Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Geographic Variation in the Urinary Microbiota of Patients with Urolithiasis

Hsiang Ying Lee
Kaohsiung Medical University Hospital
Chun Kai Chang
Kaohsiung Medical University Hospital
Wen-Jeng Wu
Kaohsiung Medical University Hospital
Deng-Chyang Wu
Kaohsiung Medical University Hospital
Sung Yong Cho
moretry@snu.ac.kr

Seoul National University College of Medicine, Seoul National University Hospital

Article

Keywords: Urolithiasis, Urinary microbiota, Geographic variation, Full-length 16S rRNA sequencing

Posted Date: September 10th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10609570/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Scientific Reports on November 4th, 2026.
See the published version at https://doi.org/10.1038/s41598-026-77872-0.

Abstract

Background: Geographic variation may influence the urinary microbiota of patients with urolithiasis. This study compared urinary microbial profiles between Taiwan and Korea patients.

Materials and Methods:

This cross-national comparative study included 72 patients with clinically confirmed urolithiasis, comprising 31 patients from Taiwan and 41 from South Korea. Bladder urine samples were collected by urethral catheterization before surgery and prophylactic antibiotic administration. Full-length 16S rRNA genes were amplified using the 27F and 1492R primers and sequenced using a third-generation long-read sequencing platform. Sequence denoising and amplicon sequence variant inference were performed using DADA2, followed by taxonomic annotation and phylogenetic analysis in QIIME2. Alpha diversity, beta diversity, and differential taxonomic abundance were compared between the two groups.

Results:

No significant differences were observed in alpha diversity indices, including microbial richness, diversity, evenness, and phylogenetic diversity. However, beta diversity analyses demonstrated significant differences in overall urinary microbial community composition between the Taiwan and Korea groups, as shown by ANOSIM, MRPP, and perMANOVA. Differential abundance analysis identified enrichment of Proteobacteria, *Shigella flexneri*, and several related taxa in the Taiwan group, whereas *Gardnerella swidsinskii*, Prevotellaceae, and *Veillonella* were enriched in the Korea group. At the species level, *G. swidsinskii* showed significantly greater relative abundance in the Korea cohort.

Conclusion: Taiwanese and Korean patients with urolithiasis exhibited distinct urinary microbial profiles despite similar alpha diversity. These findings suggest that geographic, dietary, and microbial factors may contribute to population-specific patterns of urinary stone disease.

Introduction

Urolithiasis is one of the most common and highly recurrent diseases of the urinary system [1–3]. Its clinical manifestations vary widely, ranging from asymptomatic small calculi, painless hematuria, and severe flank pain presenting as renal colic, to recurrent urinary tract infection, urinary tract obstruction, irreversible deterioration of renal function, and even life-threatening urosepsis [4,5]. According to the latest data from the Global Burden of Disease (GBD) study, the global number of incident cases of urolithiasis reached 106 million in 2021 [6]. The common causes of stone formation are multifactorial which are influenced by genetic, dietary, metabolic syndrome and environmental factors [7]. In recent years, the role of the microbiota in stone formation has been increasingly investigated.

Commensal microbiota in both the gut and urine also serve as indispensable contributors to this process, an interaction increasingly referred to as the “gut–kidney axis” [8]. Microorganisms may participate in the pathogenesis of urolithiasis through multiple complex and deeply interconnected mechanisms [9]. Some previous research have discovered important microbes such as *Oxalobacter formigenes*, *Bifidobacterium*, and certain *Lactobacillus* species which possess the capacity to degrade dietary oxalate [10]. Schmidt et al. [11] employed advanced materials science techniques, including

focused ion beam–scanning electron microscopy (FIB-SEM) and confocal fluorescence microscopy, and for the first time identified bacterial biofilm structures intercalated within polycrystalline mineral layers in human calcium oxalate stones.

Geographic location, dietary patterns and microbiota environment may influence stone formation, intercountry differences in urinary microbial profiles may provide important insights into the pathogenesis of urolithiasis. Therefore, we conducted a comparative study of the urinary microbiota between patients from Korea and Taiwan to explore potential geographic and population-based differences associated with stone disease.

Material and Methods

Patient Selection and Data Collection

The study was approved by the Institutional Review Board of Kaohsiung Medical University Hospital (KMUHIRB-F(I)-20250207) and the Institutional Review Board of Seoul National University Hospital (IRB No. 2207-202-1346). Written informed consent was obtained from all participants prior to study participation and sample collection. All methods were performed in accordance with the relevant guidelines and regulations. This study was designed as a cross-regional comparative analysis of the urinary microbiota in patients with clinically confirmed urolithiasis from Taiwan and South Korea. Patients in the Taiwan group were recruited from Kaohsiung Medical University Chung-Ho Memorial Hospital, whereas urine samples from the South Korea group were provided by Seoul National University Hospital. After excluding samples that failed quality control, a total of 72 urine samples from patients with urolithiasis were included in the final analysis, comprising 31 patients from Taiwan and 41 patients from South Korea.

All included patients underwent operative management for urolithiasis and had a confirmed diagnosis based on clinical evaluation and imaging studies, including plain abdominal radiography, urinary tract ultrasonography, or computed tomography. To minimize the potential influence of therapeutic procedures and antibiotic exposure on urinary microbiota profiles, urine samples were collected after the patient had entered the operating room and before the administration of prophylactic antibiotics and performing surgery. Bladder urine was obtained by urethral catheterization to reduce the possibility of contamination from the distal urethral or skin microbiota and to improve the reliability of urinary microbiota analysis. Patients with any antibiotic exposure within one month prior to urine sample collection were excluded. In addition, to minimize potential confounding from other urinary tract diseases or indwelling medical devices that could affect the interpretation of urinary microbiota profiles, patients were excluded if they had recurrent urinary tract infections, sexually transmitted infections, urinary tract malignancies, or long-term indwelling urinary catheters.

