



# The gut microbiota-aromatic hydrocarbon receptor (AhR) axis mediates the anticolitic effect of polyphenol-rich extracts from *Sanghuangporus*.

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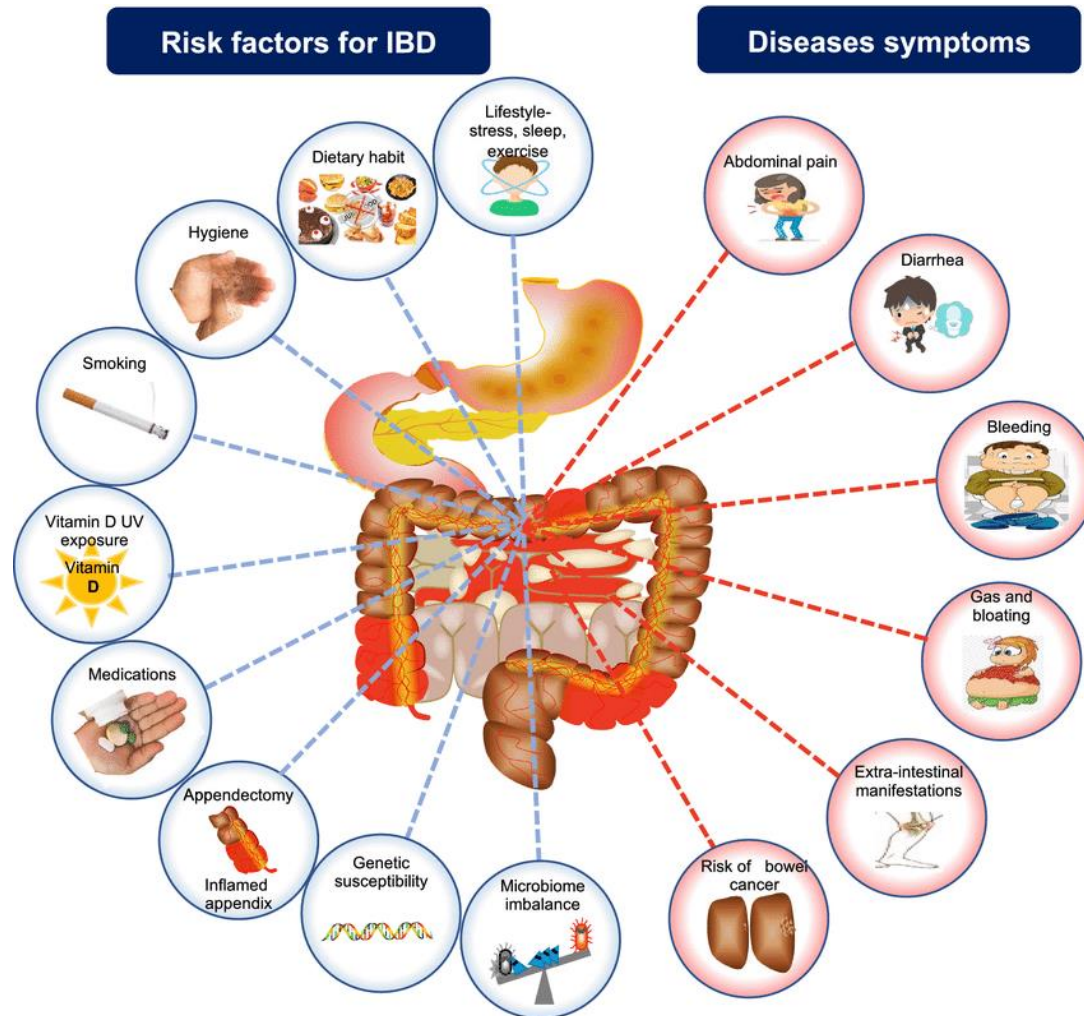


