive
g__Moraxella	Lenticin	−0.205	0.253	negtive
g__Alloprevotella	Lenticin	0.194	0.279	positive
g__Neisseria	Lenticin	0.190	0.289	positive
g__Veillonella	Lenticin	0.188	0.295	positive
g__Gardnerella	Lenticin	−0.126	0.484	negtive
g__Mycoplasma	Lenticin	0.118	0.515	positive
g__Aeromonas	Lenticin	−0.113	0.530	negtive
g__Streptococcus	Lenticin	0.112	0.534	positive
g__Prevotella_7	Lenticin	0.087	0.630	positive
g__Vibrio	Lenticin	−0.085	0.640	negtive
g__Pseudoalteromonas	Lenticin	−0.082	0.652	negtive
g__Lactobacillus	Lenticin	0.032	0.861	positive
g__Tropheryma	Lenticin	0.021	0.909	positive
g__Acinetobacter	Malondialdehyde	−0.621	0.000	negtive
g__Hydrogenophaga	Malondialdehyde	−0.589	0.000	negtive
g__Porphyromonas	Malondialdehyde	0.435	0.011	positive
g__Veillonella	Malondialdehyde	0.386	0.027	positive
g__Vibrio	Malondialdehyde	−0.359	0.040	negtive
g__Brevundimonas	Malondialdehyde	−0.354	0.044	negtive
g__Aeromonas	Malondialdehyde	−0.317	0.072	negtive
g__Leifsonia	Malondialdehyde	−0.303	0.087	negtive
g__Pseudoalteromonas	Malondialdehyde	−0.297	0.093	negtive
g__Moraxella	Malondialdehyde	−0.274	0.122	negtive
g__Haemophilus	Malondialdehyde	0.274	0.122	positive
g__Streptococcus	Malondialdehyde	0.271	0.128	positive
g__Mycoplasma	Malondialdehyde	0.256	0.150	positive
g__Lactobacillus	Malondialdehyde	−0.252	0.156	negtive
g__Alloprevotella	Malondialdehyde	0.181	0.313	positive
g__Prevotella	Malondialdehyde	0.147	0.415	positive
g__Gardnerella	Malondialdehyde	−0.139	0.440	negtive
g__Tropheryma	Malondialdehyde	0.110	0.541	positive
g__Neisseria	Malondialdehyde	0.086	0.634	positive
g__Prevotella_7	Malondialdehyde	0.051	0.779	positive
g__Hydrogenophaga	MANNOSE	−0.534	0.002	negtive
g__Acinetobacter	MANNOSE	−0.533	0.002	negtive
g__Porphyromonas	MANNOSE	0.510	0.002	positive
g__Veillonella	MANNOSE	0.462	0.007	positive
g__Haemophilus	MANNOSE	0.357	0.041	positive
g__Lactobacillus	MANNOSE	−0.349	0.047	negtive
g__Mycoplasma	MANNOSE	0.313	0.076	positive
g__Streptococcus	MANNOSE	0.295	0.095	positive
g__Prevotella	MANNOSE	0.289	0.103	positive
g__Alloprevotella	MANNOSE	0.283	0.110	positive
g__Vibrio	MANNOSE	−0.278	0.117	negtive
g__Brevundimonas	MANNOSE	−0.274	0.123	negtive
g__Leifsonia	MANNOSE	−0.229	0.200	negtive
g__Aeromonas	MANNOSE	−0.229	0.200	negtive
g__Neisseria	MANNOSE	0.227	0.205	positive
g__Pseudoalteromonas	MANNOSE	−0.203	0.256	negtive
g__Moraxella	MANNOSE	−0.179	0.318	negtive
g__Prevotella_7	MANNOSE	0.142	0.429	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Tropheryma	MANNOSE	0.137	0.449	positive
g__Gardnerella	MANNOSE	−0.132	0.464	negtive
g__Moraxella	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.403	0.020	negtive
g__Acinetobacter	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.363	0.039	negtive
g__Hydrogenophaga	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.275	0.121	negtive
g__Lactobacillus	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.243	0.173	negtive
g__Brevundimonas	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.237	0.184	negtive
g__Leifsonia	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.223	0.212	negtive
g__Mycoplasma	N−Acetyl−alpha−D−glucosamine 1−phosphate	0.206	0.250	positive
g__Aeromonas	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.188	0.295	negtive
g__Tropheryma	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.185	0.301	negtive
g__Gardnerella	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.172	0.340	negtive
g__Vibrio	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.164	0.363	negtive
g__Pseudoalteromonas	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.149	0.408	negtive