16S rRNA Gene Sequencing

After urine sample collection, all specimens were processed according to a standardized protocol and subsequently subjected to full-length 16S rRNA gene sequencing analysis. Full-length 16S rRNA sequencing data from all 72 urine samples were newly generated specifically for the present study. All samples were frozen at − 80°C after collection. In the experimental workflow, the full-length 16S rRNA gene was first amplified from urine samples by polymerase chain reaction (PCR) using barcoded universal 16S primers 27F and 1492R. After PCR amplification, the barcoded DNA amplicons underwent quality control and were subsequently pooled according to the analytical workflow before SMRTbell library preparation. The constructed SMRTbell libraries were purified using AMPure PB beads to remove potential noise fragments that could affect downstream sequencing quality. The purified samples then underwent DNA damage repair and adapter ligation, followed by sequencing on a third-generation long-read sequencing platform.

Filtered sequences were subsequently subjected to denoising analysis using the DADA2 package in R (v1.20). Prior to denoising, primer sequences were removed from the amplicons. The forward primer sequence was AGRGTTYGATYMTGGCTCAG, and the reverse primer sequence was RGYTACCTTGTTACGACTT. The DADA2 workflow included sequence quality filtering, dereplication, error correction, inference of true biological sequences, and chimera removal. This approach corrects potential artificial errors arising from sequencing, PCR amplification, or chimera formation based on sequence abundance, quality scores, and sequence-level differences, thereby generating sequence features that more accurately represent the true microbial composition. After denoising and chimera removal, the resulting non-chimeric sequence features were defined as amplicon sequence variants (ASVs).

Representative ASV sequences and the ASV table were then imported into QIIME2 (v2022.11) for taxonomic annotation and phylogenetic analysis. Taxonomic classification was performed using the QIIME2 feature-classifier classify-consensus-vsearch method, with the NCBI 16S ribosomal RNA database used as the reference database. Taxonomic assignments for each ASV were summarized at multiple taxonomic levels, including kingdom, phylum, class, order, family, genus, and species, and were used for subsequent analyses of urinary microbiota composition.

To further evaluate sequence similarity and evolutionary relationships among ASVs, multiple sequence alignment was performed using QIIME2 alignment mafft, and a phylogenetic tree of the representative ASV sequences was constructed using QIIME2 phylogeny fasttree. After taxonomic annotation and phylogenetic tree construction, the generated ASV table served as the basis for downstream analyses, including taxonomic composition profiling, alpha diversity analysis, beta diversity analysis, differential abundance analysis between groups, and other statistical analyses.

Statistical analysis

Species composition, microbial diversity, and between-group differences in urinary microbiota were analyzed in patients with urolithiasis from the Taiwan and Korea groups. For differential abundance analysis, urinary microbiota profiles between the Taiwan and Korea groups were compared based on

taxonomic abundance data at different classification levels. Partial least squares discriminant analysis (PLS-DA) was performed to evaluate differences in overall urinary microbial composition between the Taiwan and Korea groups. PLS-DA was applied to the taxonomic abundance data to project high-dimensional microbial features into latent components that maximized separation between the predefined groups and to identify taxa contributing to the observed group discrimination. Differences in alpha diversity indices and taxonomic abundance between the two groups were assessed using the Wilcoxon rank-sum test or Welch's t-test, depending on the data distribution and characteristics. In addition, linear discriminant analysis effect size (LEfSe) was used to identify potential discriminatory taxa between the two groups, and the LDA score was used to evaluate the contribution of each taxonomic feature to group discrimination. LEfSe analysis was performed using the bioBakery LEfSe Python version and the microeco package in R (v0.16.0), with results generated according to different LDA score thresholds. Statistical significance was determined based on p values, with $p < 0.05$ considered statistically significant.

Results

After sequencing, raw HiFi reads were first obtained for each urine sample. Subsequent preprocessing was performed sequentially. Following this quality-control workflow, the resulting non-chimeric reads were used as the basis for ASV inference, taxonomic annotation, microbial community composition analysis, and diversity analysis. A summary of sequencing data quality control and denoising results for each group is presented in Table 1. In the Korean group, the mean number of raw HiFi reads was 16,377 ± 2,289 reads. After quality filtering, denoising, and chimera removal, the mean number of non-chimeric reads was 14,290 ± 2,463 reads, corresponding to a final retention rate of 87.0 ± 7.1%. In the Taiwan group, the mean number of raw HiFi reads was 27,099 ± 17,221 reads, and the mean number of non-chimeric reads was 20,774 ± 10,123 reads, with a final retention rate of 84.0 ± 17.4%. Across all 72 samples, the mean number of raw HiFi reads was 20,993 ± 12,524 reads, while the mean number of non-chimeric reads was 17,082 ± 7,561 reads, resulting in an overall final retention rate of 85.7 ± 12.6%.

Table 1
Sequencing Data Quality Control and DADA2 Denoising Results

Group	n	Raw HiFi reads	Primer-removed reads	Filtered reads	Denoised reads	Non-chimera reads	Final retention rate (%)
Korea group	41	16,377 ± 2,289	15,046 ± 2,480	14,568 ± 2,431	14,445 ± 2,443	14,290 ± 2,463	87.0 ± 7.1
Taiwan group	31	27,099 ± 17,221	22,012 ± 10,840	21,238 ± 10,469	21,160 ± 10,456	20,774 ± 10,123	84.0 ± 17.4
Overall	72	20,993 ± 12,524	18,045 ± 8,074	17,440 ± 7,791	17,336 ± 7,795	17,082 ± 7,561	85.7 ± 12.6

In Fig. 1, in the Taiwan group, species such as *Shigella flexneri*, *Enterococcus faecalis*, and *Proteus mirabilis* were observed to account for a certain proportion of the microbial community. In contrast, the Korean group showed distributions of *Gardnerella swidsinskii*, *Lactobacillus iners*, *Streptococcus agalactiae*, and several *Gardnerella*-related species. The rarefaction curve results are shown in Fig. 2. The curves of most samples gradually reached a plateau with increasing sequencing depth, indicating that the number of newly detected ASVs decreased as additional sequences were obtained. These findings suggest that the current sequencing depth was sufficient to capture most of the detectable microbial communities. PLS-DA demonstrated a clear separation in urinary microbial profiles between the Taiwan and Korea groups. The first and second latent components explained 3.37% and 2.61% of the total variation, respectively. Although limited overlap was observed between the confidence ellipses, most Taiwanese samples clustered toward negative PLSDA1 values, whereas Korean samples were predominantly distributed toward positive PLSDA1 values, indicating distinct group-specific microbial community patterns (Fig. 3).

