Probiotics and Antimicrobial Proteins
https://doi.org/10.1007/s12602-025-10556-9

RESEARCH

Lactiplantibacillus plantarum GMNL-661 Ameliorates *Clostridioides difficile* Infection and Reconfigures Intestinal Microbiota in a Murine Model

Meng-Jia Li[1] · Hong-Ming Chen[1,9] · Yueh-Lin Chen[6] · Yi-Hsin Lai[3] · Cheng-Yu Lai[8] · Jhen-Wei Ruan[3] · Jenn-Wei Chen[2] · Wan-Hua Tsai[7] · Wen-Chien Ko[4,5] · Pei-Jane Tsai[3]

Accepted: 21 April 2025

Abstract

Clostridioides difficile infection (CDI) is a significant global health threat, often resulting from antibiotic-induced disruption of the gut microbiota, which leads to severe gastrointestinal issues. Current treatments, such as vancomycin, are effective but can cause subsequent relapses, further microbiota disruption, and high treatment costs. Probiotics offer a promising microbiota-based therapeutic strategy. Following an in vitro screening for novel lactic acid bacterial (LAB) strains with strong anti-*C. difficile* ability and good tolerance to digestive challenges, *Lactiplantibacillus plantarum* GMNL-661 emerged as a potential solution to combat CDI. In a CDI mice model, the appropriate dose of GMNL-661 effectively alleviated CDI, which caused weight loss, gut inflammation, and mucin depletion. GMNL-661 alleviated CDI symptoms through increased gut barrier genes and downregulated IL-1 and IL-18. 16s rDNA analysis of mice stool from CDI and CDI supplemented with GMNL-661 showed distinct microbiota ecology. GMNL-661 dramatically affected the microbiome of CDI, increasing *Lactobacillus* spp. and *Clostridium* cluster XVIII while reducing *Clostridium* and *Enterococcus* species. Genome analysis of GMNL-661 revealed minimal safety concerns in antibiotic resistance and virulence genes, confirming that it is suitable for inclusion in the food chain. Antimicrobial peptide (AMP) prediction on GMNL-661 and 299v genome suggested a strong potential candidate for anti-CD antimicrobial peptides. These findings highlighted *L. plantarum* GMNL-661 as an effective and highly safe therapeutic agent against CDI in clinical.

Keywords *Lactiplantibacillus plantarum* · *Clostridioides difficile* · Probiotics · Microbiota · Mice model

Introduction

Clostridioides difficile infection (CDI) remains a critical concern for global public health, manifesting in a spectrum of conditions from mild diarrhea to life-threatening

Meng-Jia Li and Hong-Ming Chen contributed equally to this work.

✉ Wen-Chien Ko
winston3415@gmail.com

✉ Pei-Jane Tsai
peijtsai@mail.ncku.edu.tw

1 Institute of Basic Medical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan

2 Department of Microbiology and Immunology, College of Medicine, National Cheng Kung University, Tainan, Taiwan

3 Department of Medical Laboratory Science and Biotechnology, College of Medicine, National Cheng Kung University, Tainan, Taiwan

4 National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan

5 Department of Medicine, National Cheng Kung University, Tainan, Taiwan

6 EirGenix Inc./Research & Development/Cell Line Engineering, Taipei, Taiwan

7 Research and Development Department, GenMont Biotech Incorporation, Tainan, Taiwan

8 Inong Agriculture Company Limited, Tainan, Taiwan

9 Yanshuei District Health Station, Tainan, Taiwan

Published online: 06 May 2025