

# Taxonomic identification of bile salt hydrolase-encoding lactobacilli: Modulation of the enterohepatic bile acid profile

Ziwei Song, Shuo Feng, Xingchen Zhou, Zhengxing Song, Jing Li, Ping Li

State Key Laboratory of Natural Medicines, China Pharmaceutical University

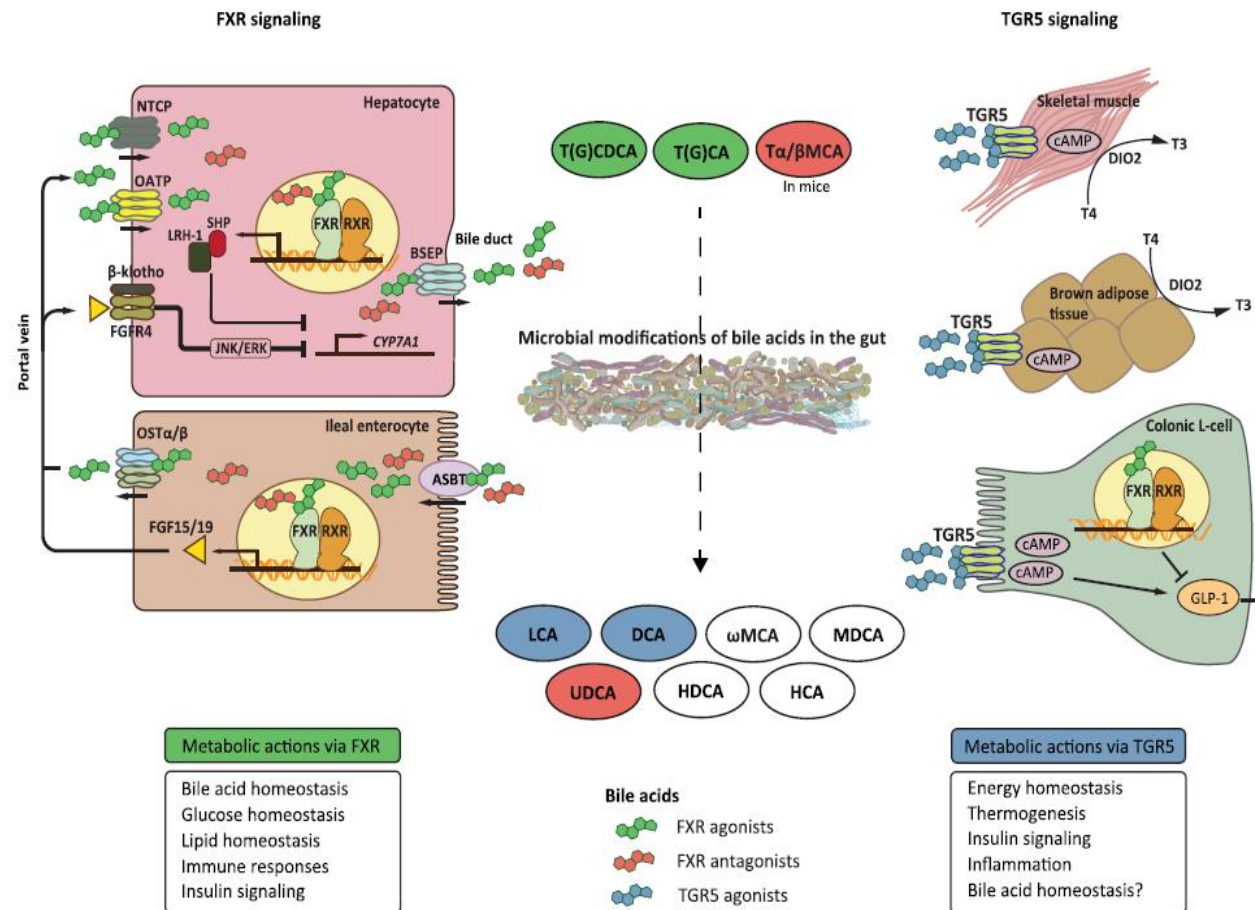
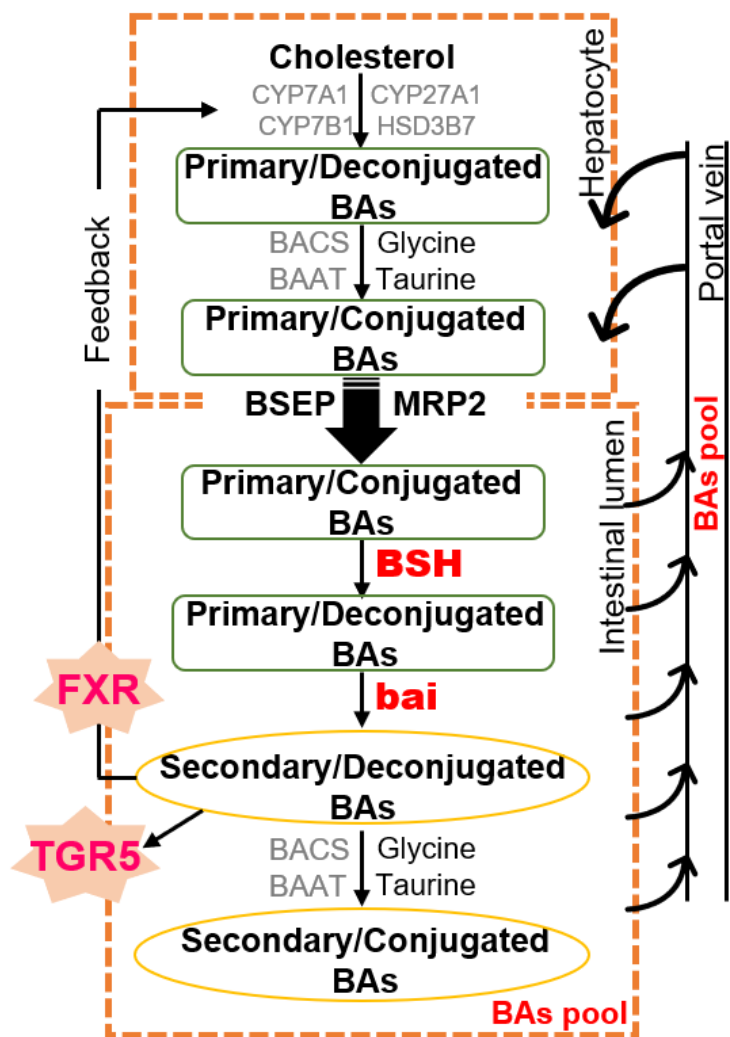