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# Introduction

## ➤ Background—Inflammatory bowel disease (IBD) is a global public health concern

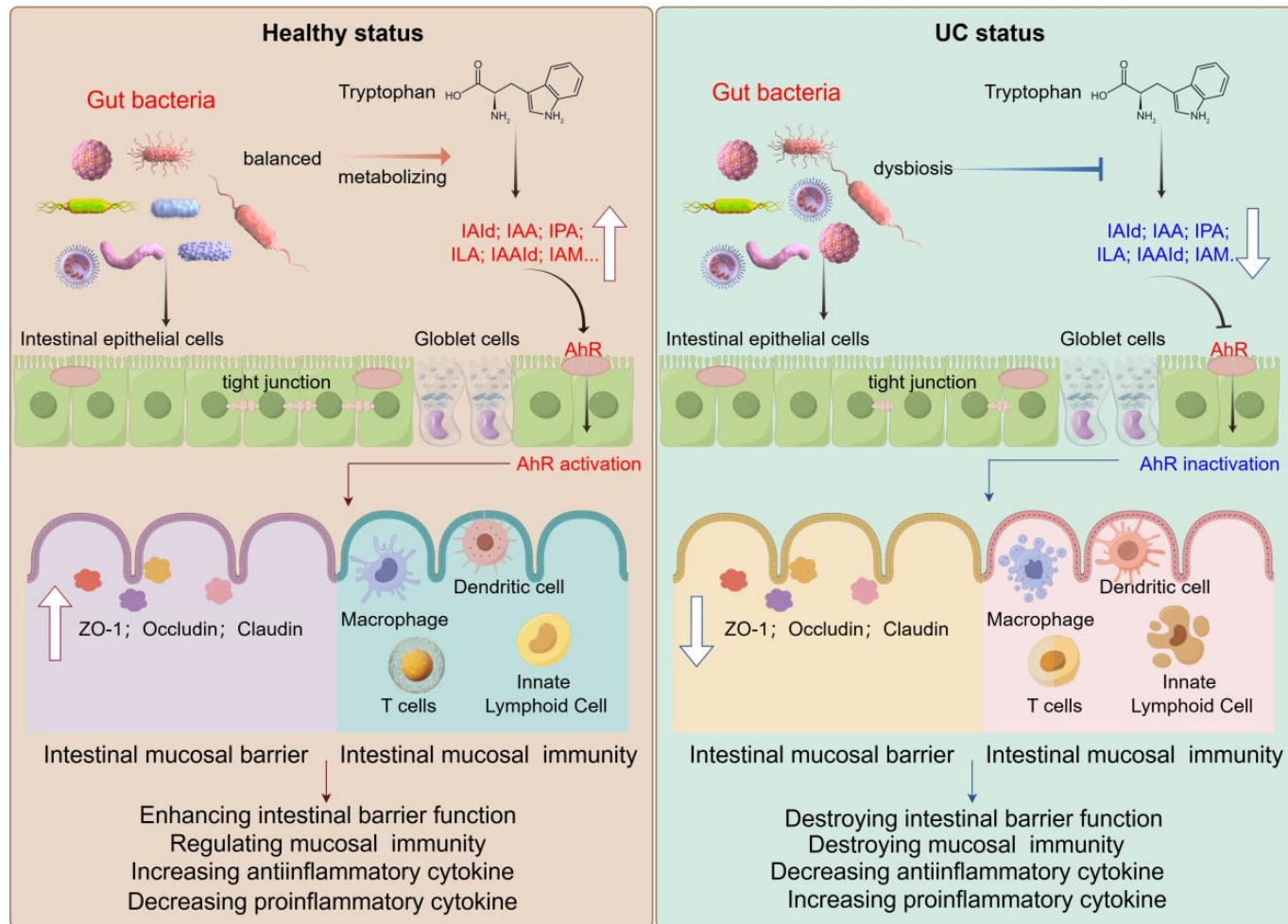


- Inflammatory bowel disease (IBD) mainly comprises ulcerative colitis (UC) and Crohn's disease (CD);
- IBD affects approximately 0.5% of the global population;
- Typical symptoms of IBD include urgent diarrhea, intermittent abdominal pain, rectal bleeding, and weight loss;
- IBD significantly decreases quality of life, and elevates the risk of colon cancer;
- IBD lacks a definitive medical cure, and is often accompanied by subsequent instances of secondary failure.



# Introduction

## ➤ Background—“Gut microbiota-indole derivative-AhR” participates in the occurrence and development of IBD



- The dysbiosis of the gut microbiota is closely related with the onset and progression of IBD;
- Gut microbiota-derived indole derivatives obviously ameliorate experimental ulcerative colitis;
- Indole derivatives are natural ligands of the aryl hydrocarbon receptor (AhR);
- Gut microbiota and its microbial metabolites, especially indole derivatives, may represent promising reservoirs for the development of new therapeutic interventions against IBD.



# Introduction

## ➤ Background—The anti-colitis effect and mechanism of SH still remains unknown



polyphenol-rich extract  
of *Sanghuangporus* (SH)



colitis mice



efficacy?  
mechanism?

- *Sanghuangporus* is an edible medicinal fungus that is used in both medicine and as a dietary supplement;
- *Sanghuangporus* possess multiple pharmacological effects, including anti-inflammatory, antitumour and antioxidant effects;
- *Sanghuangporus* has the capacity to modulate the gut microbiota.

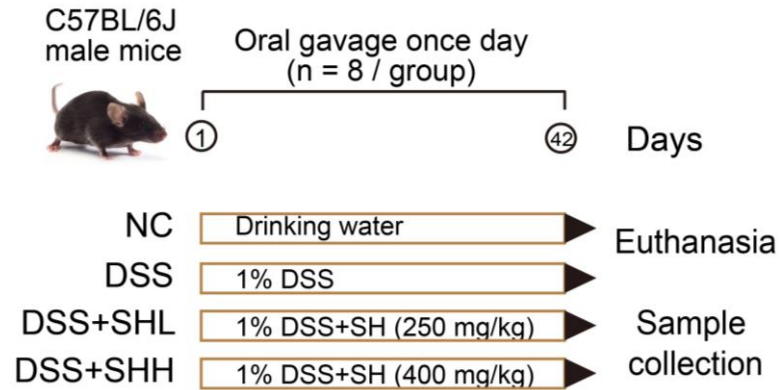




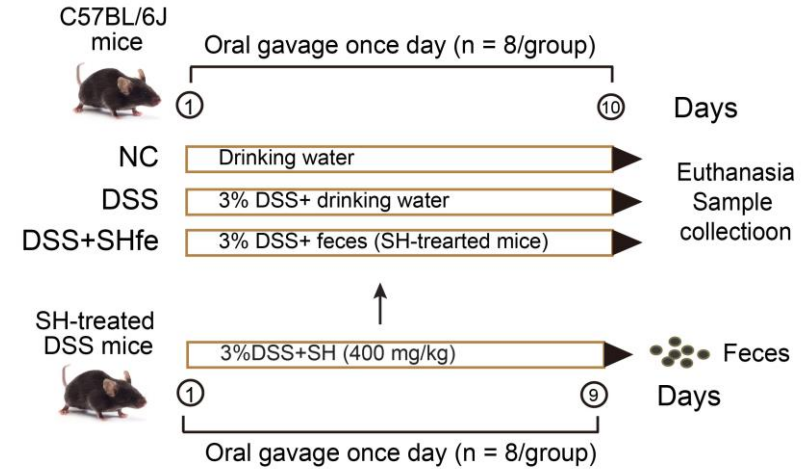
# Main text

## Study design

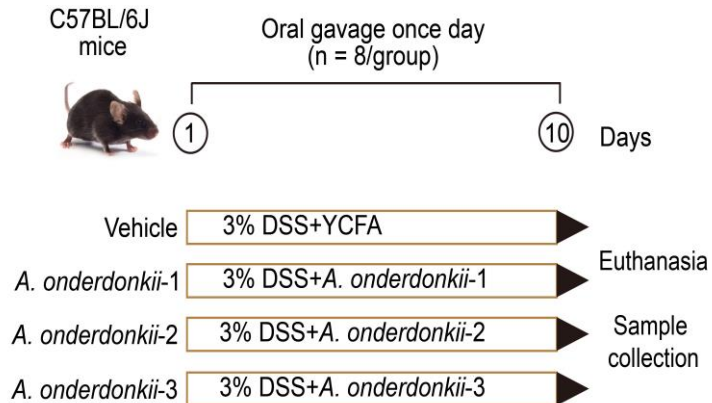
### (1) The anti-colitis effect of SH



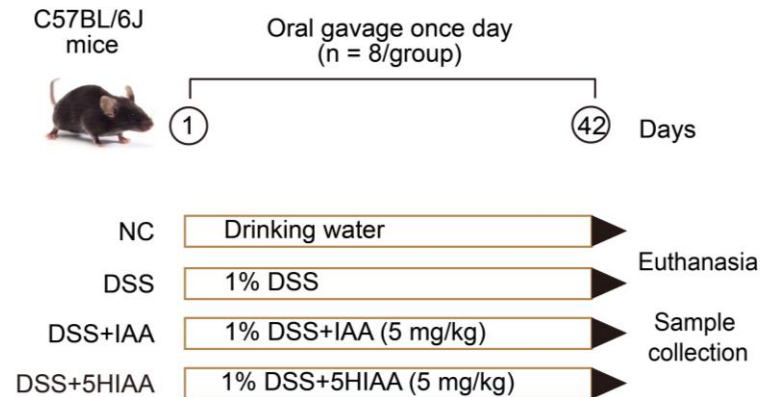
### (2) The contribution of the gut microbiota to the anti-colitis effect of SH



