



Isolation of potentially novel species expands the genomic and functional diversity of Lachnospiraceae

Xiaoqian Lin, Tongyuan Hu, Zhinan Wu, Lingne Li, Yuhao Wang, Dingyang Wen, Xudong Liu, Wenxi Li, Hwei Liang, Xin Jin, Xun Xu, Jian Wang, Huanming Yang, Karsten Kristiansen*, Liang Xiao*, Yuanqiang Zou*

BGI Research, Shenzhen, China



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Introduction

Lachnospiraceae:

It is highly abundant in the healthy human gut, and also colonizes the rumen and environment.

Probiotic functions:

- ✓ Convert bile acids
- ✓ Produce short chain fatty acids
- ✓ Antibacterial substances



Next generation probiotics with great potential

Cohort studies, animal experiments:

Species	Function
<i>Anaerobutyricum soehngenii</i>	Improved insulin sensitivity in db/db mice
<i>Anaerobutyricum hallii</i>	Improve postprandial blood sugar control
<i>Anaerostipes hadrus</i> BPB5	Exacerbating colitis in mice
<i>Eisenbergiella tayi</i>	Pathogen
<i>Clostridium boltea</i>	Pathogen
<i>Clostridium clostridioforme</i>	Pathogen

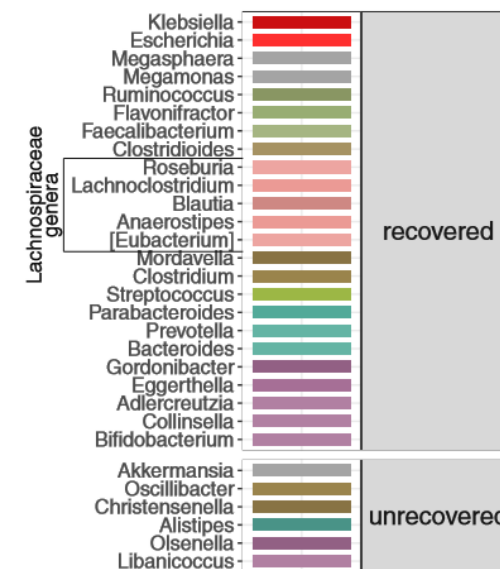
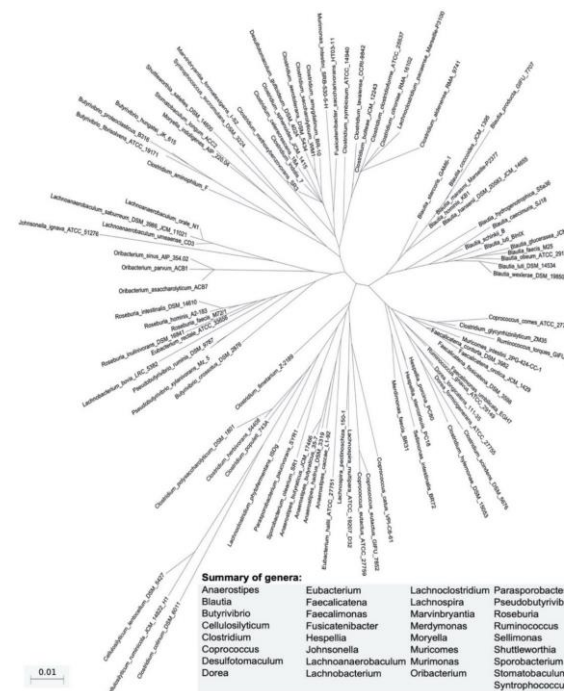


beneficial



harmful

It is crucial to select the appropriate strain for study from the large collection of strains available



