



Effects of *Lactiplantibacillus plantarum* FBT215 and prebiotics on the gut microbiota structure of mice

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Abstract

Imbalanced intestinal microbiota is associated with diseases, including inflammatory bowel disease and obesity, and diet can alter the structure of the gut microbiota. In this study, the effects of dietary treatments including the potential probiotic *Lactiplantibacillus plantarum* FBT215 with/without prebiotics on the intestinal microbiota composition of mice were investigated. *Lactiplantibacillus plantarum* FBT215 administration significantly decreased the Firmicutes/Bacteroidetes ratio and increased the abundance of *Muribaculum* and *Duncaniella*. The diversity within and between groups was measured according to α and β diversity metrics, respectively. The Shannon index of α diversity decreased significantly in all treatment groups except the probiotic group, although this group showed an increase in the Chao1 index. Principal coordinate analysis of β diversity showed that the groups had different species distributions. Finally, gamma-aminobutyric acid (GABA) concentration increased in groups fed *L. plantarum* FBT215. These findings improve our understanding of the association between the gut microbiota structure and specific probiotic/prebiotic-containing diets.

Keywords Gut microbiota · *Lactiplantibacillus plantarum* · Bacterial composition · α/β Diversity · GABA

Introduction

The gut microbiota of humans comprises approximately 10^{14} microorganisms, including viruses, yeast, and bacteria (Anwar et al., 2021). The gut microbiota population can be influenced by the administration of antibiotics or by diarrhea (Noh et al., 2018), and an imbalance of microbiota (dysbiosis) is associated with obesity, inflammatory bowel disease, and immune responses (Claesson et al., 2011). Therefore, the gut microbiota play a major role in human health and disease.

Probiotics are live microorganisms that are beneficial to the health of the host when administered in adequate amounts (Fuller, 1991). Prebiotics are nondigestible oligosaccharides that benefit the host by stimulating the growth of bacteria. Synbiotics are a combination of probiotics and prebiotics (Roberfroid, 1998). The consumption of probiotics can affect the composition of intestinal microbial

communities as the probiotics compete with the microbiota for nutritional substrates. Specifically, altering carbohydrate utilization dynamics via substrate availability through probiotic supplementation affects microbial community structure (O'Toole and Cooney, 2008). Additionally, changes in metabolic profiles, including short-chain fatty acids (SCFAs) concentration, are known to affect the composition of microbiota (Li et al., 2008), and exopolysaccharides produced by probiotics can act as substrates for microbial components. Studies on mice have indicated that probiotics influence the regulation of depressive symptoms (Liu et al., 2020) and obesity (Soundharrajan et al., 2020) as well as altering microbiota composition. For instance, the Firmicutes/Bacteroidetes (F/B) ratio was shown to increase in obese mice but decrease in lean mice (Ley et al., 2005), and an imbalance in this ratio can be restored via the appropriate use of probiotics (Stojanov et al., 2020). The fermentation of prebiotics, e.g., fructooligosaccharide (FOS), galactooligosaccharide, and inulin, causes the proliferation of beneficial microorganisms in the gastrointestinal tract (Hemarajata and Versalovic, 2013), protects the microorganisms from species that have pernicious effects on energy sources, and promotes the production of SCFAs with immunomodulatory properties (Guarino et al., 2020). Moreover, synbiotics

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have been shown to alleviate disease by improving metabolic profiles (Li et al., 2021) and releasing specific enzyme such as β -fructofuranosidase (Cui et al., 2022).

The effects of probiotics on the structure of the gut microbiota differ according to the probiotic strain. Thus, it is important to select an appropriate strain for a specific therapeutic purpose (Stojanov et al., 2020). In addition, *Lactiplantibacillus plantarum* has been shown to regulate the gut microbial composition through the hydrolysis of FOS (Chen et al., 2015). In the present study, we investigated the effects of administering *L. plantarum* FBT215 as a potential probiotic with or without prebiotics (FOS and inulin) on the gut microbiota composition of WT mouse model using the Illumina platform to conduct metagenomic analysis of the 16S rRNA gene. In general, since healthy individual intakes probiotics and prebiotics as food supplements, healthy model was used for study, not a disease model.

Materials and methods

Isolation of *L. plantarum* FBT215

In previous study, *Lactiplantibacillus plantarum* FBT215 was isolated from Korean traditional food, kimchi (Kim et al., 2022).

Experimental animals

Six-week-old male C57BL/6J mice (DaeHan Biolink, Eum-sung, Korea) weighing 21–23 g were housed under a 12/12 h light/dark cycle with controlled temperature ($22 \pm 1^\circ\text{C}$) and relative humidity ($55 \pm 1\%$). The mice were acclimated for one week and randomly divided into six groups ($n=5$ mice per group) as follows: control (G1), FOS (Sigma-Aldrich, St. Louis, MO, USA; G2), inulin (Sigma-Aldrich; G3), *L. plantarum* FBT215 (G4), FOS + *L. plantarum* FBT215 (G5), and inulin + *L. plantarum* FBT215 (G6) treatment groups.

