



Enhancement of gut barrier integrity by a *Bacillus subtilis* secreted metabolite through the GADD45A-Wnt/ β -catenin pathway

Shiqi Liu¹, Peiran Cai¹, Wenjing You¹, Mingshun Yang¹, Yuang Tu¹, Yanbing Zhou¹, Teresa G. Valencak¹, Yingping Xiao², Yizhen Wang¹, Tizhong Shan¹

¹Zhejiang University College of Animal Sciences

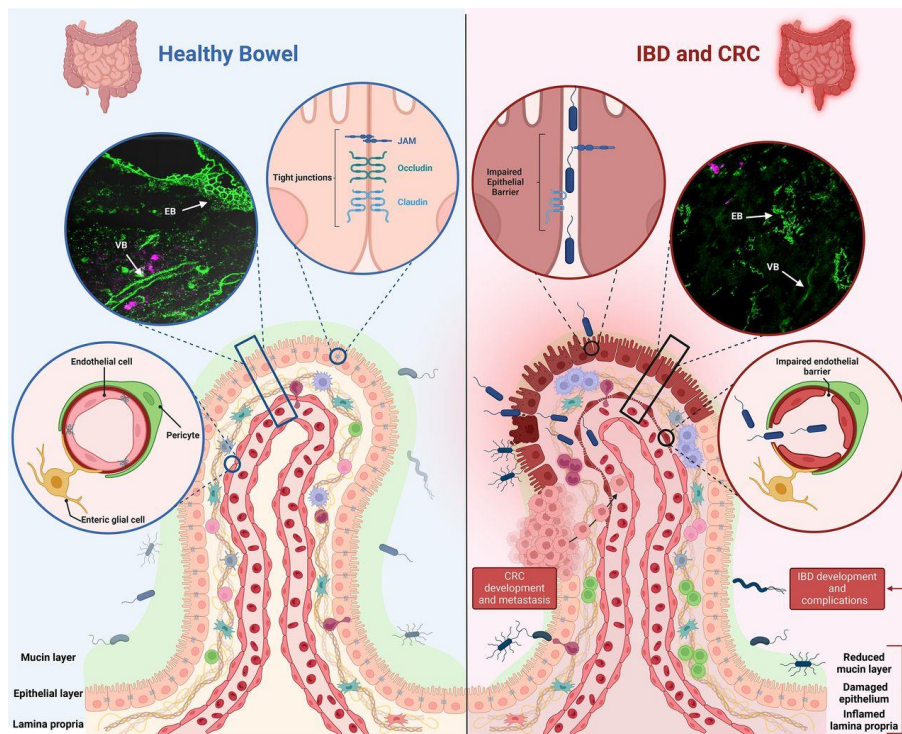
²Zhejiang Academy of Agricultural Sciences



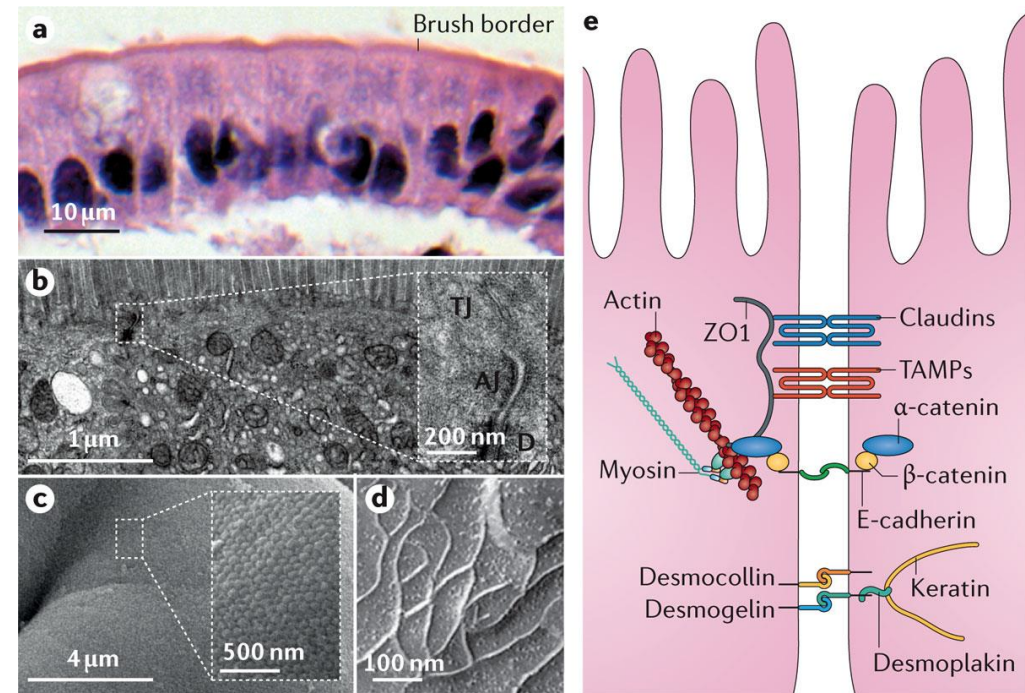
Shiqi Liu, Peiran Cai, Wenjing You, Mingshun Yang, Yuang Tu, Yanbing Zhou, Teresa G, Yingping Xiao, Yizhen Wang, Tizhong Shan. 2025. Enhancement of gut barrier integrity by a *Bacillus subtilis* secreted metabolite through the GADD45A-Wnt/ β -catenin pathway. *iMeta* 4: e70005. <https://doi.org/10.1002/imt2.70005>

Background

- ❑ Inflammatory bowel disease (IBD) is a major challenge to global health, characterized by intestinal inflammation, impaired barrier function, and dysbiosis, with limited treatment options currently available. In animal production, damage to the intestinal barrier directly affects intestinal health and production efficiency.
- ❑ Probiotics have shown great potential in maintaining intestinal homeostasis and treating intestinal diseases. However, the function and underlying mechanisms of a novel strain of *Bacillus subtilis* (*B. subtilis*) in alleviating acute intestinal inflammatory injury remain unclear.