The comparison of alpha diversity indices between the Taiwan and Korean groups is presented in Table 2. Good's coverage was 1.000 in both groups, indicating adequate sequencing coverage of the detectable microbial composition in the study samples. Overall, no statistically significant differences were observed between the Taiwan and Korean groups in within-sample richness, diversity, evenness, or phylogenetic diversity of the urinary microbiota among patients with urolithiasis.

Table 2
Comparison of Alpha Diversity Between the Taiwan and Korean Groups

Alpha diversity index	Taiwan group, median (IQR)	Korea group, median (IQR)	p value
Observed features	37.0 (10.5–73.5)	30.0 (17.0–60.0)	0.92
Shannon entropy	2.36 (1.82–4.75)	2.59 (1.94–4.14)	0.87
Simpson index	0.764 (0.627–0.925)	0.749 (0.641–0.918)	0.75
Pielou evenness	0.701 (0.419–0.812)	0.593 (0.438–0.767)	0.27
Menhinick index	0.299 (0.072–0.473)	0.260 (0.139–0.468)	0.78
Margalef index	3.74 (0.97–7.18)	3.05 (1.65–6.08)	0.95
Faith's PD	5.91 (3.06–7.85)	4.86 (3.80–6.11)	0.32
Good's coverage	1.000 (1.000–1.000)	1.000 (1.000–1.000)	1.00

Intergroup differences were assessed using ANOSIM, MRPP, and perMANOVA. The ANOSIM analysis showed significant differences in community structure between the Taiwan and Korean groups, with an R value of 0.1502 and a p value of 0.0010. The MRPP analysis also demonstrated statistically significant differences in microbial composition between the two groups, with an A value of 0.0023 and a significance value of 0.0290. The perMANOVA analysis indicated that group assignment was statistically

associated with differences in urinary microbiota composition, with an F value of 1.2909, an R^2 of 0.0181, and both the p value and adjusted p value of 0.0090 (Table 3).

The LEfSe analysis results are shown in Fig. 4. In the Taiwan group, taxa with higher LDA scores mainly included *Proteobacteria*, *Shigella flexneri*, *Flavobacteriales*, *Alphaproteobacteria*, *Flavobacteriia*, *Denitrificimonas caeni*, *Denitrificimonas*, *Pseudomonadales*, *Pseudomonadaceae*, *Bradyrhizobium embrapense*, and *Bradyrhizobium*. In contrast, taxa relatively enriched in the Korean group included *Gardnerella swidsinskii*, *Prevotellaceae*, and *Veillonella*. These findings indicate distinct enrichment patterns of specific taxa in the urinary microbiota between the Taiwan and Korean groups. The results of the species-level Welch's t-test analysis are shown in Fig. 5. Species with higher relative abundance in the Taiwan group included *Bradyrhizobium embrapense*, *Denitrificimonas caeni*, *Myroides guanonis*, *Flavobacterium*-related species, *Albibacterium bauzanense*, *Lascolabacillus massiliensis*, *Myroides odoratus*, *Eoetvoesia caeni*, and *Corynebacterium lowii*. In contrast, *Gardnerella swidsinskii* showed a significantly higher relative abundance in the Korean group.

Discussion

The key findings of our research revealed no significant differences between the Taiwan and Korea groups across any alpha diversity indices. However, significant geographic variation was observed in the overall microbial community structure, as reflected by beta diversity, as well as in the relative abundance of specific taxonomic groups. Previous study had highlighted geographic variation as a critical consideration when applying microbiota-based models to predict host phenotypes across different populations [12].

From intergroup differences analysis, *Shigella flexneri* was found to be significantly enriched in the Taiwan group. However, because *Escherichia coli* and *Shigella* diverged relatively recently in evolutionary history, their 16S rRNA gene sequences share more than 99.8% similarity [13]. Therefore, we hypothesize that uropathogenic *Escherichia coli* (UPEC) or related members of the family Enterobacteriaceae are enriched in the Taiwan cohort of patients with urolithiasis. UPEC possesses a highly specialized virulence factors that enables firm adhesion to urothelial umbrella cells through type 1 fimbriae and P fimbriae. Such bacterial colonization may not only induce persistent local inflammation through activation of the NF-κB signaling pathway, but also promote the excessive generation of reactive oxygen species (ROS), resulting in epithelial injury. This sustained bacteria-induced urothelial damage may compromise the protective, anti-adhesive mucin layer covering the urothelial surface, thereby exposing the underlying collagen-rich interstitial matrix. The resulting inflamed and damaged urinary tract microenvironment may provide a favorable substrate for the deposition of supersaturated calcium oxalate crystals, potentially facilitating the development of Randall's plaques and their subsequent growth into clinically apparent calculi [14,15]. Furthermore, the prevalence of uric acid urolithiasis and metabolic syndrome in Taiwan may contribute to a more acidic urinary environment with an increased metabolic waste burden, potentially conferring a selective survival advantage on highly adaptable members of the family Enterobacteriaceae.