Probiotic, prebiotic, and probiotic + prebiotic treatments

L. plantarum FBT215 was administered orally as a potential probiotic strain at a concentration of 1×10^{10} CFU/mice/day for 4 weeks. Probiotic, prebiotic, and probiotic + prebiotic combination treatments were each dissolved in 0.15 mL of water. The mice in G1 were treated with 0.15 mL of water only; those in G2 and G3 were treated with 0.15 g of FOS and inulin, respectively; those in G4 were treated with 1×10^{10} CFU/mice/day of *L. plantarum* FBT215; and those in G5 and G6 were each treated with 1×10^{10} CFU/mice/day of *L. plantarum* FBT215 combined with 0.15 g of either FOS or inulin, respectively. Over a 4-week period, the mice were gavaged orally for

the first 2 weeks and probiotic and/or prebiotic were provided ad libitum for the last 2 weeks by mixing with Labdiet 5053 (Orientbio, Sungnam, Korea). After the 4-week experimental period, the mice were sacrificed using CO₂ inhalation and their cecal tissues were collected. Tissue samples were immediately frozen at -80°C .

Sampling, 16S rRNA gene sequencing, and bioinformatic analysis

The cecal samples were used for analysis of the intestinal microbiota composition. Libraries were constructed using a Herculase II Fusion DNA Polymerase Nextra XT Index Kit V2 (Macrogen, Daejeon, Korea) according to 16S Metagenomic Sequencing Library Preparation Part #15044223 Rev. B. The V3–V4 region was amplified to construct the libraries using the Bakt_341F (5'-CCTACGGGNGGCWGCAG-3') and 805R (5'-GACTACHVGGGTATCTAATCC-3') primer set. These libraries were sequenced via the MiSeq Illumina platform. To produce amplicon sequence variants (ASVs), the Divisive Amplicon Denoising Algorithm 2 (DADA2) was used for denoising. Prior to this analysis, both the adapters and primers were removed via Cutadapt. Quality filtering, merging, and chimera removal were then performed using DADA2.

γ -Aminobutyric acid measurement via an enzyme-linked immunosorbent assay

γ -Aminobutyric acid (GABA) concentrations in the cecal tissues were measured using a GABA enzyme-linked immunosorbent assay (ELISA; LDN Immunoassays, Nordhorn, Germany). Samples were diluted 1:10 (w/v) in lysis solution (0.1 N of HCl, 1 mM of EDTA, and 4 mM of sodium metabisulphite) and homogenized. After centrifugation at $5000 \times g$ for 5 min, the resultant aqueous solution was used to quantify GABA according to the ELISA manufacturer's instructions. All reactions were performed in duplicate and measured at 450 nm.

Statistical analysis

A *t*-test was used to determine the differences between two groups, e.g., the control group and an experimental group. Statistical analyses were performed via IBM SPSS statistics 26 (IBM Corp., Armonk, NY, USA), and $p < 0.05$ was considered statistically significant.

Results and discussion

The 16S rRNA gene sequencing conducted for each sample generated > 140,000 reads. The number of ASVs produced using denoising methods was 39,401–86,598 after filtering, denoising, and chimera removal. The average GC content was 55.04%, and the rarefaction curve reached a plateau depending on the sequencing depth (data not shown). As > 100,000 reads per sample is generally regarded as a sufficient number for the analysis of gut microbiota (Illumina, 2013), the number of reads obtained via our methods was sufficient for the present analysis.

Relative abundance of bacterial composition

The intestinal microbiota structure can be altered by various factors, including drugs, toxins, and pathogens, but particularly by diet (Carding et al., 2015). FOS and inulin are generally regarded as prebiotics that selectively stimulate the growth of gut microorganisms (Ballan et al., 2020). Previous study found that FOS improves intestinal conditions and regulates the immune system (Fukasawa et al., 2010). In the present study, the effects of *L. plantarum* FBT215, prebiotics, and combinations of these treatments on the gut microbiota composition were examined, and the relative abundance of phyla and genera is shown in Figs. 1 and 2, respectively.

Bacteroidetes (55.68–81.52%) was the most abundant phylum in all groups, followed by Firmicutes (10.40–38.25%) and Proteobacteria (0.65–6.60%) (Fig. 1).