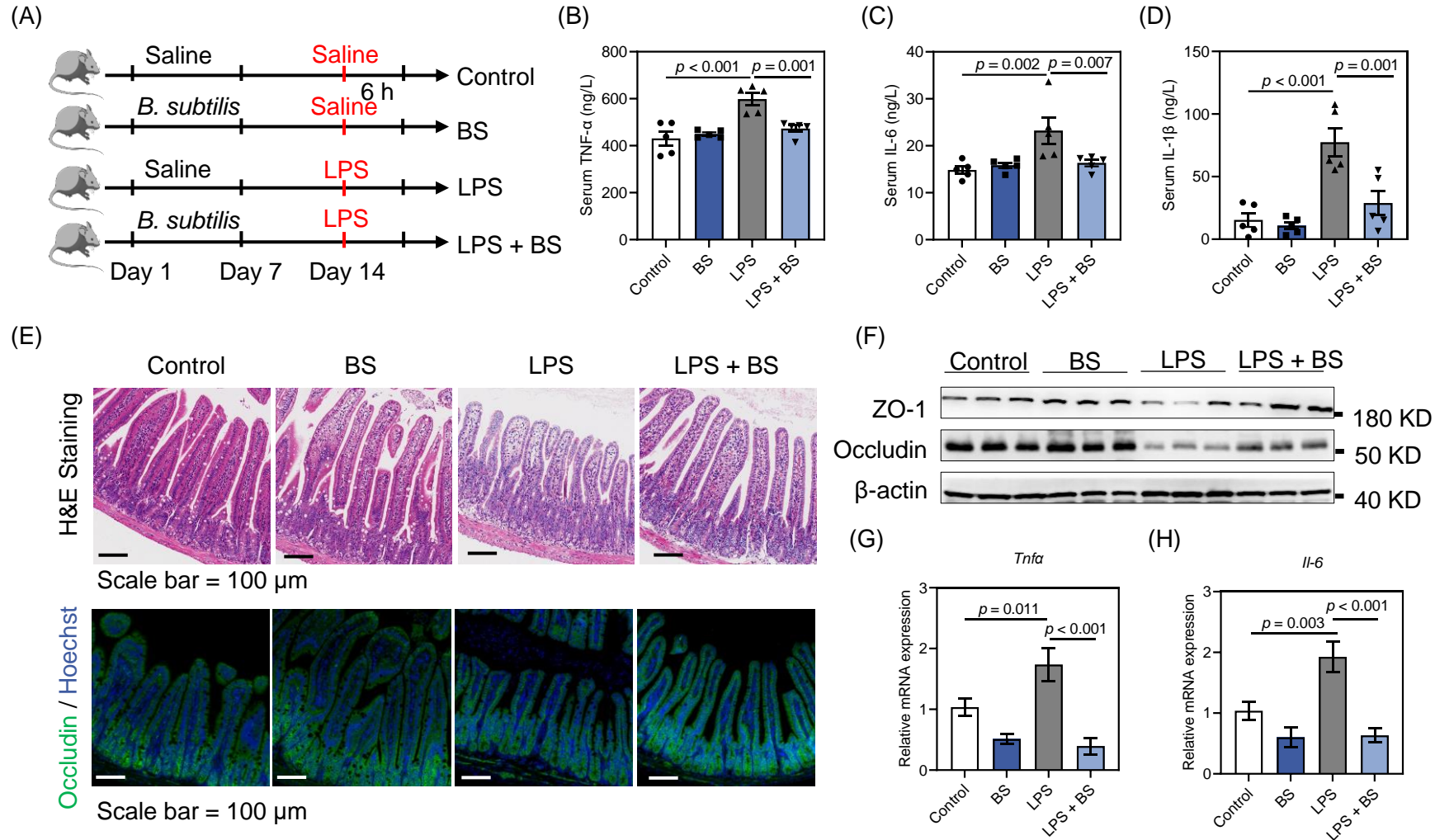


(Gut, 2024)



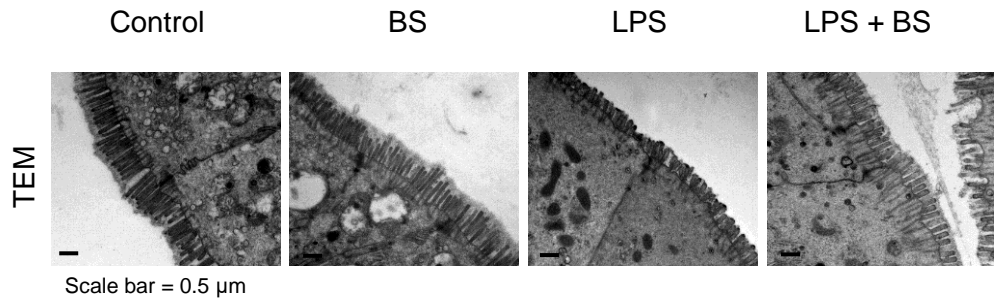
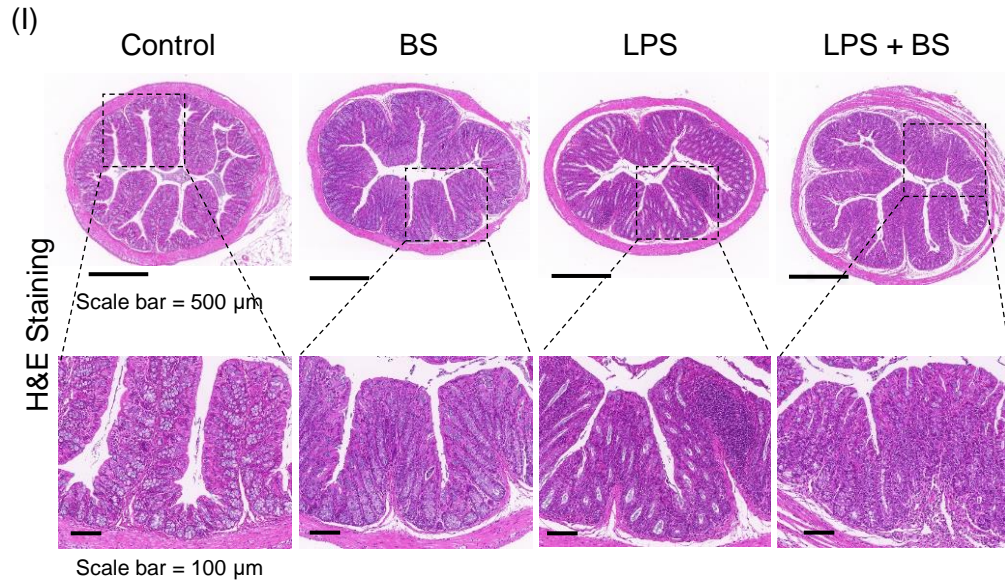
Results

- Bacillus subtilis* alleviates LPS-induced acute intestinal inflammation and epithelial barrier damage.