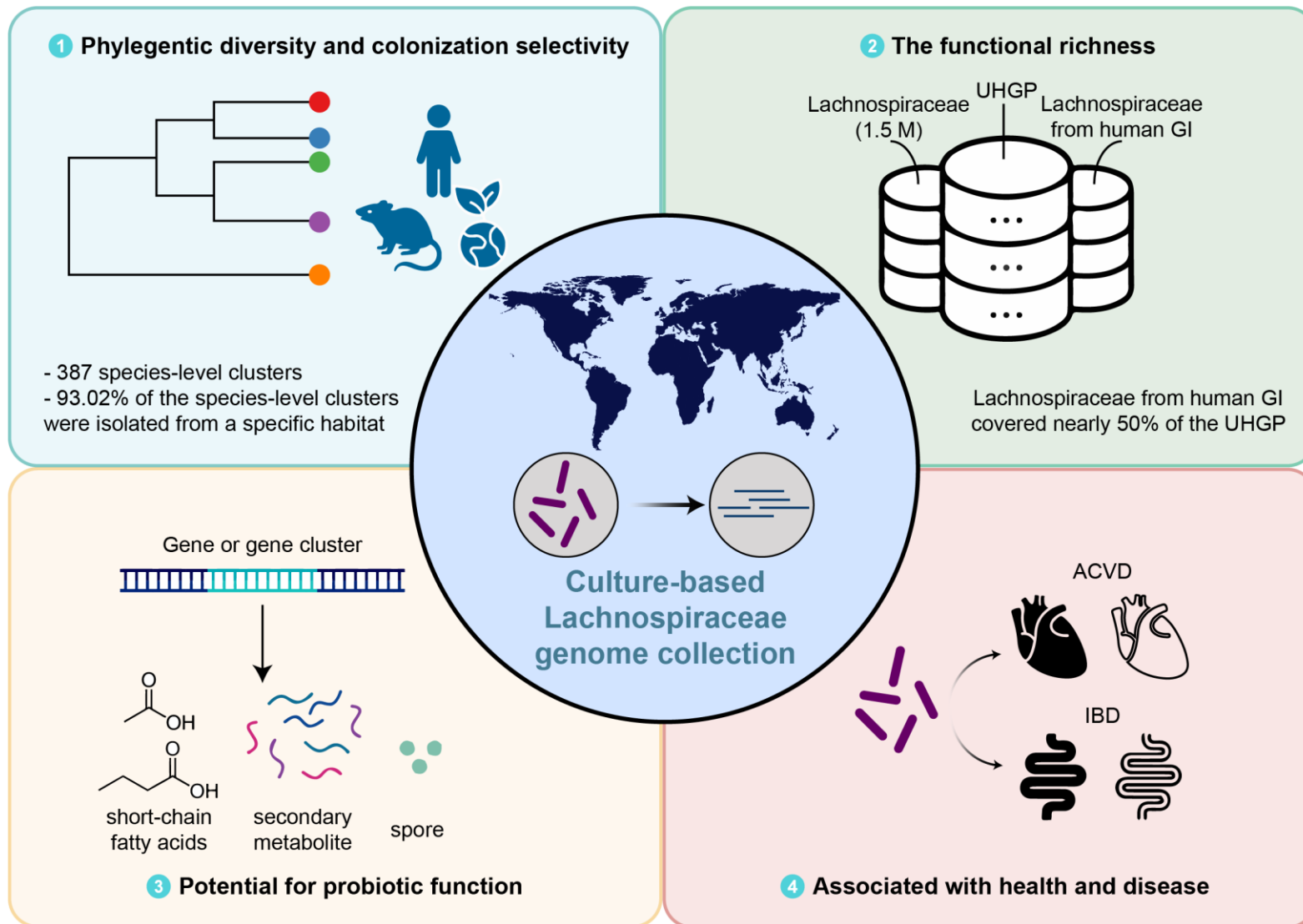
Sorbara M T, Littmann E R, Fontana E, et al. Cell host & microbe, 2020, 28(1): 134-146. e4.

