读书报告

胡文攀

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Original Article

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Loss of MicroRNA-21 Influences the Gut Microbiota, Causing Reduced Susceptibility in a Murine Model of Colitis

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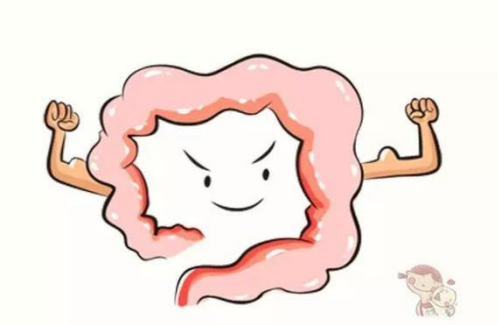
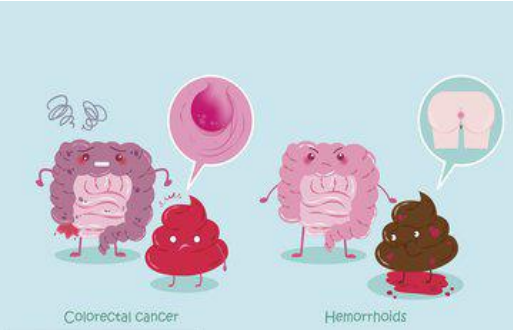
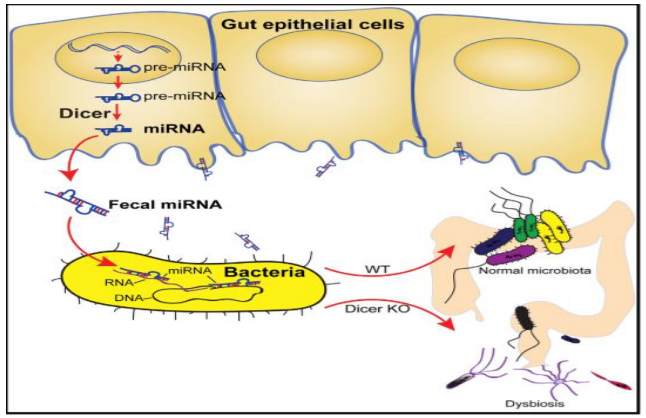




炎症性肠病[IBD]，是胃肠道慢性炎症的统称。一般来说累及回肠、直肠、结肠这些的都可以叫炎性肠病，主要临床表现为腹痛、腹泻、肠鸣、大便带黏液或脓血等。病程长，且反复发作。会造成消化功能紊乱，营养来源不足，引发消瘦、贫血、乏力等相应并发症，严重者会导致肠道大出血、肠穿孔，甚至癌变。

IBD 的病因和发病机制目前尚未完全明确，一般认为它是由遗传因素、环境因素和宿主免疫系统之间的复杂相互作用引起的。IBD不仅在人类群体中高发，在其他哺乳类也十分常见。该病也使养殖行业受到损失。

背景与意义



- **miR-21与IBD：** miR-21可通过增强上皮细胞凋亡和靶向紧密连接蛋白RhoB，使肠上皮细胞屏障变得更具有渗透性，从而对疾病产生了机械上的影响。由此我们猜想，miR-21在炎症性肠病中超表达，不只是炎症反应生成的额外产物， miR-21很可能是**引发肠道炎症的一种调控物质**。
- **肠道微生物与IBD：** IBD已经被证明与肠道菌群失调有关，而且IBD患者的肠道屏障会受到不同程度的损伤，这可能是导致疾病的原因，也可能是炎症引起的，从而加剧疾病。但是微生物失调是否会导致屏障功能受损和炎症发展，或者失调是否是屏障改变的结果，仍有待研究。此外**肠道菌群与黏膜下层免疫系统的异常作用导致的免疫激活和慢性炎症，被越来越多的人认为是产生IBD的主要原因**。

研究内容

1. 探究miR-21的表达与DSS诱导的结肠炎之间的关系
2. 探究在结肠炎恢复过程中miR-21是否也起作用
3. 探究混养下粪菌自然转移对照组是否也能起到实验组一样作用
4. 无菌小鼠粪菌移植进行验证
5. 抗生素干扰实验
6. 探究缺乏miR-21对肠道菌的影响

材料与方法

- DSS-induced experimental colitis
- Colonization of germ-free mice with fecal microbiota
- Co-housing experiments
- Antibiotic treatment of mice
- Histology
- 16S sequencing and analysis
- qRT-PCR
- Colonoscopy