On the contrary, *Gardnerella swidsinskii* was significantly enriched in the Korea group. Although there is no evidence that *Gardnerella swidsinskii* is related to urinary stone disease. However, previous studies have demonstrated that *Gardnerella*-associated bacterial communities can be detected within the urinary tract. Animal models further indicate that transient bladder exposure to *Gardnerella* can induce alterations in urothelial gene expression, epithelial exfoliation, and tissue repair responses, while potentially lowering the threshold for recurrent infection by uropathogenic *Escherichia coli* [16]. These findings suggest that *Gardnerella* may modify urothelial integrity and the local immune environment even in the absence of a typical acute infection [17, 18]. Based on this background, we speculate that the enrichment of *G. swidsinskii* in the Korean group may reflect a microbial signature associated with disruption of the urothelial barrier. They could theoretically increase opportunities for calcium oxalate or other inorganic crystals in the urine to contact and adhere to damaged urothelial surfaces, thereby contributing to the establishment of a local microenvironment conducive to stone formation. However, this proposed mechanism remains hypothetical and requires further experimental validation.

In addition to *Gardnerella*, the Korea group also showed significant enrichment of anaerobic taxa, including Prevotellaceae and *Veillonella*. Multiple cross-national microbiome studies have linked the abundance of these bacteria in the gut microbiota to dietary patterns characterized by a high intake of carbohydrate-rich plant-derived fiber and fermented foods [19, 20]. Accordingly, the enrichment of *Prevotella* and *Veillonella* observed in the our Korea group is consistent with the high-fiber characteristics of the traditional Korean diet. In microbial ecology, *Prevotella* and *Veillonella* frequently form a closely interconnected metabolic syntrophic network. *Prevotella* efficiently ferments complex polysaccharides and dietary fiber derived from the host diet, producing short-chain fatty acids and lactate. By contrast, because *Veillonella* lacks the enzymatic machinery required for direct carbohydrate degradation, its growth is highly dependent on lactate produced by other bacteria, such as *Prevotella* or *Lactobacillus*, as a major carbon source [21, 22].

This study has several limitations. First, the relatively small sample size and recruitment from only two medical centers may limit the generalizability of the findings. Second, the cross-sectional design precludes causal inference, and the absence of healthy controls makes it difficult to distinguish stone-associated microbial signatures from geographic variation. Third, potential confounders, including diet, metabolic status, urinary chemistry, and stone composition, were not fully assessed. Although full-length 16S rRNA sequencing improves taxonomic resolution, it may not reliably differentiate closely related species such as *Escherichia coli* and *Shigella* or provide functional and strain-level information. Larger multicenter studies incorporating healthy controls and complementary metagenomic and metabolomic analyses are therefore needed. Despite these limitations, this study represents an initial step toward understanding geographic variation in the urinary microbiota of patients with urolithiasis. By identifying distinct microbial patterns between populations from different countries, our findings provide a foundation for future larger-scale, multicenter studies aimed at clarifying the biological and clinical relevance of population-specific urinary microbial signatures.

Conclusions

Using a rigorous cross-national cohort design and third-generation full-length 16S rRNA gene sequencing, this study systematically compared the urinary microbiota profiles of patients with urolithiasis from Taiwan and South Korea. No significant differences in alpha diversity were observed. However, beta diversity analyses revealed significant geographic heterogeneity in urinary microbial community composition between the two groups. The enrichment of *Gardnerella swidsinskii* in the Korea group may reflect a distinct microbial signature associated with urothelial barrier dysfunction. In addition, the enriched anaerobic metabolic syntrophic network formed by *Prevotella* and *Veillonella* may contribute to reshaping the local urinary microbiota through the gut–kidney–bladder axis. Further studies are needed to elucidate the complex pathogenic axis linking environmental exposures, dietary patterns, microbial ecology, and urinary stone formation.

Declarations

Funding:

This study was supported in part by a research grant from AJU PHARM Co., Ltd.

Author Contribution

H.Y.L. and S.Y.C. conceived and designed the study. H.Y.L., C.K.C., and S.Y.C. collected the clinical samples and data. H.Y.L. and D.C.W. performed the microbiome and statistical analyses. H.Y.L. drafted the manuscript and prepared the figures and tables. W.J.W., D.C.W., and S.Y.C. critically revised the manuscript and supervised the study. All authors reviewed and approved the final manuscript.

Acknowledgement

This study was supported in part by a research grant from AJU PHARM Co., Ltd. (IRB No. 2207-202-1346). This study was partially supported by the Ministry of Science and Technology (NSTC 113-2324-B-037-027), Kaohsiung Medical University Hospital (KMUH-113-3R49, KMUH114-4M52), and Regenerative Medicine and Cell Therapy Research Center (KMU-TC114A202).

Data Availability

The raw full-length 16S rRNA sequencing datasets generated and analysed during the current study are available in the National Center for Biotechnology Information (NCBI) Sequence Read Archive (SRA) under BioProject accession number [PRJNA1511942]. The datasets are publicly available through the NCBI SRA.