g__Porphyromonas	N−Acetyl−alpha−D−glucosamine 1−phosphate	0.134	0.457	positive
g__Haemophilus	N−Acetyl−alpha−D−glucosamine 1−phosphate	0.134	0.457	positive
g__Neisseria	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.109	0.547	negtive
g__Prevotella_7	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.096	0.596	negtive
g__Alloprevotella	N−Acetyl−alpha−D−glucosamine 1−phosphate	0.072	0.690	positive
g__Veillonella	N−Acetyl−alpha−D−glucosamine 1−phosphate	0.065	0.719	positive
g__Streptococcus	N−Acetyl−alpha−D−glucosamine 1−phosphate	−0.050	0.784	negtive
g__Prevotella	N−Acetyl−alpha−D−glucosamine 1−phosphate	0.015	0.935	positive
g__Acinetobacter	N−Acetyl−D−tryptophan	−0.364	0.038	negtive
g__Vibrio	N−Acetyl−D−tryptophan	−0.329	0.062	negtive
g__Hydrogenophaga	N−Acetyl−D−tryptophan	−0.327	0.064	negtive
g__Brevundimonas	N−Acetyl−D−tryptophan	−0.318	0.072	negtive
g__Pseudoalteromonas	N−Acetyl−D−tryptophan	−0.305	0.084	negtive
g__Aeromonas	N−Acetyl−D−tryptophan	−0.300	0.090	negtive
g__Leifsonia	N−Acetyl−D−tryptophan	−0.221	0.217	negtive
g__Moraxella	N−Acetyl−D−tryptophan	−0.180	0.316	negtive
g__Tropheryma	N−Acetyl−D−tryptophan	0.153	0.397	positive
g__Lactobacillus	N−Acetyl−D−tryptophan	0.151	0.401	positive
g__Gardnerella	N−Acetyl−D−tryptophan	−0.133	0.462	negtive
g__Haemophilus	N−Acetyl−D−tryptophan	0.109	0.545	positive
g__Neisseria	N−Acetyl−D−tryptophan	−0.075	0.680	negtive
g__Alloprevotella	N−Acetyl−D−tryptophan	−0.066	0.714	negtive
g__Prevotella_7	N−Acetyl−D−tryptophan	−0.051	0.777	negtive
g__Veillonella	N−Acetyl−D−tryptophan	0.036	0.843	positive
g__Streptococcus	N−Acetyl−D−tryptophan	0.025	0.889	positive
g__Porphyromonas	N−Acetyl−D−tryptophan	−0.014	0.940	negtive
g__Prevotella	N−Acetyl−D−tryptophan	−0.001	0.994	negtive
g__Mycoplasma	N−Acetyl−D−tryptophan	−0.001	0.997	negtive
g__Mycoplasma	N−Acetyl−L−cysteine	0.379	0.030	positive
g__Hydrogenophaga	N−Acetyl−L−cysteine	−0.332	0.060	negtive
g__Prevotella	N−Acetyl−L−cysteine	0.328	0.062	positive
g__Porphyromonas	N−Acetyl−L−cysteine	0.285	0.107	positive
g__Acinetobacter	N−Acetyl−L−cysteine	−0.280	0.114	negtive
g__Haemophilus	N−Acetyl−L−cysteine	0.260	0.144	positive
g__Lactobacillus	N−Acetyl−L−cysteine	−0.218	0.222	negtive
g__Veillonella	N−Acetyl−L−cysteine	0.180	0.317	positive
g__Gardnerella	N−Acetyl−L−cysteine	−0.166	0.355	negtive
g__Prevotella_7	N−Acetyl−L−cysteine	0.121	0.504	positive
g__Neisseria	N−Acetyl−L−cysteine	0.120	0.508	positive
g__Alloprevotella	N−Acetyl−L−cysteine	0.112	0.536	positive
g__Tropheryma	N−Acetyl−L−cysteine	0.102	0.573	positive
g__Leifsonia	N−Acetyl−L−cysteine	−0.095	0.600	negtive
g__Moraxella	N−Acetyl−L−cysteine	−0.089	0.621	negtive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Brevundimonas	N-Acetyl-L-cysteine	−0.073	0.685	negtive
g__Pseudoalteromonas	N-Acetyl-L-cysteine	0.058	0.746	positive
g__Aeromonas	N-Acetyl-L-cysteine	−0.008	0.965	negtive
g__Streptococcus	N-Acetyl-L-cysteine	−0.003	0.987	negtive
g__Vibrio	N-Acetyl-L-cysteine	−0.001	0.996	negtive
g__Streptococcus	N-Acetyl-L-phenylalanine	0.463	0.007	positive
g__Porphyromonas	N-Acetyl-L-phenylalanine	0.424	0.014	positive
g__Lactobacillus	N-Acetyl-L-phenylalanine	−0.404	0.020	negtive
g__Veillonella	N-Acetyl-L-phenylalanine	0.391	0.025	positive
g__Mycoplasma	N-Acetyl-L-phenylalanine	0.325	0.065	positive
g__Acinetobacter	N-Acetyl-L-phenylalanine	−0.319	0.071	negtive
g__Alloprevotella	N-Acetyl-L-phenylalanine	0.301	0.089	positive
g__Haemophilus	N-Acetyl-L-phenylalanine	0.281	0.113	positive
g__Neisseria	N-Acetyl-L-phenylalanine	0.281	0.113	positive
g__Prevotella	N-Acetyl-L-phenylalanine	0.257	0.149	positive