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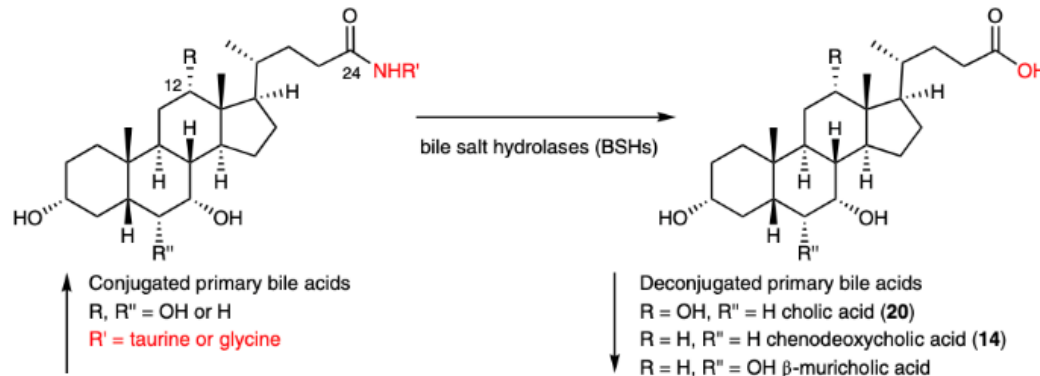
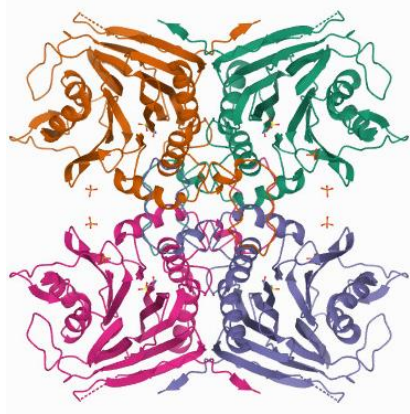
# Introduction