Current understanding of the diversity of Lachnospiraceae is incomplete



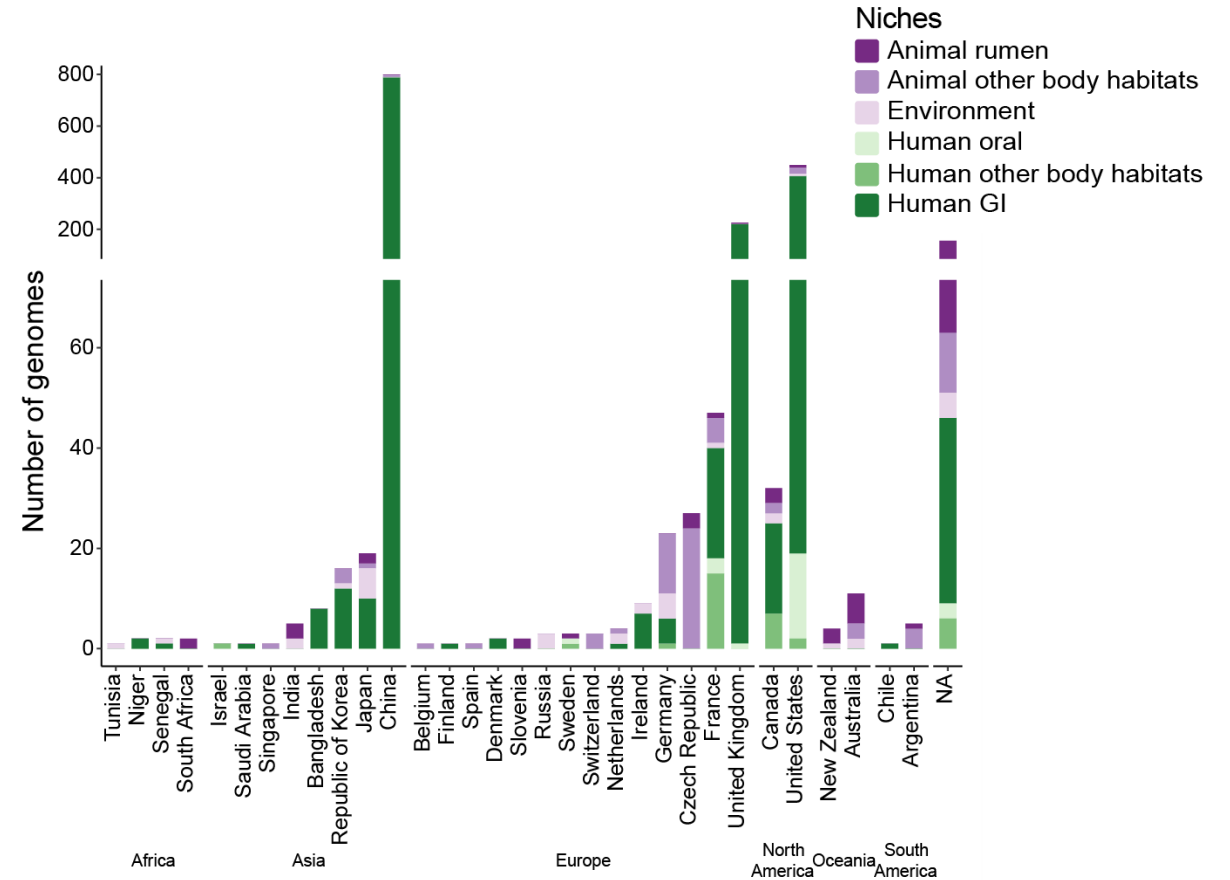
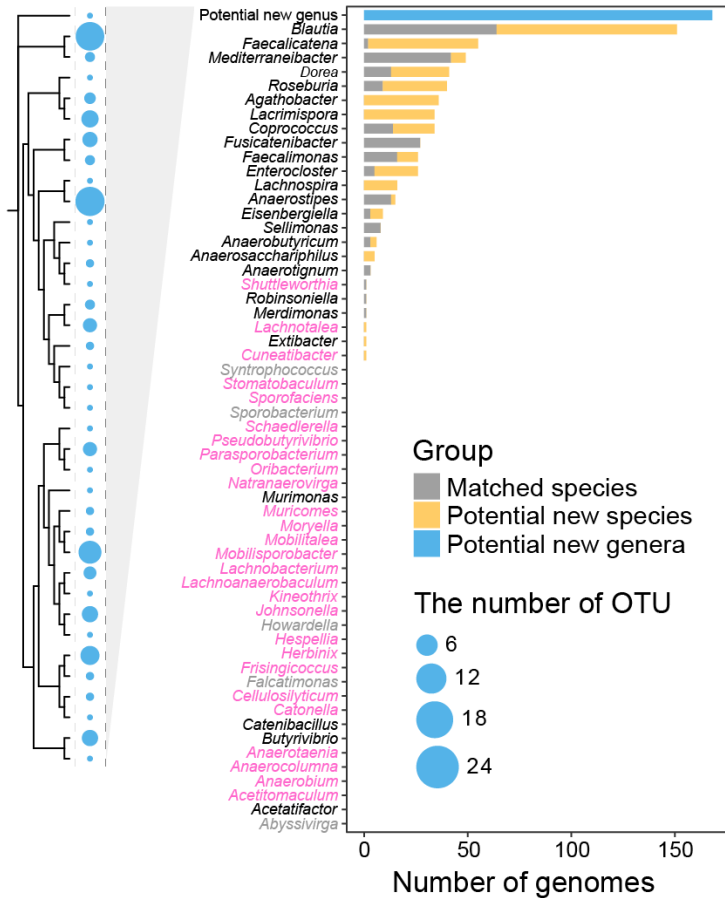
Highlight