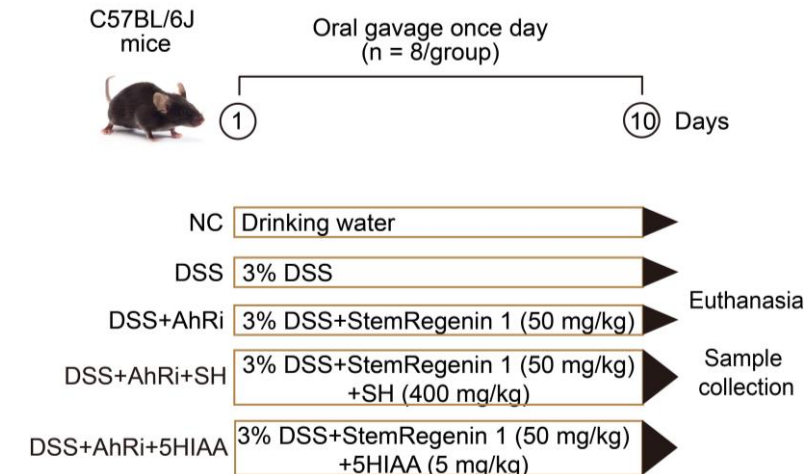
### (3) The anti-colitis effect of gut microbiota



### (4) The anti-colitis effect of metabolite



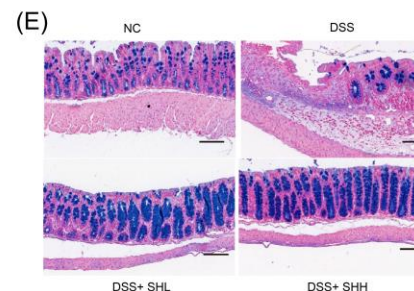
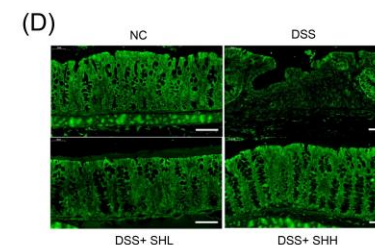
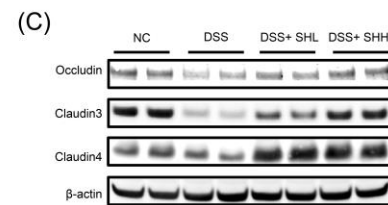
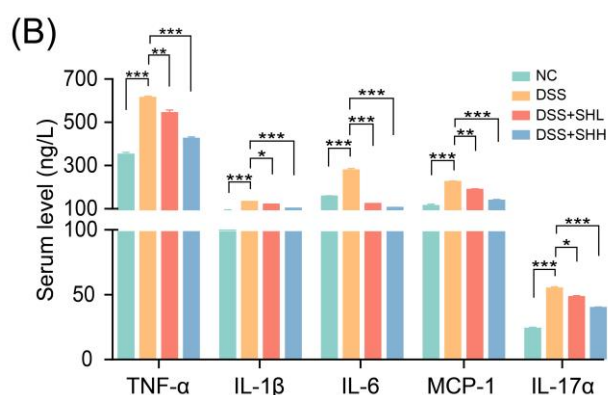
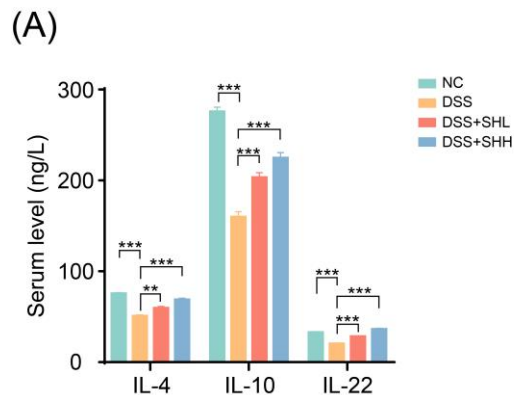
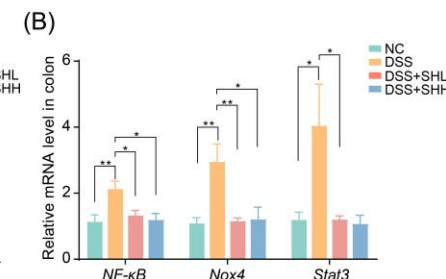
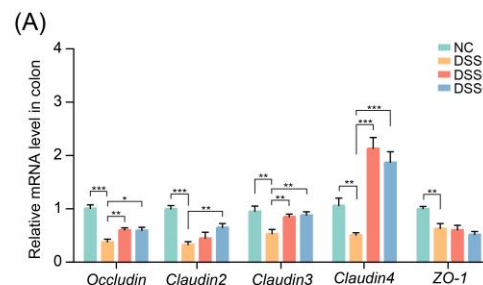
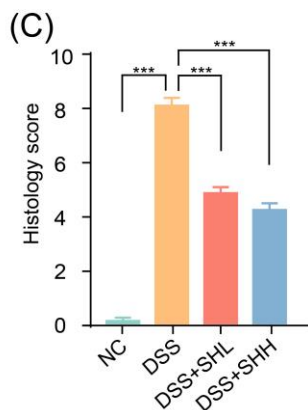
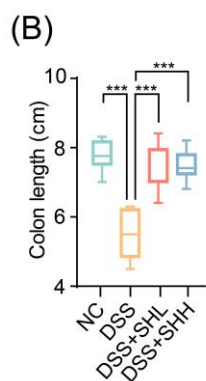
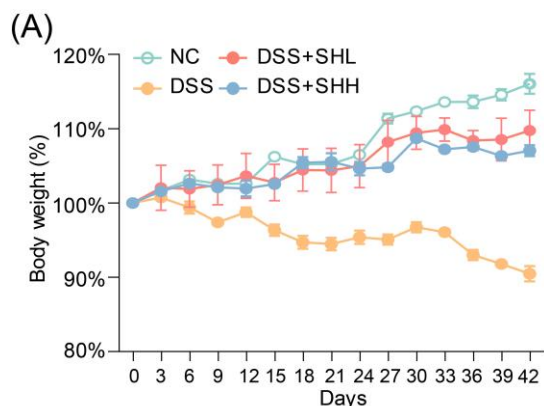
### (5) The contribution of the AhR to the anti-colitis effect of SH