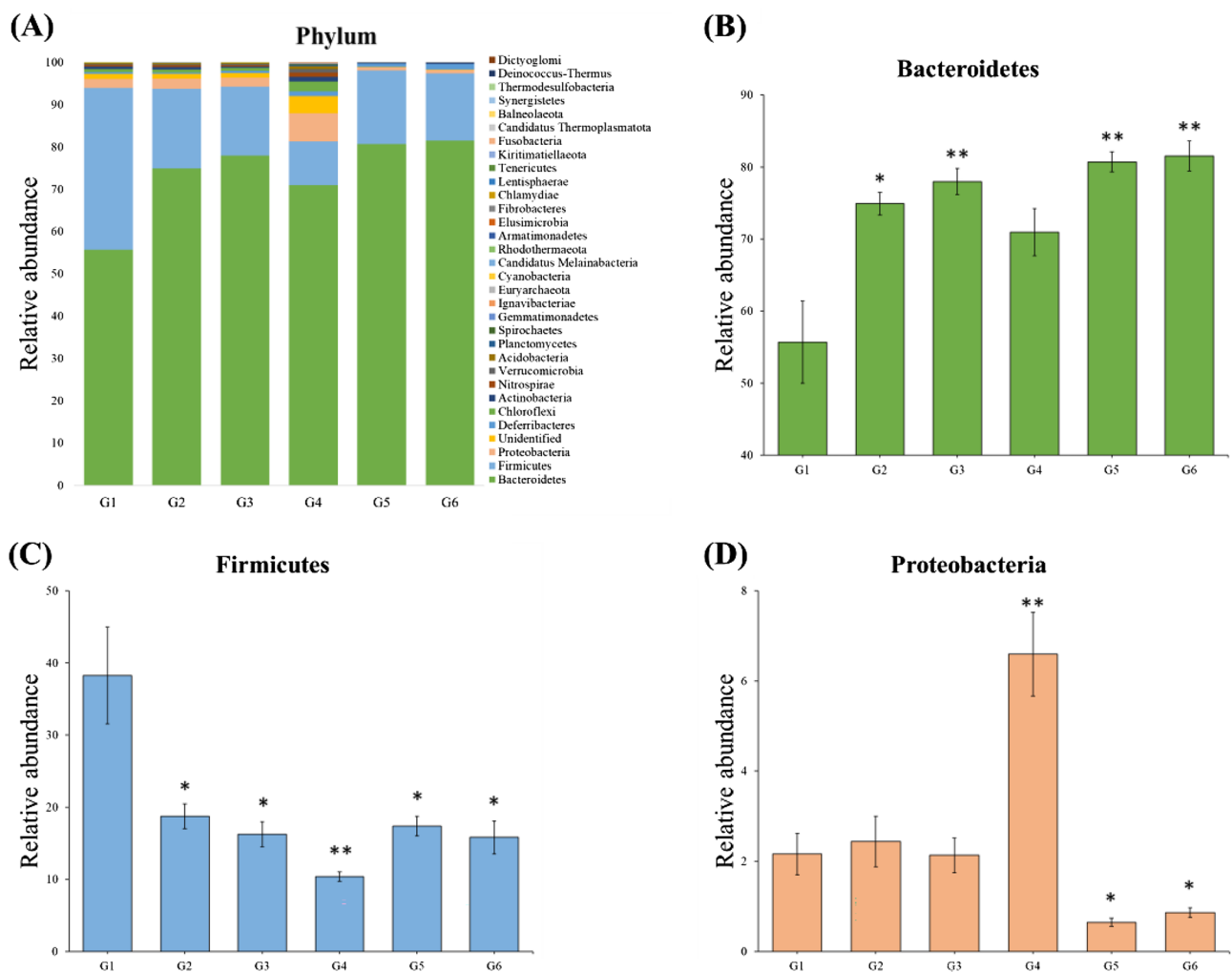


Fig. 1 Composition of bacterial taxa at the phylum level. **A** Stacked bar graph showing the relative abundance of phyla in G1–G6. Bar graphs showing the relative abundance of **B** Bacteroidetes, **C** Firmi-

cutes, and **D** Proteobacteria. * $p < 0.05$ and ** $p < 0.01$ represent significant differences compared with the control group

