

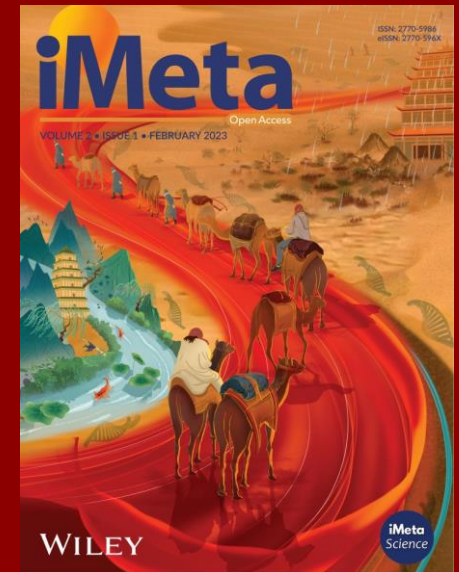


新型枯草芽孢杆菌分泌的代谢产物通过GADD45A-Wnt/ β -catenin途径增强肠道屏障的完整性

刘事奇¹, 蔡沛燃¹, 有文静¹, 杨明顺¹, 涂羽昂¹, 周炎冰¹,
Teresa G. Valencak¹, 肖英平², 汪以真¹, 单体中¹

¹浙江大学动物科学学院

²浙江省农业科学院

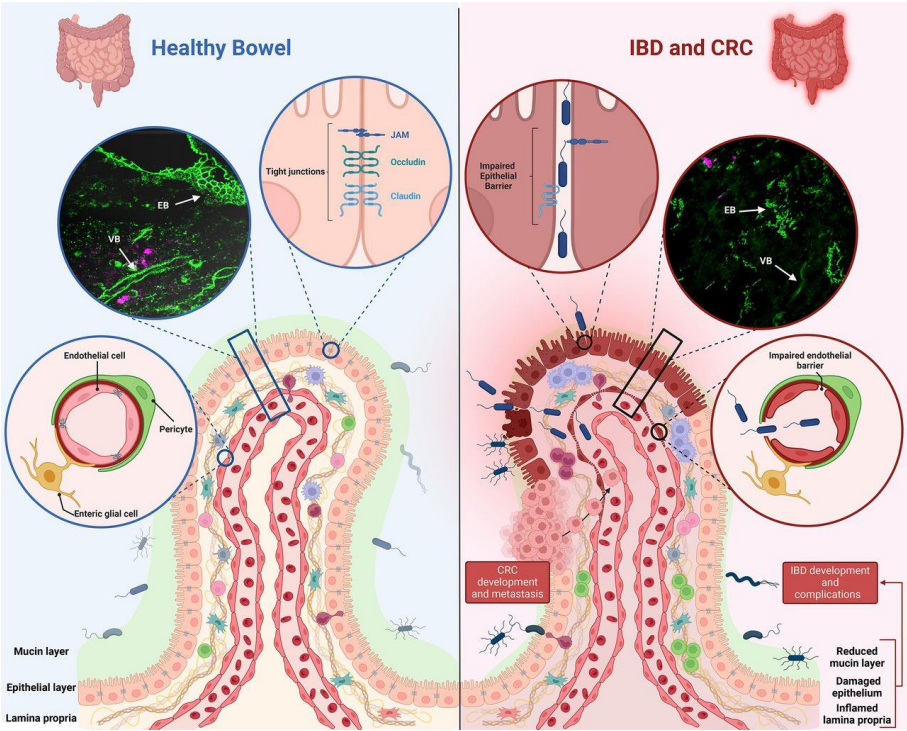


Shiqi Liu, Peiran Cai, Wenjing You, Mingshun Yang, Yuang Tu, Yanbing Zhou, Teresa G, Yingping Xiao, Yizhen Wang, Tizhong Shan. 2025. Enhancement of gut barrier integrity by a *Bacillus subtilis* secreted metabolite through the GADD45A-Wnt/ β -catenin pathway. *iMeta* 4: e70005. <https://doi.org/10.1002/imt2.70005>

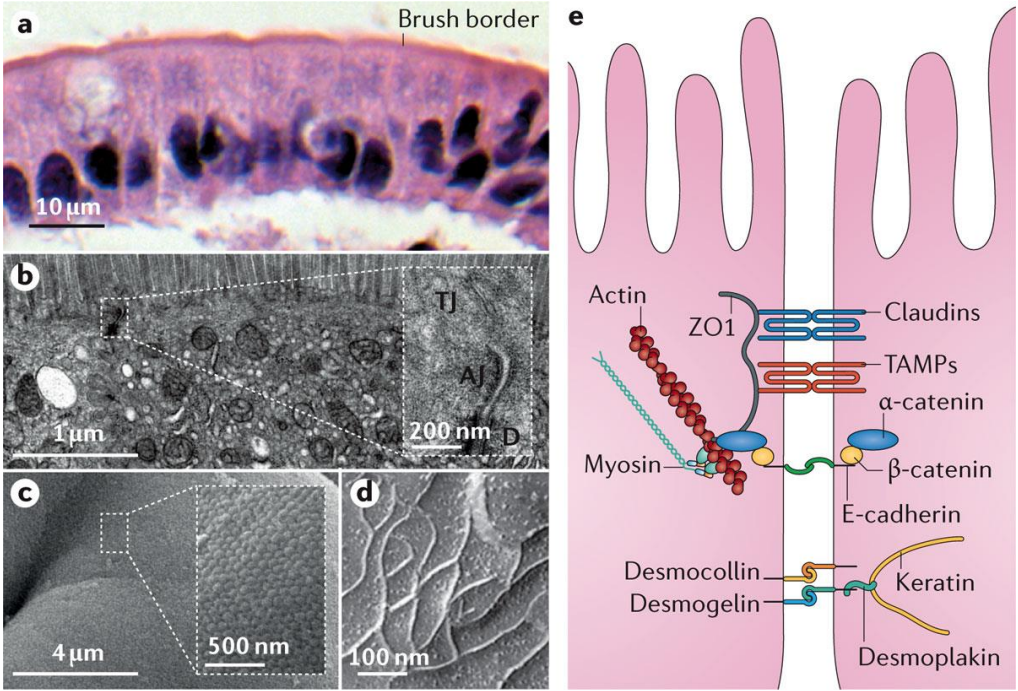


研究背景

- ❑ 炎症性肠病（IBD）是全球健康面临的重大挑战，其特征为肠道炎症、屏障功能受损及菌群失调，且目前针对IBD的治疗方法有限。在动物生产中，肠道屏障受损直接影响动物肠道健康和生产效益；
- ❑ 益生菌在维持肠道稳态和治疗肠道疾病中展示出巨大潜力。新型枯草芽孢杆菌（*B. subtilis*）缓解肠道急性炎症损伤的功能及其潜在的作用机制尚不清楚。