# Main text

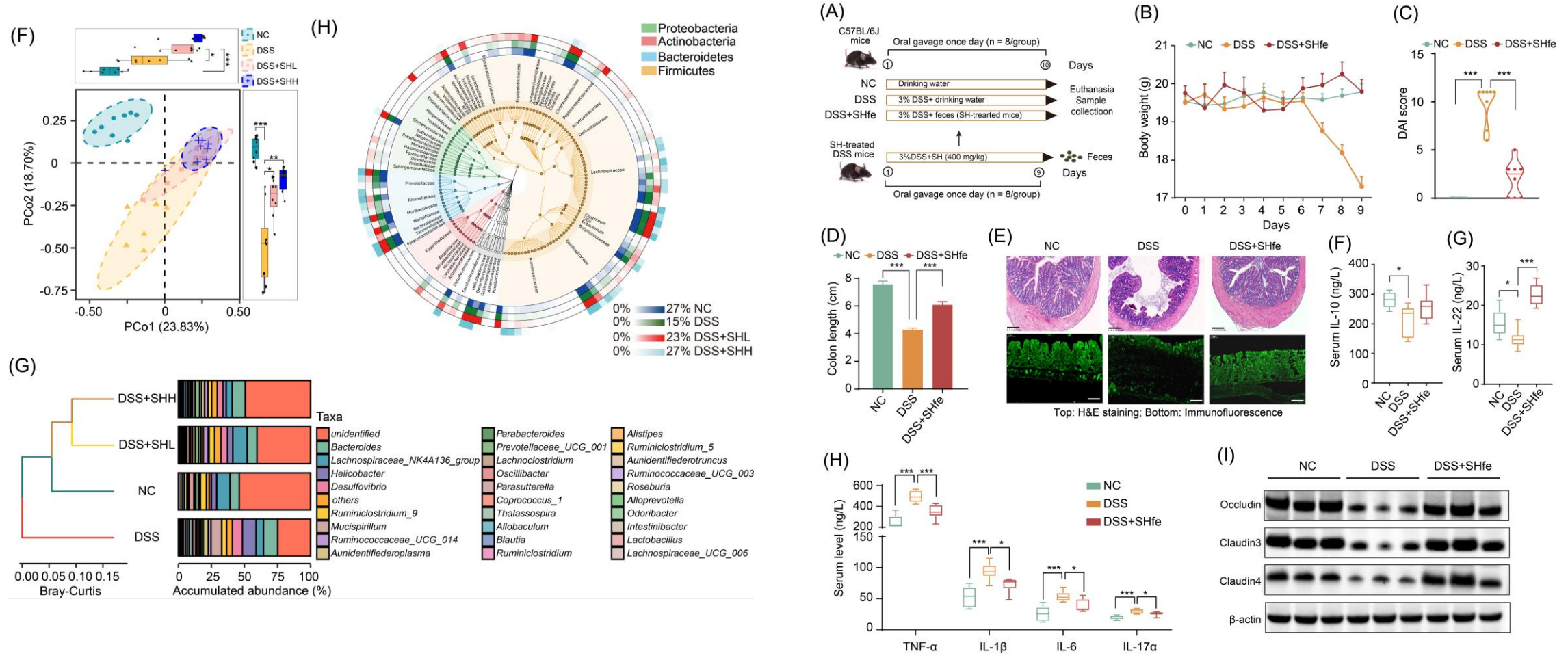
## Results—SH alleviates DSS-induced colitis in C57BL/6 mice



- SH reverses DSS-induced weight loss, increased DAI, shortened colon, and damaged crypt and colon tissue;
- SH decreases pro-inflammatory cytokine, whereas increases anti-inflammatory cytokine;
- SH increases the expression of tight junction genes and proteins, while reducing the oxidative stress-related genes.

