DDW2026
Digestive Disease Week®
MAY 2–5, 2026 | CHICAGO, IL
EXHIBIT DATES: MAY 3–5, 2026

EMBARGOED UNTIL 12:01 a.m. CDT; Sunday, May 3, 2026

Probiotic reshapes gut microbiome and reduces histamine burden in long COVID patients

Abstract 389

Background: Long COVID affects 10-30% of COVID-19 convalescents, with persistent gut dysbiosis implicated as a central pathogenic mechanism. Acute infection disrupts gut integrity, depletes beneficial bacteria (e.g., Faecalibacterium prausnitzii), and expands histamine-producing pathobionts (e.g., Klebsiella), while diamine oxidase (DAO) activity declines. This establishes a self-sustaining dysbiotic state that drives systemic endotoxemia, inflammation, and neuroinflammation, mechanistically linking gut instability to core symptoms such as fatigue, insomnia, and cognitive dysfunction. Systemic histamine elevation acts as a key pathophysiological driver, amplifying cytokine storms and neuroinflammation.

Methods: In a six-month randomized, double-blind trial, 280 Long COVID patients received either the synbiotic formula SIM01 (Bifidobacterium adolescentis, B. bifidum, B. longum with galacto-oligosaccharides [GOS], xylooligosaccharides [XOS], resistant dextrin) or placebo (low-dose vitamin C). Longitudinal multi-omics analysis (stool metagenomics, untargeted metabolomics, plasma proteomics/cytokine profiling) was performed on 695 stool and 476 blood samples collected at baseline, six months (end-of-treatment), and 12 months (six-months post-treatment). Clinical symptom assessments tracked fatigue, insomnia, cognitive symptoms, and gastrointestinal distress.

Results: SIM01 induced significant, durable remodeling of the gut microbiome, increasing alpha diversity and enriching beneficial commensals (F. prausnitzii, Akkermansia muciniphila, Roseburia hominis) while depleting pathobionts (Ruminococcus gnavus, Clostridium spp.). Metabolomics revealed a profound reduction in fecal histamine, the most significantly altered metabolite, persisting at 12 months. Histamine reduction correlated strongly with alleviation of fatigue, insomnia, memory loss, and dyspnea ($FDR<0.05$) and decreased plasma IL-1β. Mechanistically, histamine reduction occurred potentially via: 1) Competitive microbiota remodeling (SIM01 strains positively correlated with histamine-negative species, negatively with histamine-positive species); and 2) Enhanced host histamine clearance (significantly increased plasma DAO activity). Baseline gut microbiota composition accurately predicted SIM01 strain colonization success and subsequent clinical symptom response (AUC=0.982).

Conclusion: The synbiotic SIM01 durably reshapes the gut microbiome and reduces histamine burden in Long COVID patients via a dual mechanism, thereby significantly alleviating core symptoms such as fatigue and insomnia. Reduced histamine and IL-1β mechanistically link microbiome remodeling to symptom resolution. Baseline microbiota signatures predict treatment response, enabling precision deployment of probiotics for Long COVID management and informing next-generation biotherapeutics.