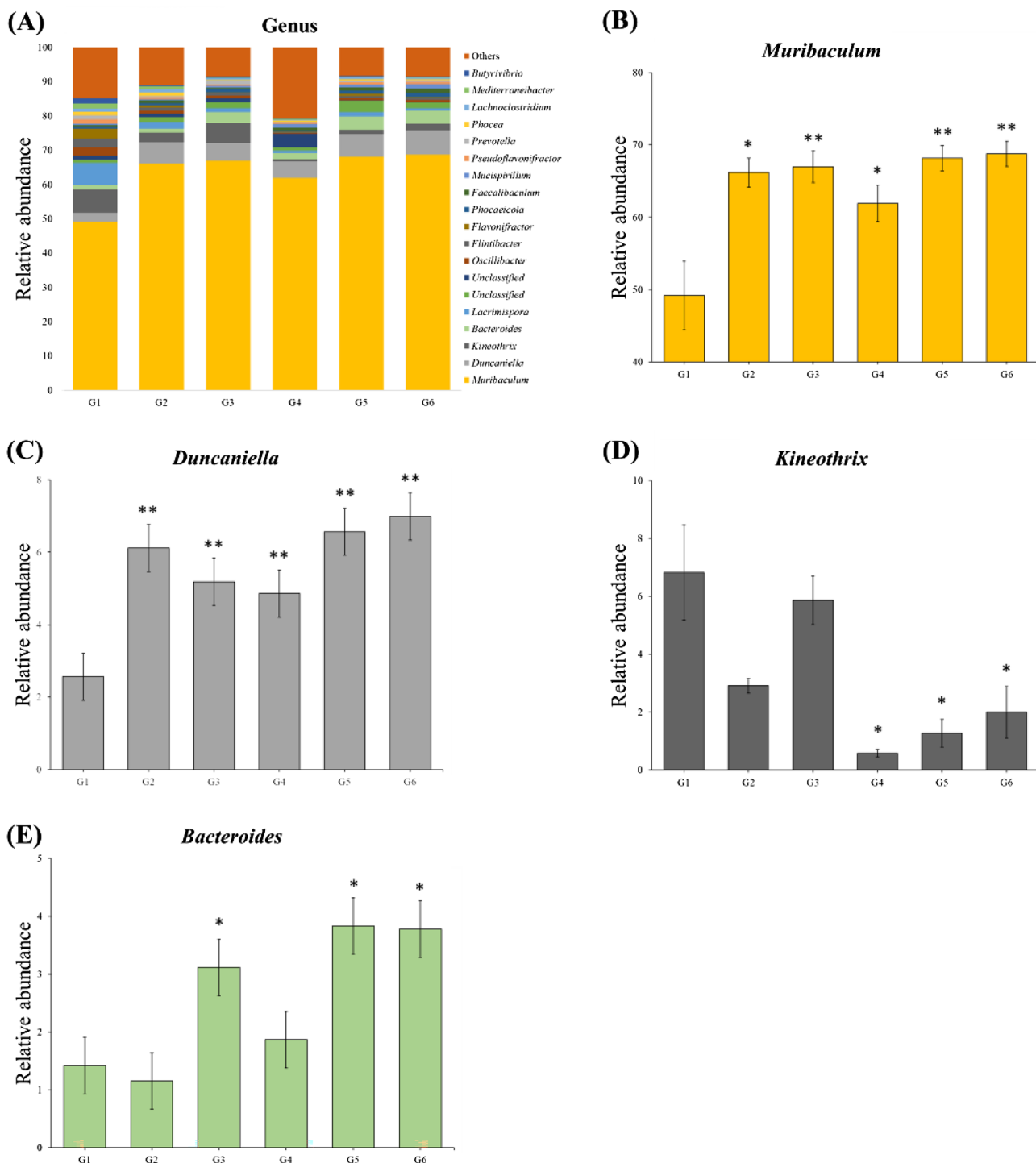


Fig. 2 Composition of bacterial taxa at the genus level. **A** Stacked bar graph showing the relative abundance of genera in G1–G6 (at least one sample > 1%). Bar graphs showing the relative abundance

of **B** *Muribaculum*, **C** *Duncaniella*, **D** *Kineothrix*, and **E** *Bacteroides*. * $p < 0.05$ and ** $p < 0.01$ represent significant differences compared with the control group

The abundance of Bacteroidetes was significantly increased in all groups except G4 (Fig. 1B), whereas the abundance of Firmicutes was significantly decreased in all groups (Fig. 1C). The abundance of Proteobacteria increased in

G4 like previous study that administered the *L. plantarum* ZDY2013 for 3 weeks (Xie et al., 2016) but decreased in the combined treatment groups (Fig. 1D). Proteobacteria decreased in existing study using synbiotics composed of