# Main text

## Results—Gut microbiota plays a crucial role in mediating the anti-colitis efficacy of SH

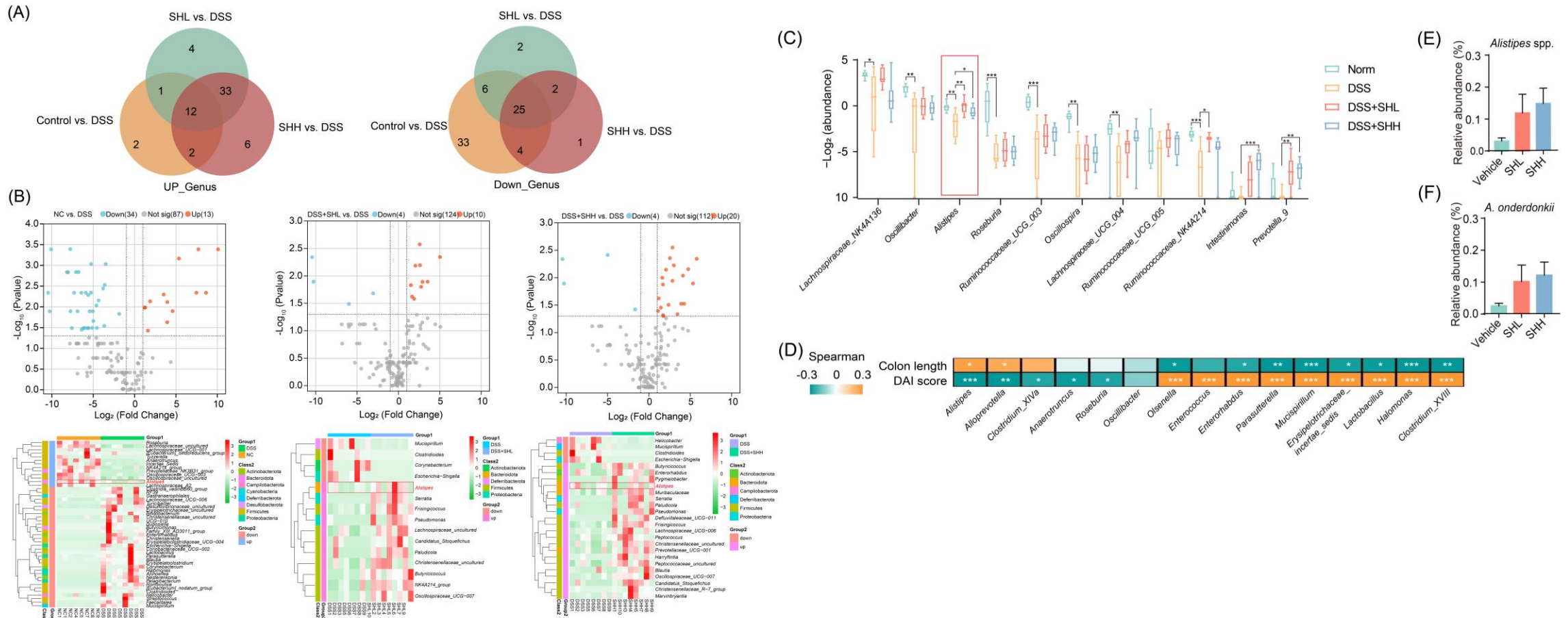


- SH significantly modulates the gut microbial community in DSS-induced colitis mice;
- Gut microbes from SH-treated mice exhibit potent colitis-ameliorating effects.



# Main text

## Results—SH enriches *Alistipes onderdonkii* to ameliorate colitis

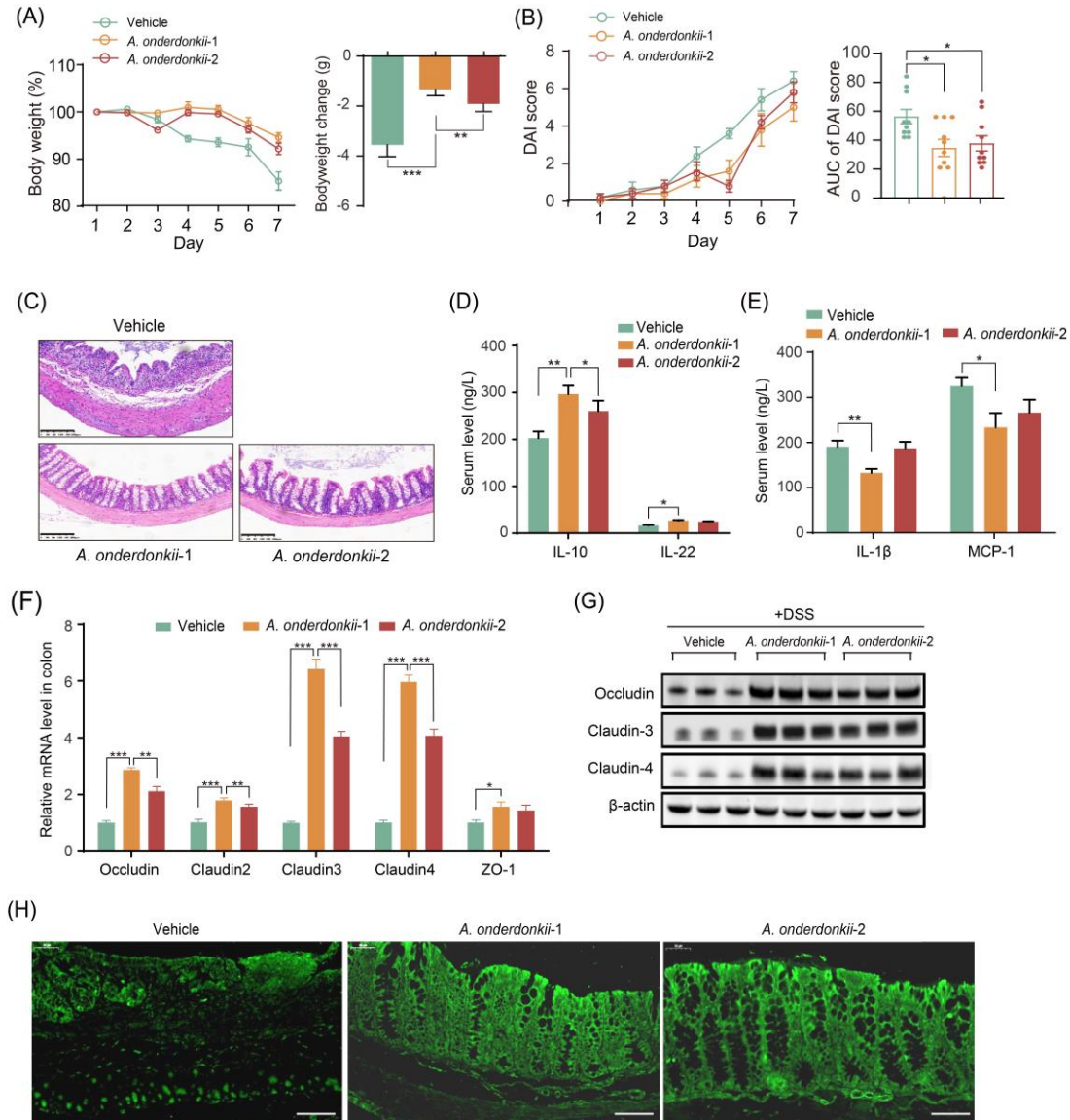


- SH significantly enriched *Alistipes*, which is negatively related with DAI score, and positively related with colon length.