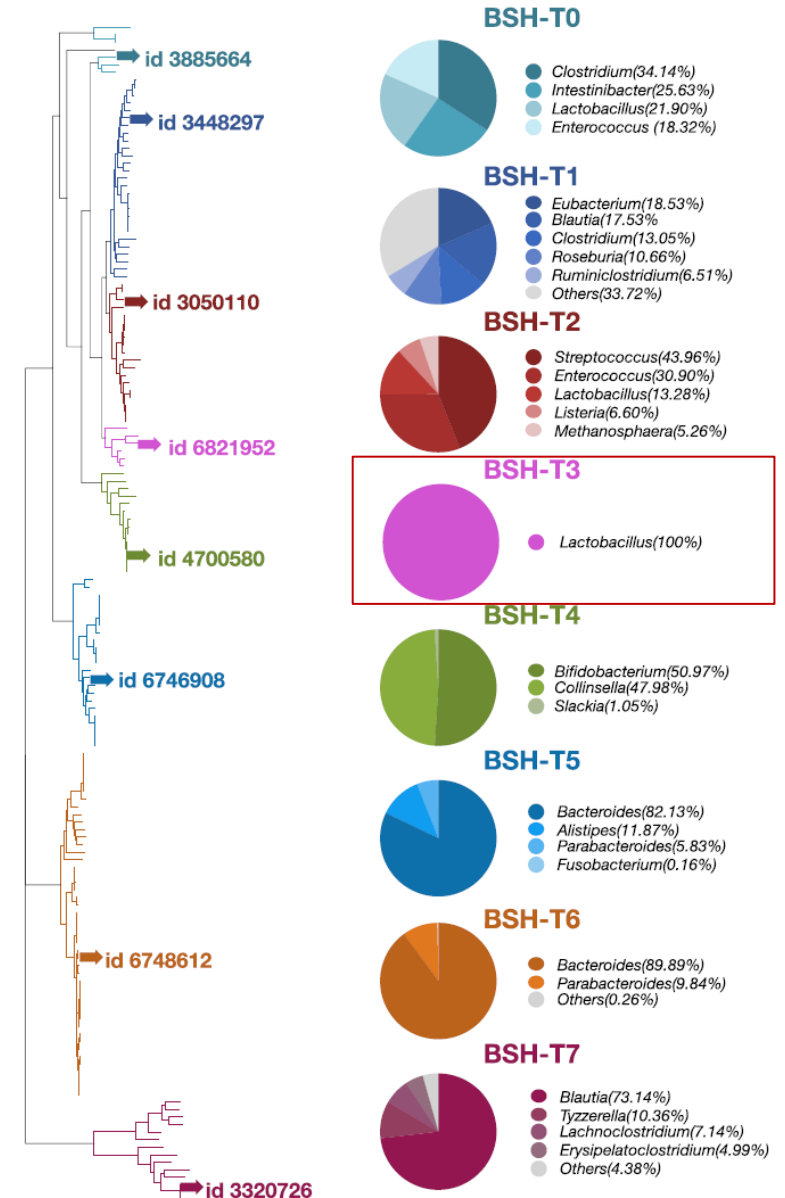
- ◆ Bile acids are produced by **cholesterol** in the liver and **metabolized in the gut by the gut microbiota.**
- ◆ These bile acids can regulate many metabolic pathways in the host by **activating FXR and TGR5 receptors.**

# Introduction

## Bile salt hydrolases



- ◆ **Bile salt hydrolases (BSH)** is a key enzyme in the metabolism of bile acids in the gut.
- ◆ In our previous study, BSH-encoding strains were systematically identified and classified into **eight phylotypes** based on phylogenetic analyses.
- ◆ **BSH-T3 has the highest enzyme activity** and is found only in *Lactobacillus*.