g__Tropheryma	N-Acetyl-L-phenylalanine	0.237	0.185	positive
g__Hydrogenophaga	N-Acetyl-L-phenylalanine	−0.233	0.191	negtive
g__Gardnerella	N-Acetyl-L-phenylalanine	−0.212	0.237	negtive
g__Prevotella_7	N-Acetyl-L-phenylalanine	0.153	0.397	positive
g__Vibrio	N-Acetyl-L-phenylalanine	−0.120	0.506	negtive
g__Moraxella	N-Acetyl-L-phenylalanine	0.044	0.807	positive
g__Pseudoalteromonas	N-Acetyl-L-phenylalanine	−0.036	0.843	negtive
g__Aeromonas	N-Acetyl-L-phenylalanine	−0.022	0.901	negtive
g__Brevundimonas	N-Acetyl-L-phenylalanine	−0.020	0.911	negtive
g__Leifsonia	N-Acetyl-L-phenylalanine	−0.012	0.948	negtive
g__Haemophilus	Neobyakangelicol	0.521	0.002	positive
g__Porphyromonas	Neobyakangelicol	0.354	0.043	positive
g__Leifsonia	Neobyakangelicol	−0.310	0.079	negtive
g__Gardnerella	Neobyakangelicol	−0.310	0.079	negtive
g__Acinetobacter	Neobyakangelicol	−0.274	0.122	negtive
g__Veillonella	Neobyakangelicol	0.263	0.139	positive
g__Streptococcus	Neobyakangelicol	0.250	0.161	positive
g__Hydrogenophaga	Neobyakangelicol	−0.248	0.164	negtive
g__Tropheryma	Neobyakangelicol	0.223	0.213	positive
g__Brevundimonas	Neobyakangelicol	−0.221	0.216	negtive
g__Prevotella	Neobyakangelicol	0.190	0.290	positive
g__Prevotella_7	Neobyakangelicol	0.187	0.299	positive
g__Lactobacillus	Neobyakangelicol	−0.175	0.328	negtive
g__Vibrio	Neobyakangelicol	−0.146	0.418	negtive
g__Pseudoalteromonas	Neobyakangelicol	−0.111	0.537	negtive
g__Alloprevotella	Neobyakangelicol	0.106	0.557	positive
g__Aeromonas	Neobyakangelicol	−0.082	0.649	negtive
g__Neisseria	Neobyakangelicol	0.081	0.654	positive
g__Moraxella	Neobyakangelicol	−0.057	0.754	negtive
g__Mycoplasma	Neobyakangelicol	−0.022	0.903	negtive
g__Mycoplasma	N-Formylmethionine	0.451	0.008	positive
g__Gardnerella	N-Formylmethionine	−0.394	0.023	negtive
g__Acinetobacter	N-Formylmethionine	−0.369	0.035	negtive
g__Lactobacillus	N-Formylmethionine	−0.363	0.038	negtive
g__Hydrogenophaga	N-Formylmethionine	−0.358	0.042	negtive
g__Haemophilus	N-Formylmethionine	0.276	0.121	positive
g__Tropheryma	N-Formylmethionine	0.214	0.231	positive
g__Moraxella	N-Formylmethionine	−0.203	0.257	negtive
g__Porphyromonas	N-Formylmethionine	0.202	0.261	positive
g__Streptococcus	N-Formylmethionine	0.165	0.358	positive
g__Neisseria	N-Formylmethionine	0.117	0.517	positive
g__Alloprevotella	N-Formylmethionine	0.115	0.523	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Veillonella	N-Formylmethionine	0.108	0.549	positive
g__Pseudoalteromonas	N-Formylmethionine	0.105	0.561	positive
g__Aeromonas	N-Formylmethionine	0.103	0.569	positive
g__Prevotella	N-Formylmethionine	0.084	0.642	positive
g__Vibrio	N-Formylmethionine	0.046	0.801	positive
g__Prevotella_7	N-Formylmethionine	−0.037	0.840	negtive
g__Brevundimonas	N-Formylmethionine	−0.030	0.868	negtive
g__Leifsonia	N-Formylmethionine	−0.028	0.877	negtive
g__Acinetobacter	N-Nitrosodimethylamine	0.399	0.022	positive
g__Hydrogenophaga	N-Nitrosodimethylamine	0.378	0.031	positive
g__Haemophilus	N-Nitrosodimethylamine	−0.280	0.114	negtive
g__Leifsonia	N-Nitrosodimethylamine	0.213	0.233	positive
g__Mycoplasma	N-Nitrosodimethylamine	−0.197	0.272	negtive
g__Brevundimonas	N-Nitrosodimethylamine	0.179	0.318	positive
g__Moraxella	N-Nitrosodimethylamine	0.159	0.377	positive
g__Prevotella_7	N-Nitrosodimethylamine	0.149	0.409	positive
g__Veillonella	N-Nitrosodimethylamine	0.139	0.442	positive
g__Streptococcus	N-Nitrosodimethylamine	0.112	0.536	positive
g__Porphyromonas	N-Nitrosodimethylamine	−0.110	0.541	negtive
g__Gardnerella	N-Nitrosodimethylamine	−0.077	0.669	negtive
g__Aeromonas	N-Nitrosodimethylamine	0.056	0.758	positive