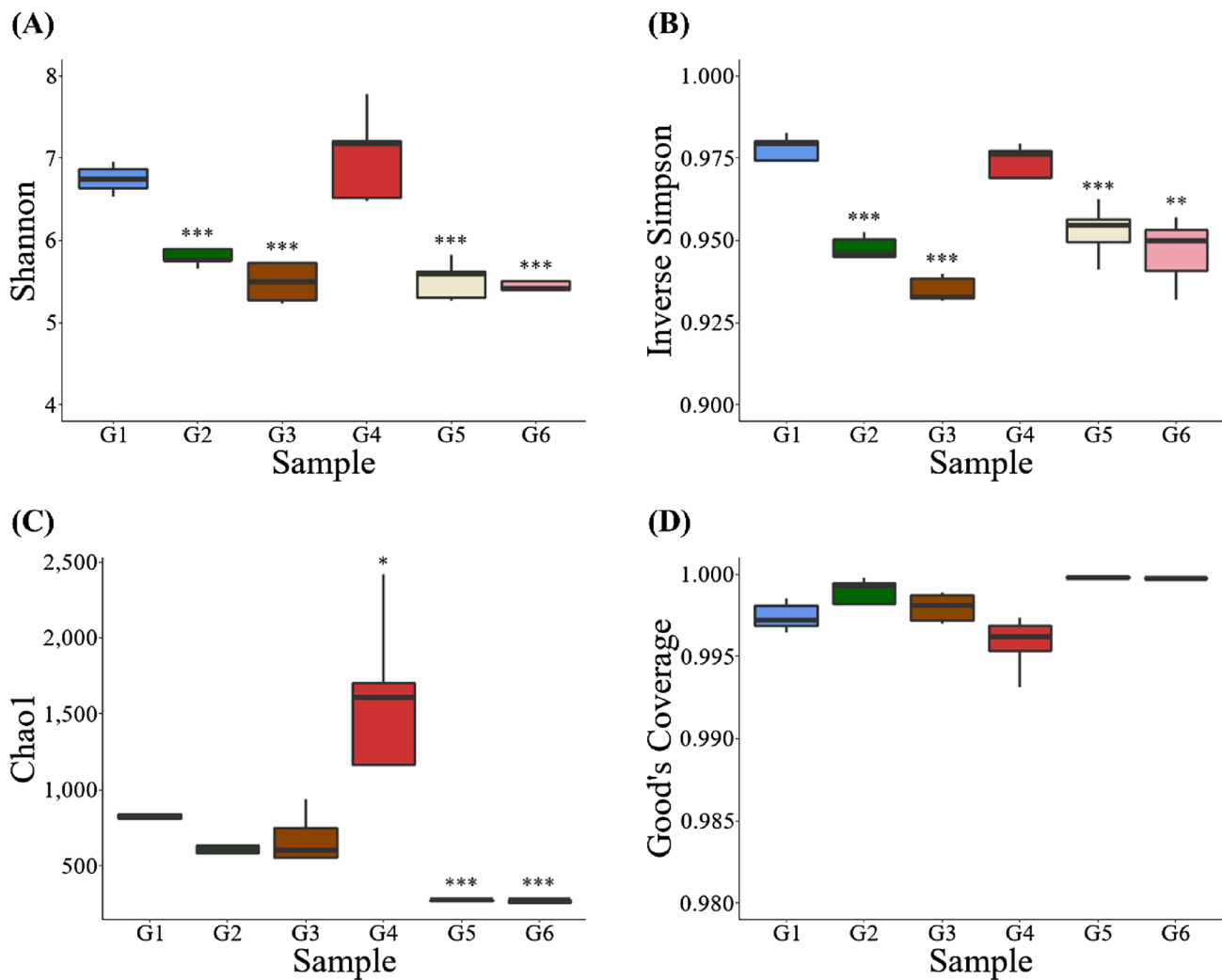


Fig. 3 Boxplots of α diversity parameters. Boxes represent the interquartile range between 25 and 75th percentiles. Horizontal line in the box is the median value. **A** Shannon, **B** Inverse Simpson, **C** Chao1,

and **D** Good's coverage indice in G1–G6. * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$ represent significant differences compared with the control group

Bifidobacterium longum and inulin-based prebiotics (MacFarlane et al., 2013). However, further study will be needed to identify the association between probiotic *L. plantarum* and/or prebiotics in Proteobacteria abundance. Similarly, previous research showed that the abundance of Bacteroidetes and Firmicutes increased and decreased, respectively, when FOS and inulin were administered (Zhu et al., 2017). In the present study, treatment with *L. plantarum* FBT215 significantly reduced the F/B ratio. Several dysbiosis-related diseases, such as obesity or inflammatory bowel disease, are associated with an increase or decrease in the F/B ratio, and effects of this ratio are known to differ according to probiotic administration (Stojanov et al., 2020). Indeed, balancing the F/B ratio is important for improving dysbiosis and maintaining health (Stojanov et al., 2020); thus, *L. plantarum* FBT215 could potentially be used in supplements for

improving, for example, obesity. However, further studies on the efficacy of *L. plantarum* FBT215 supplementation are needed in obese mice.

The most abundant genus was *Muribaculum* (49.18–68.79%), followed by *Duncaniella* (2.56–6.99%) (Fig. 2), and these two genera were significantly more abundant in the experimental groups than in the control group, which explains the increase in the abundance of Bacteroidetes (Fig. 2B and C). Previous studies have indicated that *Muribaculum* is depleted under inflamed conditions (Dobranowski et al., 2019; Zhou et al., 2022), and the abundance of *Muribaculum intestinale* is reduced in mice with Crohn's disease (Dobranowski et al., 2019). *Duncaniella* is known to help protect the host from dextran sulfate sodium-induced colonic injury (Chang et al., 2021). In contrast, the abundance of *Kineothrix* (0.58–6.82%), a butyrate-producing

