



# Draft Genome Sequences of Two Strains of *Bifidobacterium dentium* Isolated from a Crude Fecal Extract Used for Fecal Microbiota Transplantation in the Republic of Korea

Erin Simpson,<sup>a</sup> Fatemeh Sanjar,<sup>a</sup> Dennis Wylie,<sup>b</sup> Sowon Park,<sup>c</sup> Hong Koh,<sup>c</sup> Jaewoong Bae,<sup>d</sup> Sun-Young Kook,<sup>e</sup> Seokjin Kim,<sup>e</sup> Hyun Jung Kim<sup>a,f</sup>

<sup>a</sup>Department of Biomedical Engineering, The University of Texas at Austin, Austin, Texas, USA

<sup>b</sup>Center for Biomedical Research Support, The University of Texas at Austin, Austin, Texas, USA

<sup>c</sup>Department of Pediatrics, Yonsei University College of Medicine, Severance Fecal Microbiota Transplantation Center, Severance Hospital, Seoul, Republic of Korea

<sup>d</sup>Hecto Innovation Lab, Hecto Co., Ltd., Seoul, Republic of Korea

<sup>e</sup>R&D Institute, BioEleven Co., Ltd., Seoul, Republic of Korea

<sup>f</sup>Department of Oncology, Dell Medical School, The University of Texas at Austin, Austin, Texas, USA

Erin Simpson and Fatemeh Sanjar contributed equally in performing this work. Author order was determined based on the writing and editing contributions.

**ABSTRACT** We present the draft genome sequences of two *Bifidobacterium dentium* strains isolated from a fecal extract for fecal microbiota transplantation at a hospital in the Republic of Korea. Phylogenetic and functional analyses were performed to understand the physiological characteristics and functions of *Bifidobacterium* spp. in the human intestine.

*Bifidobacterium* is a genus of Gram-positive, anaerobic, nonmotile, and non-spore-forming bacteria considered to be key contributors to the healthy commensal gut microbiome (1). Predicted to constitute less than 10% of the adult human microbiota, *Bifidobacterium* has long been studied as an important class of probiotics due to many beneficial functions, including the inhibition of pathogen colonization, host immune modulation, and the maintenance of intestinal barrier function (2–5). These physiological functions are essential for gut homeostasis and the prevention of numerous gastrointestinal disorders (1, 6). To better understand the underlying mechanisms of these beneficial functions and how they can be utilized therapeutically, it is critical to identify the genetic composition of naturally occurring *Bifidobacterium* populations in healthy individuals (7).

In this report, we describe draft genome sequences of two *Bifidobacterium dentium* strains (FMTc1 and FMTc3) isolated from the processed fecal extract provided by a qualified, healthy South Korean donor. This crude fecal extract derived from a fecal sample has been used for fecal microbiota transplantation (FMT) for patients with inflammatory bowel disease in the Severance Fecal Microbiota Transplantation Center at Severance Hospital in the Republic of Korea (institutional review board [IRB] approval number 4-2017-0223). The fecal specimen was collected and processed according to the standard operating procedures at a commercial stool bank, BioEleven Co. in the Republic of Korea (IRB approval number P01-201803-31-009; ClinicalTrials registration number NCT03399188). Healthy fecal donors were screened based on the IRB-approved protocol. A fresh fecal sample collected from a fecal donor was resuspended (0.2% [wt/vol]) with a sterilized saline solution (0.9% [wt/vol]) containing autoclaved glycerol (final concentration, 12.5% [vol/vol]). The fecal homogenate was then filtered (cutoff size, 300  $\mu$ m) and homogenized at room temperature under aerobic conditions for 10 min (BagMixer; Interscience). Aliquots were stored at  $-80^{\circ}\text{C}$  until use.