g__Lactobacillus	N-Nitrosodimethylamine	0.052	0.771	positive
g__Alloprevotella	N-Nitrosodimethylamine	−0.050	0.780	negtive
g__Pseudoalteromonas	N-Nitrosodimethylamine	0.025	0.892	positive
g__Vibrio	N-Nitrosodimethylamine	0.021	0.908	positive
g__Tropheryma	N-Nitrosodimethylamine	0.020	0.910	positive
g__Prevotella	N-Nitrosodimethylamine	−0.015	0.934	negtive
g__Neisseria	N-Nitrosodimethylamine	−0.009	0.960	negtive
g__Lactobacillus	O-Phospho-L-serine	−0.261	0.142	negtive
g__Acinetobacter	O-Phospho-L-serine	−0.259	0.145	negtive
g__Hydrogenophaga	O-Phospho-L-serine	−0.247	0.165	negtive
g__Mycoplasma	O-Phospho-L-serine	0.216	0.228	positive
g__Tropheryma	O-Phospho-L-serine	0.207	0.249	positive
g__Streptococcus	O-Phospho-L-serine	−0.192	0.286	negtive
g__Prevotella_7	O-Phospho-L-serine	−0.142	0.430	negtive
g__Moraxella	O-Phospho-L-serine	−0.119	0.511	negtive
g__Neisseria	O-Phospho-L-serine	−0.090	0.620	negtive
g__Gardnerella	O-Phospho-L-serine	−0.090	0.620	negtive
g__Vibrio	O-Phospho-L-serine	−0.078	0.665	negtive
g__Aeromonas	O-Phospho-L-serine	−0.058	0.748	negtive
g__Prevotella	O-Phospho-L-serine	0.052	0.774	positive
g__Leifsonia	O-Phospho-L-serine	−0.052	0.774	negtive
g__Brevundimonas	O-Phospho-L-serine	−0.048	0.788	negtive
g__Alloprevotella	O-Phospho-L-serine	−0.034	0.850	negtive
g__Porphyromonas	O-Phospho-L-serine	−0.033	0.854	negtive
g__Veillonella	O-Phospho-L-serine	0.012	0.948	positive
g__Pseudoalteromonas	O-Phospho-L-serine	−0.002	0.993	negtive
g__Haemophilus	O-Phospho-L-serine	−0.001	0.995	negtive
g__Hydrogenophaga	Pelargonidin	−0.542	0.001	negtive
g__Acinetobacter	Pelargonidin	−0.429	0.013	negtive
g__Mycoplasma	Pelargonidin	0.423	0.014	positive
g__Moraxella	Pelargonidin	−0.417	0.016	negtive
g__Porphyromonas	Pelargonidin	0.335	0.057	positive
g__Brevundimonas	Pelargonidin	−0.321	0.069	negtive
g__Haemophilus	Pelargonidin	0.217	0.224	positive
g__Prevotella	Pelargonidin	0.217	0.225	positive
g__Gardnerella	Pelargonidin	−0.197	0.272	negtive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Veillonella	Pelargonidin	0.162	0.368	positive
g__Leifsonia	Pelargonidin	−0.151	0.403	negtive
g__Alloprevotella	Pelargonidin	0.143	0.427	positive
g__Aeromonas	Pelargonidin	−0.126	0.483	negtive
g__Lactobacillus	Pelargonidin	−0.119	0.508	negtive
g__Vibrio	Pelargonidin	−0.094	0.602	negtive
g__Neisseria	Pelargonidin	0.082	0.651	positive
g__Tropheryma	Pelargonidin	−0.067	0.711	negtive
g__Pseudoalteromonas	Pelargonidin	−0.065	0.718	negtive
g__Streptococcus	Pelargonidin	0.006	0.973	positive
g__Prevotella_7	Pelargonidin	−0.001	0.996	negtive
g__Hydrogenophaga	Pentedrone	0.607	0.000	positive
g__Acinetobacter	Pentedrone	0.518	0.002	positive
g__Moraxella	Pentedrone	0.379	0.030	positive
g__Brevundimonas	Pentedrone	0.346	0.049	positive
g__Haemophilus	Pentedrone	−0.328	0.062	negtive
g__Porphyromonas	Pentedrone	−0.316	0.073	negtive
g__Leifsonia	Pentedrone	0.253	0.156	positive
g__Mycoplasma	Pentedrone	−0.220	0.219	negtive
g__Aeromonas	Pentedrone	0.141	0.435	positive
g__Tropheryma	Pentedrone	0.135	0.455	positive
g__Prevotella	Pentedrone	−0.122	0.500	negtive
g__Pseudoalteromonas	Pentedrone	0.116	0.520	positive
g__Veillonella	Pentedrone	−0.115	0.526	negtive
g__Gardnerella	Pentedrone	0.108	0.548	positive
g__Vibrio	Pentedrone	0.104	0.566	positive
g__Neisseria	Pentedrone	−0.084	0.643	negtive
g__Alloprevotella	Pentedrone	−0.069	0.703	negtive
g__Lactobacillus	Pentedrone	−0.045	0.804	negtive
g__Streptococcus	Pentedrone	−0.029	0.872	negtive
g__Prevotella_7	Pentedrone	0.012	0.946	positive
g__Mycoplasma	PROPANIL	0.304	0.086	positive
g__Moraxella	PROPANIL	−0.252	0.157	negtive