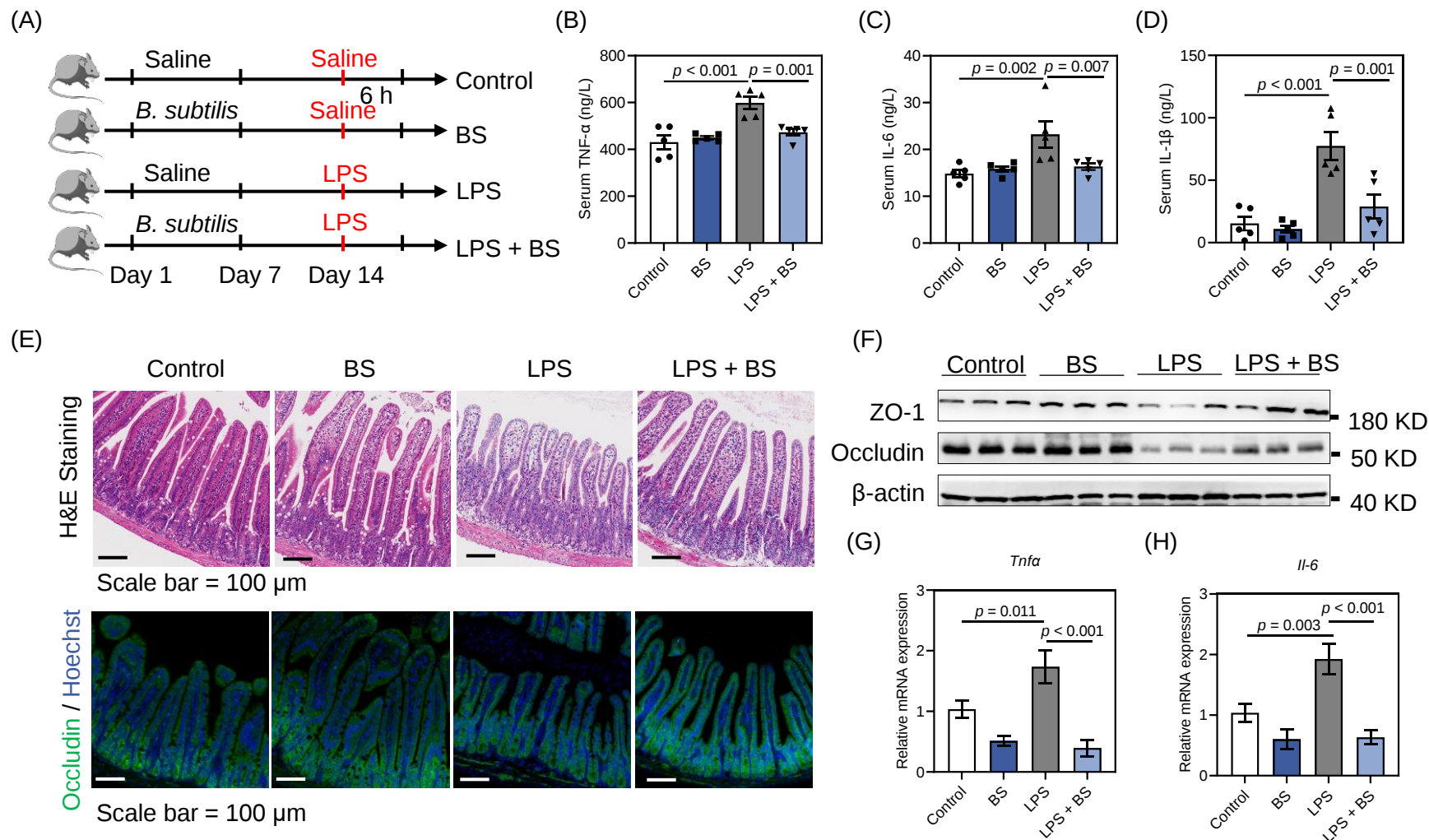
(Gut, 2024)



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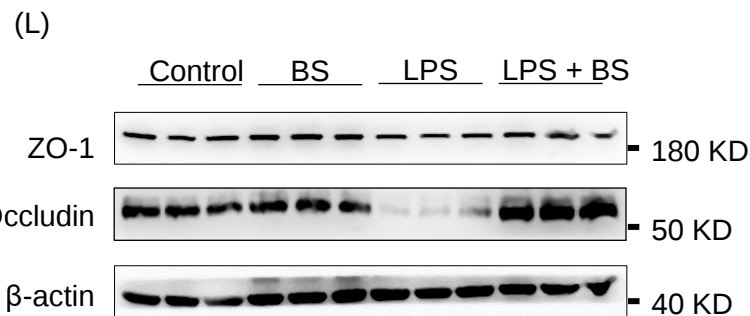
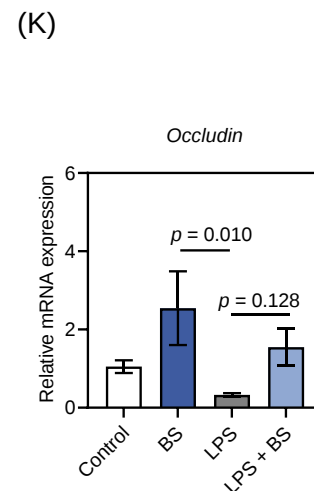
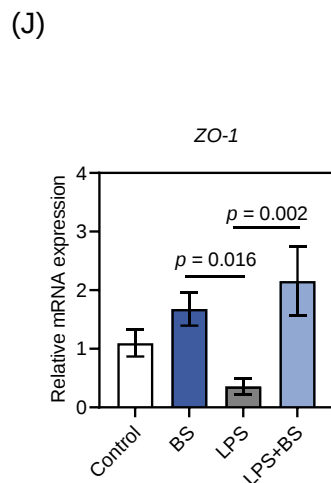
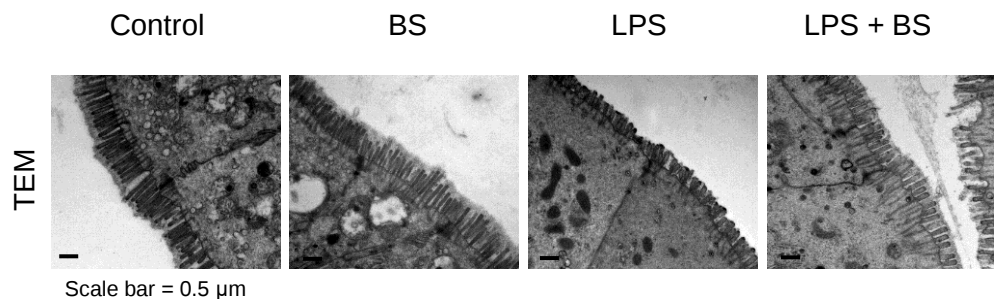
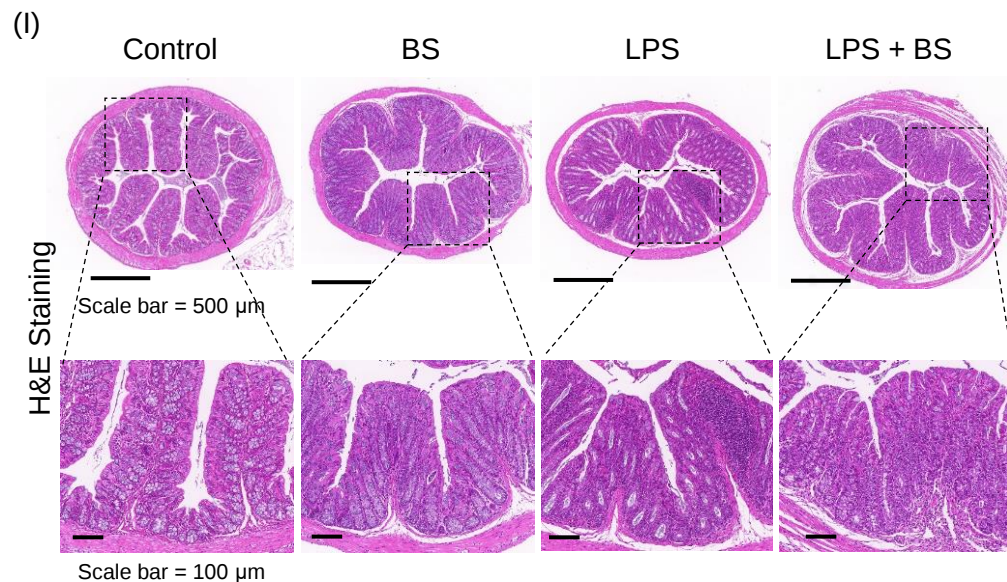
研究结果