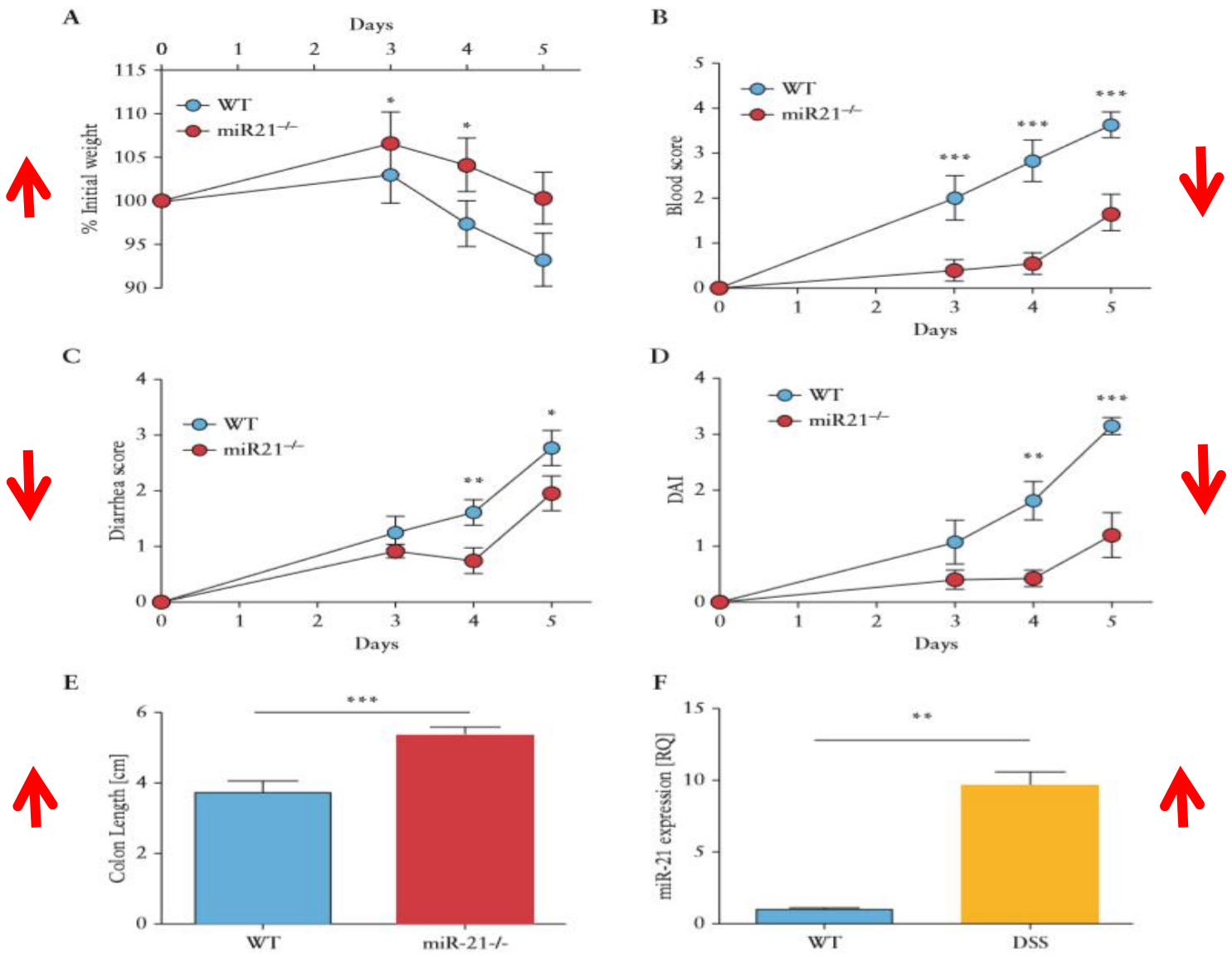
结果与讨论

Fig1 **miR-21缺失对DSS诱导的结肠炎具有保护作用—降低易感性**

WT and miR-21$^{-/-}$ mice
（8 -12 weeks ）

given 2.5% DSS [w/v] ad libitum for 5 days

weight | Blood score | diarrhea score | DAI | colons measured