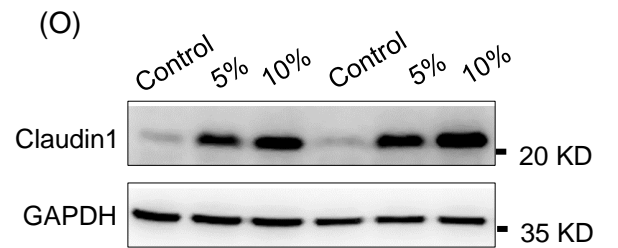
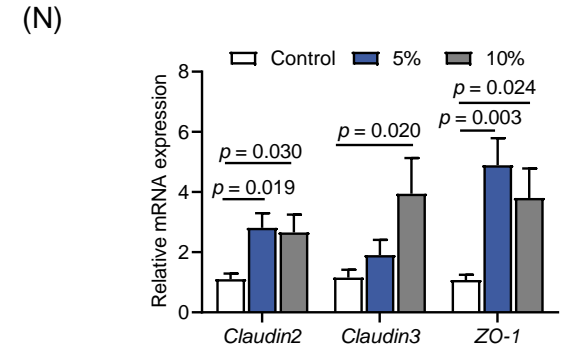
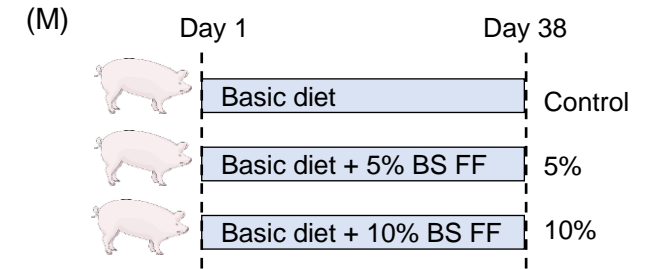
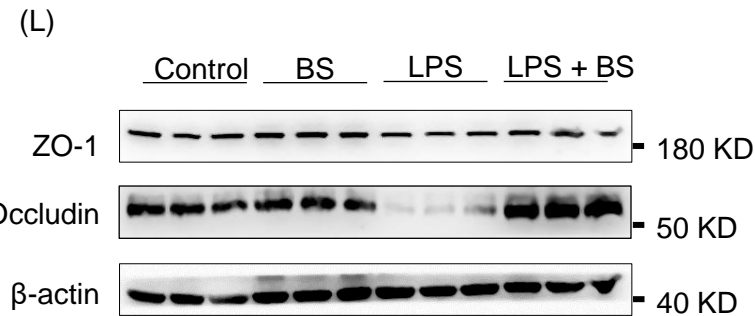
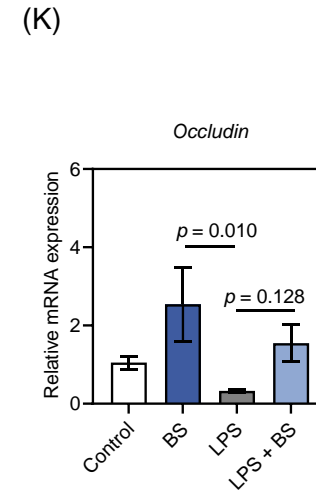
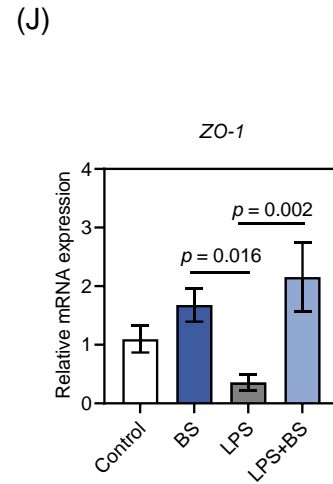


Results

□ *Bacillus subtilis* alleviates LPS-induced acute intestinal inflammation and epithelial barrier damage.



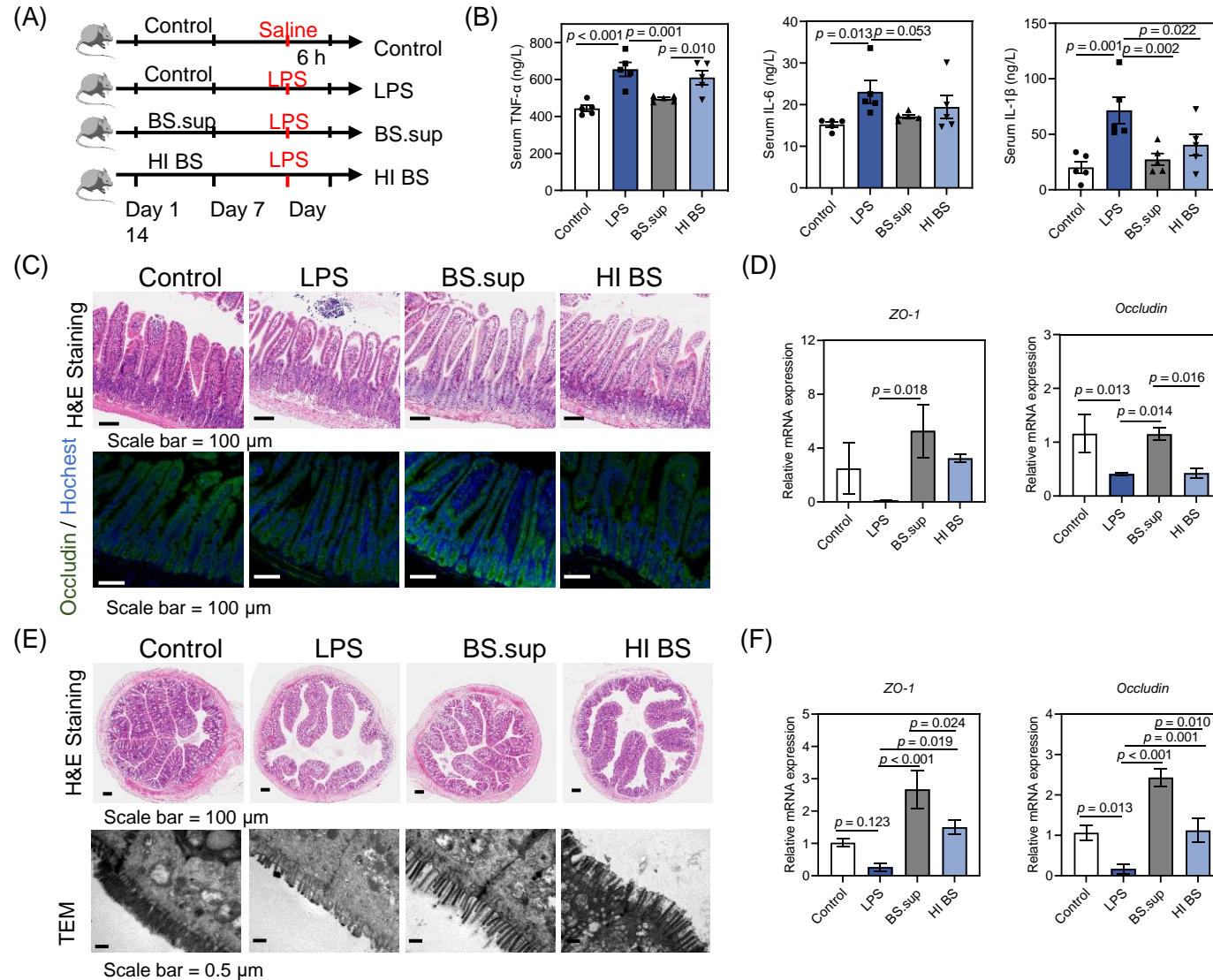
In mice



In pigs

Results

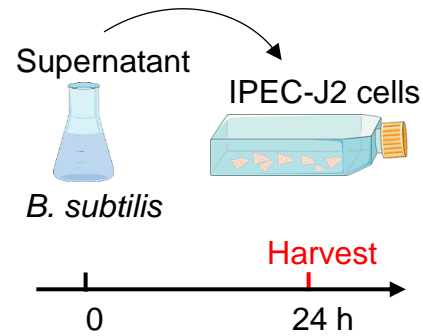
- The culture supernatant of *Bacillus subtilis* can mimic the effects of live bacteria when administered orally to mice, maintaining the integrity of the intestinal barrier.