□ 新型枯草芽孢杆菌缓解LPS诱导的急性肠道炎症和屏障损伤

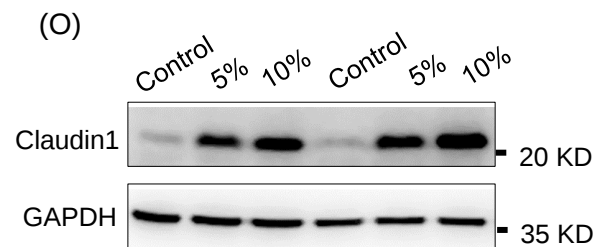
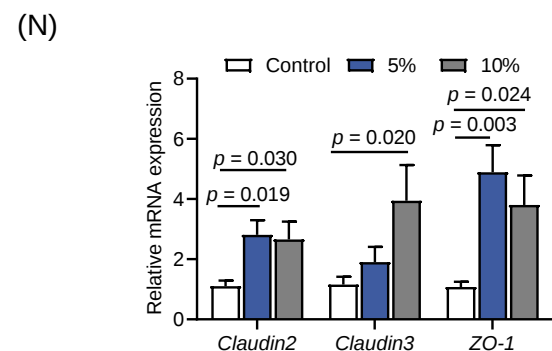
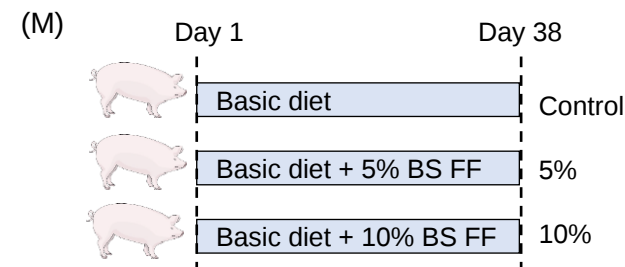


