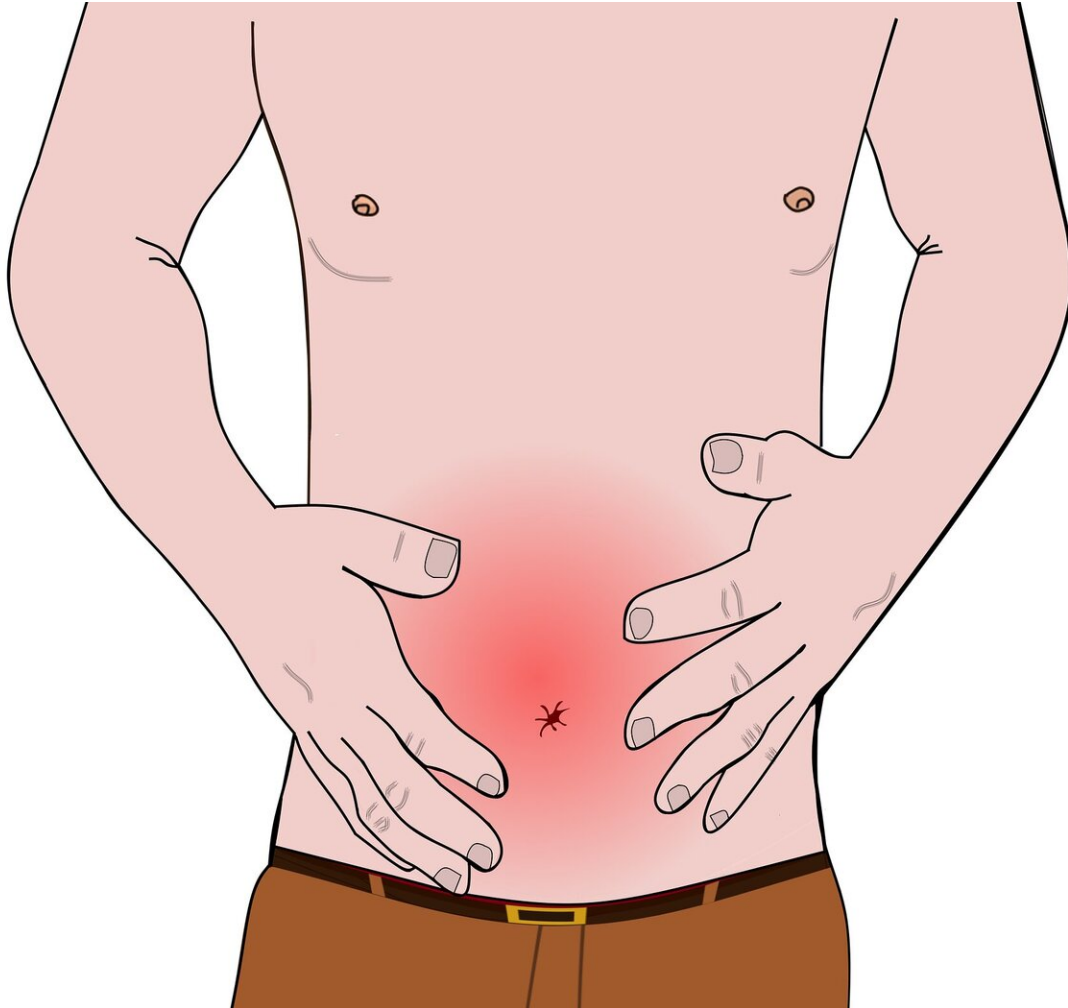


How gut microbes help alleviate constipation

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Scientists have identified the genes in the probiotic Bifidobacteria

B. longum responsible for improving gut motility. A research team reporting November 21 in the journal *Cell Host & Microbe* found that *B. longum* strains possessing the *abfA* cluster of genes can ameliorate constipation through enhanced utilization of an indigestible fiber called arabinan in the gut.

"We established the [causal link](#) between a genetic variant—the *abfA* cluster—to the key functional difference of probiotic *B. longum* in multiple model organisms, including mice and humans, and provided mechanistic and ecological insights into how a single gene cluster can affect the gut motility of hosts through arabinan metabolism," says Qixiao Zhai of Jiangnan University, one of the paper's co-senior authors.