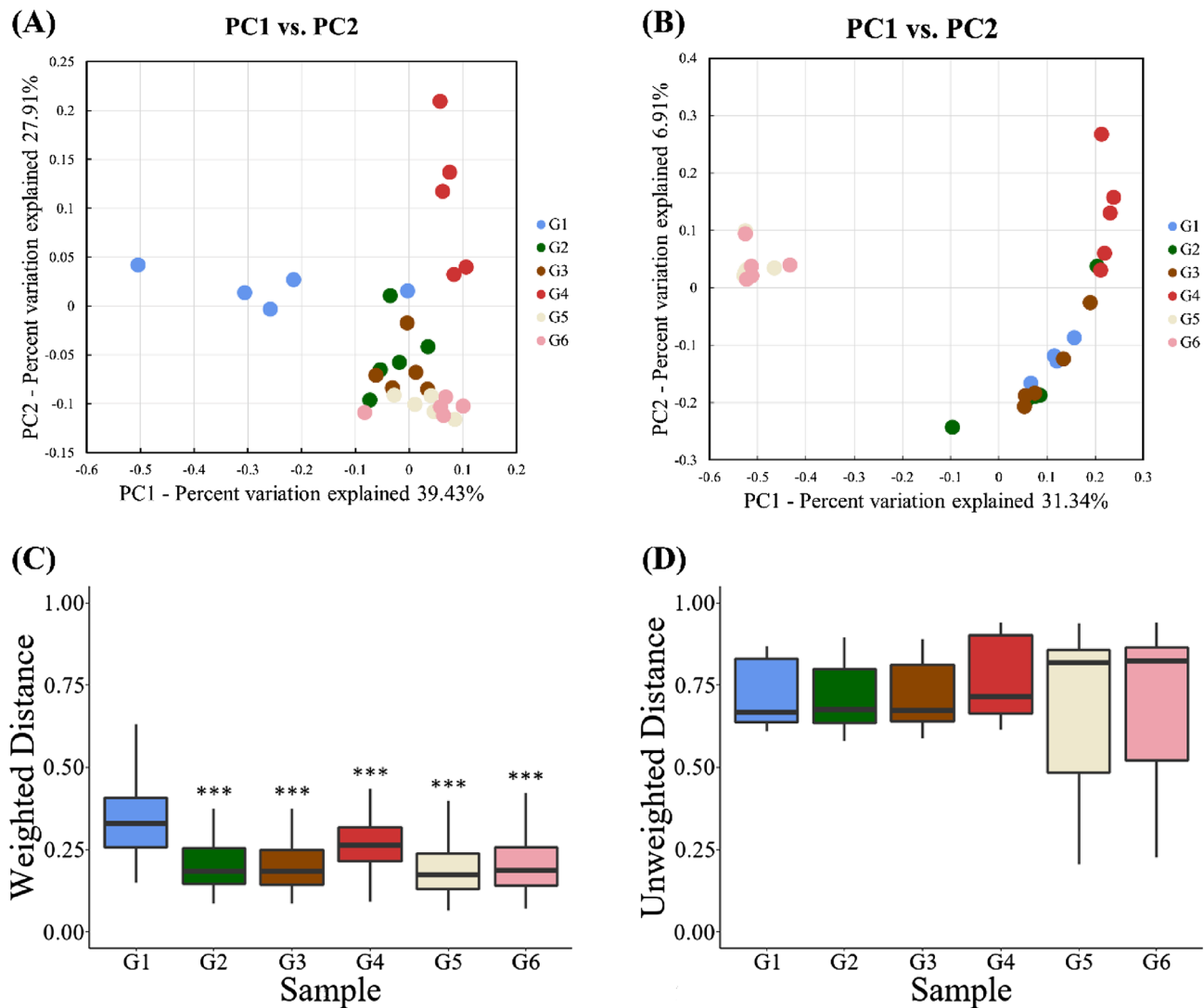


Fig. 4 PCoA plots based on microbial ASVs of samples. **A, C** Weighted UniFrac distance and **B, D** unweighted UniFrac distance are represented by two-dimensional plots and boxplots. *** $p < 0.001$ represents significant difference compared with the control group

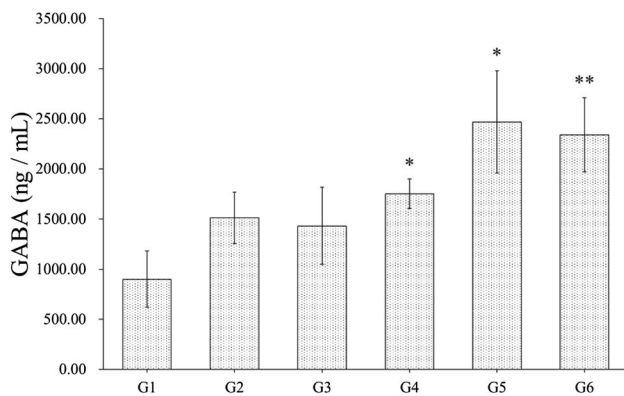


Fig. 5 GABA concentrations in cecal content using ELISA. * $p < 0.05$ and ** $p < 0.01$ represent significant differences compared with the control group

bacteria (Haas and Blanchard, 2017), significantly decreased in G4–G6 (Fig. 2D), and the abundance of *Bacteroides*, i.e., acetate-, propionate-, and lactate-producing bacteria, increased in G3 and G5–G6 (Fig. 2E). SCFAs, including acetate and butyrate, are synthesized by intestinal microbiota via indigestible carbohydrate fermentation, and the concentration of SCFAs is influenced by external factors, including probiotic usage, which regulate the gut microbiota structure (Cui et al., 2022). Although the abundance of certain SCFAs-producing bacteria decreased in several experimental groups, it remains necessary to determine how the concentration of SCFAs changes with the administration of probiotics and/or prebiotics. At the species level, *L. plantarum* increased markedly, as expected, in G4–G6 following treatment with *L. plantarum* FBT215 (data not shown).

Diversity of gut microbiota

To identify the diversity of bacterial communities within (α) and between (β) groups, various parameters were used. For α diversity, the Shannon, Inverse Simpson, and Chao1 indices (Fig. 3A–C, respectively) were measured. All experimental groups except G4 showed significantly decreased Shannon index values, which provides more weight to the value of species richness than evenness in measurement (Kim et al., 2017), and Inverse Simpson index values (Fig. 3A and B). These findings are consistent with a previous study in which the Shannon index decreased after FOS, *L. plantarum*, and *L. plantarum* + FOS supplementations (Cui et al., 2022). However, according to the Chao1 index, species richness increased in the probiotic treatment group (Fig. 3C), whereas it decreased in a previous study using *L. plantarum* ST-III (Cui et al., 2022). Therefore, *L. plantarum* FBT215-fed mice had more rare microbial species and a higher abundance of microbial species than the control mice. Good's coverage index (Fig. 3D) of all groups was > 0.99, indicating that only 1% of reads were not covered during sequencing, i.e., > 99% of the total species were represented in the analysis and the degree of sequencing coverage was high.

To assess β diversity, principal coordinate analysis (PCoA) was performed (Fig. 4). According to weighted UniFrac, which considers species abundance (Chen et al., 2012), the distribution of the control group was clustered far from the experimental groups, and the two clusters were statistically different (Fig. 4A and C). However, a plot based on the unweighted UniFrac distance, which calculates only the presence or absence of species (Chen et al., 2012), showed an ambiguous dispersion among the G1–G4 groups. The distribution of G5 and G6 groups were different with other groups. However, there were no statistically significant differences (Fig. 4B and D). These results suggest that the experimental treatments may not affect the growth of new microorganisms in mice but may affect the growth of existing microorganisms.