# Results

## Lactobacilli species encoding bile salt hydrolases in human gut microbiota

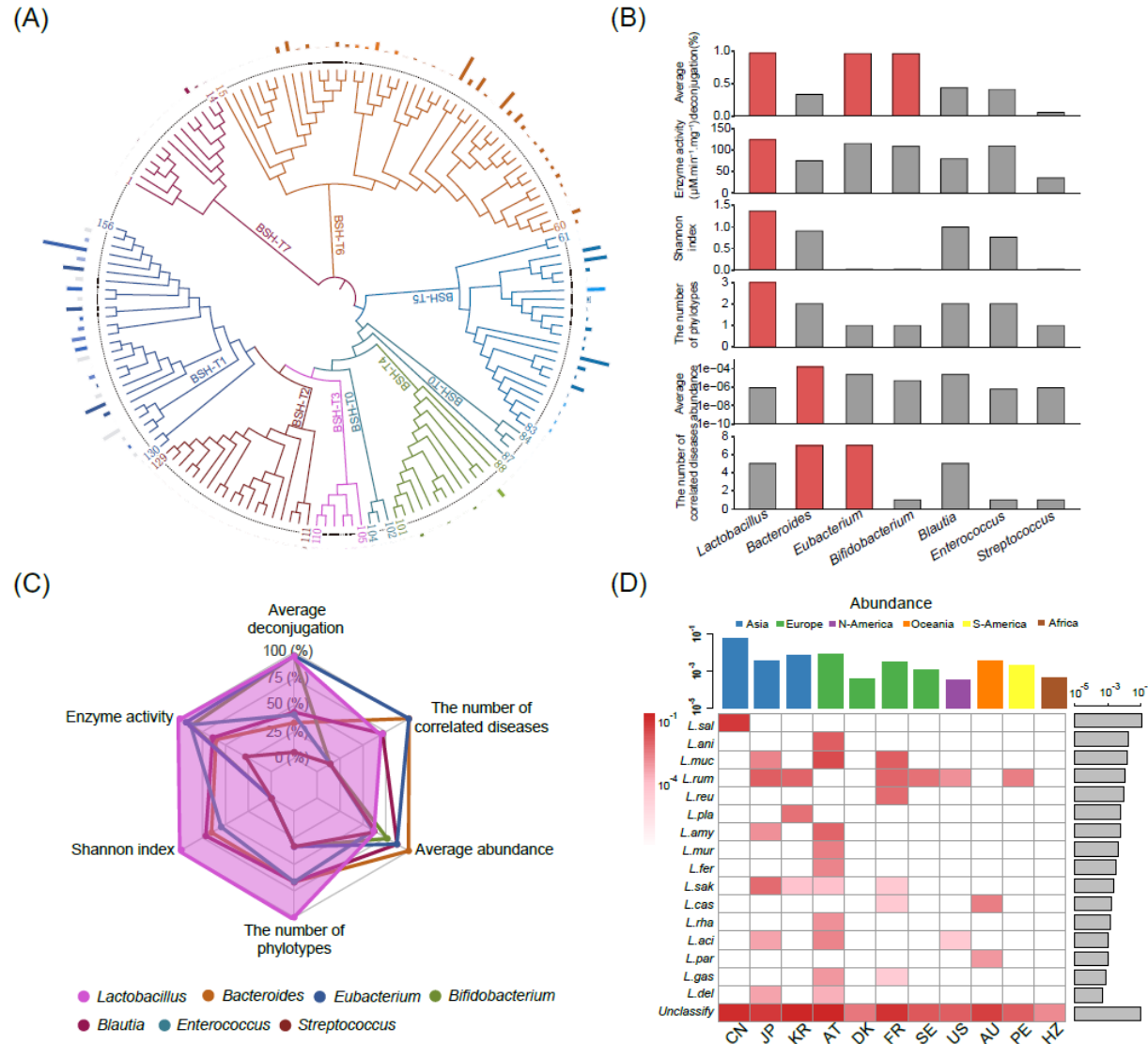


FIGURE 1 Comprehensive analysis of bile salt hydrolase (BSH)-encoding bacteria.

- ◆ The 156 BSHs from 90 species were mainly distributed in **seven genera** including: *Enterococcus*, *Eubacterium*, *Streptococcus*, *Lactobacillus*, *Bifidobacterium*, *Bacteroides*, and *Blautia*.
- ◆ Multi-factor analysis showed that *Lactobacillus* was the most critical bacterium.
- ◆ The main **16 BSH-encoding lactobacilli** species were identified in the gut of healthy humans.
- ◆ The abundance and distribution characteristics of 16 BSH-encoding lactobacilli species were analyzed in humans from 11 populations.