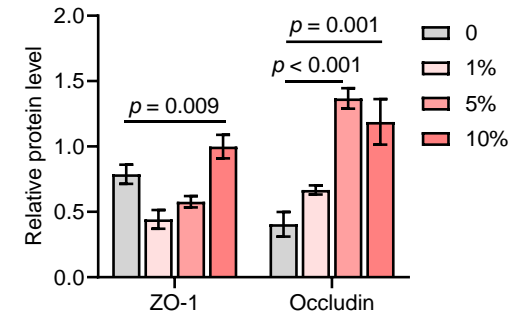
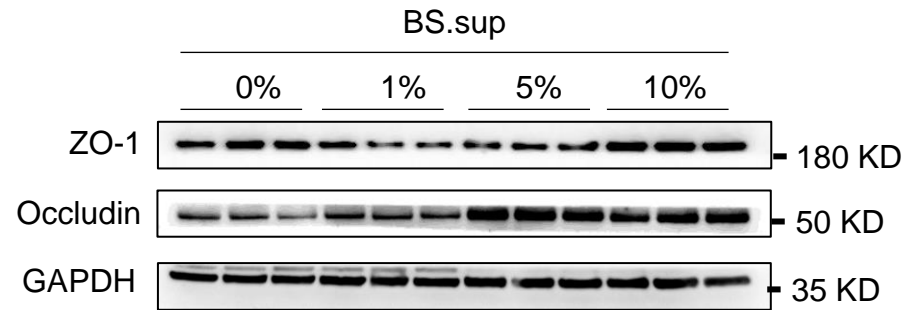
Results

- The protective effect of *Bacillus subtilis* against LPS-induced acute intestinal injury is mainly related to its metabolites.

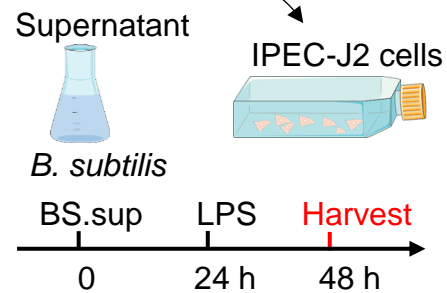
(G)



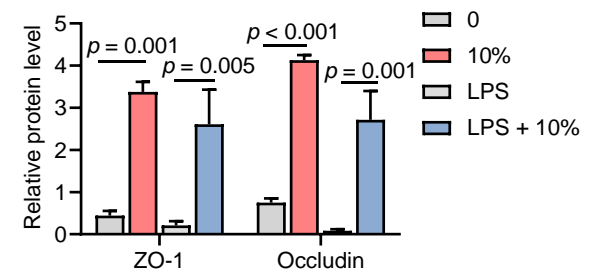
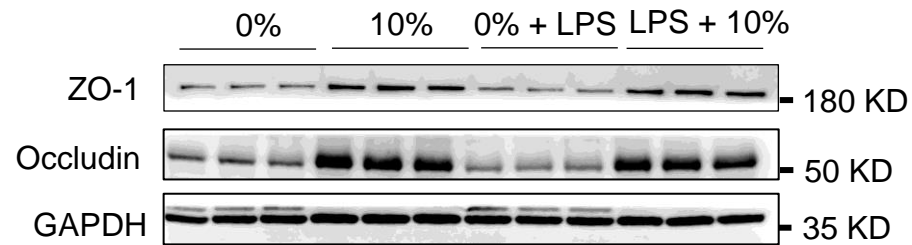
(H)



(I)