To collect publicly available cultured genome sequences of Lachnospiraceae and conduct a comprehensive diversity analysis to guide the selection of potential probiotics



Results

The expanded Cultivated Genome Reference increases the taxonomic diversity of Lachnospiraceae

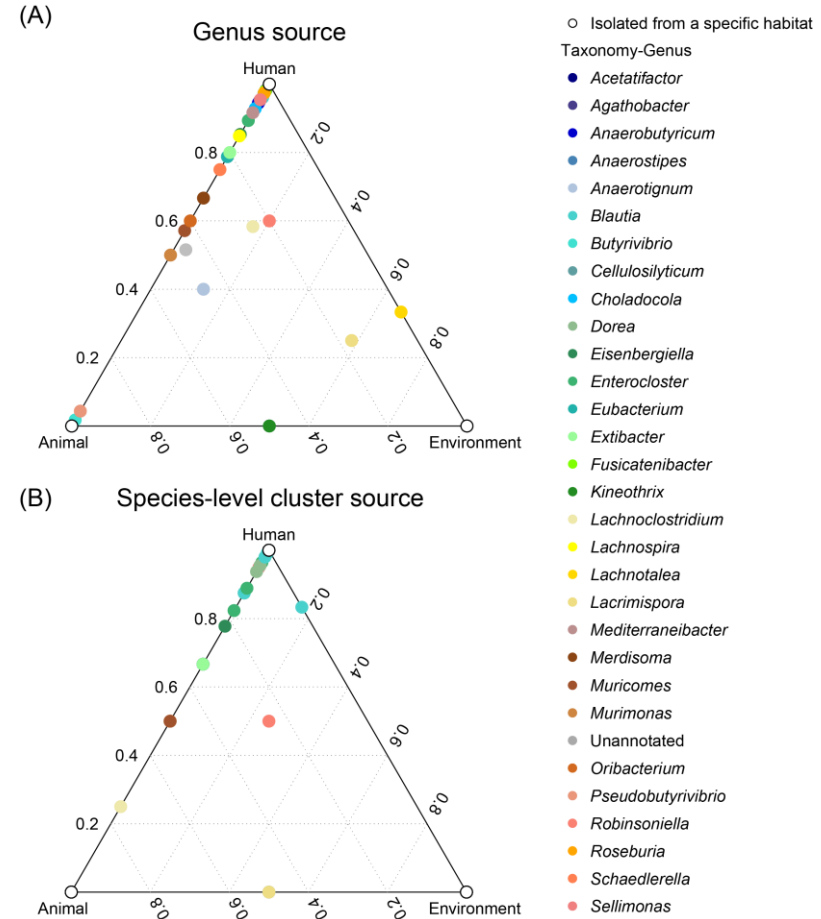
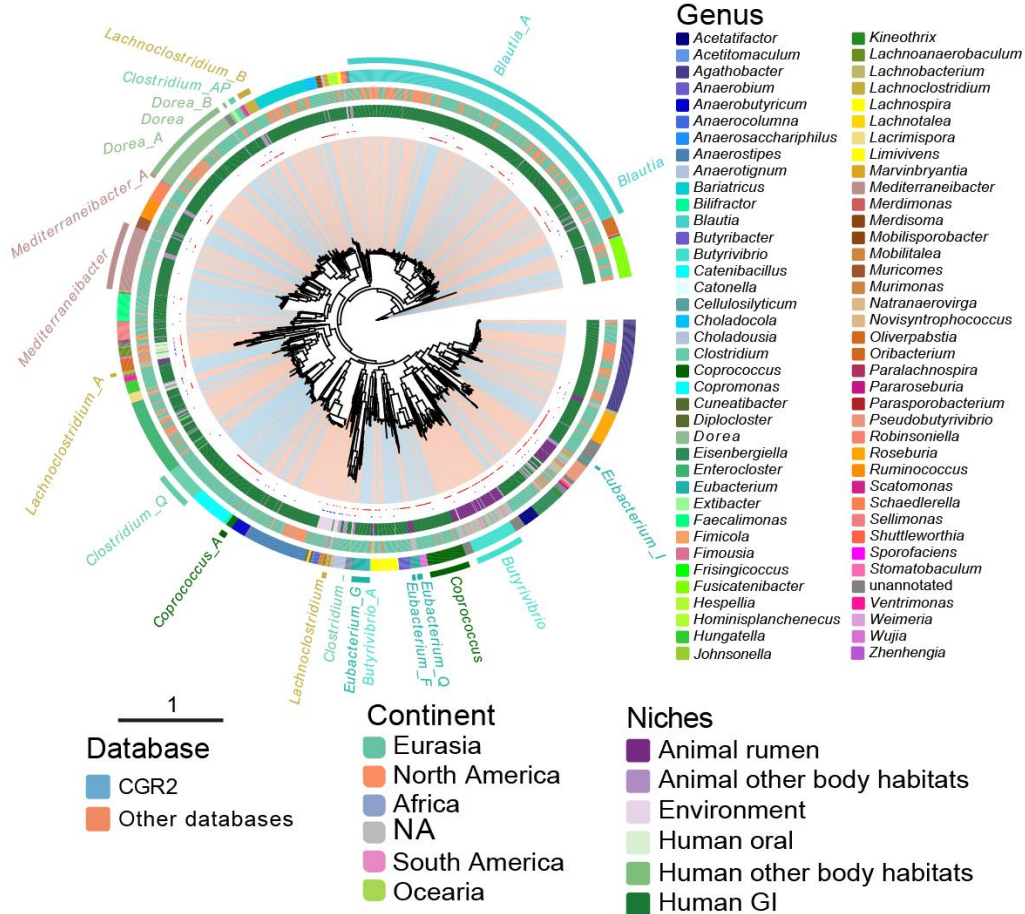


- 756 high-quality Lachnospiraceae genomes
- 47.88% potential new species and 22.22% potential new genera