# Main text

## ► Results—SH enriches *Alistipes onderdonkii* to ameliorate colitis

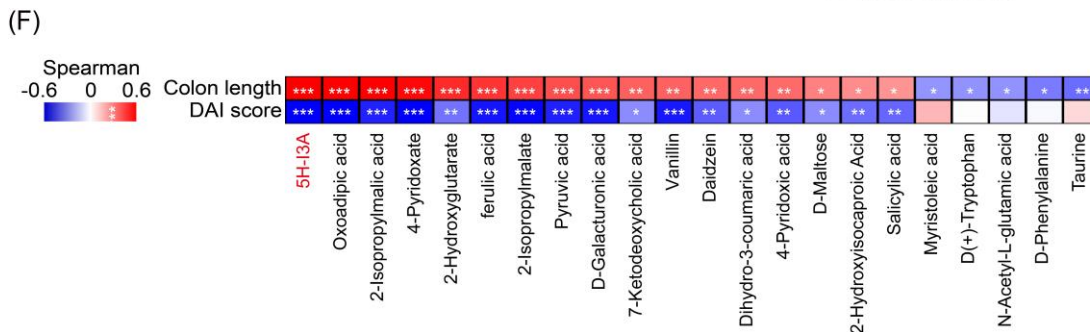
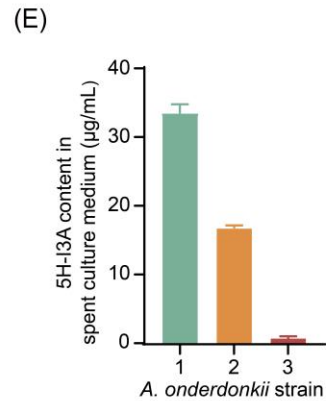
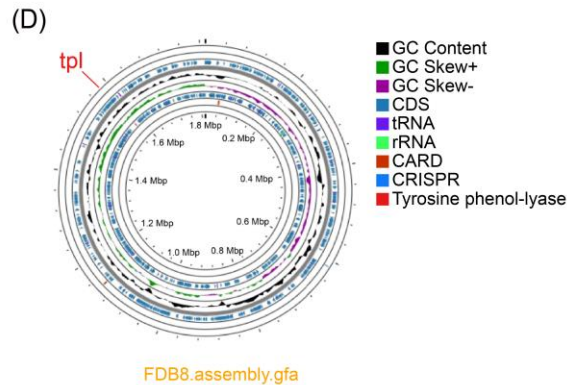
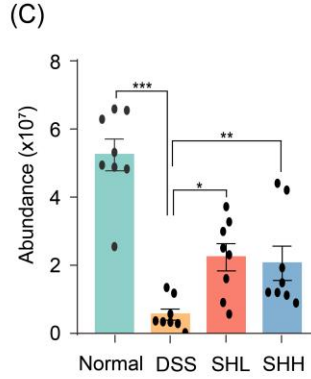
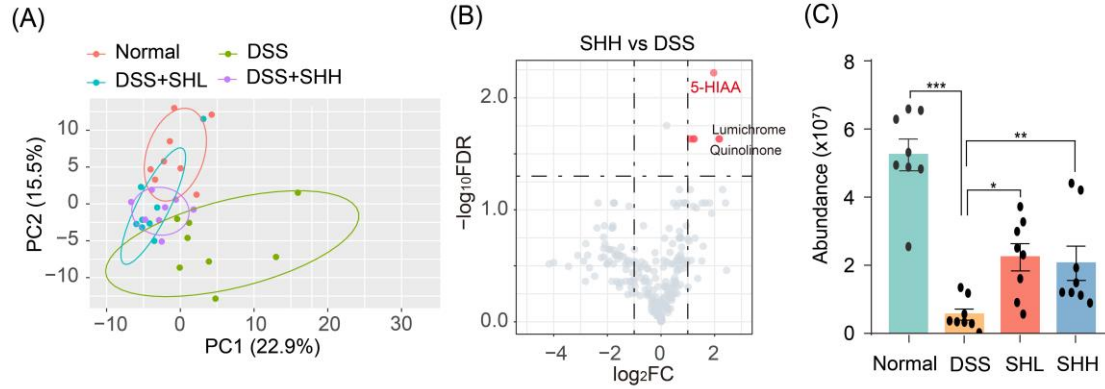


- *A. onderdonkii* strains (#1: FDB8和#2: FDFM) effectively prevented body weight loss, decreased DAI scores, recovered colon tissue injury, and improved inflammatory status;
- *A. onderdonkii* elevated the expression of TJ proteins to enhance gut barrier function
- The anti-colitis effect of *A. onderdonkii* exhibits strain-specific.