**Citation** Simpson E, Sanjar F, Wylie D, Park S, Koh H, Bae J, Kook S-Y, Kim S, Kim HJ. 2020. Draft genome sequences of two strains of *Bifidobacterium dentium* isolated from a crude fecal extract used for fecal microbiota transplantation in the Republic of Korea. Microbiol Resour Announc 9:e00197-20. <https://doi.org/10.1128/MRA.00197-20>.

**Editor** David Rasko, University of Maryland School of Medicine

**Copyright** © 2020 Simpson et al. This is an open-access article distributed under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/).

Address correspondence to Hyun Jung Kim, [hyunjung.kim@utexas.edu](mailto:hyunjung.kim@utexas.edu).

**Received** 2 March 2020

**Accepted** 9 May 2020

**Published** 4 June 2020

**TABLE 1** Genome assembly statistics and strain information

Strain	GenBank accession no.	Total no. of reads	Genome coverage (x)	Avg contig coverage (x)	No. of contigs	No. of genes	No. of coding sequences	Genome size (bp)	No. of tRNAs	G+C content (%)	$N_{50}$ (bp)
FMTc1	<a href="#">ERS4331523</a>	3,907,594	269.3952	54.1136	29	2,202	2,143	2,538,385	58	58.49	137,183
FMTc3	<a href="#">ERS4331524</a>	3,921,209	270.2438	50.4725	33	2,209	2,152	2,539,231	56	58.49	162,381

The crude fecal extract obtained from BioEleven Co. was used to isolate the reported strains by performing single-colony isolation using *Bifidobacterium*-selective medium (BSM) agar (Anaerobe Systems) at 37°C in an anaerobic glove box (5% H<sub>2</sub>, 5% CO<sub>2</sub>, and 90% N<sub>2</sub>). After incubation for 36 h, individual colonies were independently subcultured in 5 ml of liquid BSM for 48 h at 37°C in the same anaerobic glove box, without shaking.

Genomic DNA was isolated and purified (QIAamp PowerFecal DNA kit; Qiagen), qualified (NanoDrop UV spectrophotometer; Thermo Fisher Scientific), and then submitted for whole-genome sequencing (CosmosID). Libraries were prepared using the Ion Xpress Plus fragment library kit (Thermo Fisher Scientific) according to the manufacturer's protocol and then sequenced with the Ion S5 next-generation sequencing system (Thermo Fisher Scientific). A summary of genome assembly statistics and strain information is provided in Table 1. The raw single-end reads were trimmed and processed using BBDuk (BBMap v36.49) with a reading quality trimming parameter of 20 (8). The genome assembly was achieved using the SPAdes assembler (v3.9.0) (9). Completeness of the assembled isolates was evaluated using the CheckM lineage\_wf function (v1.0.13) (10). Genome annotation of assembled isolates was achieved using the Prokka Annotation Pipeline (v1.13) with the added parameters mincontiglen 200 and compliant (11). Default parameters were used for all software unless otherwise specified.

Genome sizes for isolates FMTc1 and FMTc3 were 2,538,385 and 2,539,231 bp, respectively. Annotation of each genome revealed 2,202 genes, 2,143 protein-coding regions, and 58 tRNA genes in *B. dentium* FMTc1 and 2,209 genes, 2,152 protein-coding regions, and 56 tRNA genes in *B. dentium* FMTc3, with a G+C content of 58.49% in both isolates. Both isolates were found to produce toxins A and HipA and to possess ESX secretion systems.

**Data availability.** Draft genome sequences for *B. dentium* FMTc1 and *B. dentium* FMTc3 are available in GenBank under accession numbers [ERS4331523](#) and [ERS4331524](#), respectively. The accession numbers for the genome assemblies are [JAAWWM000000000](#) (for *B. dentium* FMTc1) and [JAAWWN000000000](#) (for *B. dentium* FMTc3), under BioProject numbers [PRJNA622788](#) and [PRJNA622792](#).