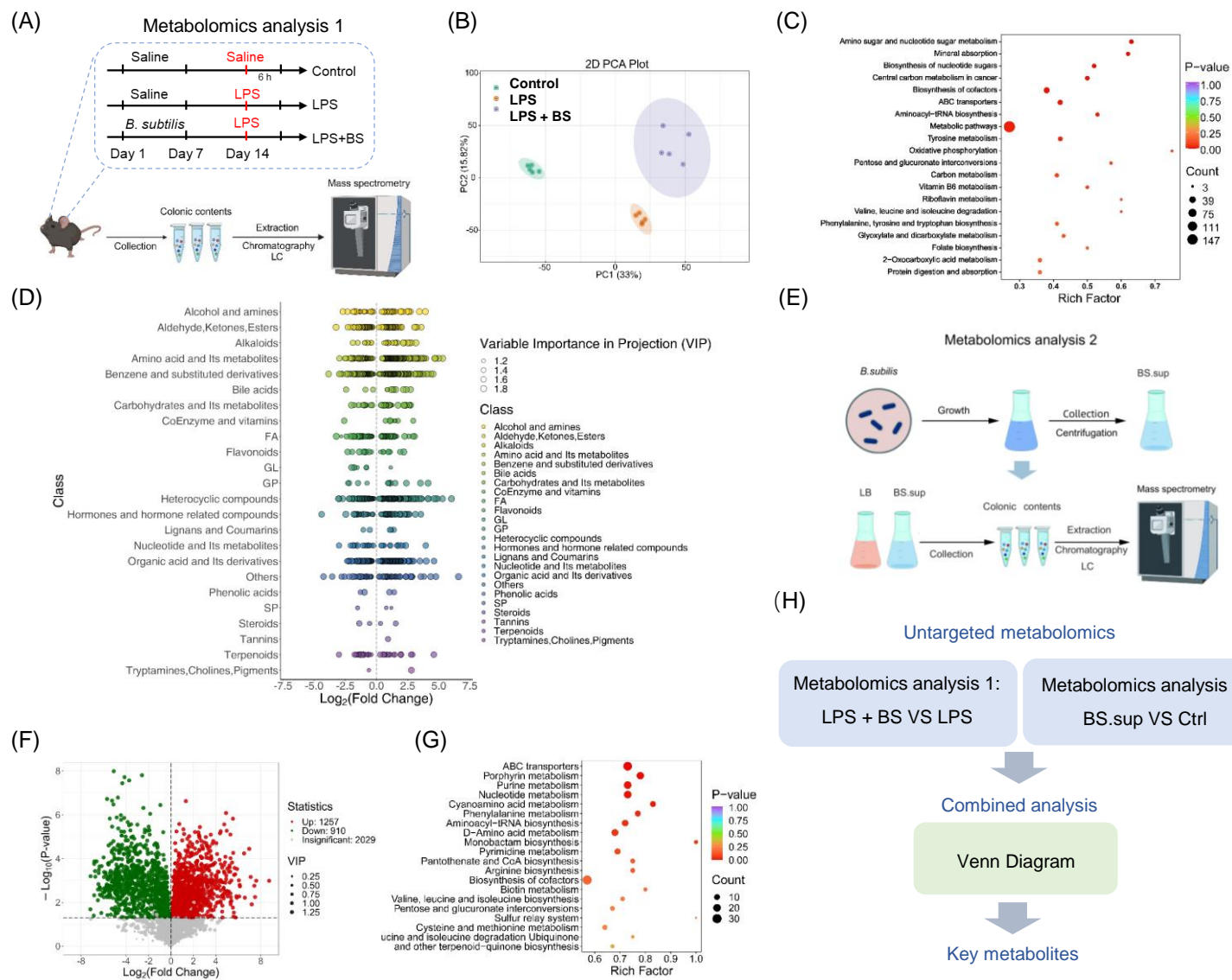


(J)



Results

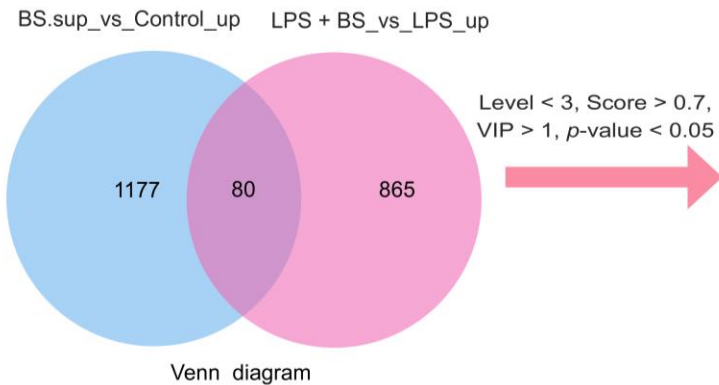
□ *Bacillus subtilis* alters the metabolic profiles of the intestine.



Results

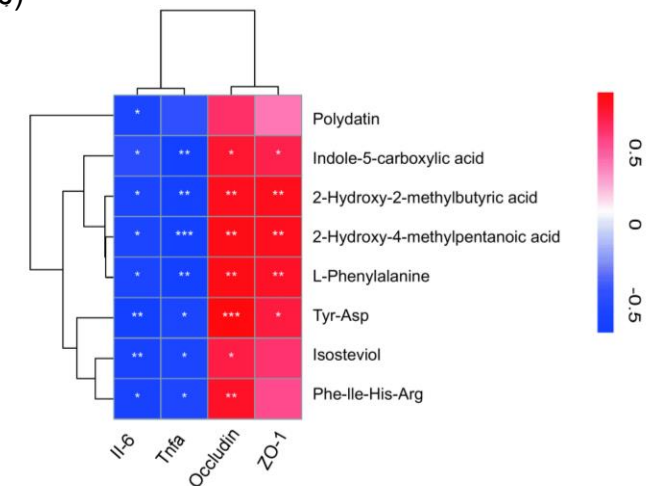
- Eight potential key metabolites that may regulate intestinal barrier function were identified: HMP, 2-hydroxy-2-methylbutyric acid (HMBA), polydatin, indole-5-carboxylic acid (ICA), isosteviol, L-phenylalanine (L-Phe), Tyr-Asp, and Phe-Ile-His-Arg.

(I)