研究结果

□ 新型枯草芽孢杆菌缓解LPS诱导的肠道损伤、维持肠道屏障完整性



小鼠模型

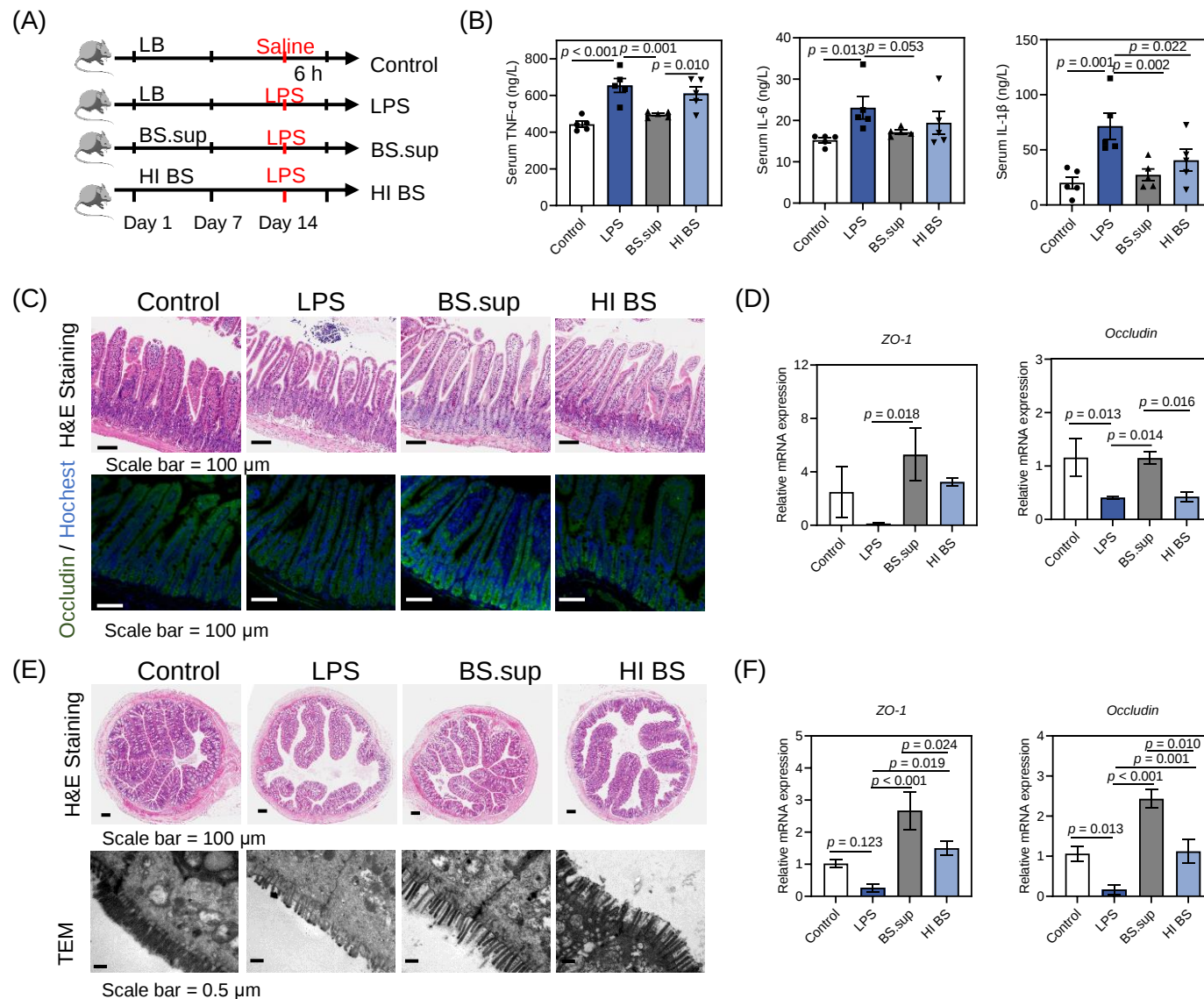


猪模型



研究结果

□ 新型枯草芽孢杆菌的培养基上清灌胃小鼠能模拟活菌的效果，可以维持肠道屏障完整性

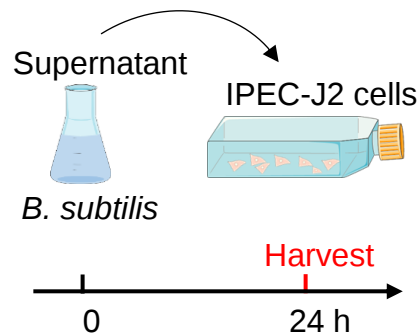




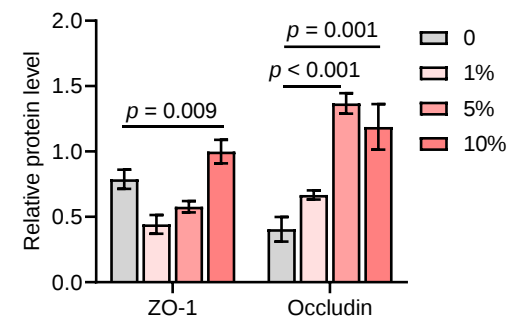
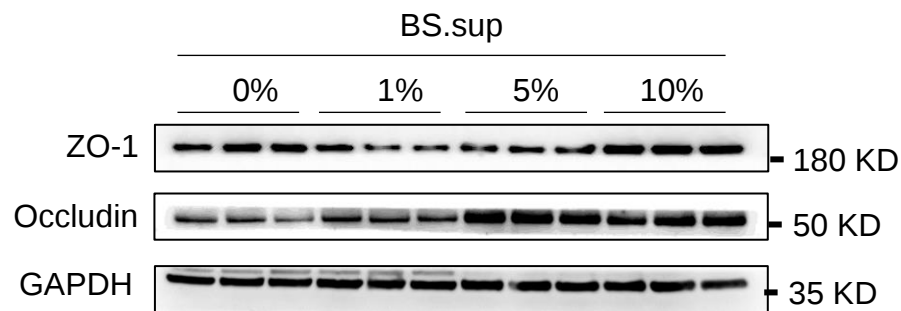
研究结果

枯草芽孢杆菌主要是通过代谢物发挥功能

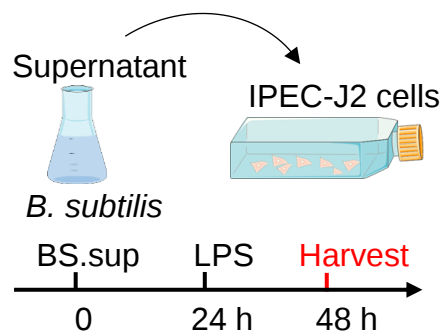
(G)



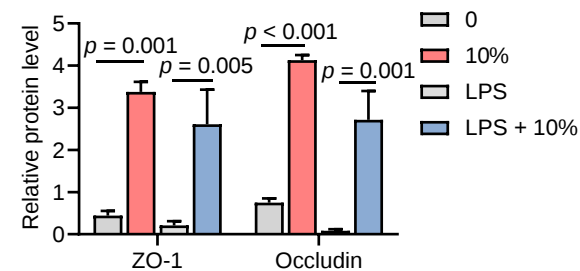
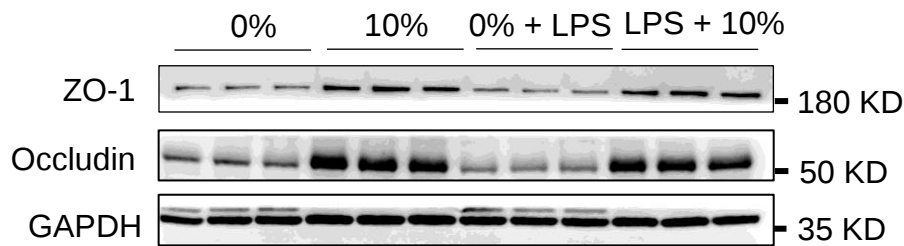
(H)



(I)