g__Acinetobacter	PROPANIL	−0.181	0.312	negtive
g__Streptococcus	PROPANIL	−0.178	0.323	negtive
g__Hydrogenophaga	PROPANIL	−0.168	0.349	negtive
g__Prevotella	PROPANIL	0.107	0.553	positive
g__Leifsonia	PROPANIL	0.058	0.748	positive
g__Haemophilus	PROPANIL	0.051	0.779	positive
g__Gardnerella	PROPANIL	−0.050	0.784	negtive
g__Lactobacillus	PROPANIL	−0.044	0.808	negtive
g__Aeromonas	PROPANIL	−0.038	0.834	negtive
g__Prevotella_7	PROPANIL	0.036	0.844	positive
g__Vibrio	PROPANIL	0.034	0.852	positive
g__Brevundimonas	PROPANIL	−0.032	0.858	negtive
g__Pseudoalteromonas	PROPANIL	0.030	0.869	positive
g__Alloprevotella	PROPANIL	0.025	0.888	positive
g__Porphyromonas	PROPANIL	0.024	0.894	positive
g__Veillonella	PROPANIL	0.021	0.908	positive
g__Tropheryma	PROPANIL	0.003	0.985	positive
g__Neisseria	PROPANIL	0	1	
g__Porphyromonas	Propyzamide	0.543	0.001	positive
g__Haemophilus	Propyzamide	0.531	0.001	positive
g__Hydrogenophaga	Propyzamide	−0.422	0.015	negtive
g__Prevotella	Propyzamide	0.421	0.015	positive
g__Alloprevotella	Propyzamide	0.386	0.027	positive
g__Veillonella	Propyzamide	0.369	0.034	positive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Acinetobacter	Propyzamide	−0.362	0.039	negtive
g__Neisseria	Propyzamide	0.339	0.054	positive
g__Moraxella	Propyzamide	−0.313	0.076	negtive
g__Brevundimonas	Propyzamide	−0.287	0.105	negtive
g__Prevotella_7	Propyzamide	0.261	0.142	positive
g__Tropheryma	Propyzamide	−0.204	0.255	negtive
g__Gardnerella	Propyzamide	−0.203	0.256	negtive
g__Leifsonia	Propyzamide	−0.185	0.302	negtive
g__Vibrio	Propyzamide	−0.152	0.400	negtive
g__Streptococcus	Propyzamide	0.141	0.434	positive
g__Aeromonas	Propyzamide	−0.135	0.452	negtive
g__Pseudoalteromonas	Propyzamide	−0.103	0.569	negtive
g__Lactobacillus	Propyzamide	−0.058	0.746	negtive
g__Mycoplasma	Propyzamide	0.039	0.828	positive
g__Mycoplasma	Pyroglutamic acid	0.353	0.044	positive
g__Lactobacillus	Pyroglutamic acid	−0.341	0.053	negtive
g__Tropheryma	Pyroglutamic acid	0.267	0.132	positive
g__Hydrogenophaga	Pyroglutamic acid	−0.25	0.160	negtive
g__Vibrio	Pyroglutamic acid	−0.236	0.186	negtive
g__Acinetobacter	Pyroglutamic acid	−0.211	0.239	negtive
g__Haemophilus	Pyroglutamic acid	0.208	0.245	positive
g__Alloprevotella	Pyroglutamic acid	0.205	0.251	positive
g__Gardnerella	Pyroglutamic acid	−0.203	0.256	negtive
g__Porphyromonas	Pyroglutamic acid	0.193	0.282	positive
g__Prevotella	Pyroglutamic acid	0.190	0.290	positive
g__Neisseria	Pyroglutamic acid	0.185	0.301	positive
g__Veillonella	Pyroglutamic acid	0.175	0.329	positive
g__Streptococcus	Pyroglutamic acid	0.149	0.407	positive
g__Aeromonas	Pyroglutamic acid	−0.149	0.408	negtive
g__Brevundimonas	Pyroglutamic acid	−0.108	0.547	negtive
g__Pseudoalteromonas	Pyroglutamic acid	−0.106	0.557	negtive
g__Leifsonia	Pyroglutamic acid	−0.098	0.589	negtive
g__Moraxella	Pyroglutamic acid	−0.052	0.773	negtive
g__Prevotella_7	Pyroglutamic acid	0.043	0.811	positive
g__Hydrogenophaga	S−adenosylmethionine	−0.464	0.007	negtive
g__Prevotella_7	S−adenosylmethionine	−0.426	0.013	negtive
g__Acinetobacter	S−adenosylmethionine	−0.390	0.026	negtive
g__Leifsonia	S−adenosylmethionine	−0.387	0.026	negtive
g__Brevundimonas	S−adenosylmethionine	−0.372	0.034	negtive
g__Streptococcus	S−adenosylmethionine	−0.358	0.041	negtive
g__Veillonella	S−adenosylmethionine	−0.339	0.054	negtive
g__Lactobacillus	S−adenosylmethionine	0.311	0.079	positive
g__Alloprevotella	S−adenosylmethionine	−0.306	0.083	negtive
g__Moraxella	S−adenosylmethionine	−0.301	0.088	negtive
g__Vibrio	S−adenosylmethionine	−0.263	0.138	negtive
g__Prevotella	S−adenosylmethionine	−0.204	0.256	negtive