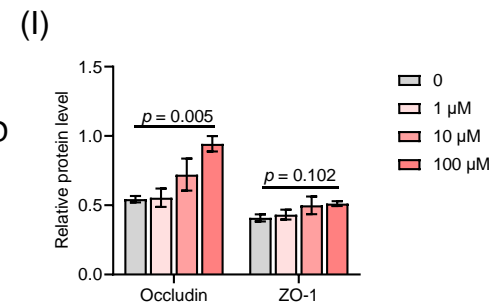
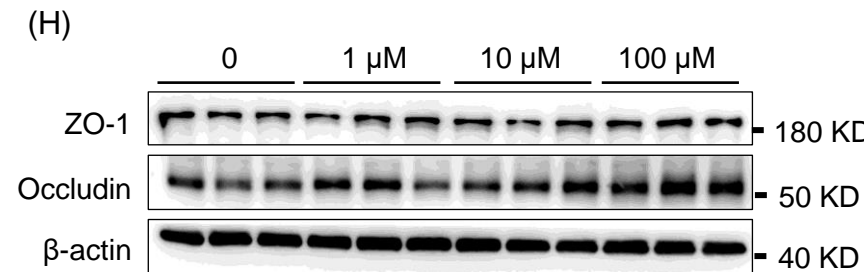
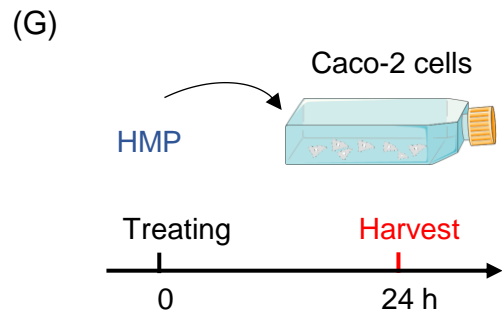
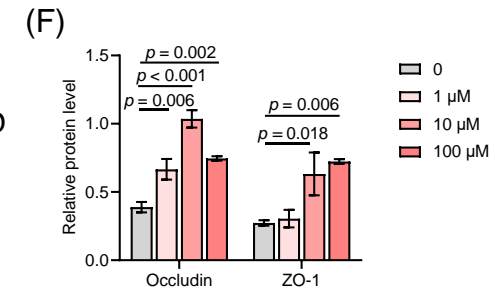
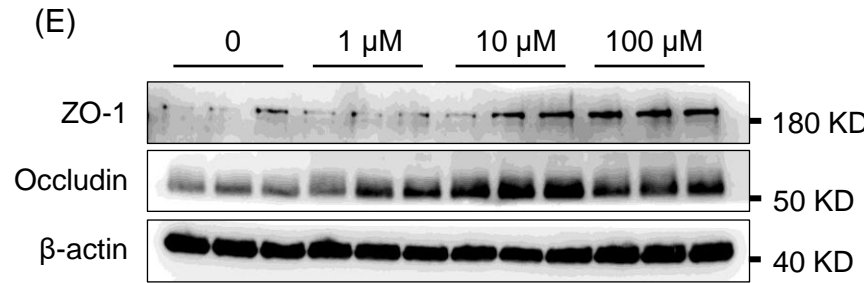
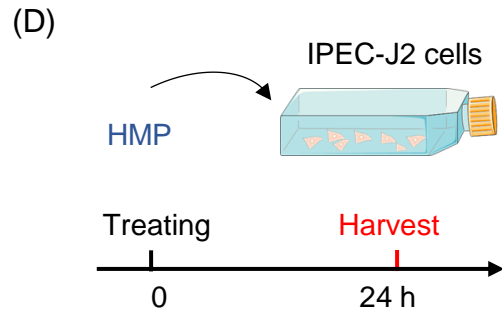
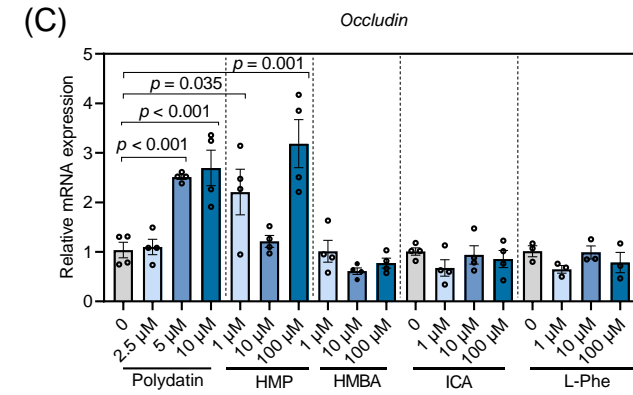
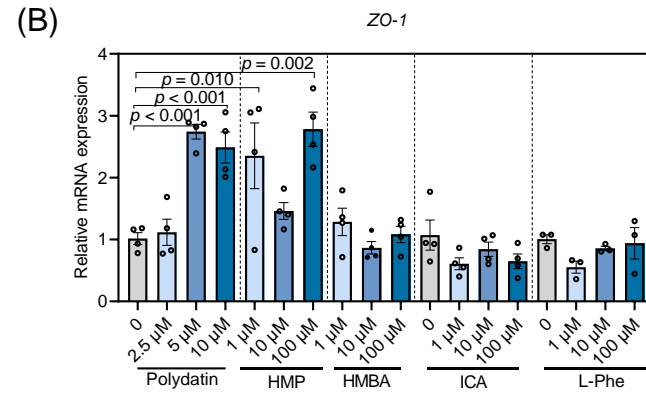
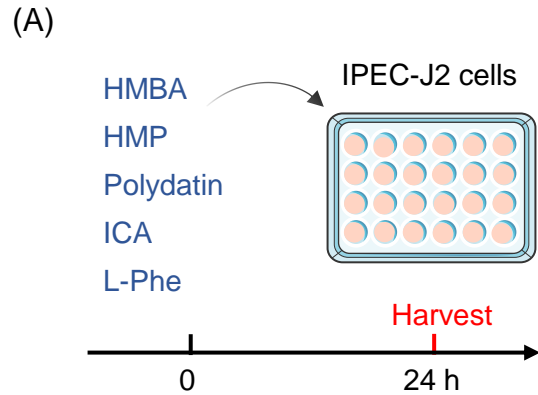
Key metaboltes	Level	Score	VIP	p-value
Polydatin	2	0.836	1.824120548	0.000161384
2-Hydroxy-4-methylpentanoic acid	1a	0.9587	1.768467265	0.005869386
2-Hydroxy-2-methylbutyric acid	1a	0.9289	1.685298765	0.014059252
Isosteviol	1b	0.7566	1.814884198	0.002805972
Indole-5-carboxylic acid	1b	0.7325	1.709865084	0.006898485
L-Phenylalanine	1a	0.9725	1.718958617	0.012859551
Tyr-Asp	1b	0.7844	1.695183498	0.000243087
Phe-Ile-His-Arg	2	0.9398	1.751870369	0.006246878

(J)