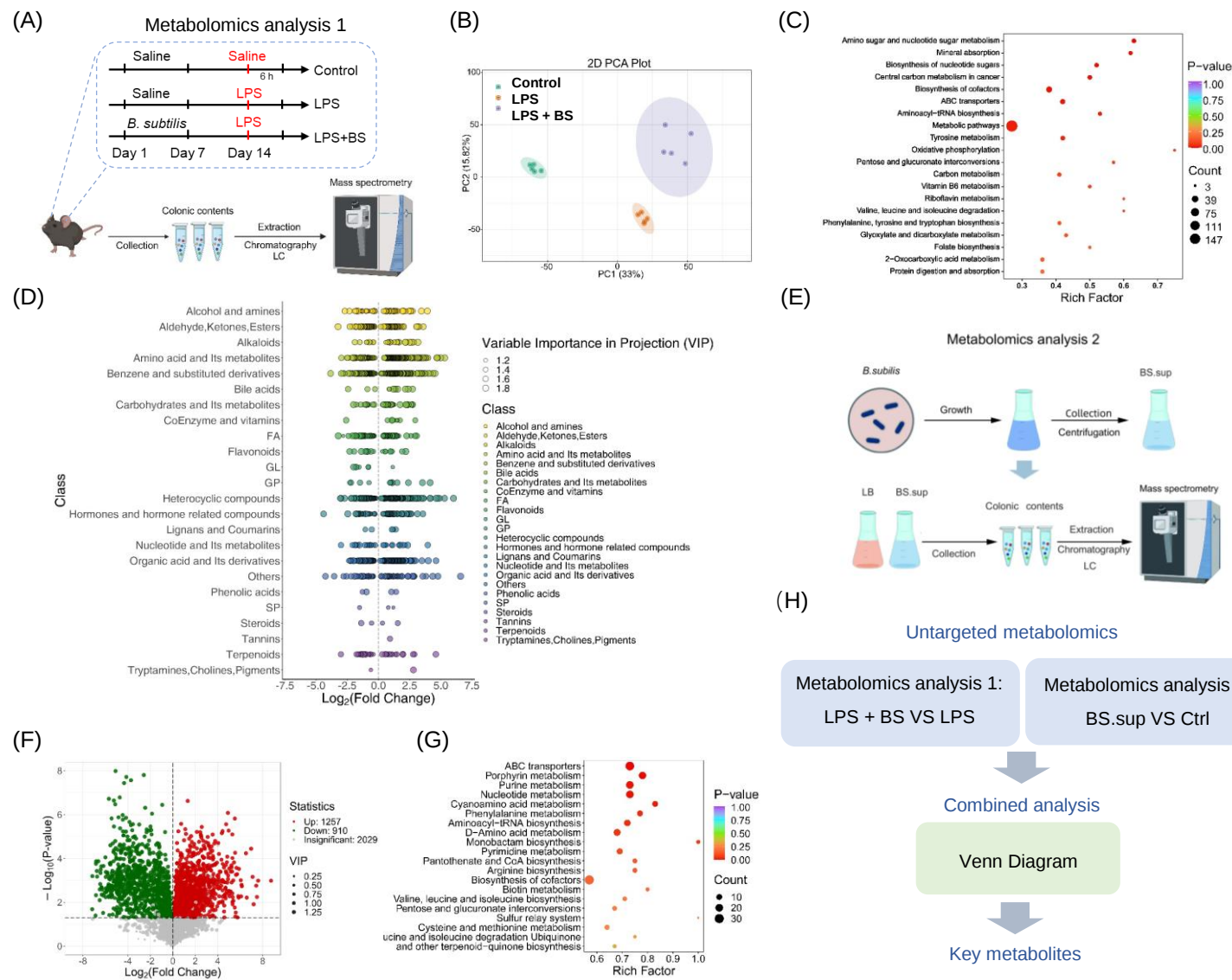


(J)



研究结果

枯草芽孢杆菌改变肠道代谢物的图谱



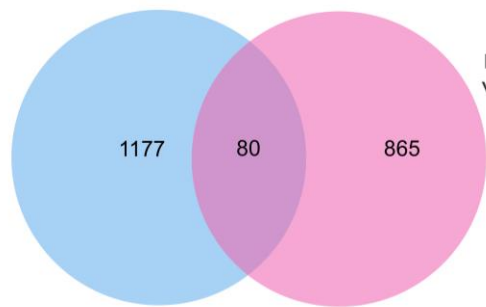


研究结果

- ❑ 鉴定得到8种可能具有调节肠道屏障功能的潜在关键代谢物：HMP、2-羟基-2-甲基丁酸 (HMBA)、虎杖苷、吲哚-5-羧酸 (ICA)、异甜菊醇、L-苯丙氨酸 (L-Phe)、Tyr-Asp和 Phe-Ile-His-Arg

(I)