g__Neisseria	S−adenosylmethionine	−0.184	0.304	negtive
g__Aeromonas	S−adenosylmethionine	−0.183	0.307	negtive
g__Pseudoalteromonas	S−adenosylmethionine	−0.168	0.351	negtive
g__Porphyromonas	S−adenosylmethionine	−0.120	0.505	negtive
g__Haemophilus	S−adenosylmethionine	0.069	0.705	positive
g__Mycoplasma	S−adenosylmethionine	0.067	0.709	positive
g__Tropheryma	S−adenosylmethionine	−0.016	0.931	negtive
g__Gardnerella	S−adenosylmethionine	0.011	0.951	positive
g__Hydrogenophaga	Sedoheptulose 7−phosphate	−0.699	0.000	negtive
g__Acinetobacter	Sedoheptulose 7−phosphate	−0.541	0.001	negtive
g__Brevundimonas	Sedoheptulose 7−phosphate	−0.514	0.003	negtive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	p value	relation
g__Leifsonia	Sedoheptulose 7-phosphate	−0.452	0.008	negtive
g__Porphyromonas	Sedoheptulose 7-phosphate	0.438	0.011	positive
g__Haemophilus	Sedoheptulose 7-phosphate	0.419	0.015	positive
g__Vibrio	Sedoheptulose 7-phosphate	−0.408	0.018	negtive
g__Aeromonas	Sedoheptulose 7-phosphate	−0.391	0.025	negtive
g__Pseudoalteromonas	Sedoheptulose 7-phosphate	−0.381	0.029	negtive
g__Moraxella	Sedoheptulose 7-phosphate	−0.303	0.087	negtive
g__Veillonella	Sedoheptulose 7-phosphate	0.195	0.276	positive
g__Prevotella	Sedoheptulose 7-phosphate	0.191	0.287	positive
g__Neisseria	Sedoheptulose 7-phosphate	0.137	0.446	positive
g__Gardnerella	Sedoheptulose 7-phosphate	−0.130	0.470	negtive
g__Streptococcus	Sedoheptulose 7-phosphate	0.119	0.511	positive
g__Alloprevotella	Sedoheptulose 7-phosphate	0.093	0.605	positive
g__Lactobacillus	Sedoheptulose 7-phosphate	0.053	0.768	positive
g__Mycoplasma	Sedoheptulose 7-phosphate	0.052	0.772	positive
g__Tropheryma	Sedoheptulose 7-phosphate	0.023	0.897	positive
g__Prevotella_7	Sedoheptulose 7-phosphate	0.017	0.924	positive
g__Vibrio	Serotonin	0.334	0.057	positive
g__Leifsonia	Serotonin	0.290	0.101	positive
g__Pseudoalteromonas	Serotonin	0.266	0.134	positive
g__Aeromonas	Serotonin	0.238	0.182	positive
g__Neisseria	Serotonin	0.229	0.201	positive
g__Prevotella_7	Serotonin	0.185	0.302	positive
g__Hydrogenophaga	Serotonin	0.171	0.339	positive
g__Brevundimonas	Serotonin	0.160	0.373	positive
g__Acinetobacter	Serotonin	0.154	0.390	positive
g__Alloprevotella	Serotonin	0.153	0.394	positive
g__Porphyromonas	Serotonin	0.111	0.540	positive
g__Gardnerella	Serotonin	0.110	0.544	positive
g__Prevotella	Serotonin	0.094	0.603	positive
g__Veillonella	Serotonin	0.080	0.656	positive
g__Mycoplasma	Serotonin	−0.069	0.703	negtive
g__Haemophilus	Serotonin	0.056	0.756	positive
g__Streptococcus	Serotonin	0.046	0.800	positive
g__Tropheryma	Serotonin	−0.038	0.835	negtive
g__Lactobacillus	Serotonin	0.035	0.845	positive
g__Moraxella	Serotonin	−0.007	0.971	negtive
g__Mycoplasma	Sojagol	−0.423	0.014	negtive
g__Acinetobacter	Sojagol	0.366	0.037	positive
g__Lactobacillus	Sojagol	0.357	0.042	positive
g__Hydrogenophaga	Sojagol	0.317	0.073	positive
g__Moraxella	Sojagol	0.295	0.095	positive
g__Porphyromonas	Sojagol	−0.252	0.158	negtive
g__Gardnerella	Sojagol	0.236	0.185	positive
g__Veillonella	Sojagol	−0.232	0.193	negtive
g__Tropheryma	Sojagol	−0.148	0.411	negtive
g__Haemophilus	Sojagol	−0.141	0.434	negtive
g__Brevundimonas	Sojagol	0.101	0.576	positive
g__Leifsonia	Sojagol	0.094	0.602	positive
g__Pseudoalteromonas	Sojagol	−0.078	0.668	negtive
g__Streptococcus	Sojagol	−0.072	0.692	negtive
g__Prevotella	Sojagol	−0.063	0.726	negtive
g__Aeromonas	Sojagol	−0.063	0.727	negtive
g__Vibrio	Sojagol	−0.063	0.730	negtive
g__Alloprevotella	Sojagol	−0.039	0.828	negtive
g__Prevotella_7	Sojagol	−0.008	0.963	negtive
g__Neisseria	Sojagol	−0.004	0.981	negtive

(*continues*)

Table S1 Continued.