结果与讨论

Fig-2 在DSS诱导的结肠炎恢复模型中，mir -21缺陷小鼠受到保护

WT ; miR-21$^{-/-}$

↓

2.5% DSS
for 5 days

↓

water for a
further
5 days

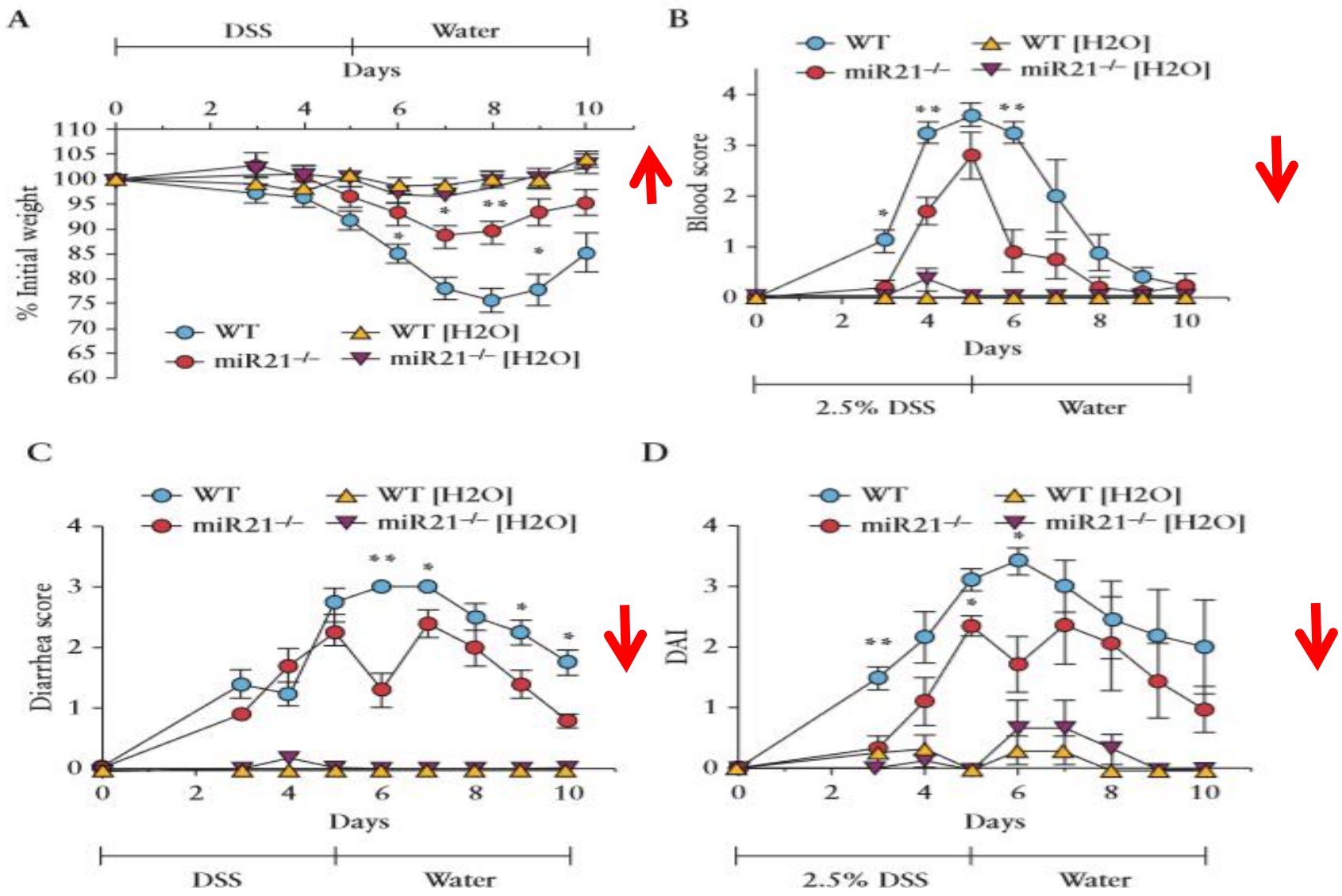
↓

……

WT[H2O] ;
miR-21$^{-/-}$ [H2O]