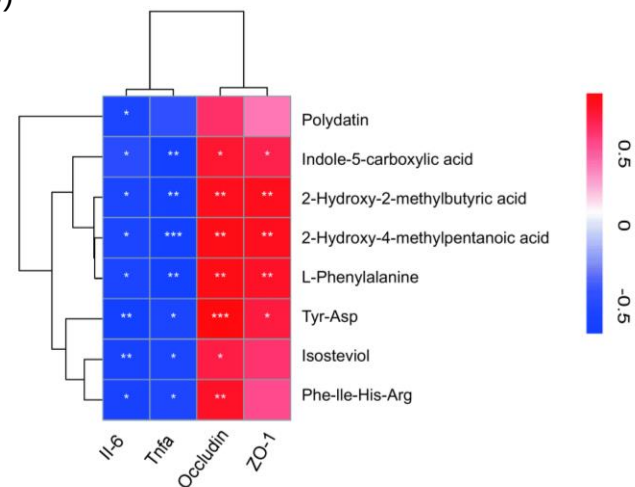
BS.sup_vs_Control_up LPS + BS_vs_LPS_up



Level < 3, Score > 0.7,
VIP > 1, *p*-value < 0.05

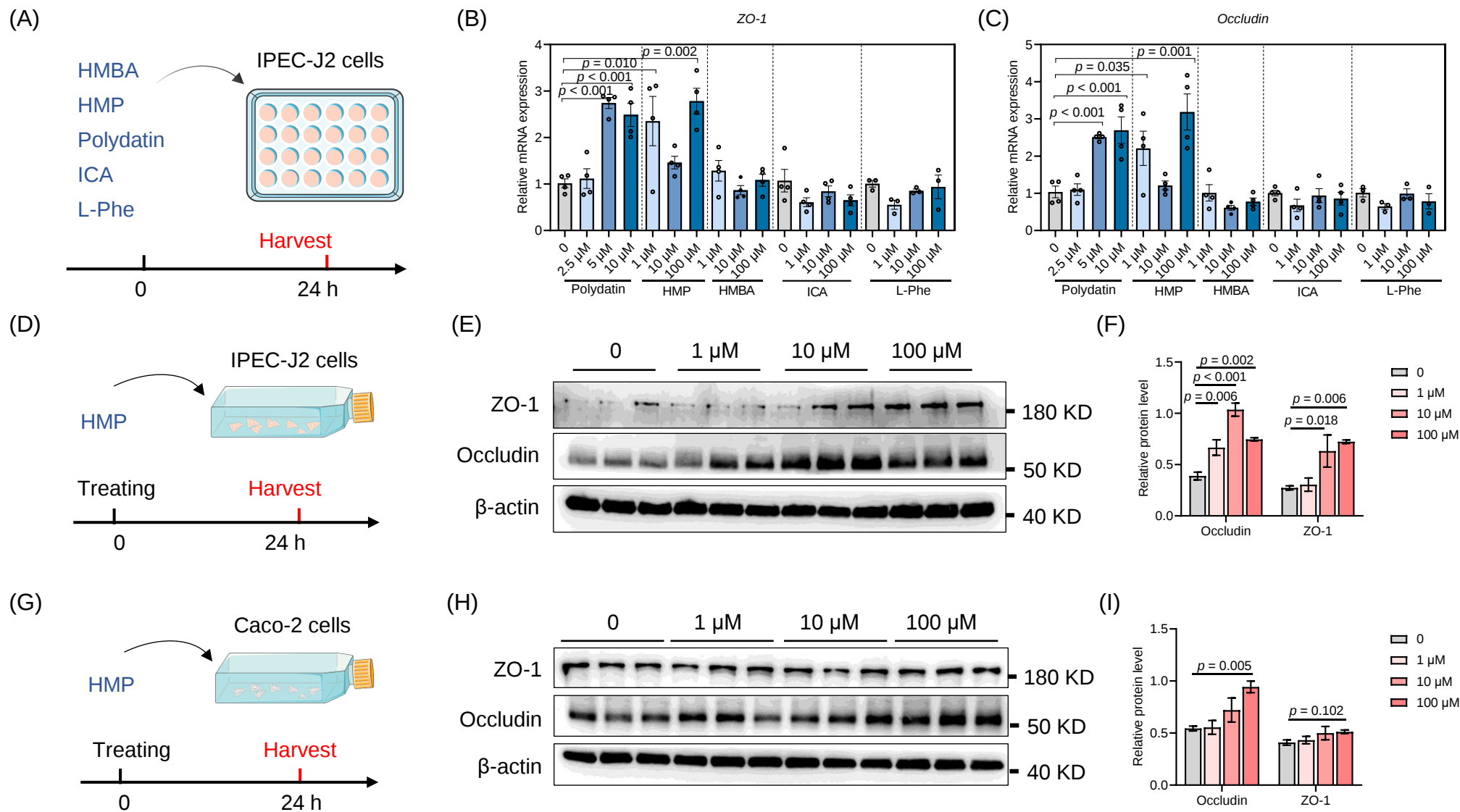
Key metaboltes	Level	Score	VIP	<i>p</i> -value
Polydatin	2	0.836	1.824120548	0.000161384
2-Hydroxy-4-methylpentanoic acid	1a	0.9587	1.768467265	0.005869386
2-Hydroxy-2-methylbutyric acid	1a	0.9289	1.685298765	0.014059252
Isosteviol	1b	0.7566	1.814884198	0.002805972
Indole-5-carboxylic acid	1b	0.7325	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)



研究结果

□ HMP在体外可显著促进肠道上皮细胞紧密连接蛋白的表达

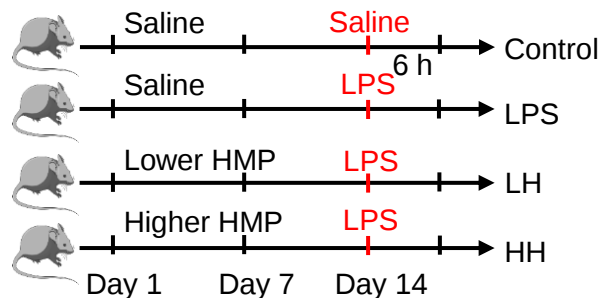




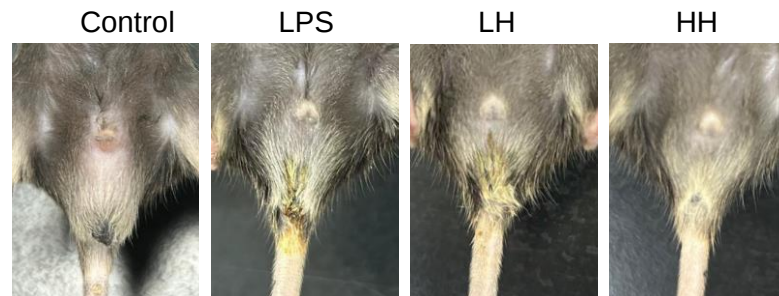
研究结果

□ HMP能够恢复LPS处理后紧密连接蛋白的表达、缓解肠道上皮屏障损伤

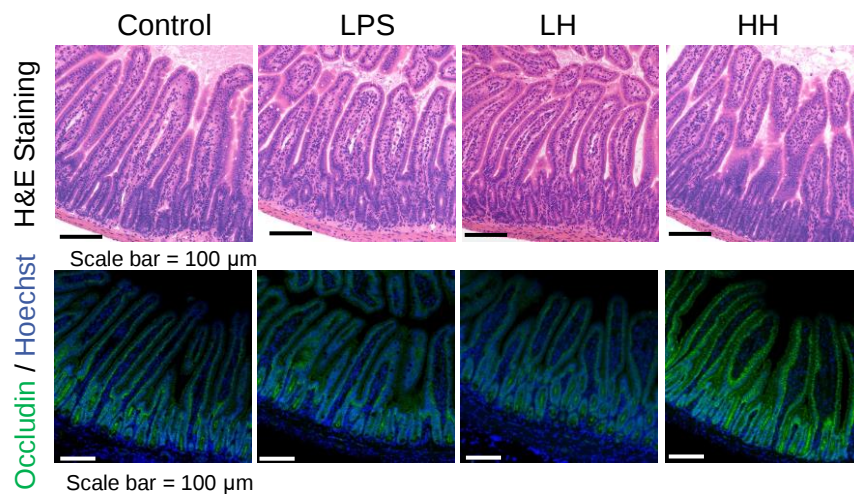
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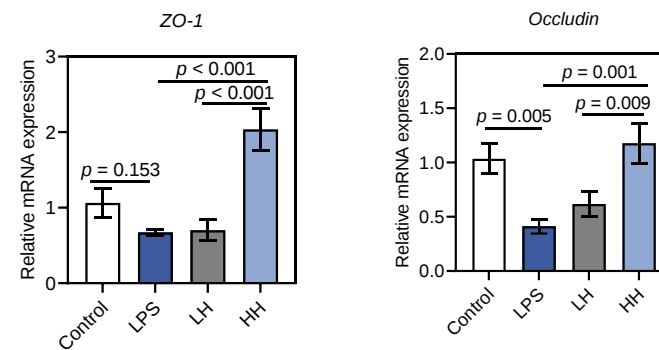
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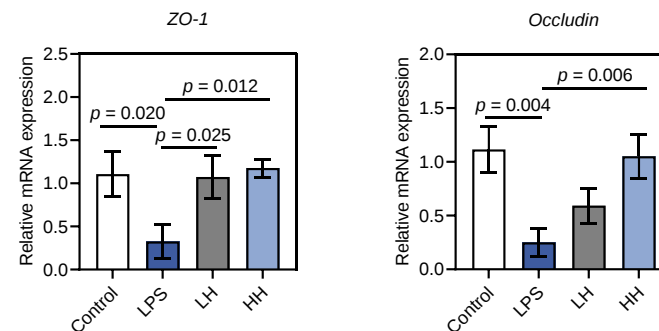
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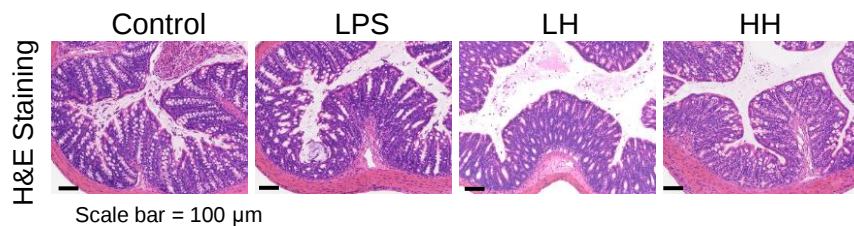
(M)