- Covers most of the genera derived from human gut, and fills in 3 genera that have not been previously isolated from human gut.

- 1,868 high-quality genomes included in the analysis
- isolated from 32 countries across 6 continents and include multiple ecological niches

Results

Phylogenetic analysis reveals phyletic diversity and colonization selectivity



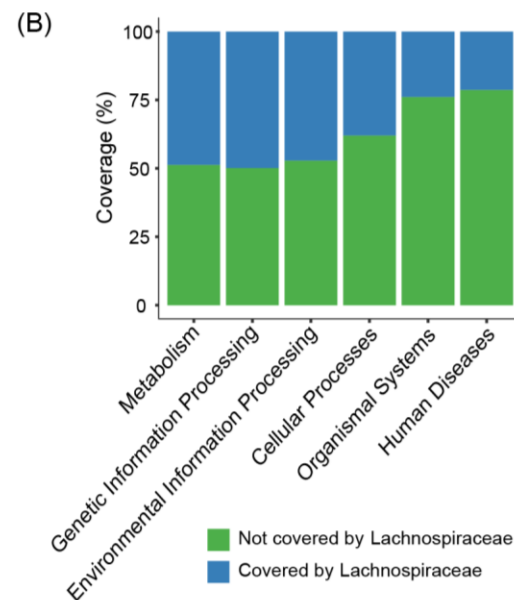
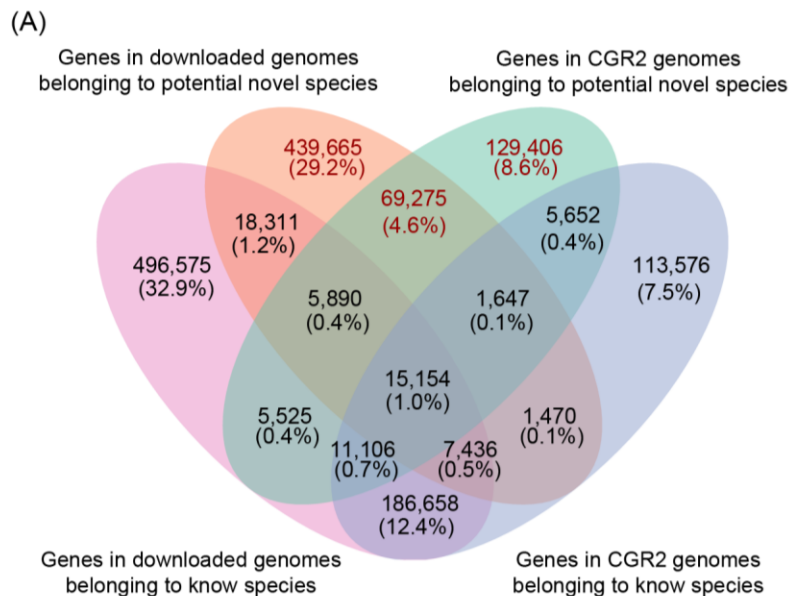
- 387 species-level clusters, more than three times the number of existing species
- 8 genera show great diversity on the phylogenetic tree