## ACKNOWLEDGMENTS

This work was partially supported by the Bio and Medical Technology Development Program of the National Research Foundation funded by the Ministry of Science and ICT (grant 2018M3A9H3025030 to H.J.K. and H.K.), a Technology Impact Award from the Cancer Research Institute (grant UTA18-000889 to H.J.K.), the National Cancer Institute of the National Institutes of Health (grant R21CA236690 to H.J.K.), and the Leona M. and Harry B. Helmsley Charitable Trust (grant 1912-03604 to H.J.K.).

H.J.K. is a founder of 3D Health Solutions, Inc., and holds an equity interest in the company. The other authors declare no conflicts of interest.

## REFERENCES

- O'Callaghan A, van Sinderen D. 2016. Bifidobacteria and their role as members of the human gut microbiota. *Front Microbiol* 7:925. <https://doi.org/10.3389/fmicb.2016.00925>.
- Turrioni F, Ribbera A, Foroni E, van Sinderen D, Ventura M. 2008. Human gut microbiota and bifidobacteria: from composition to functionality. *Antonie Van Leeuwenhoek* 94:35–50. <https://doi.org/10.1007/s10482-008-9232-4>.
- Valdés-Varela L, Hernández-Barranco AM, Ruas-Madiedo P, Gueimonde M. 2016. Effect of *Bifidobacterium* upon *Clostridium difficile* growth and toxicity when co-cultured in different prebiotic substrates. *Front Microbiol* 7:738. <https://doi.org/10.3389/fmicb.2016.00738>.
- Vazquez-Gutierrez P, de Wouters T, Werder J, Chassard C, Lacroix C. 2016. High iron-sequestering bifidobacteria inhibit enteropathogen growth and adhesion to intestinal epithelial cells in vitro. *Front Microbiol* 7:1480. <https://doi.org/10.3389/fmicb.2016.01480>.
- Hiiippala K, Jouhten H, Ronkainen A, Hartikainen A, Kainulainen V, Jalanka J, Satokari R. 2018. The potential of gut commensals in reinforcing

- ing intestinal barrier function and alleviating inflammation. *Nutrients* 10:988. <https://doi.org/10.3390/nu10080988>.
6. Giannetti E, Maglione M, Alessandrella A, Strisciuglio C, De Giovanni D, Campanozzi A, Miele E, Staiano A. 2017. A mixture of 3 bifidobacteria decreases abdominal pain and improves the quality of life in children with irritable bowel syndrome: a multicenter, randomized, double-blind, placebo-controlled, crossover trial. *J Clin Gastroenterol* 51:e5–e10. <https://doi.org/10.1097/MCG.0000000000000528>.
  7. Daliri E-M, Tango CN, Lee BH, Oh D-H. 2018. Human microbiome restoration and safety. *Int J Med Microbiol* 308:487–497. <https://doi.org/10.1016/j.ijmm.2018.05.002>.
  8. Bushnell B. 2014. BBMap: a fast, accurate, splice-aware aligner. Lawrence Berkeley National Laboratory, Berkeley, CA.
  9. Bankevich A, Nurk S, Antipov D, Gurevich AA, Dvorkin M, Kulikov AS, Lesin VM, Nikolenko SI, Pham S, Pribelski AD, Pyshkin AV, Sirotkin AV, Vyahhi N, Tesler G, Alekseyev MA, Pevzner PA. 2012. SPAdes: a new genome assembly algorithm and its applications to single-cell sequencing. *J Comput Biol* 19:455–477. <https://doi.org/10.1089/cmb.2012.0021>.
  10. Parks DH, Imelfort M, Skennerton CT, Hugenholtz P, Tyson GW. 2015. CheckM: assessing the quality of microbial genomes recovered from isolates, single cells, and metagenomes. *Genome Res* 25:1043–1055. <https://doi.org/10.1101/gr.186072.114>.
  11. Seemann T. 2014. Prokka: rapid prokaryotic genome annotation. *Bioinformatics* 30:2068–2069. <https://doi.org/10.1093/bioinformatics/btu153>.