# Results

## Classification of lactobacilli species and comparison of deconjugation ability in vitro

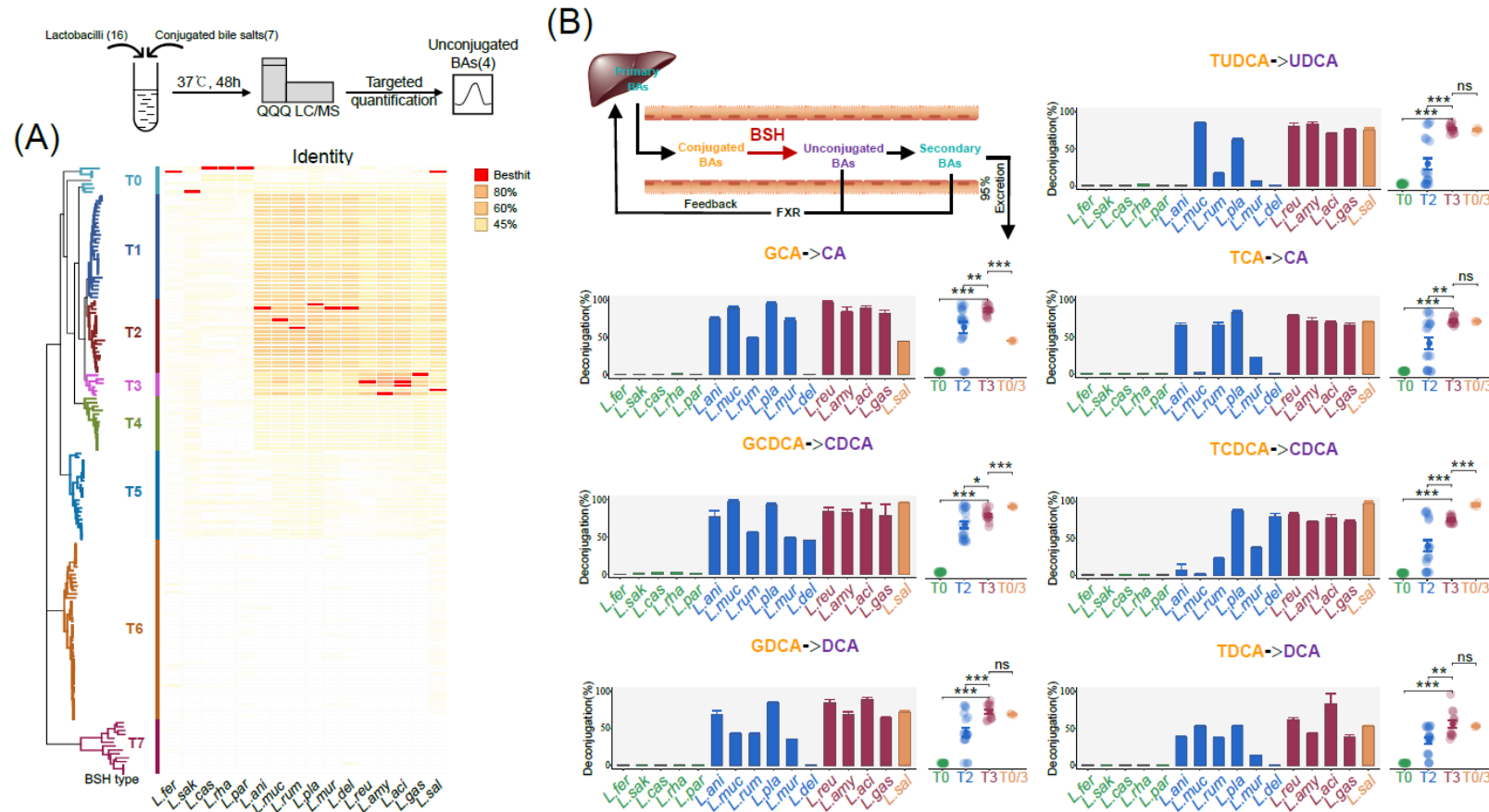


FIGURE 2 Deconjugation activity of bile salt hydrolase (BSH)-encoding lactobacilli.

- ◆ According to the phylogenetic-based system, the 16 strains of lactobacilli were divided into four categories such as: **Lac(BSH-T0)**, **Lac(BSH-T2)**, **Lac(BSH-T3)** and ***L. salivarius***.
- ◆ The in vitro deconjugation ability of 16 strains was ranked as follows: **Lac(BSH-T3)  $\approx$  *L. salivarius* > Lac(BSH-T2)  $\gg$  Lac(BSH-T0)**.



# Results

## Administration of lactobacilli alters the gut microbiome of mice

### Administration of BSH-T3-encoding *L. reuteri*

- ◆ In the structure of gut microbiota,  **$\alpha$  diversity and  $\beta$  diversity were significantly increased.**
- ◆ In the composition of gut microbiota, most species abundance changes were caused.

### QPCR quantification of each lactobacillus species

- ◆ The administration of four lactobacilli successfully colonized in mice gut.