Data 1	Data 2	rho	pv alue	relation
g__Mycoplasma	Thioacetamide	0.393	0.024	positive
g__Hydrogenophaga	Thioacetamide	−0.308	0.082	negtive
g__Acinetobacter	Thioacetamide	−0.264	0.137	negtive
g__Vibrio	Thioacetamide	−0.259	0.146	negtive
g__Tropheryma	Thioacetamide	0.247	0.166	positive
g__Brevundimonas	Thioacetamide	−0.201	0.260	negtive
g__Aeromonas	Thioacetamide	−0.198	0.270	negtive
g__Lactobacillus	Thioacetamide	−0.196	0.273	negtive
g__Pseudoalteromonas	Thioacetamide	−0.163	0.364	negtive
g__Leifsonia	Thioacetamide	−0.147	0.413	negtive
g__Moraxella	Thioacetamide	−0.128	0.478	negtive
g__Haemophilus	Thioacetamide	0.103	0.567	positive
g__Porphyromonas	Thioacetamide	0.101	0.577	positive
g__Gardnerella	Thioacetamide	−0.084	0.641	negtive
g__Prevotella	Thioacetamide	0.083	0.645	positive
g__Alloprevotella	Thioacetamide	0.078	0.666	positive
g__Neisseria	Thioacetamide	0.077	0.670	positive
g__Veillonella	Thioacetamide	0.063	0.729	positive
g__Streptococcus	Thioacetamide	0.054	0.767	positive
g__Prevotella_7	Thioacetamide	0.005	0.977	positive
g__Brevundimonas	XMP	0.422	0.015	positive
g__Acinetobacter	XMP	0.364	0.038	positive
g__Aeromonas	XMP	0.360	0.040	positive
g__Pseudoalteromonas	XMP	0.355	0.042	positive
g__Prevotella	XMP	−0.322	0.068	negtive
g__Leifsonia	XMP	0.310	0.079	positive
g__Vibrio	XMP	0.291	0.100	positive
g__Hydrogenophaga	XMP	0.233	0.191	positive
g__Lactobacillus	XMP	−0.230	0.197	negtive
g__Moraxella	XMP	0.223	0.213	positive
g__Alloprevotella	XMP	−0.175	0.331	negtive
g__Haemophilus	XMP	−0.155	0.390	negtive
g__Streptococcus	XMP	−0.129	0.473	negtive
g__Porphyromonas	XMP	−0.120	0.505	negtive
g__Mycoplasma	XMP	0.074	0.681	positive
g__Veillonella	XMP	−0.056	0.755	negtive
g__Neisseria	XMP	−0.027	0.879	negtive
g__Tropheryma	XMP	0.020	0.914	positive
g__Prevotella_7	XMP	0.012	0.948	positive
g__Gardnerella	XMP	−0.004	0.984	negtive

Table S2

Pathway	Description	# compounds_ num(dem)	Compounds(dem)	Total	Percent	Rich Factor	Raw_p	-ln(p)	ms2_description
hsa01100	Metabolic pathways	27	C00144;C00164;C00655;C02814;C03056;C01586;C00793;C00120;C05904;C00037;C01112;C00092;C00989;C01005;C00160;C06102;C00159;C00858;C00719;C03519;C00019;C04501;C05382;C00197;C00780;C01879;C00246	2974	87.097	0.009	0.016	4.146	Global and overview maps
hsa01200	Carbon metabolism	6	C00160;C05382;C00037;C00197;C00989;C01005	114	19.355	0.053	0.000	8.992	Global and overview maps
hsa00270	Cysteine and methionine metabolism	5	C00019;C00793;C00197;C03145;C01005	66	16.129	0.076	0.000	9.342	Amino acid metabolism
hsa01230	Biosynthesis of amino acids	5	C00019;C05382;C00197;C00037;C01005	128	16.129	0.039	0.002	6.267	Global and overview maps
hsa00260	Glycine, serine and threonine metabolism	4	C01005;C00197;C00719;C00037	48	12.903	0.083	0.000	8.005	Amino acid metabolism
hsa02010	ABC transporters	4	C00159;C00719;C00120;C00037	138	12.903	0.029	0.016	4.145	Membrane transport
hsa01250	Biosynthesis of nucleotide sugars	4	C00159;C04501;C05382;C01112	200	12.903	0.02	0.052	2.954	Global and overview maps
hsa01240	Biosynthesis of cofactors	4	C00197;C00120;C00037;C00019	328	12.903	0.012	0.204	1.591	Global and overview maps
hsa05230	Central carbon metabolism in cancer	3	C00092;C00197;C00037	37	9.677	0.081	0.002	6.128	Cancer: overview
hsa00650	Butanoate metabolism	3	C00164;C00989;C00246	47	9.677	0.064	0.004	5.441	Carbohydrate metabolism
hsa00630	Glyoxylate and dicarboxylate metabolism	3	C00160;C00197;C00037	62	9.677	0.048	0.009	4.666	Carbohydrate metabolism
hsa00230	Purine metabolism	3	C00144;C00037;C00655	99	9.677	0.030	0.033	3.421	Nucleotide metabolism
hsa04721	Synaptic vesicle cycle	2	C00780;C00037	12	6.452	0.167	0.003	5.769	Nervous system
hsa04973	Carbohydrate digestion and absorption	2	C00092;C00246	27	6.452	0.074	0.016	4.165	Digestive system
hsa04742	Taste transduction	2	C00144;C00780	32	6.452	0.063	0.021	3.841	Sensory system
hsa00030	Pentose phosphate pathway	2	C00197;C05382	35	6.452	0.057	0.025	3.672	Carbohydrate metabolism
hsa00480	Glutathione metabolism	2	C01879;C00037	38	6.452	0.053	0.030	3.519	Metabolism of other amino acids
hsa04974	Protein digestion and absorption	2	C00037;C00246	47	6.452	0.043	0.044	3.128	Digestive system
hsa00120	Primary bile acid biosynthesis	2	C15519;C00037	47	6.452	0.043	0.044	3.128	Lipid metabolism

(*continues*)

Table S2 Continued.