- 40% of genus were non-single niche
- 93.02% clusters are isolated from specific ecological niches

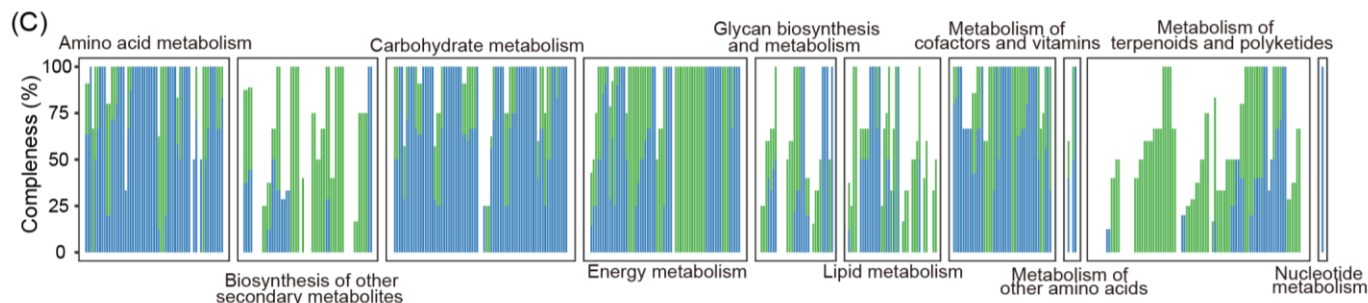


Results

Sets of genes and proteins in Lachnospiraceae genomes

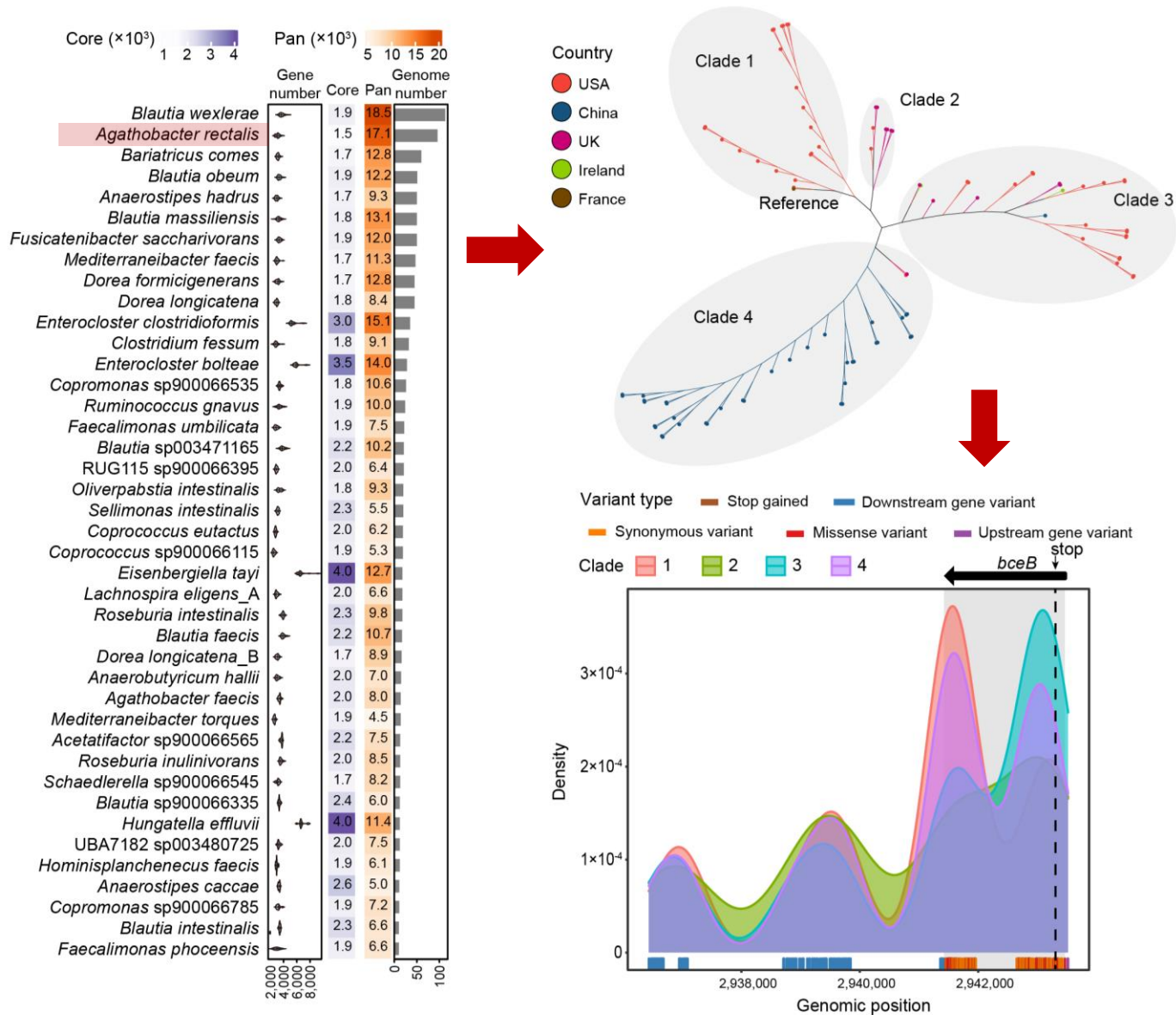


- Constructed 1.5 M gene set and 1.4 M protein set
- Potential novel species contributed **42.34%** of genes
- Proteins from the human gut Lachnospiraceae genomes cover 50% of UHGP, **perform about half of the metabolic functions of the human gut.**



Results

Pan-genome analysis reveals the ecological diversity of representatives of Lachnospiraceae



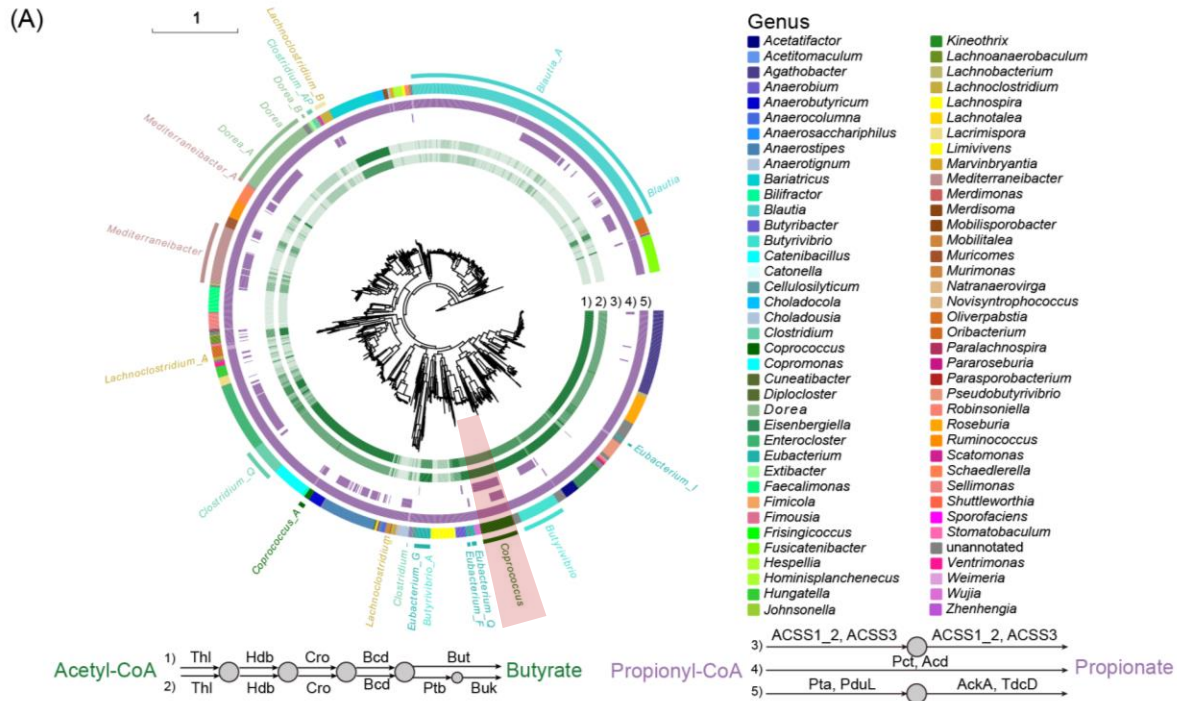
Agathobacter rectalis

- The core genome is smaller and the pan-genome is larger, indicating a more diverse genetic composition
- There are functional differences related to **geographical location** (Bacitracin export permease protein BceB)



Results

The diversity of species taxonomy, body habitats, and geography shapes the various functions of Lachnospiraceae