GABA concentrations in cecal content

L. plantarum FBT215 is a GABA-producing bacterium (Kim et al., 2022). Thus, GABA concentrations were measured after dietary treatments. GABA levels were significantly higher in *L. plantarum* FBT215-fed groups than in the control group (Fig. 5). However, there were no significant differences between the G4 and G5–G6 groups. Previous study showed that GABA concentrations significantly different according to the type of prebiotics in vitro (Kim et al., 2022), but further research about the effects of probiotics and/or prebiotics on GABA production will be needed in vivo.

Thus, these results provide some evidence of a relationship between GABA-producing bacteria and health benefits.

In general, the diversity of intestinal microbiota increases with health status (Larsen and Claassen, 2018). Our data show that the administration of probiotics and/or prebiotics alters the intestinal microbiota structure and the indices of microbial diversity in mice. The F/B ratio decreased significantly in the *L. plantarum* FBT215 supplement group, indicating that *L. plantarum* FBT215 has the potential to increase and decrease Bacteroidetes and Firmicutes levels, respectively, and thereby help prevent obesity. One limitation of the current study that affects the interpretation of the results is the use of normal mice rather than a specific disease-induced mouse model. In addition, commonly used amounts of probiotics and prebiotics were tested without determining the probiotic concentration that produce the maximum effect and the prebiotic concentration expected to produce synergetic effects with the probiotic. Therefore, concentration of treatment that produce the synergetic effects should be tested for identifying maximum effect in future studies. Nevertheless, we found that *L. plantarum* FBT215 dietary supplementation with or without prebiotics can alter the abundance of bacteria in the intestine of mice.

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Declarations

Conflict of interest The authors declare no conflict or interest.

Ethical approval This study was approved by the Institutional Animal Care and Use Committee (IACUC) at Yonsei University (YWCI-202104-005-02).

References

- Anwar H, Iftikhar A, Muzaffar H, Almatroudi A, Allemailem KS, Navaid S, Saleem S, Khurshid M. Biodiversity of gut microbiota: impact of various host and environmental factors. *BioMed Research International*. 2021: 5575245 (2021)
- Ballan R, Battistini C, Xavier-Santos D, Saad SMI. Interactions of probiotics and prebiotics with the gut microbiota. *Progress in Molecular Biology and Translational Science*. 171: 265-300 (2020)
- Carding S, Verbeke K, Vipond DT, Corfe BM, Owen LJ. Dysbiosis of the gut microbiota in disease. *Microbial Ecology in Health and Disease*. 26: 26191 (2015)
- Chang CS, Liao YC, Huang CT, Lin CM, Cheung CHY, Ruan JW, Yu WH, Tsai YT, Lin IJ, Huang CH, Liou JS, Chou YH, Chien HJ, Chuang HL, Juan HF, Huang HC, Chan HL, Liao YC, Tang SC, Su YW, Tan TH, Baumler AJ, Kao CY. Identification of a gut microbiota member that ameliorates DSS-induced colitis in intestinal barrier enhanced Dusp6-deficient mice. *Cell Reports*. 37: 110016 (2021)

