Intra-specific difference of *Latilactobacillus sakei* on inflammatory bowel diseases: insights into potential mechanisms through comparative genomics and metabolomics analyses

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**Introduction**

**Research Background**

**Inflammatory bowel diseases (IBD)** are chronic inflammatory diseases of the gastrointestinal tract that have become a global health burden.

*Latilactobacillus sakei* can effectively alleviate various immune diseases, including colitis.

**Purpose and Significance of Study:**
Screen *L. sakei* from different sources and explore the intra-specific differences of *L. sakei* on IBD, establishing a theoretical basis for further research on *L. sakei* with probiotic functions.

*More than five million people worldwide live with inflammatory bowel disease (IBD).*
Results

Exploring the *in vitro* immunomodulatory capacity of *L. sakei*

- **CCFM1267, QGZZYRHMT1L6, QJSSZ1L4, QJSSZ4L10** up-regulated Caco-2 cell activity
- *L. sakei* regulated the expression of tight junction protein and the genes of immune-related pathways

- **4 effective:** CCFM1267, QGZZYRHMT1L6, QJSSZ1L4, QJSSZ4L10
- **2 ineffective:** QJSNT1L10, QGZZYRHMT2L6

(A) Flow chart of screening of *L. sakei* *in vitro*. (B) Impact of *L. sakei* on Caco-2 cell viability after DSS stimulation. (C) Effects of *L. sakei* on TJ protein in Caco-2 cells after DSS stimulation. (D) Influence of *L. sakei* on the expression of Caco-2 cell related immune pathway after DSS stimulation.
Results

Evaluation of alleviating effect of *L. sakei* on DSS-induced colitis in mice

- **CCFM1267**: colon length, weight, tight junction proteins ↑
  pro-inflammatory factors, inflammatory enzymes ↓

- **QJSNT1L10**: less effective

1 effective: CCFM1267
1 ineffective: QJSNT1L10

(A) Flow chart of animal experiment. (B, C) Effects of *L. sakei* on physiological indexes of mice with colitis.
(D) Effects of *L. sakei* on the histological morphology of colonic in mice with colitis. (E) Effects of *L. sakei* on colon tight junction protein content in colitis mice. (F-H) Effects of *L. sakei* on inflammatory enzyme content in colitis mice. (I-M) Effects of *L. sakei* on cytokine content in colitis mice.
Results

Influence of *L. sakei* on gut microbiota and SCFAs

(A) α diversity of gut microbiota in colitis mice. (B) β diversity of the gut microbiota in colitis mice. (C) Effects of *L. sakei* on SCFAs content in colitis mice. (D, F) Effects of *L. sakei* on the phylum level of the gut microbiota in colitis mice. (E) LEfSe difference of gut microbiota in colitis mice after intervention by *L. sakei*. (G) The relative abundance of different bacteria species after *L. sakei* intervention.

- **SCFA-producing bacteria**: Enterorhabdus, *Roseburia*, *Alloprevotella*, *Adlercreutzia*
- **anti-inflammatory**

- CCFM1267 revealed a pronounced upregulatory trend of SCFAs compared to QJSNT1L10
Results

The mechanism of different strains on relieving colitis

- CCFM1267 and QJSNT1L10 belonged to two subspecies
- There were significant differences in carbohydrate-active enzymes
- Acetylcholine and indole-3-acetic acid may be the key metabolites

(A) Flow chart of comparative genomic analysis and metabolome analysis of different genera. (B) Analysis of homologous genes of *L. sakei*. (C) Average nucleotide consistency analysis of *L. sakei*. (D) Phylogenetic analysis of *L. sakei*. (E, F) Carbohydrate active enzyme analysis of *L. sakei* from different sources. (G) OPLS-DA score plot of all metabolites in *L. sakei*. (H) Volcanic map of differential metabolites.
Intra-specific variations in the effects of *L. sakei* on IBD have been observed in both *in vitro* and *in vivo* models. Differences in the carbohydrate-active enzymes of *L. sakei* may exert an indirect influence on the gut microbiota. Acetylcholine and indole-3-acetic acid were tentatively identified as key substances.

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