(O)



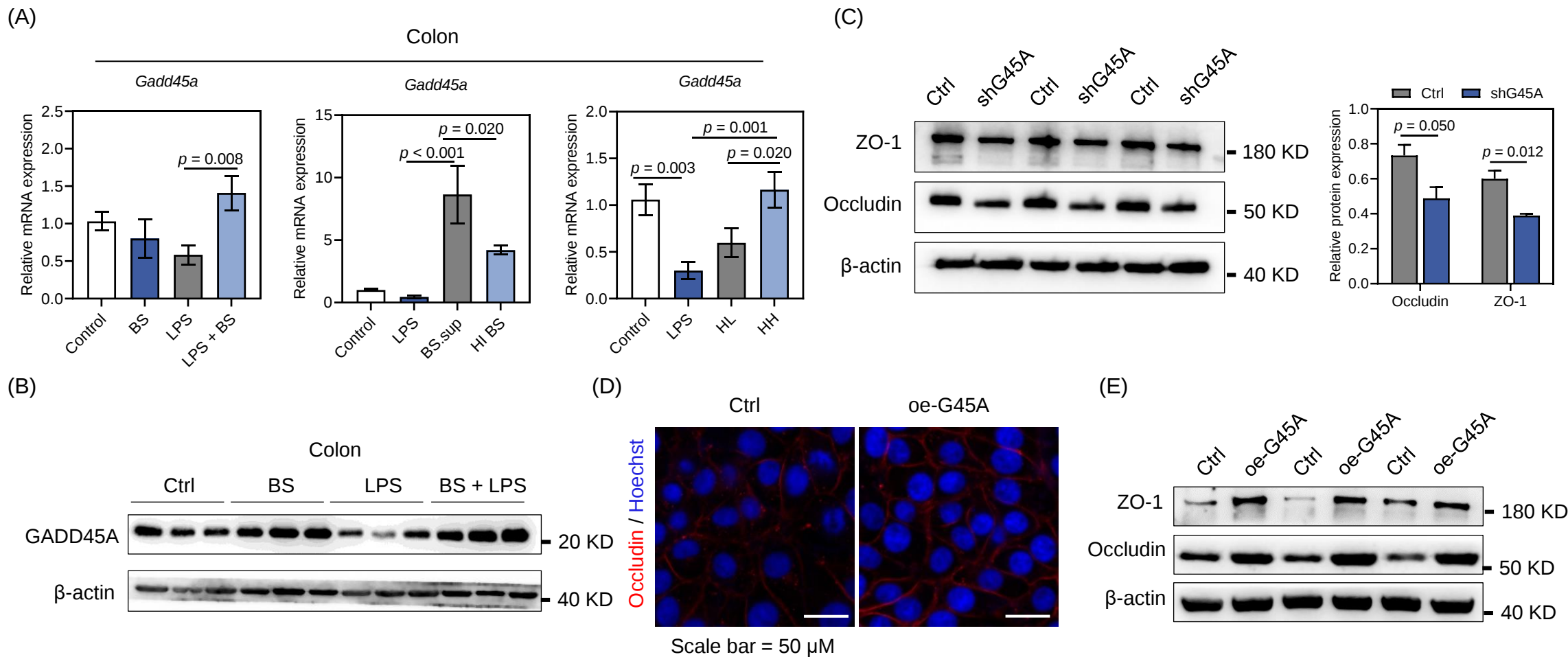
(N)





研究结果

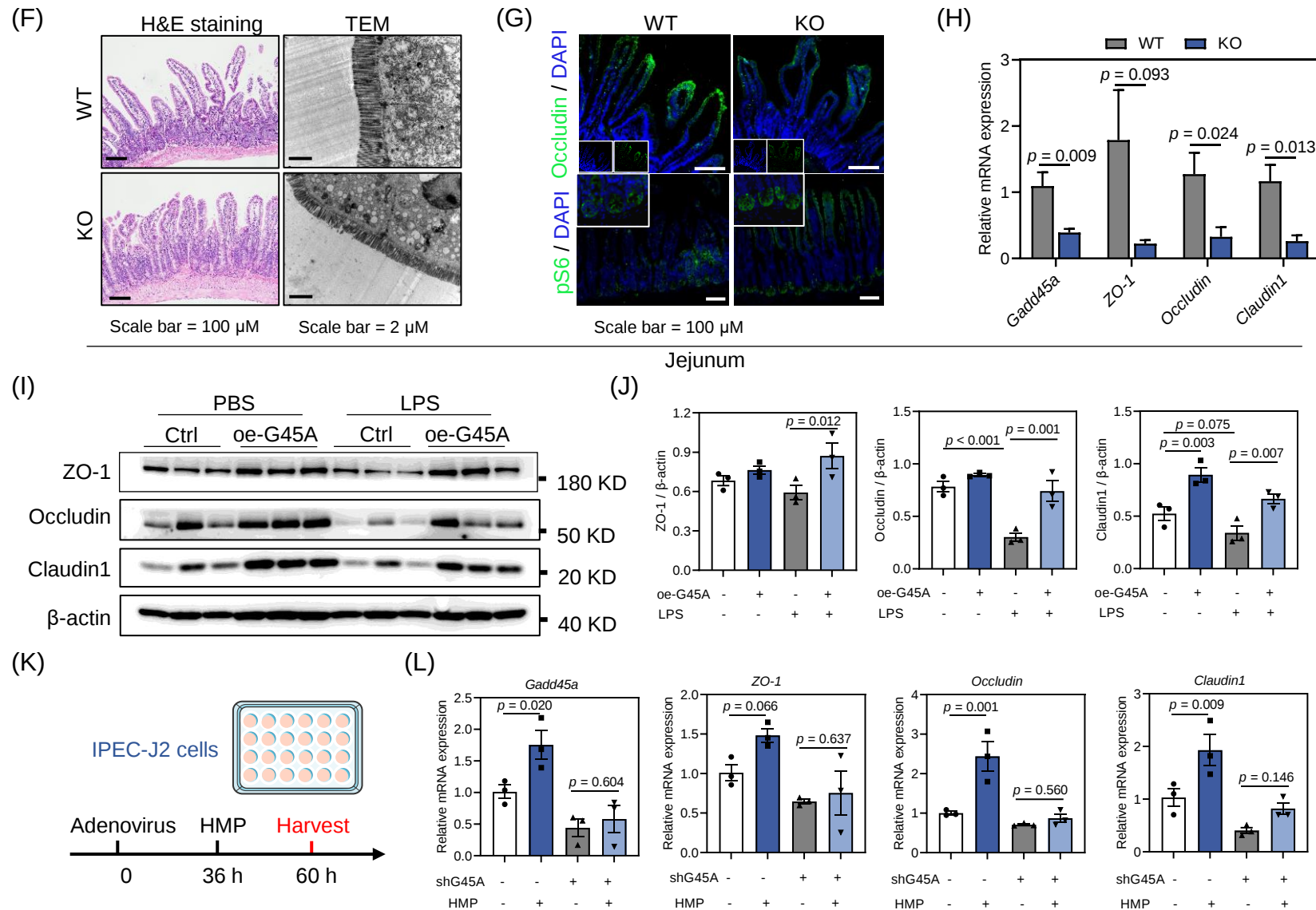
- ❑ GADD45A是维持肠道上皮屏障功能的新调控因子
- ❑ HMP调节肠道上皮屏障的功能与GADD45A的表达有关