# Main text

## Results—5-Hydroxyindole-3-acetic acid (5HIAA) is a key active microbial metabolite

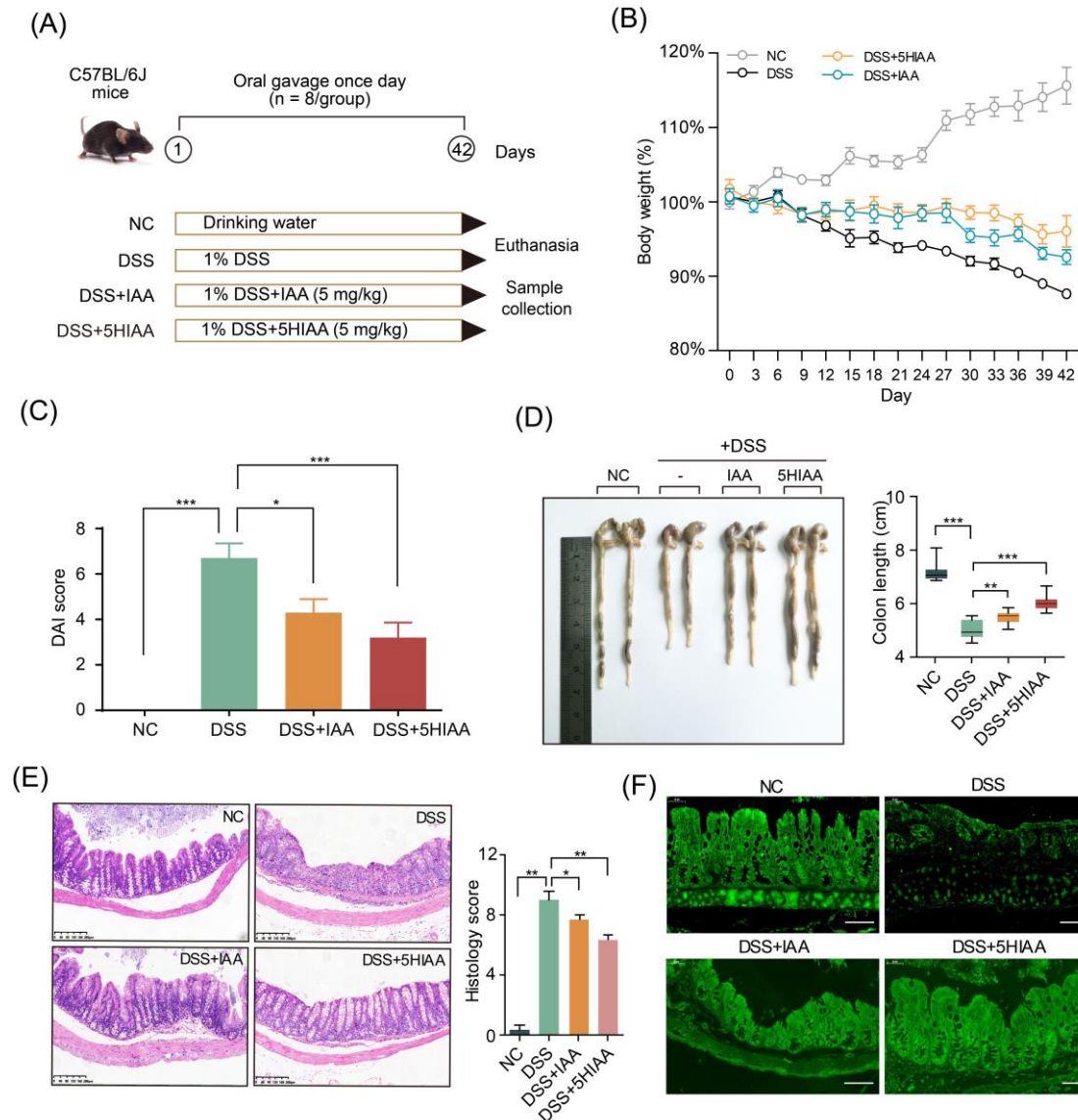


- SH prominently restored the profiles of microbial metabolites;
- SH treatment significantly elevated 5HIAA;
- *A. onderdonkii* strains (#1: FDB8 and #2: FDFM) contained a *tpl* gene associated with the biosynthesis of indole compounds;
- The concentrations of 5HIAA in spent culture supernatants of *A. onderdonkii* is as high as 33.5  $\mu\text{g/mL}$ ;
- 5HIAA was most strongly positively correlated with colon length and negatively correlated with DAI score



# Main text

## ► Results—5-Hydroxyindole-3-acetic acid (5HIAA) is a key active microbial metabolite

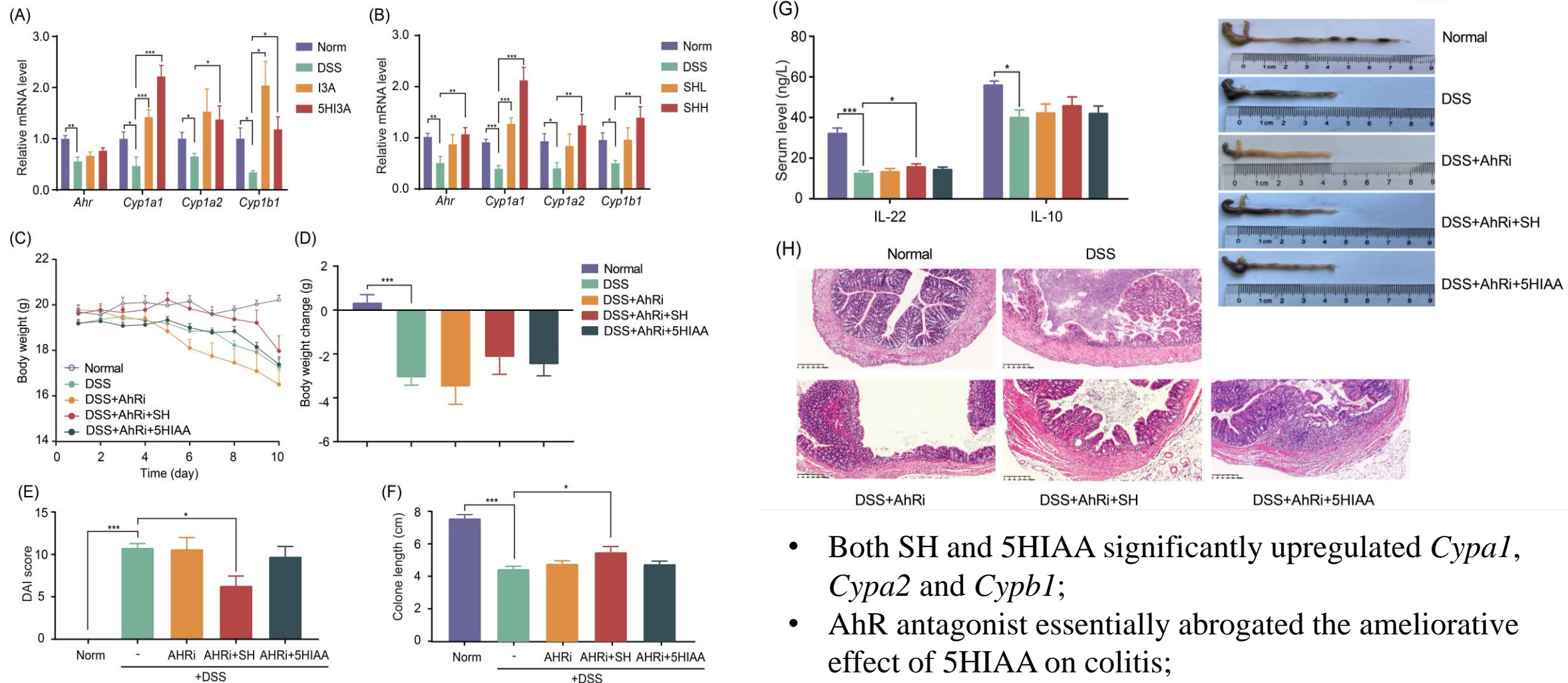


- 5HIAA performed much better than IAA at alleviating colitis;
- 5HIAA efficiently elevated the levels of anti-inflammatory factors to attenuate inflammation and decrease the levels of proinflammatory factors;
- 5HIAA reduced the relative expression of oxidative stress-related genes (*NFkappaB*, *Nox4* and *Stat3*);
- 5HIAA and IAA upregulated the expression of the tight junction factors Occludin and Claudins.