- Chen J, Bittinger K, Charlson ES, Hoffmann C, Lewis J, Wu GD, Collman RG, Bushman FD, Li HZ. Associating microbiome composition with environmental covariates using generalized UniFrac distances. *Bioinformatics*. 28: 2106–2113 (2012)
- Chen C, Zhao G, Chen W, Guo B. Metabolism of fructooligosaccharides in *Lactobacillus plantarum* ST-III via differential gene transcription and alteration of cell membrane fluidity. *Applied and Environmental Microbiology*. 81: 7697–7707 (2015)
- Claesson MJ, Cusack S, O'Sullivan O, Greene-Diniz R, de Weerd H, Flannery E, Marchesi JR, Falush D, Dinan T, Fitzgerald G, Stanton C, van Sinderen D, O'Connor M, Harnedy N, O'Connor K, Henry C, O'Mahony D, Fitzgerald AP, Shanahan F, Twomey C, Hill C, Ross RP, O'Toole PW. Composition, variability, and temporal stability of the intestinal microbiota of the elderly. *Proceedings of the National Academy of Sciences of the United States of America*. 108: 4586–4591 (2011)
- Cui S, Guo W, Chen C, Tang X, Zhao J, Mao B, Zhang H. Metagenomic analysis of the effects of *Lactiplantibacillus plantarum* and fructooligosaccharides (FOS) on the fecal microbiota structure in mice. *Foods*. 11: 1187 (2022)
- Dobranowski PA, Tang C, Sauve JP, Menzies SC, Sly LM. Compositional changes to the ileal microbiome precede the onset of spontaneous ileitis in SHIP deficient mice. *Gut Microbes*. 10: 578–598 (2019)
- Fukasawa T, Kamei A, Watanabe Y, Koga J, Abe K. Short-chain fructooligosaccharide regulates hepatic peroxisome proliferator-activated receptor alpha and farnesoid X receptor target gene expression in rats. *Journal of Agricultural and Food Chemistry*. 58: 7007–7012 (2010)
- Fuller R. Probiotics in human medicine. *Gut*. 32: 439–442 (1991)
- Guarino MPL, Altomare A, Emerenziani S, Di Rosa C, Ribolsi M, Ballestrieri P, Iovino P, Rocchi G, Cicala M. Mechanisms of action of prebiotics and their effects on gastro-intestinal disorders in adults. *Nutrients* 12: 1037 (2020)
- Haas KN, Blanchard JL. *Kineothrix alysoides*, gen. nov., sp. nov., a saccharolytic butyrate-producer within the family Lachnospiraceae. *International Journal of Systematic and Evolutionary Microbiology*. 67: 402–410 (2017)
- Hemarajata P, Versalovic J. Effects of probiotics on gut microbiota: mechanisms of intestinal immunomodulation and neuromodulation. *Therapeutic Advances in Gastroenterology*. 6: 39–51 (2013)
- Illumina, 16S metagenomic sequencing library preparation. Available from: <https://support.illumina.com>. Accessed Nov. 27, 2013
- Kim BR, Shin J, Guevarra R, Lee JH, Kim DW, Seol KH, Lee JH, Kim HB, Isaacson R. Deciphering diversity indices for a better understanding of microbial communities. *Journal of Microbiology and Biotechnology*. 27: 2089–2093 (2017)
- Kim J, Lee MH, Kim MS, Kim GH, Yoon SS. Probiotic properties and optimization of gamma-aminobutyric acid production by *Lactiplantibacillus plantarum* FBT215. *Journal of Microbiology and Biotechnology*. 32: 783–791 (2022)
- Larsen OFA, Claassen E. The mechanistic link between health and gut microbiota diversity. *Scientific Reports*. 8: 2183 (2018)
- Ley RE, Backhed F, Turnbaugh P, Lozupone CA, Knight RD, Gordon JI. Obesity alters gut microbial ecology. *Proceedings of the National Academy of Sciences of the United States of America*. 102: 11070–11075 (2005)
- Li M, Wang B, Zhang M, Rantalainen M, Wang S, Zhou H, Zhang Y, Shen J, Pang X, Zhang M, Wei H, Chen Y, Lu H, Zuo J, Su M, Qiu Y, Jia W, Xiao C, Smith LM, Yang S, Holmes E, Tang H, Zhao G, Nicholson JK, Li L, Zhao L. Symbiotic gut microbes modulate human metabolic phenotypes. *Proceedings of the National Academy of Sciences of the United States of America*. 105: 2117–2122 (2008)
- Li HY, Zhou DD, Gan RY, Huang SY, Zhao CN, Shang A, Xu XY, Li HB. Effects and mechanisms of probiotics, prebiotics, synbiotics, and postbiotics on metabolic diseases targeting gut microbiota: a narrative review. *Nutrients*. 13: 3211 (2021)
- Liu QF, Kim HM, Lim S, Chung MJ, Lim CY, Koo BS, Kang SS. Effect of probiotic administration on gut microbiota and depressive behaviors in mice. *DARU Journal of Pharmaceutical Sciences*. 28: 181–189 (2020)
- MacFarlane S, Cleary S, Bahrami B, Reynolds N, Macfarlane GT. Synbiotic consumption changes the metabolism and composition of the gut microbiota in older people and modifies inflammatory processes: a randomised, double-blind, placebo-controlled crossover study. *Alimentary Pharmacology & Therapeutics*. 38: 804–816 (2013)
- Noh CK, Kim BS, Hong G, Cheong JY, Lee KJ. Effects of the administration of probiotics on fecal microbiota diversity and composition in healthy individuals. *Journal of Neurogastroenterology and Motility*. 24: 452–459 (2018)
- O'Toole PW, Cooney JC. Probiotic bacteria influence the composition and function of the intestinal microbiota. *Interdisciplinary Perspectives on Infectious Diseases*. 2008: 175285 (2008)
- Roberfroid MB. Prebiotics and synbiotics: concepts and nutritional properties. *British Journal of Nutrition*. 80: S197–S202 (1998)
- Soundharajan I, Kuppusamy P, Srisesharam S, Lee JC, Sivanesan R, Kim D, Choi KC. Positive metabolic effects of selected probiotic bacteria on diet-induced obesity in mice are associated with improvement of dysbiotic gut microbiota. *The FASEB Journal*. 34: 12289–12307 (2020)
- Stojanov S, Berlec A, Strukelj B. The influence of probiotics on the Firmicutes/Bacteroidetes ratio in the treatment of obesity and inflammatory bowel disease. *Microorganisms*. 8: 1715 (2020)
- Xie Q, Pan M, Huang R, Tian X, Tao X, Shah NP, Wei H, Wan C. Short communication: modulation of the small intestinal microbial community composition over short-term or long-term administration with *Lactobacillus plantarum* ZDY2013. *Journal of Dairy Science*. 99: 6913–6921 (2016)
- Zhou Y, Zhang F, Mao L, Feng T, Wang K, Xu M, Lv B, Wang X. Bifico relieves irritable bowel syndrome by regulating gut microbiota dysbiosis and inflammatory cytokines. *European Journal of Nutrition*. (2022). <https://doi.org/10.1007/s00394-022-02958-0>
- Zhu L, Qin S, Zhai S, Gao Y, Li L. Inulin with different degrees of polymerization modulates composition of intestinal microbiota in mice. *FEMS Microbiology Letters*. (2017). <https://doi.org/10.1093/femsle/fnx075>

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