References

1. Moe OW. Kidney stones: pathophysiology and medical management. Lancet. 2006;367(9507):333-44.
2. Worcester EM, Coe FL. Clinical practice. Calcium kidney stones. N Engl J Med. 2010;363(10):954-63.
3. Khan SR, Pearle MS, Robertson WG, Gambaro G, Canales BK, Doizi S, et al. Kidney stones. Nat Rev Dis Primers. 2016;2:16008.
4. Teichman JM. Clinical practice. Acute renal colic from ureteral calculus. N Engl J Med. 2004;350(7):684-93.
5. Gottlieb M, Long B, Koyfman A. The evaluation and management of urolithiasis in the ED: A review of the literature. Am J Emerg Med. 2018;36(4):699-706.
6. The global, regional, and national burden of urolithiasis in 204 countries and territories, 2000-2021: a systematic analysis for the Global Burden of Disease Study 2021. EClinicalMedicine. 2024;78:102924
7. Ma Y, Cheng C, Jian Z, Wen J, Xiang L, Li H, et al. Risk factors for nephrolithiasis formation: an umbrella review. Int J Surg. 2024;110(9):5733-44.
8. Ticinesi A, Milani C, Guerra A, Allegri F, Lauretani F, Nouvenne A, et al. Understanding the gut-kidney axis in nephrolithiasis: an analysis of the gut microbiota composition and functionality of stone formers. Gut. 2018;67(12):2097-106.
9. Yuan T, Xia Y, Li B, Yu W, Rao T, Ye Z, et al. Gut microbiota in patients with kidney stones: a systematic review and meta-analysis. BMC Microbiol. 2023;23(1):143.
10. Bhardwaj M, Singhal A, Bhardwaj G, Dukic I. Probiotic and Synbiotic Interventions Targeting Oxalate-Degrading Gut Bacteria for the Prevention of Kidney Stones: A Systematic Review. Cureus. 2025;17(12):e98728
11. Schmidt WC, Mousavi A, Li J, Yang R, Gonzalez Marin G, Schreiber HLt, et al. Intercalated bacterial biofilms are intrinsic internal components of calcium-based kidney stones. Proc Natl Acad Sci U S A. 2026;123(5):e2517066123.
12. Shan Sun, Huijun Wang, Matthew Cb Tsilimigras, Annie Green Howard, Wei Sha, Jiguo Zhang et al. Does geographical variation confound the relationship between host factors and the human gut microbiota: a population-based study in China. BMJ Open. 2020;10(11):e038163.
13. Devanga Ragupathi NK, Muthuirulandi Sethuvel DP, Inbanathan FY, Veeraraghavan B. Accurate differentiation of Escherichia coli and Shigella serogroups: challenges and strategies. New Microbes New Infect. 2018;21:58-62
14. Kanlaya R, Thongboonkerd V. Persistent Escherichia coli infection in renal tubular cells enhances calcium oxalate crystal-cell adhesion by inducing ezrin translocation to apical membranes via Rho/ROCK pathway. Cell Mol Life Sci. 2022;79(7):381.
15. Miller AW, Penniston KL, Fitzpatrick K, Agudelo J, Tasian G, Lange D. Mechanisms of the intestinal and urinary microbiome in kidney stone disease. Nat Rev Urol. 2022;19(12):695-707.

16. Reitzer L, Zimmern P. Rapid Growth and Metabolism of Uropathogenic Escherichia coli in Relation to Urine Composition. Clin Microbiol Rev. 2019;33(1).
17. Gilbert NM, O'Brien VP, Waller C, Batourina E, Mendelsohn CL, Lewis AL. Gardnerella Exposures Alter Bladder Gene Expression and Augment Uropathogenic Escherichia coli Urinary Tract Infection in Mice. Frontiers in Cellular and Infection Microbiology. 2022;Volume 12 - 2022.
17. O'Brien VP, Lewis AL, Gilbert NM. Bladder Exposure to Gardnerella Activates Host Pathways Necessary for Escherichia coli Recurrent UTI. Front Cell Infect Microbiol. 2021;11:788229.
19. Shin JH, Jung S, Kim SA, Kang MS, Kim MS, Joung H, et al. Differential Effects of Typical Korean Versus American-Style Diets on Gut Microbial Composition and Metabolic Profile in Healthy Overweight Koreans: A Randomized Crossover Trial. Nutrients. 2019;11(10).
18. Jang H-H, Noh H, Kim G, Cho S-Y, Kim H-J, Choe J-S, et al. Differences in dietary patterns related to metabolic health by gut microbial enterotypes of Korean adults. Frontiers in Nutrition. 2023;Volume 9 - 2022.
19. Qin J, Shi X, Xu J, Yuan S, Zheng B, Zhang E, et al. Characterization of the Genitourinary Microbiome of 1,165 Middle-Aged and Elderly Healthy Individuals. Frontiers in Microbiology. 2021;Volume 12 - 2021.
20. Chen T, Long W, Zhang C, Liu S, Zhao L, Hamaker BR. Fiber-utilizing capacity varies in Prevotella- versus Bacteroides-dominated gut microbiota. Sci Rep. 2017;7(1):2594.