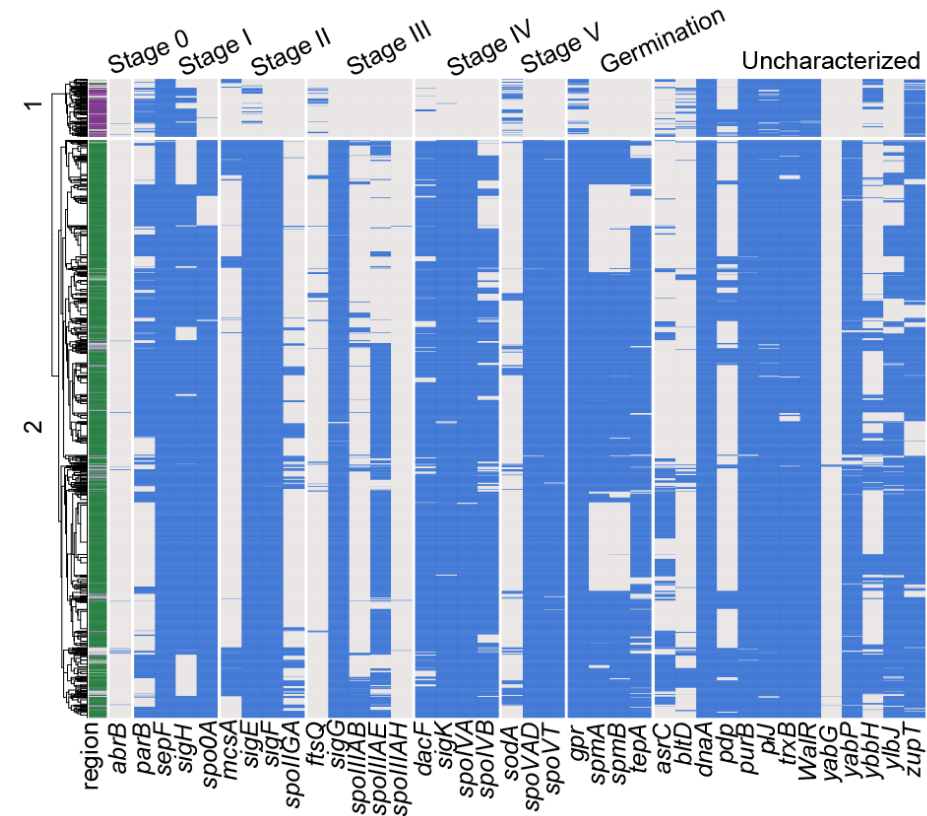
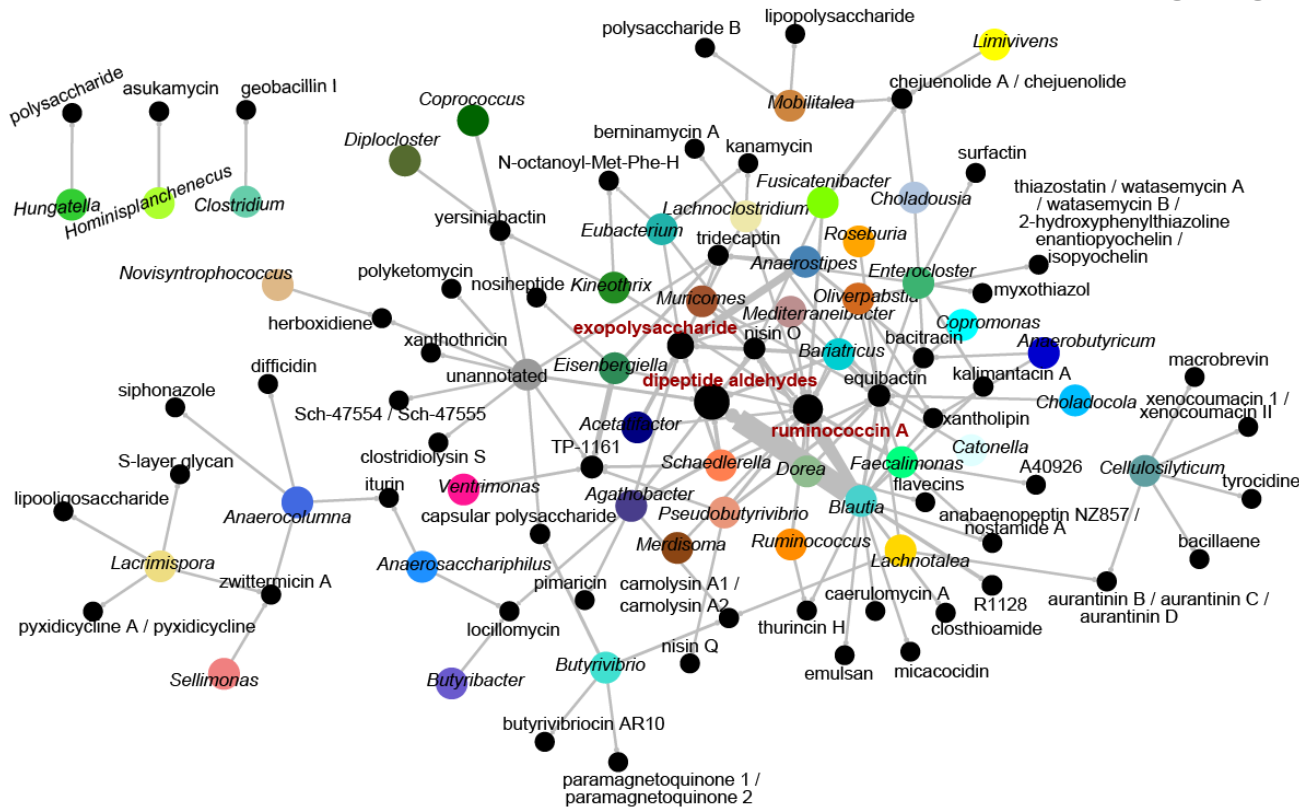


Synthesis of butyric acid and propionic acid

- 40.80% of the genomes has a complete butyrate-producing pathway, which is basically one type
- Almost all genomes have a complete propionate-producing pathway, but the types of propionate-producing pathways are different. *Coproccoccus* has a more diverse propionate-producing pathway.
- Due to different lineages within the same genus, the completeness and type of the butyrate synthesis pathway are different, such as *Coproccoccus*