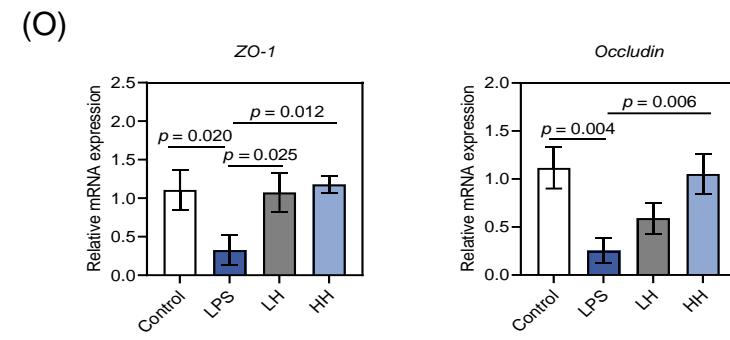
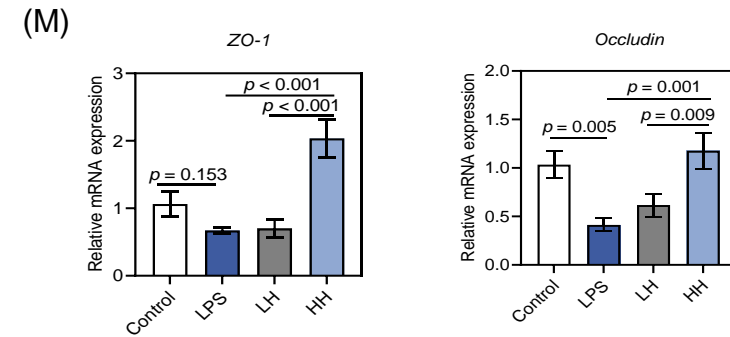
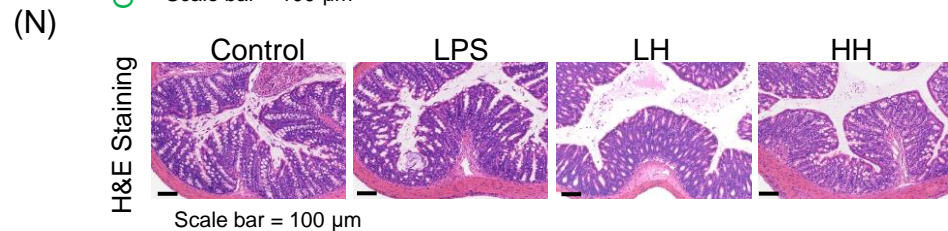
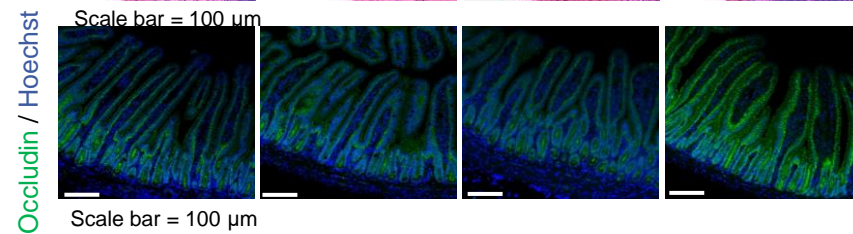
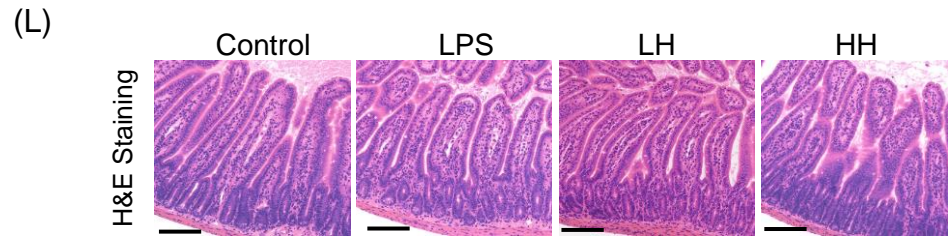
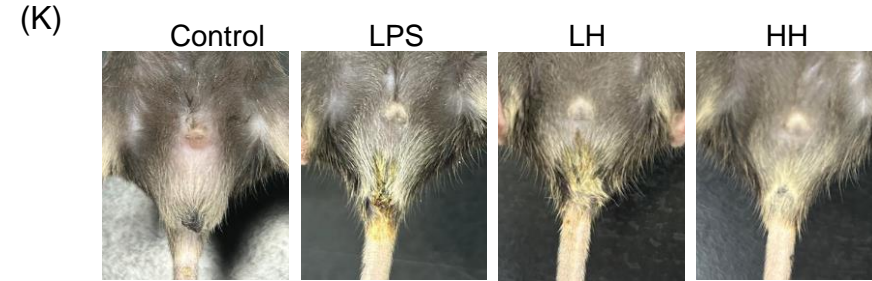
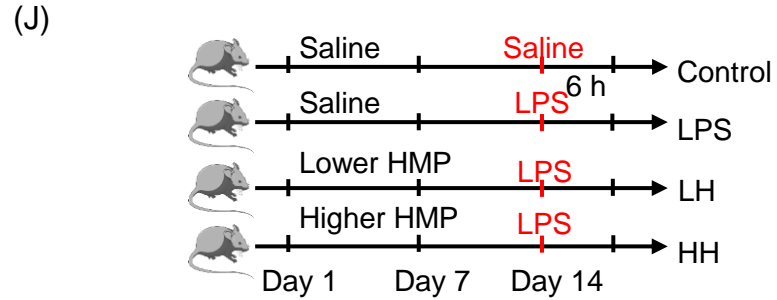
Results

□ HMP significantly promotes the expression of tight junction proteins in intestinal epithelial cells *in vitro*.



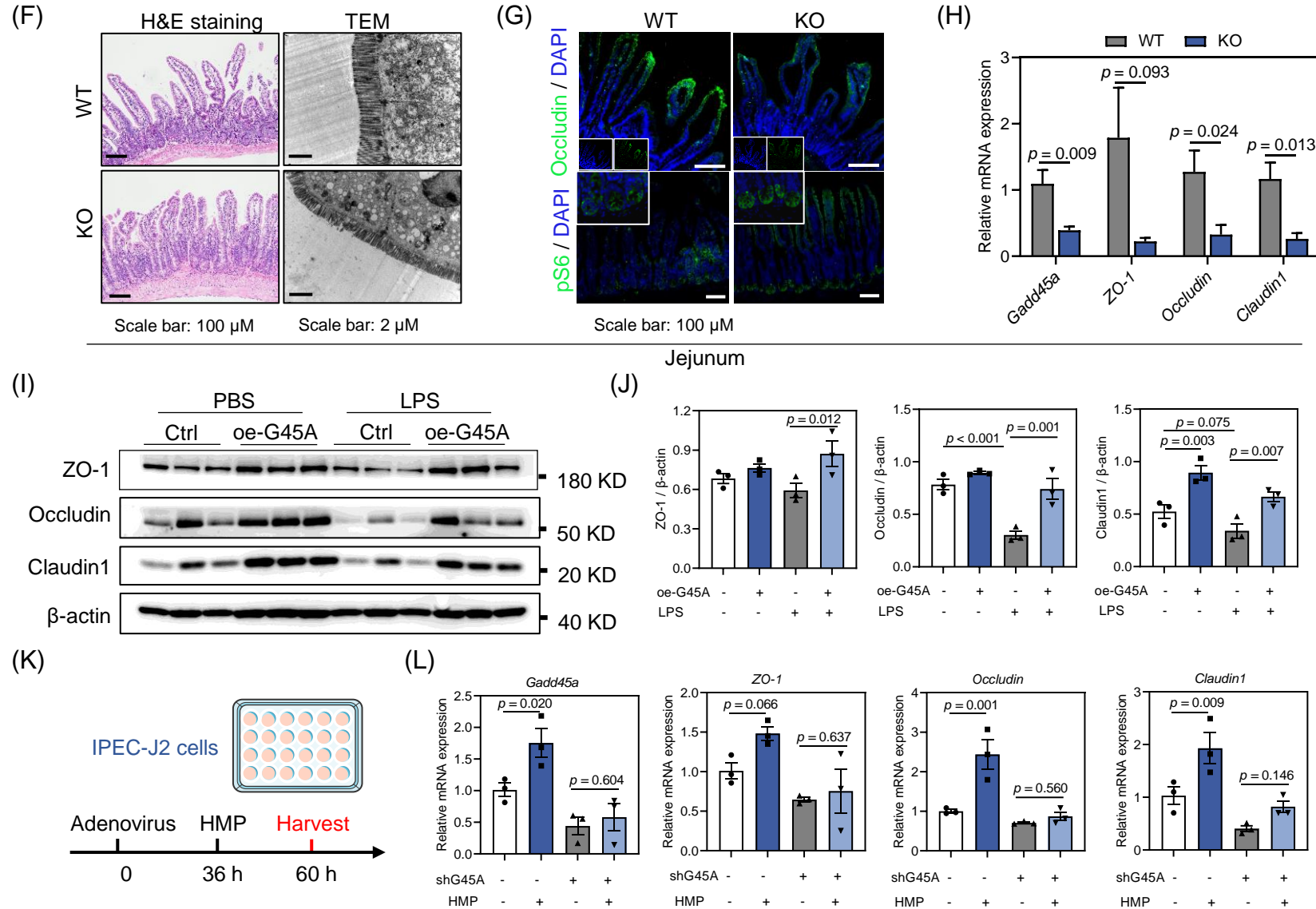
Results

- HMP can restore the expression of tight junction proteins after LPS treatment and alleviate intestinal epithelial barrier damage.