Figures

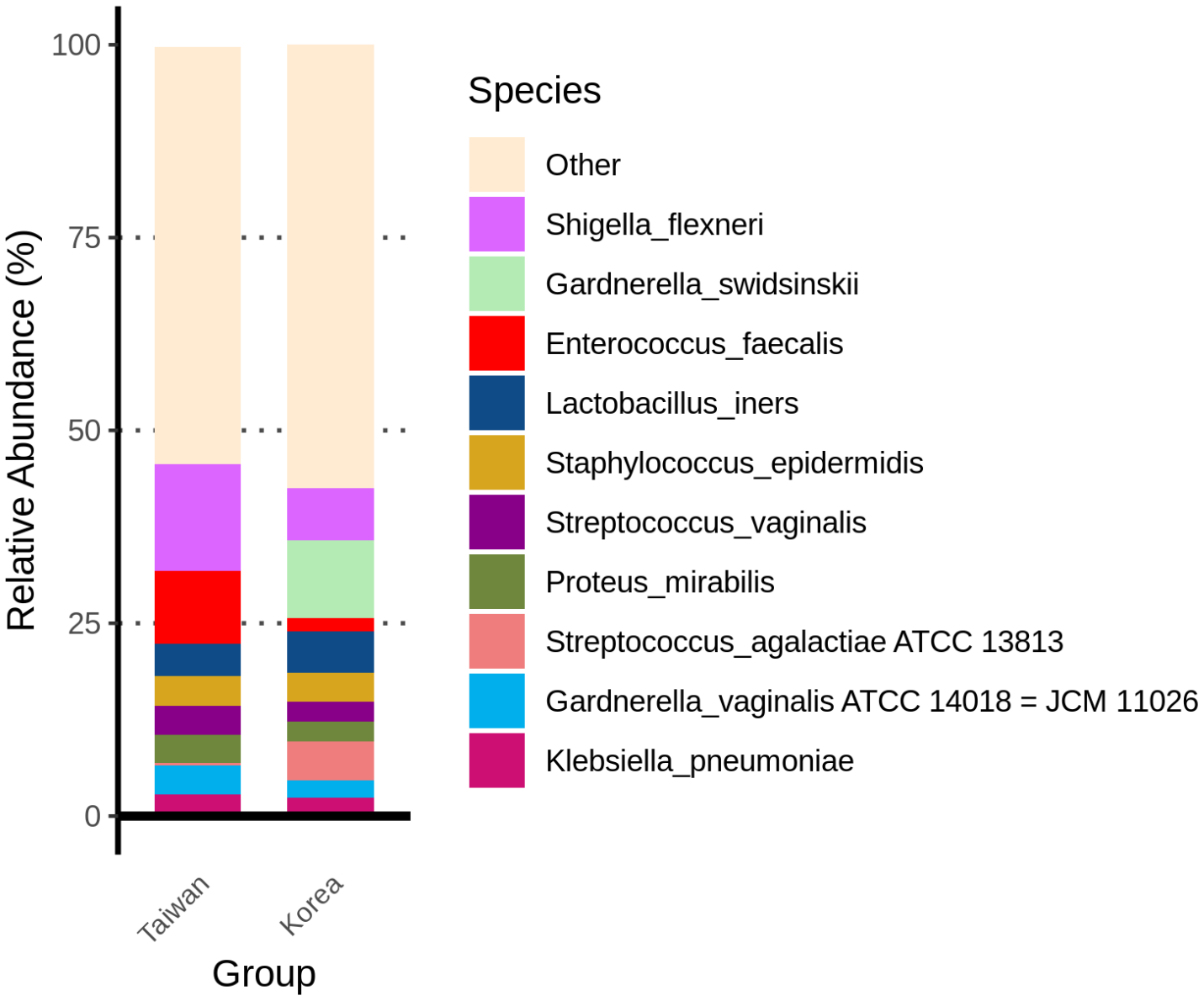


Figure 1

Relative abundance of urinary microbial species in patients with urolithiasis from Taiwan and South Korea.

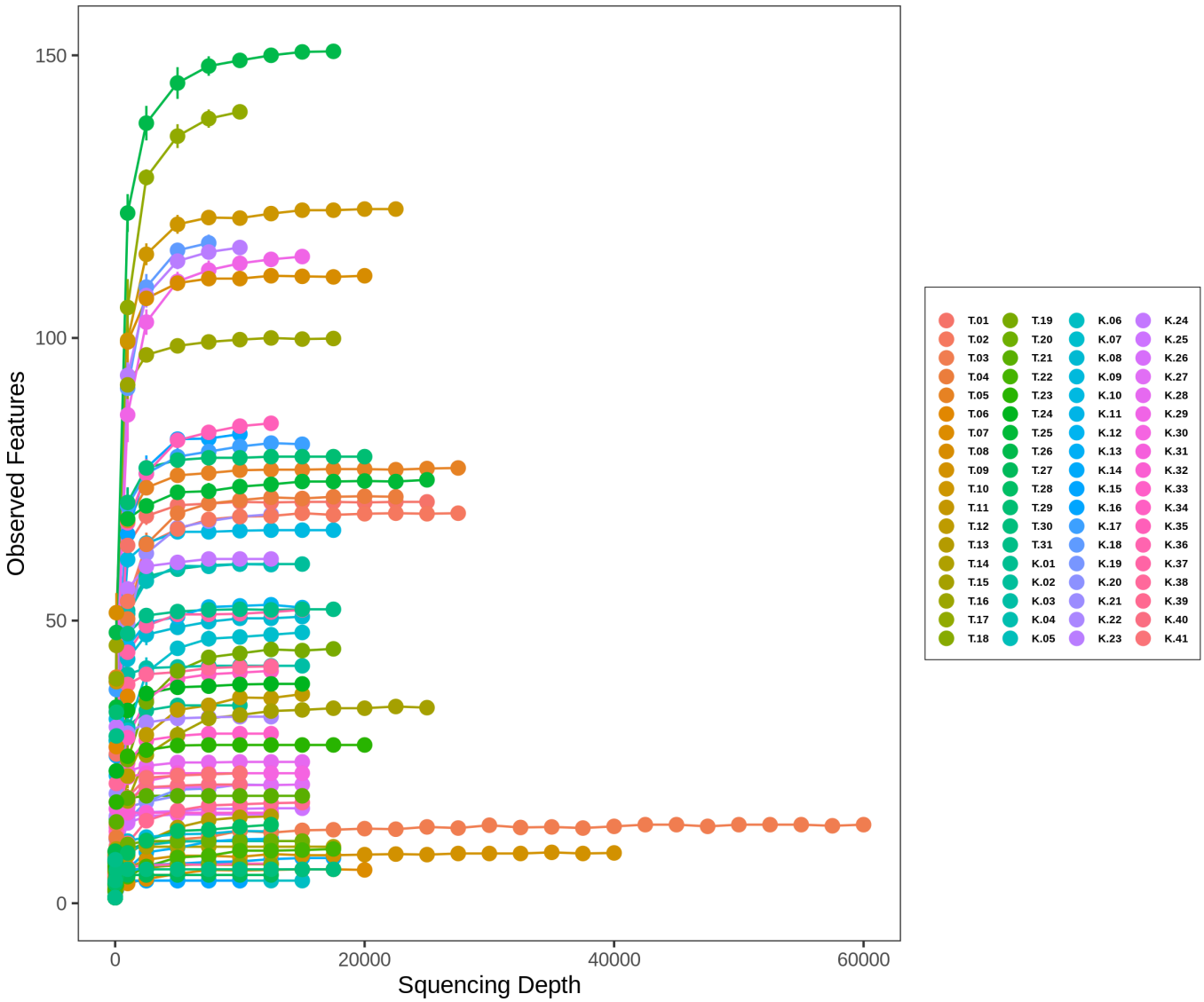


Figure 2

Rarefaction curves of observed microbial features in urine samples from patients with urolithiasis