Pathway	Description	# compounds_ num(dem)	Compounds(dem)	Total	Percent	Rich Factor	Raw_p	-ln(p)	ms2_description
hsa00310	Lysine degradation	2	C00164;C00037	50	6.452	0.04	0.049	3.016	Amino acid metabolism
hsa04080	Neuroactive ligand-receptor interaction	2	C00780;C00037	52	6.452	0.038	0.053	2.946	Signaling molecules and interaction
hsa00970	Aminoacyl-tRNA biosynthesis	2	C01005;C00037	52	6.452	0.038	0.053	2.946	Translation
hsa05208	Chemical carcinogenesis - reactive oxygen species	2	C02814;C00019	57	6.452	0.035	0.062	2.782	Cancer: overview
hsa00470	D-Amino acid metabolism	2	C00793;C00037	67	6.452	0.030	0.082	2.500	Metabolism of other amino acids
hsa00520	Amino sugar and nucleotide sugar metabolism	2	C00159;C04501	118	6.452	0.017	0.206	1.581	Carbohydrate metabolism
hsa04142	Lysosome	1	C00159	4	3.226	0.25	0.028	3.565	Transport and catabolism
hsa04740	Olfactory transduction	1	C00144	8	3.226	0.125	0.056	2.886	Sensory system
hsa04744	Phototransduction	1	C00144	8	3.226	0.125	0.056	2.886	Sensory system
hsa04022	cGMP-PKG signaling pathway	1	C00144	10	3.226	0.1	0.069	2.669	Signal transduction
hsa04122	Sulfur relay system	1	C00019	11	3.226	0.091	0.076	2.578	Folding, sorting and degradation
hsa04540	Gap junction	1	C00780	11	3.226	0.091	0.076	2.578	Cellular community - eukaryotes
hsa04625	C-type lectin receptor signaling pathway	1	C00159	11	3.226	0.091	0.076	2.578	Immune system
hsa04917	Prolactin signaling pathway	1	C00092	11	3.226	0.091	0.076	2.578	Endocrine system
hsa04911	Insulin secretion	1	C00092	12	3.226	0.083	0.083	2.494	Endocrine system
hsa01523	Antifolate resistance	1	C00144	17	3.226	0.059	0.115	2.163	Drug resistance: antineoplastic
hsa04931	Insulin resistance	1	C00092	19	3.226	0.053	0.128	2.058	Endocrine and metabolic disease
hsa04918	Thyroid hormone synthesis	1	C00092	21	3.226	0.048	0.140	1.965	Endocrine system
hsa04024	cAMP signaling pathway	1	C00780	25	3.226	0.04	0.165	1.804	Signal transduction
hsa04922	Glucagon signaling pathway	1	C00197	26	3.226	0.038	0.171	1.768	Endocrine system

hsa00780	Biotin metabolism	1	C00120	29	3.226	0.034	0.188	1.669	Metabolism of cofactors and vitamins
hsa04978	Mineral absorption	1	C00037	29	3.226	0.034	0.188	1.669	Digestive system
hsa05207	Chemical carcinogenesis - receptor activation	1	C00780	29	3.226	0.034	0.188	1.669	Cancer: overview
hsa00010	Glycolysis / Gluconeogenesis	1	C00197	31	3.226	0.032	0.200	1.609	Carbohydrate metabolism
hsa00730	Thiamine metabolism	1	C00037	31	3.226	0.032	0.200	1.609	Metabolism of cofactors and vitamins
hsa00620	Pyruvate metabolism	1	C03248	32	3.226	0.031	0.206	1.581	Carbohydrate metabolism
hsa04750	Inflammatory mediator regulation of TRP channels	1	C00780	35	3.226	0.029	0.223	1.501	Sensory system
hsa00500	Starch and sucrose metabolism	1	C00092	37	3.226	0.027	0.234	1.453	Carbohydrate metabolism
hsa00561	Glycerolipid metabolism	1	C00197	38	3.226	0.026	0.239	1.429	Lipid metabolism
hsa04977	Vitamin digestion and absorption	1	C00120	39	3.226	0.026	0.245	1.407	Digestive system
hsa05415	Diabetic cardiomyopathy	1	C00092	39	3.226	0.026	0.245	1.407	Cardiovascular disease
hsa04726	Serotonergic synapse	1	C00780	42	3.226	0.024	0.261	1.342	Nervous system
hsa00280	Valine, leucine and isoleucine degradation	1	C00164	42	3.226	0.024	0.261	1.342	Amino acid metabolism
hsa00052	Galactose metabolism	1	C00159	46	3.226	0.022	0.282	1.265	Carbohydrate metabolism
hsa00562	Inositol phosphate metabolism	1	C00092	47	3.226	0.021	0.287	1.247	Carbohydrate metabolism
hsa00360	Phenylalanine metabolism	1	C03519	49	3.226	0.020	0.298	1.211	Amino acid metabolism
hsa00051	Fructose and mannose metabolism	1	C00159	54	3.226	0.019	0.323	1.131	Carbohydrate metabolism
hsa00760	Nicotinate and nicotinamide metabolism	1	C03056	55	3.226	0.018	0.328	1.116	Metabolism of cofactors and vitamins
hsa00440	Phosphonate and phosphinate metabolism	1	C00037	56	3.226	0.018	0.333	1.101	Metabolism of other amino acids
hsa00330	Arginine and proline metabolism	1	C00019	72	3.226	0.014	0.406	0.902	Amino acid metabolism
hsa00350	Tyrosine metabolism	1	C00164	78	3.226	0.013	0.431	0.841	Amino acid metabolism

(*continues*)

Table S2 Continued.

Pathway	Description	# compounds_ num(dem)	Compounds(dem)	Total	Percent	Rich Factor	Raw_p	-ln(p)	ms2_description
hsa05204	Chemical carcinogenesis - DNA adducts	1	C14704	81	3.226	0.012	0.444	0.813	Cancer: overview
hsa00524	Neomycin, kanamycin and gentamicin biosynthesis	1	C00092	81	3.226	0.012	0.444	0.813	Biosynthesis of other secondary metabolites
hsa00380	Tryptophan metabolism	1	C00780	83	3.226	0.012	0.452	0.795	Amino acid metabolism
hsa04976	Bile secretion	1	C00780	97	3.226	0.010	0.505	0.683	Digestive system
hsa00860	Porphyrin metabolism	1	C00037	148	3.226	0.007	0.660	0.415	Metabolism of cofactors and vitamins