Constipation is a globally prevalent bowel disorder with a worldwide prevalence of 10% to 15%. Impaired gastrointestinal motility has been implicated in gut microbial dysbiosis, which is characterized by a significant decrease in the abundance of beneficial microorganisms, some of which are conventionally known as probiotics. Orally administered probiotics have therefore been widely used to alleviate symptoms.

Yet the therapeutic effect of probiotics for constipation often varies substantially across strains within the same species. Due to elusive mechanisms, the rational choice of probiotic remains challenging for medical care professionals and patients. In addition, most evidence on the beneficial effects of probiotics on gut motility mainly emerged from studies using a [mouse model](#).

"Probiotic strains were often effective in animal models yet failed in [human clinical trials](#) or were poorly validated in humans," says Jiachao Zhang of Hainan University, the study's second co-senior author. "Proof-of-concept studies based on a [human](#) cohort in combination with evidence from animal studies are urgently needed for translational

research."

Zhai, Zhang, and Shi Huang of the University of Hong Kong, the paper's third co-senior author, set out to identify and systematically validate the key genetic factors of exogenous probiotics or resident gut microbiota affecting gastrointestinal motility. They isolated 185 *B. longum* strains from 354 Chinese subjects who ranged in age from 0 to 108 years.

From a comprehensive library of wild *B. longum* strains, they discovered that the effective alleviation of constipation in mice is regulated by the *abfA* cluster. This key genetic factor preferentially enhances the utilization of arabinan—a common constituent of plant polysaccharides, an indigestible fiber for humans, and a poorly accessible source of nutrients for normal gut microbes.

The researchers further validated the *abfA* cluster's functional roles using gene-knockout experiments. In mice with constipation, *B. longum*, but not an *abfA* mutant, improved gastrointestinal transit time—an effect that was dependent upon dietary arabinan.

To establish its functional roles for ameliorating constipation in humans, the researchers used a clinical trial and a human-to-mouse fecal microbiota transplantation experiment in combination with metagenomics and metabolomics.

In the double-blind, randomized, placebo-controlled clinical trial, supplementation with *abfA*-cluster-carrying *B. longum*, but not an *abfA*-deficient strain, enriched arabinan-utilization residents, increased beneficial metabolites, and improved constipation symptoms.

Across human cohorts, *abfA*-cluster abundance in the fecal microbiomes predicted constipation, and transplantation of *abfA* cluster-enriched human microbiota to mice with constipation improved gut motility.

Notably, other than *B. longum*, the *abfA* gene/cluster is prevalent in gut residents, regulating symptoms in both mice and humans.

The authors say that the *abfA* cluster is a gut-microbiome therapeutic target for [constipation](#) in humans. More broadly, the results suggest that genetic factors governing the unique metabolic capability of probiotics should be primarily considered for screening probiotics or inferring their treatment efficacy for gastrointestinal diseases.

"Collectively, this study identified and systematically characterized a key genetic factor responsible for arabinan utilization that addressed one critical challenge in the probiotic field, namely widespread yet unknown strain specificity in [probiotic](#) treatment efficacy," Huang says.

"Our proof-of-concept study also established generalizable principles for the rational development of colonizable, functional probiotics with persistent treatment efficacy in multiple model organisms. Moreover, the *abfA* cluster is so prevalent in the gut microbiota that it can be developed as a simple yet powerful biomarker for gastrointestinal diseases."

More information: Chengcheng Zhang et al, A key genetic factor governing arabinan utilization in the gut microbiome alleviates constipation, *Cell Host & Microbe* (2023). DOI: 10.1016/j.chom.2023.10.011 , [www.cell.com/cell-host-microbe ... 1931-3128\(23\)00415-8](http://www.cell.com/cell-host-microbe/1931-3128(23)00415-8)

Peter Kuffa et al, Fiber-deficient diet inhibits colitis through the regulation of the niche and metabolism of a gut pathobiont, *Cell Host & Microbe* (2023). [DOI: 10.1016/j.chom.2023.10.016](https://doi.org/10.1016/j.chom.2023.10.016)

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