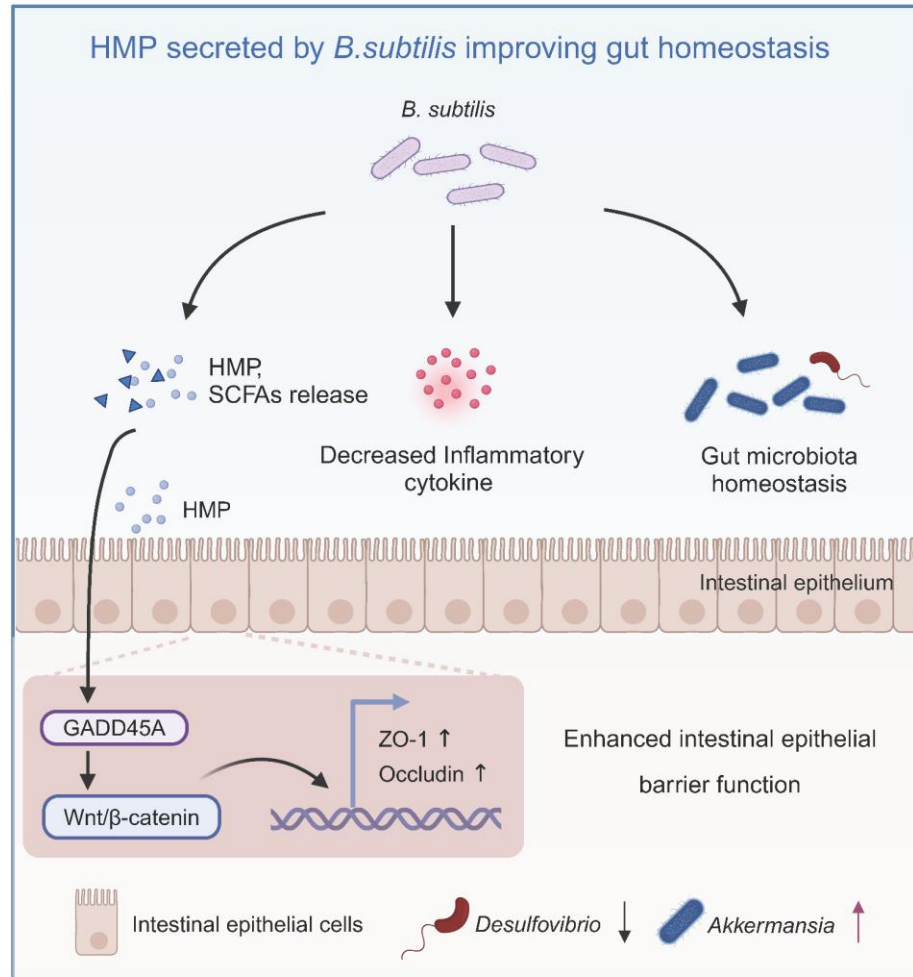


Results

□ The regulation of intestinal barrier function by HMP is dependent on GADD45A.



Conclusion

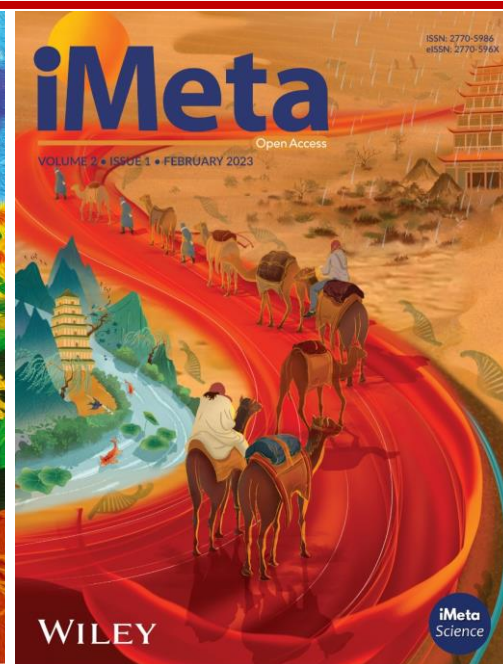


- ❑ *B. subtilis* can protect the organism from LPS-induced acute intestinal injury and inflammation;
- ❑ *B. subtilis* is capable of ameliorating LPS-induced intestinal microbiota imbalance and increasing the relative abundance of *Akkermansia*;
- ❑ HMP secreted by *B. subtilis* can enhance the integrity of the intestinal epithelial barrier;
- ❑ GADD45A is a novel regulatory factor of the intestinal epithelial barrier;
- ❑ HMP regulates the integrity of the intestinal epithelial barrier through the GADD45A-Wnt/β-catenin pathway.

Shiqi Liu, Peiran Cai, Wenjing You, Mingshun Yang, Yuang Tu, Yanbing Zhou, Teresa G, Yingping Xiao, Yizhen Wang, Tizhong Shan. 2025. Enhancement of gut barrier integrity by a *Bacillus subtilis* secreted metabolite through the GADD45A-Wnt/β-catenin pathway. *iMeta* 4: e70005. <https://doi.org/10.1002/imt2.70005>


iMeta: Integrated meta-omics to change the understanding of the biology and environment


WILEY



“***iMeta***” is a Wiley partner journal launched by iMeta Science Society in 2022, first **impact factor (IF) 23.8 in 2024, ranking 2/161 in the microbiology**. It aims to publish innovative and high-quality papers with broad and diverse audiences. **Its scope is similar to *Nature Biotechnology, Nature Methods, Nature Microbiology, Nature Food, etc.*** Its unique features include video abstract, bilingual publication, and social media dissemination, with more than 600,000 followers. It has published 220+ papers and been cited for 5600+ times, and has been indexed by **SCIE / WOS, PubMed, Google Scholar, and Scopus**.

“***iMetaOmics***” is a sister journal of “***iMeta***” launched in 2024, with a **target IF>10, and its scope is similar to *Nature Communications, Microbiome, ISME J, Nucleic Acids Research, Briefings in Bioinformatics, etc.*** All contributes are welcome!

 Society: <http://www.imeta.science>
Publisher: <https://wileyonlinelibrary.com/journal/imeta>
Submission: <https://wiley.atyponrex.com/journal/IMT2>
<https://wiley.atyponrex.com/journal/IMO2>

 office@imeta.science
imetaomics@imeta.science

 [Promotion Video](#)

 [iMetaScience](#)

 [iMetaScience](#)