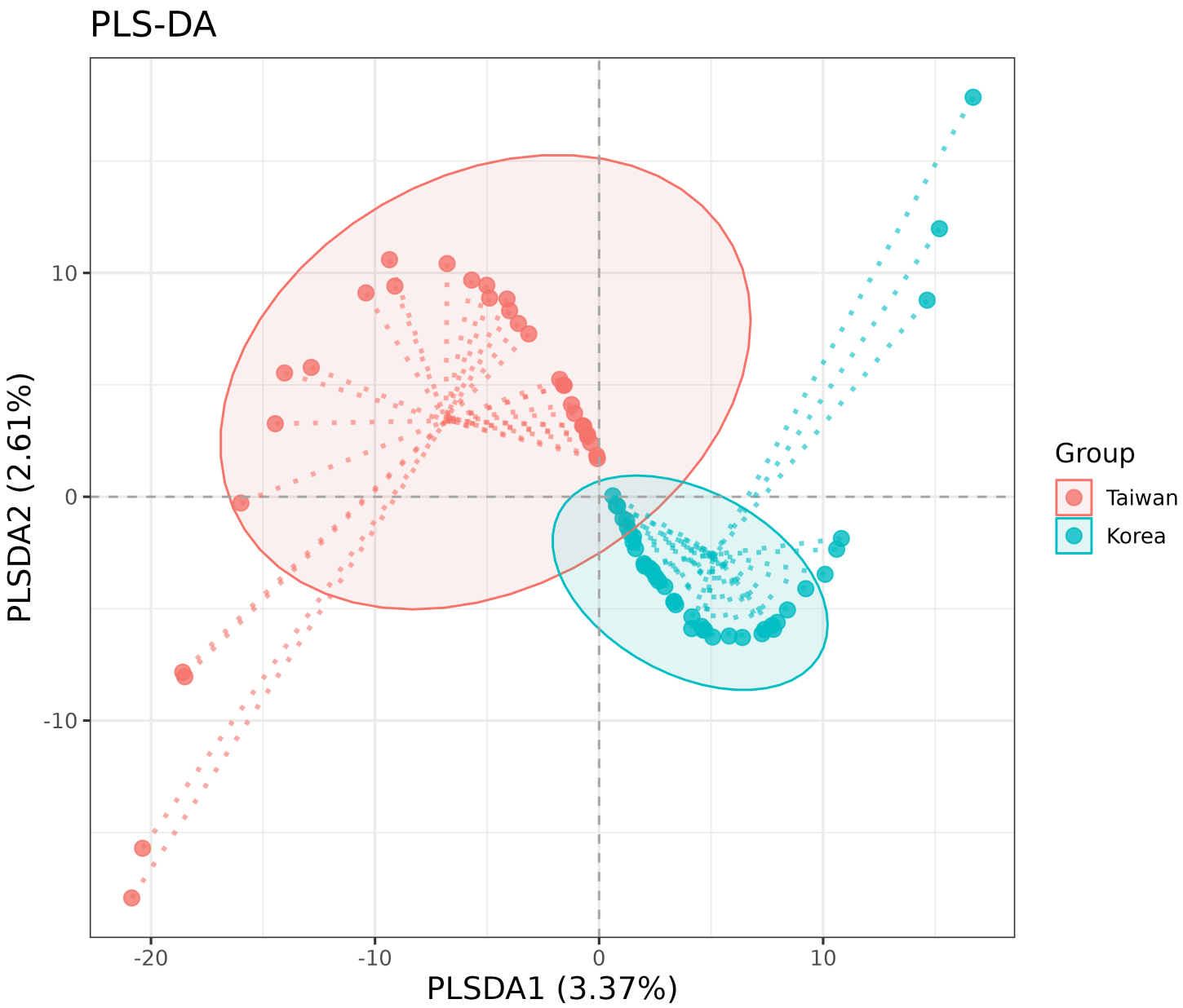


Figure 3

Partial least squares discriminant analysis (PLS-DA) of urinary microbiota profiles in Taiwan and Korea patients with urolithiasis