↓

water for
10 days



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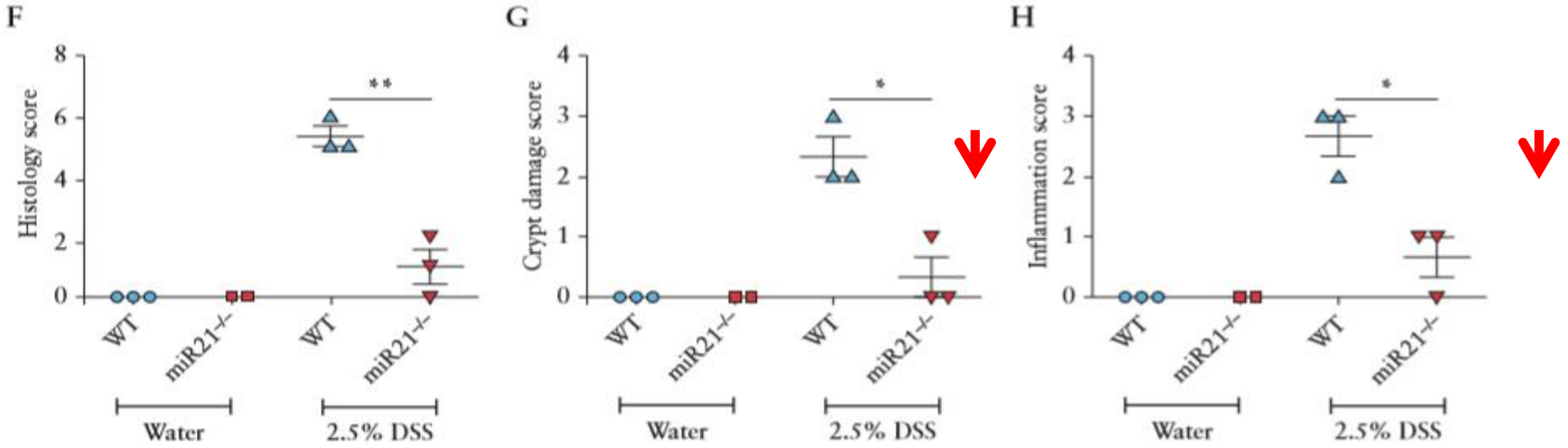
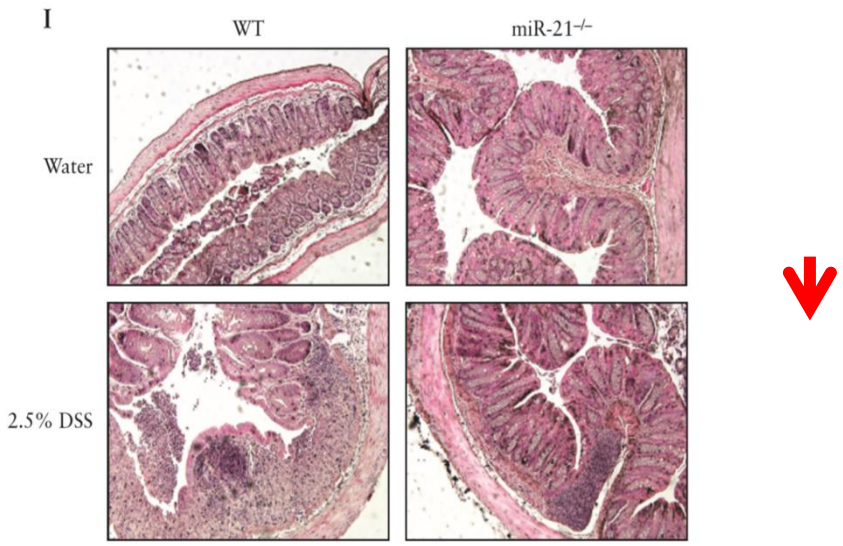
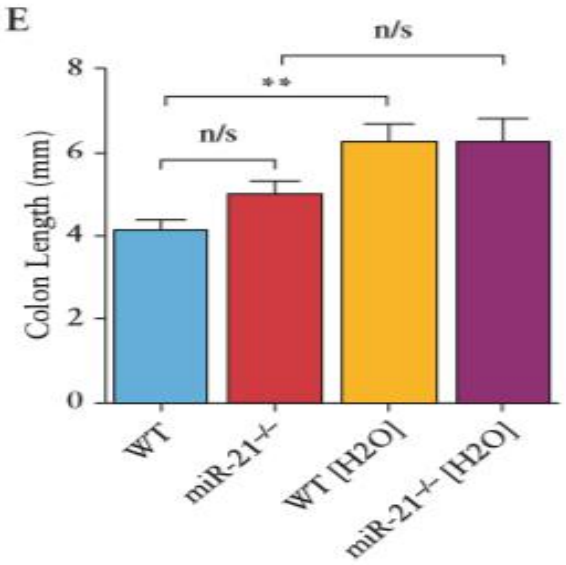