Results

The diversity of species taxonomy, body habitats, and geography shapes the various functions of Lachnospiraceae



Secondary metabolite synthesis

- Dipeptide aldehyde: a highly effective protein inhibitor
- RumA: useful in the clinical treatment of pathogenic *Clostridium* spp. infections
- Extracellular polysaccharides: can serve as a substrate for cross-feeding, stimulate the growth of specific beneficial bacteria

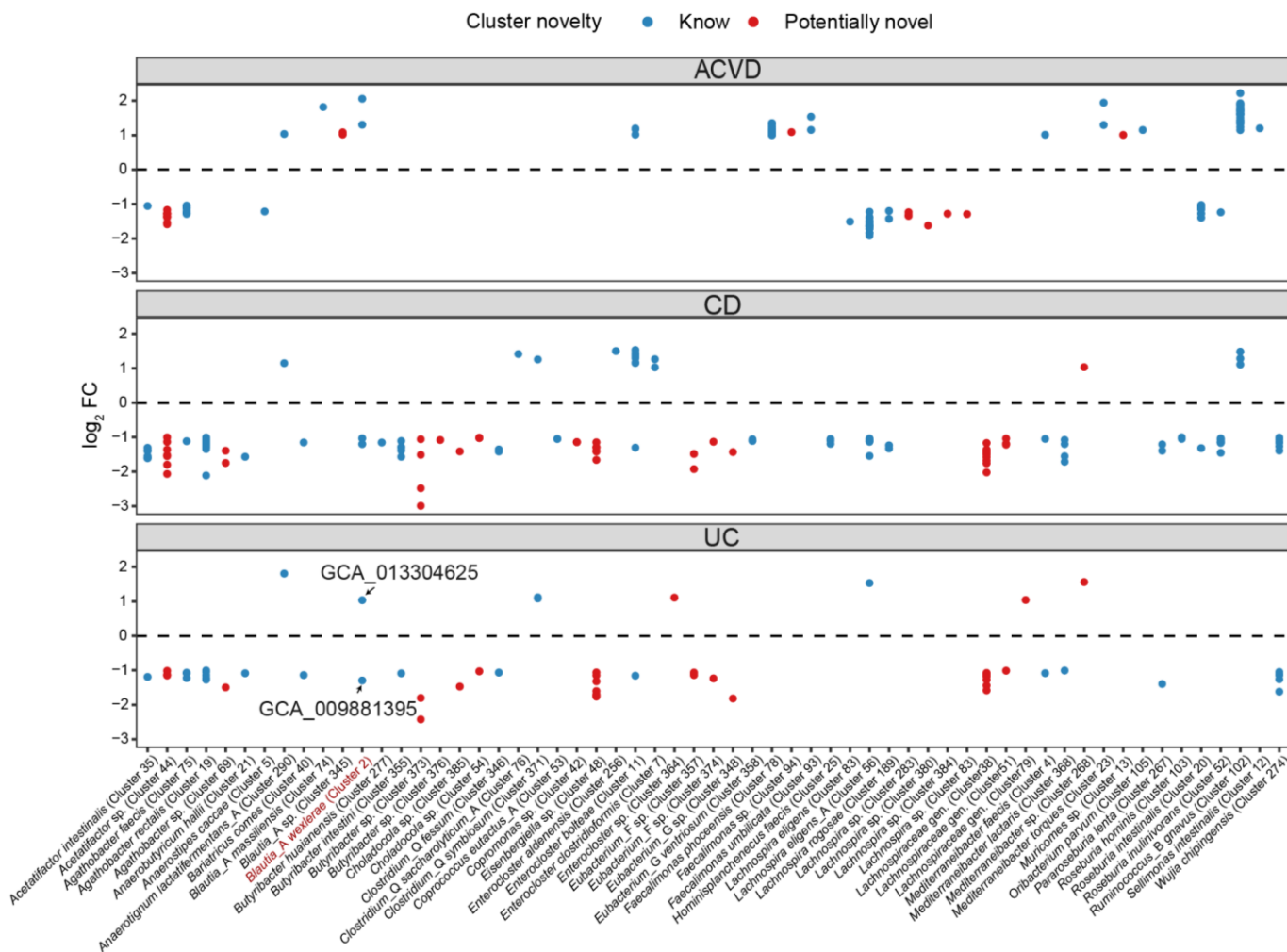
sporulation

- numerous deletions of characteristic genes in the genomes of animal rumen origin and the human oral habitat



Results

Investigating associations of the Lachnospiraceae clusters with human diseases



Genome level

- Different genomes in the same cluster have different distributions in healthy and disease cohorts



Summary

- Comprehensive genome analysis reveals underestimated species diversity and distinct functions of Lachnospiraceae.
- Cataloging 1.5M genes highlights Lachnospiraceae's significant role in the human gut microbiota, with potential novel species contributing.
- Lachnospiraceae demonstrates a vast potential for synthesizing short-chain fatty acid (SCFA), producing secondary metabolites, and forming spores, which is promising for future studies and applications.
- The abundance of Lachnospiraceae correlates inversely with diseases like atherosclerotic cardiovascular disease (ACVD) and inflammatory bowel disease (IBD), indicating a potential protective role.

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