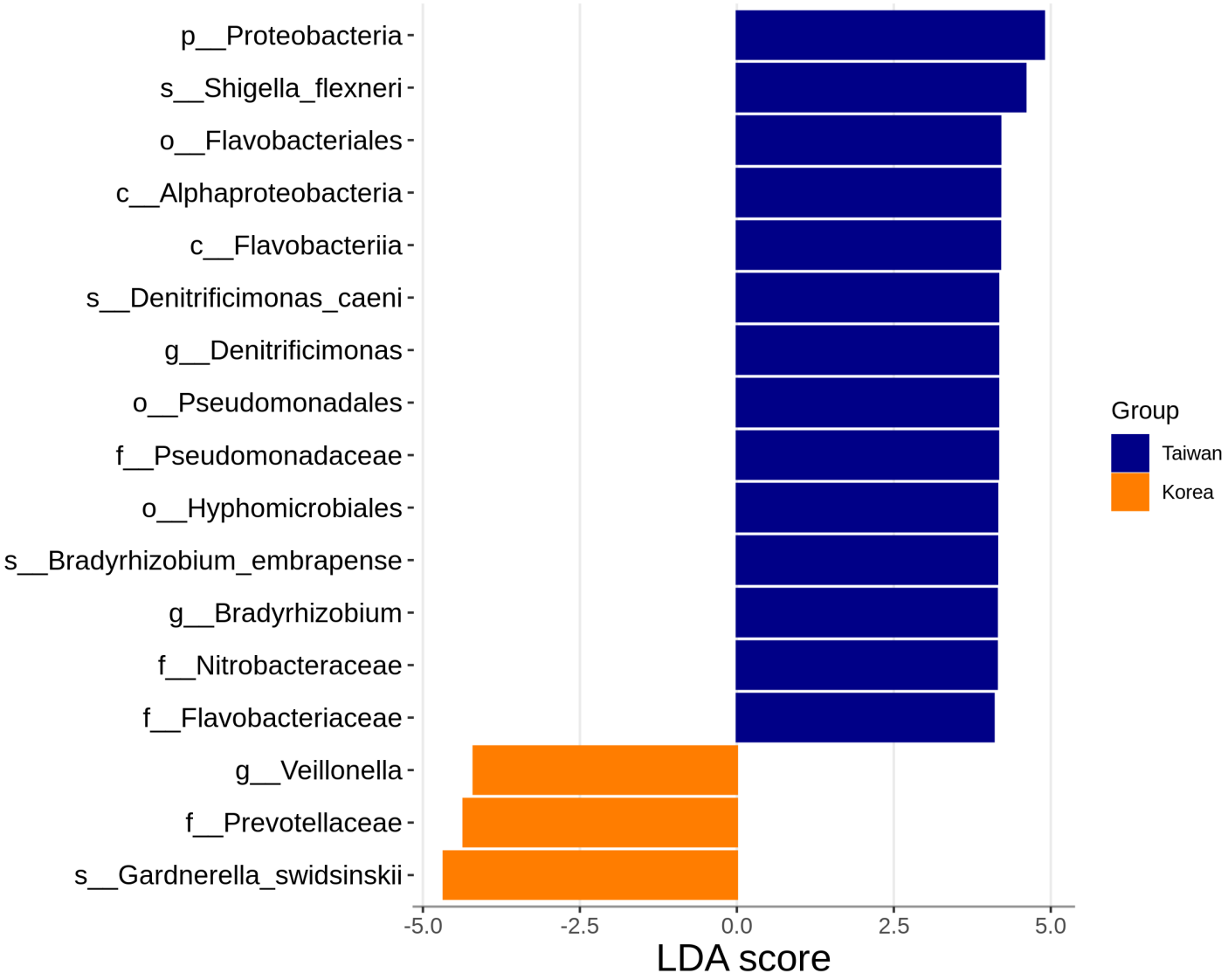


Figure 4

Differentially abundant urinary microbial taxa identified by linear discriminant analysis effect size (LEfSe) between Taiwan and Korea patients with urolithiasis.

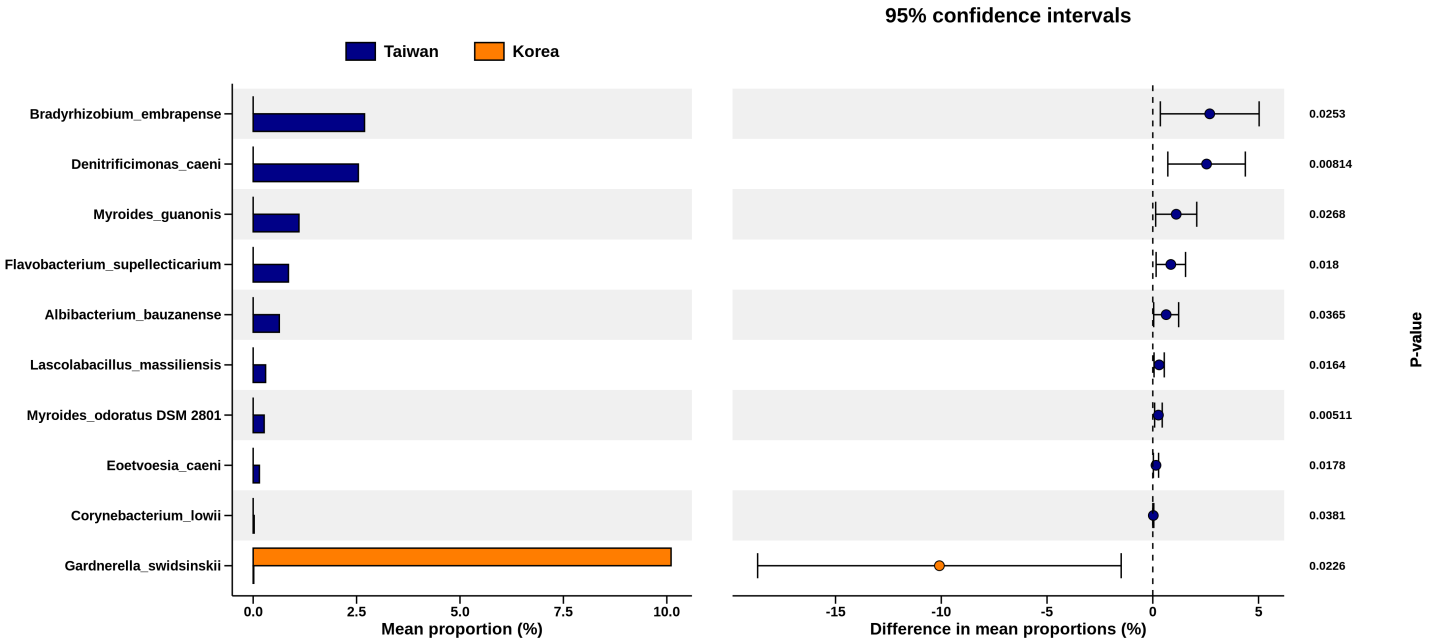


Figure 5

Species-level differences in urinary microbial abundance between Taiwanese and Korean patients with urolithiasis.