结果与讨论 Fig-3 DSS诱导下miR-21–/–中自然转移粪便微生物群对WT提供了一些保护

WT and miR-21–/–
co-housed for 4 weeks

↓

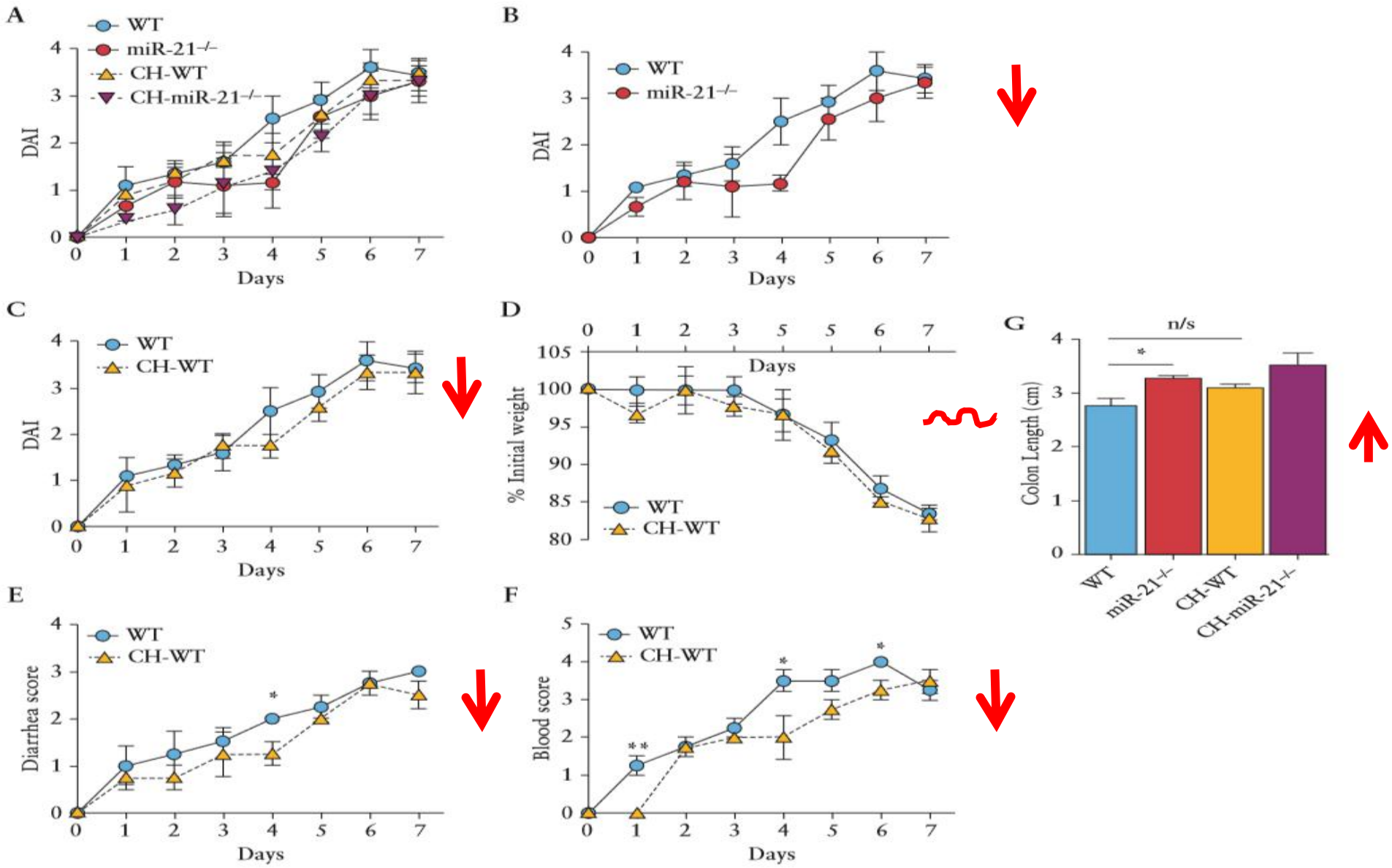
CH-WT　　CH-miR-21–/–

↓

given 2.5% DSS [w/v] ad libitum for 7 days

↓

……



结果与讨论

Fig-4

DSS诱导下mir -21缺陷小鼠的粪便微生物群对无细菌(GF)小鼠进行定殖可减少结肠炎的损害