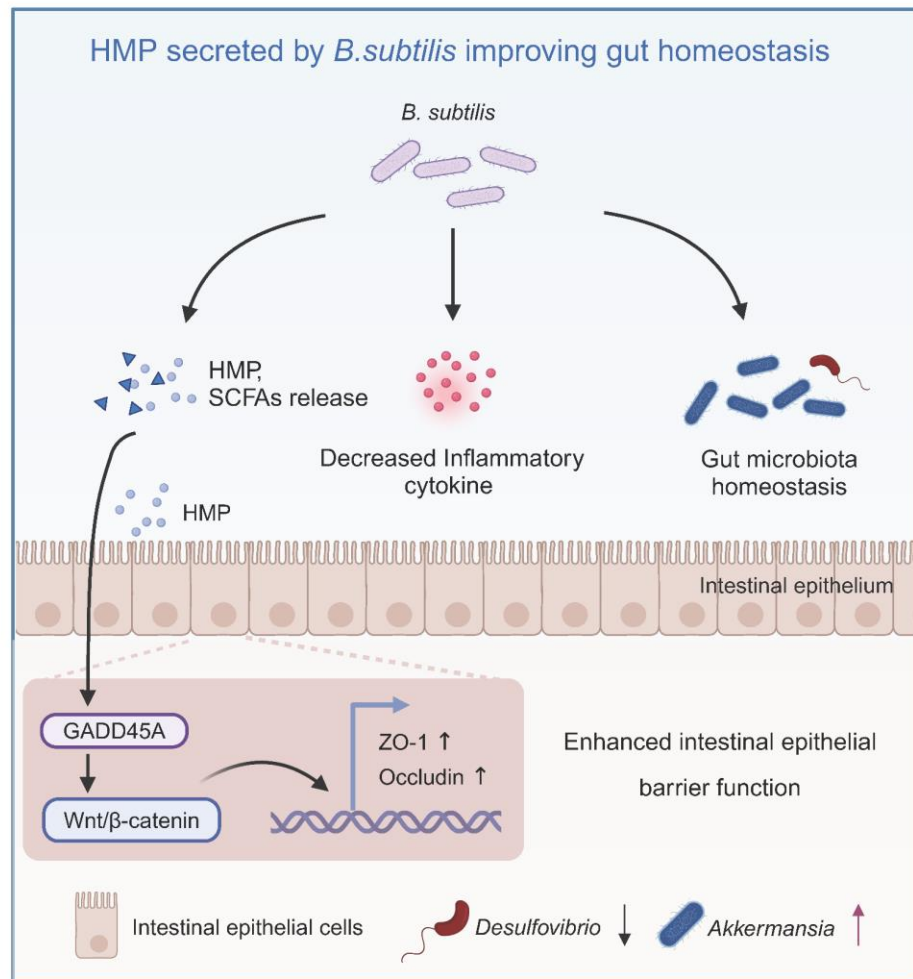
研究结果

□ HMP调节肠道屏障功能依赖于GADD45A的作用



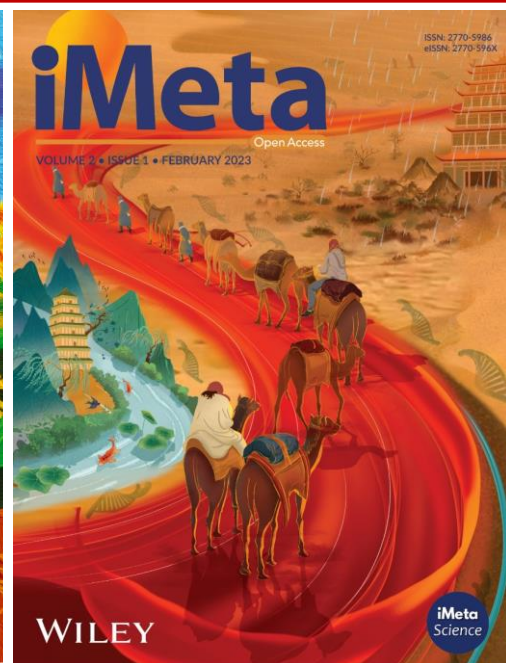


结论



- ❑ *B. subtilis* 可保护机体免受LPS诱导的急性肠道损伤和炎症;
- ❑ *B. subtilis* 能够改善LPS诱导的肠道菌群失衡, 提高阿克曼菌属的相对丰度;
- ❑ *B. subtilis* 分泌的HMP可增强肠道上皮屏障的完整性;
- ❑ GADD45A是肠道上皮屏障的一个新调控因子;
- ❑ HMP可通过GADD45A-Wnt/β-catenin通路调节肠道上皮屏障的完整性。

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