# Main text

## ► Results—Colonic AhR activation is important for mediating the anticolic effect of SH

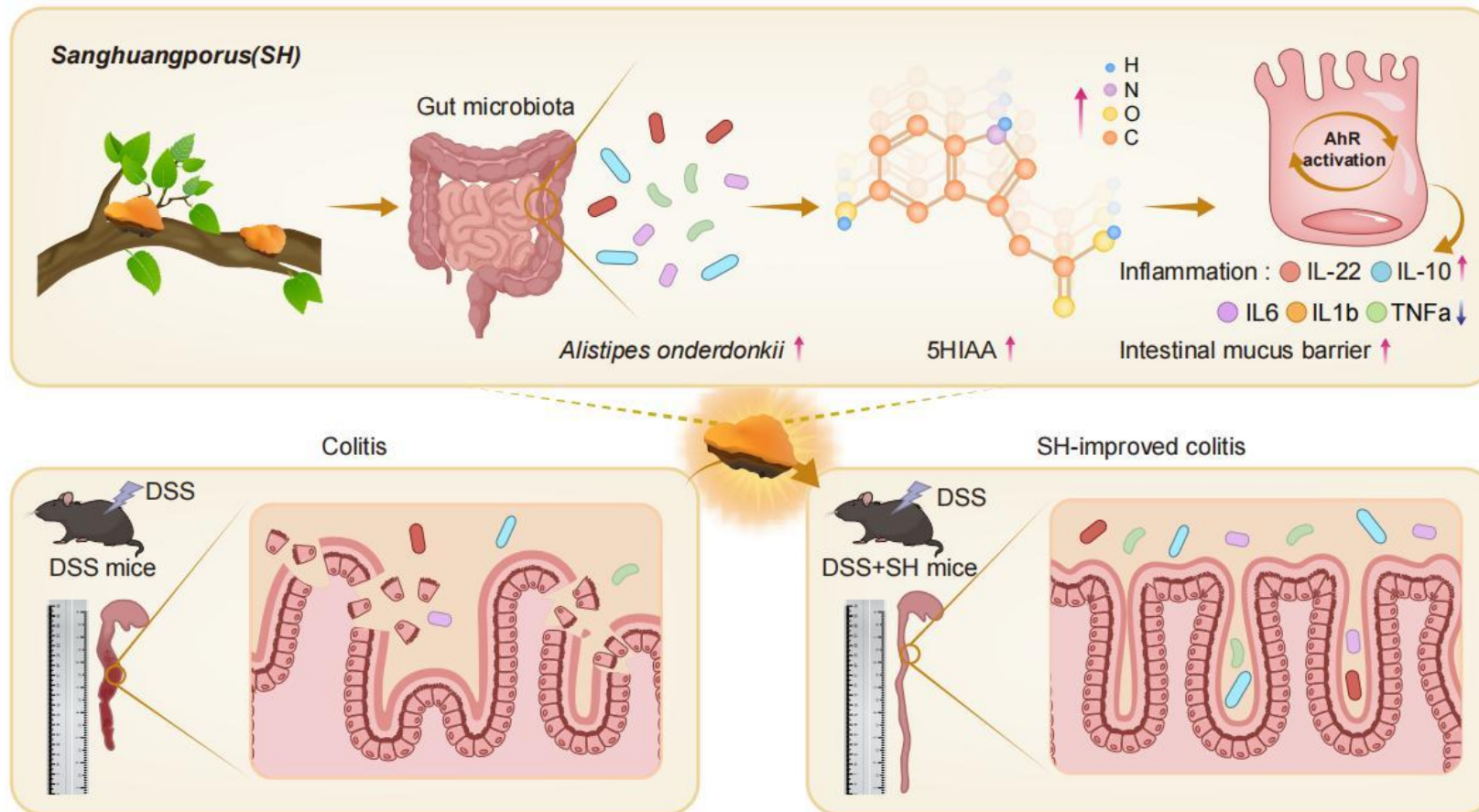


- Both SH and 5HIAA significantly upregulated *Cyp1*, *Cypa2* and *Cypb1*;
- AhR antagonist essentially abrogated the ameliorative effect of 5HIAA on colitis;
- AhR antagonists partially eliminated the ameliorative effect of SH on colitis.



# Main text

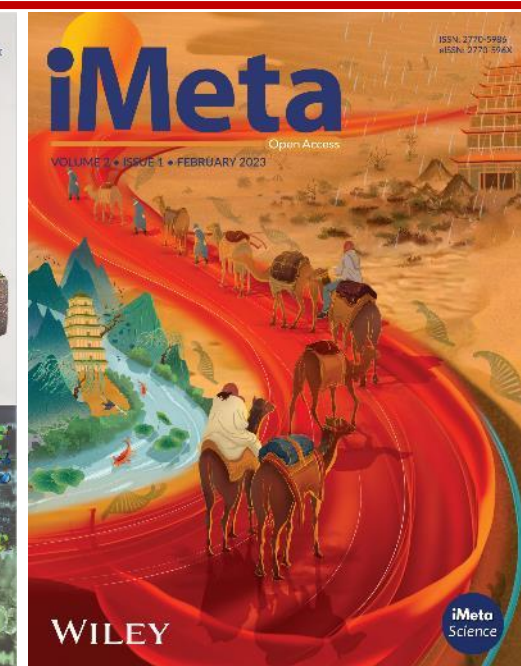
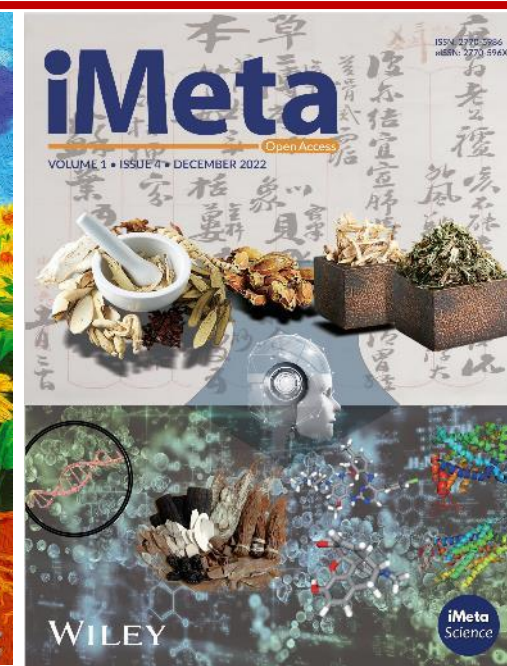
## ► Results—SH exerts anti-colitis effect via the “*A. onderdonkii*-5HIAA-AhR” axis





# Summary

- ❑ *Sanghuangporus* polyphenol extract (SH) potently alleviated symptoms of colon colitis in DSS-induced colitis mice.
- ❑ The gut microbiota especially *Alistipes onderdonkii* mediates the anticolitic effect of SH.
- ❑ The SH-enriched microbial metabolite 5-hydroxyindole-3-acetic acid (5HIAA) exhibited an anticolitic effect via the activation of the aryl hydrocarbon receptor (AhR).
- ❑ The “gut microbiota-metabolites-signaling pathway” provides an effective perspective for the study of complex Chinese medicine systems.



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