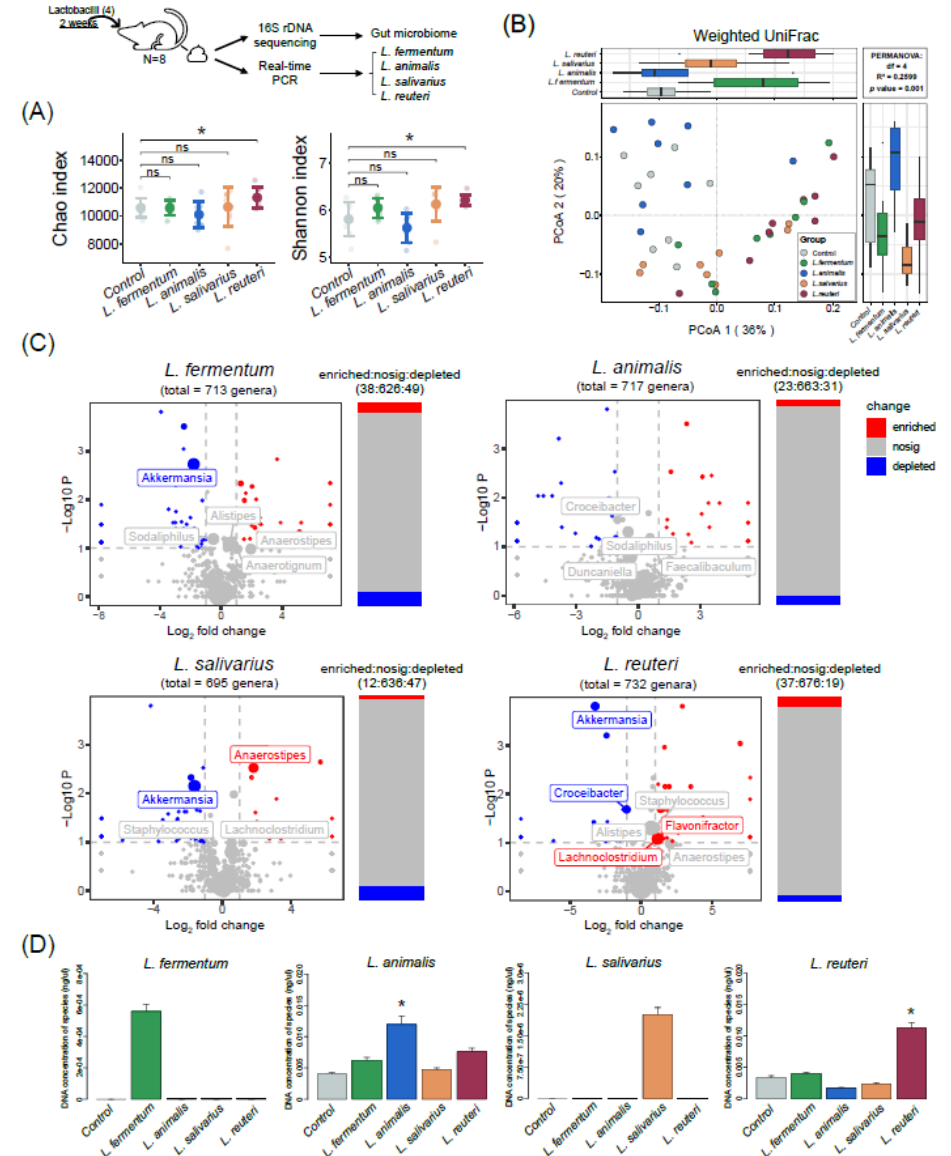


FIGURE 3 Treatment with lactobacilli alters the structure of the fecal microbiome in mice.

# Results

## Administration of lactobacilli alters serum and fecal metabolomes of mice

**Serum: 573 features;  
Fecal: 163 features.**

- ◆ Serum metabolome: *L. reuteri* administration group had the highest number of differential features, and **49 metabolites up-regulated**.
- ◆ Fecal metabolome: *L. reuteri* administration group still had the highest number of differential features, with **13 metabolites up-regulated** and **9 metabolites down-regulated**.
- ◆ In general, administration of **BSH-encoding-*L. reuteri*** has a significant effect on the serum and fecal metabolome of mice, particularly in **promoting lipid and cholesterol metabolism**.

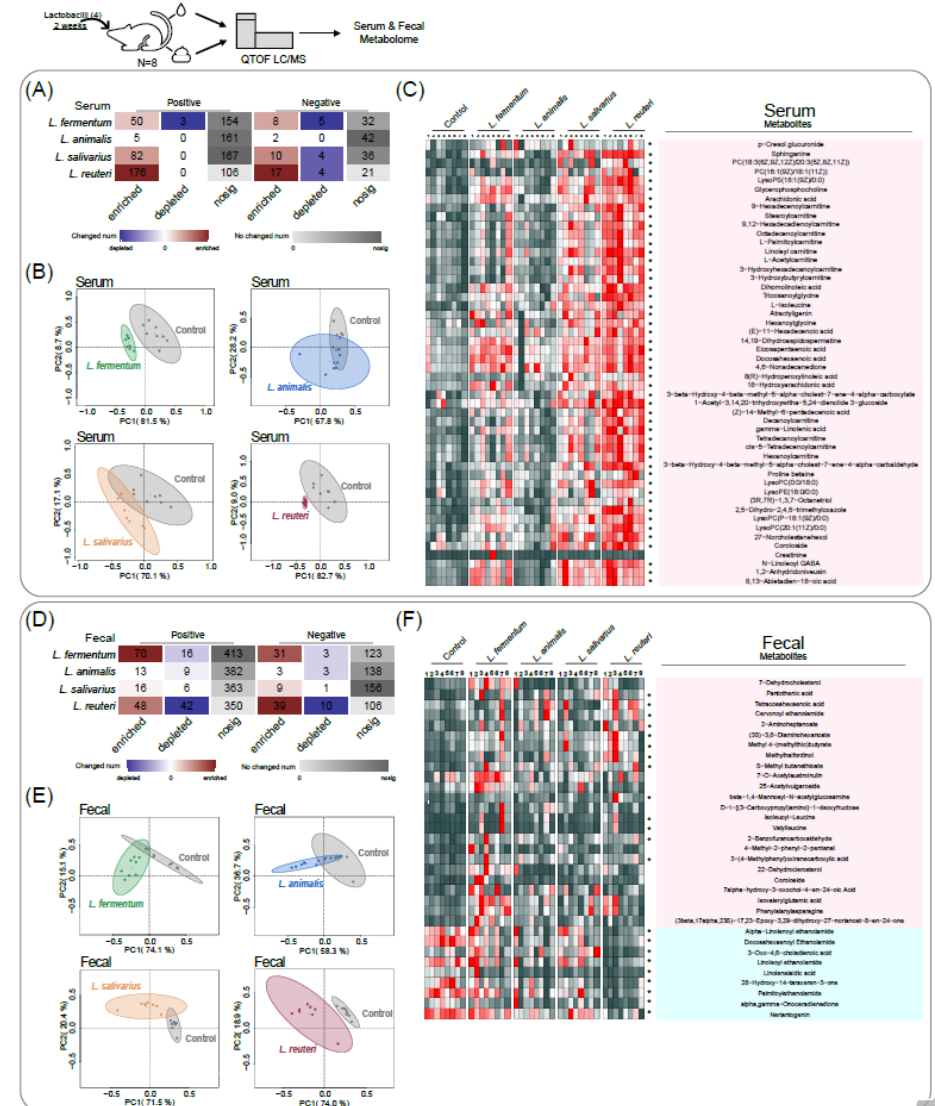


FIGURE 4 Treatment with lactobacilli alters the serum and fecal metabolomes of mice.

# Results

## Regulatory effect of lactobacilli species on enterohepatic BA pools in mice

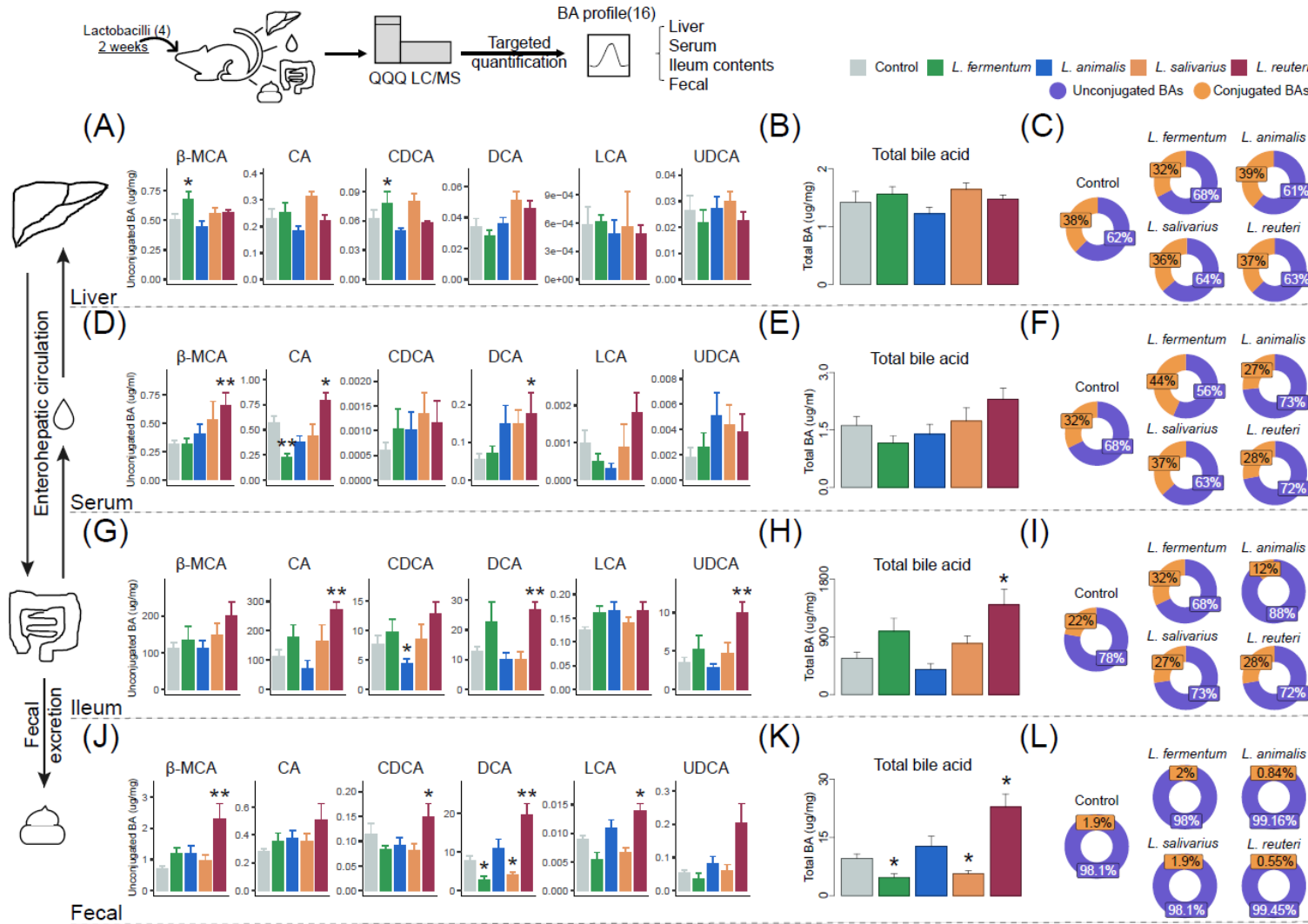
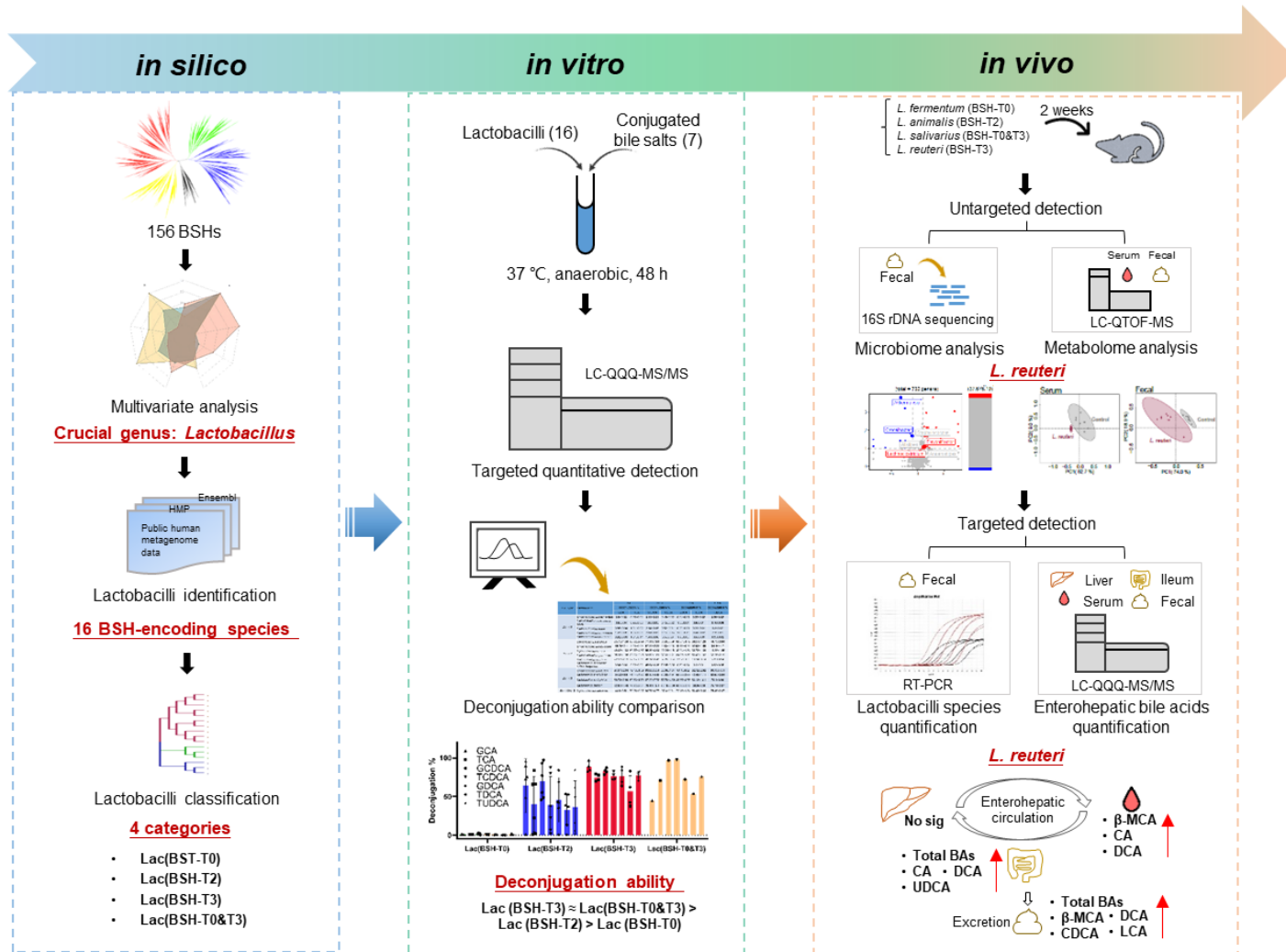


FIGURE 5 Treatment with lactobacilli alters the composition of the bile acid (BA) pool in mice.

- ◆ In liver, the bile acid pool showed minor changes.
- ◆ In serum, the concentrations of  $\beta$ -MCA, CA and DCA were significantly increased in *L. reuteri* administration group.
- ◆ In ileum, the concentrations of CA, DCA and UDCA, and the total bile acid level increased significantly in *L. reuteri* administration group.
- ◆ In faeces, the concentrations of  $\beta$ -MCA, CDCA, DCA and LCA, and the total bile acid level were significantly increased in *L. reuteri* administration group.
- ◆ Overall, the administration of **BSH-T3-encoding *L. reuteri*** had the greatest effect on the **enterohepatic bile acid profile** in mice.



# Summary



- *Lactobacillus* was identified as the crucial BSH-encoding genus.
- According to the encoded BSH, the 16 lactobacilli were **classified into four categories** in the gut of healthy **individuals**.
- In vitro experiments showed that **BSH-T3-encoding lactobacilli** had the strongest deconjugation ability.
- Administration of **BSH-T3-encoding *L. reuteri*** changed the microbiome and metabolome structure of mice, and significantly changed the enterohepatic bile acid profile in mice.

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