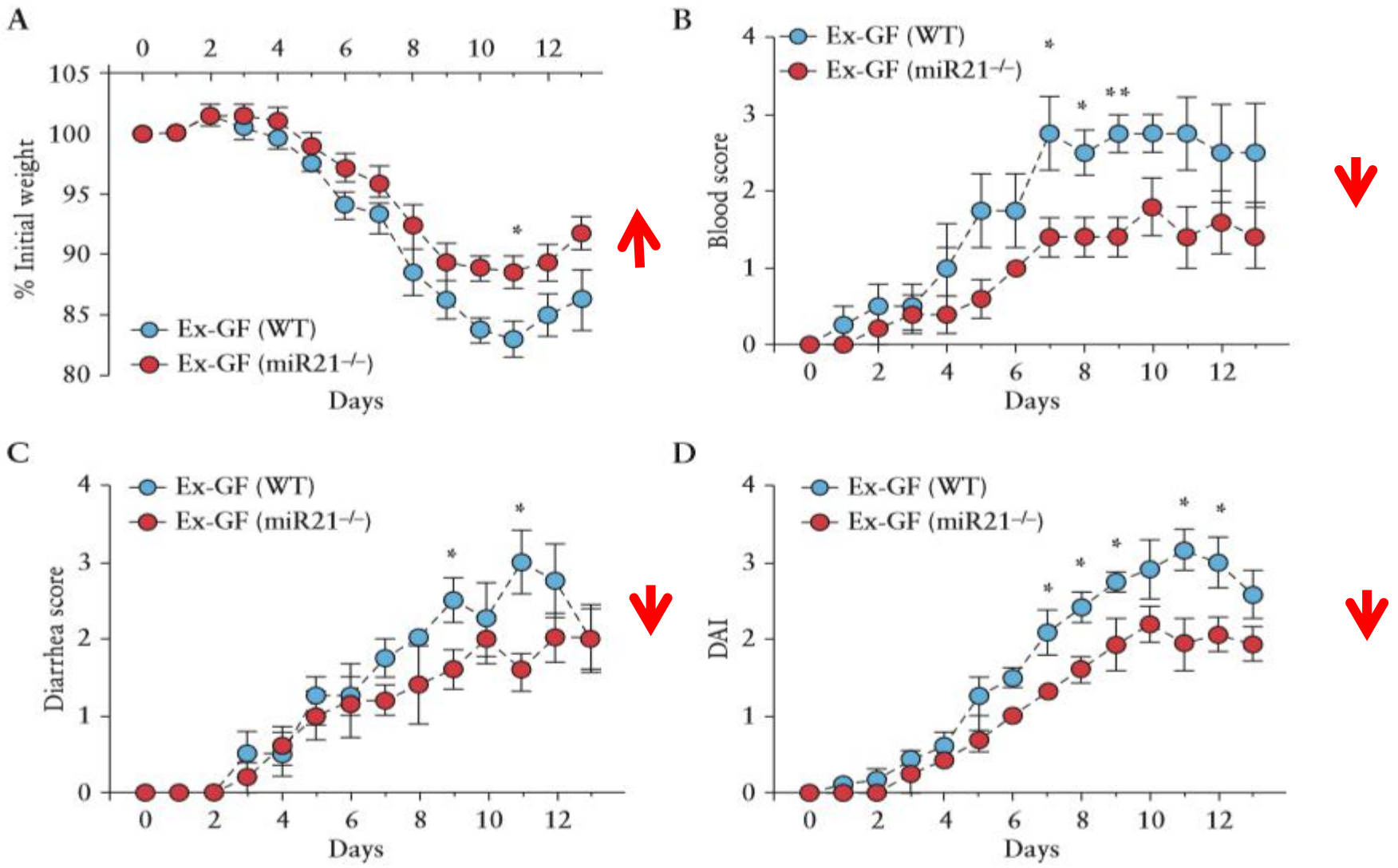
GF were colonized with WT or miR-21–/– mice fecal by oral gavage

↓ Several days

given 2.5% DSS [w/v] ad libitum for 13 days

↓

……



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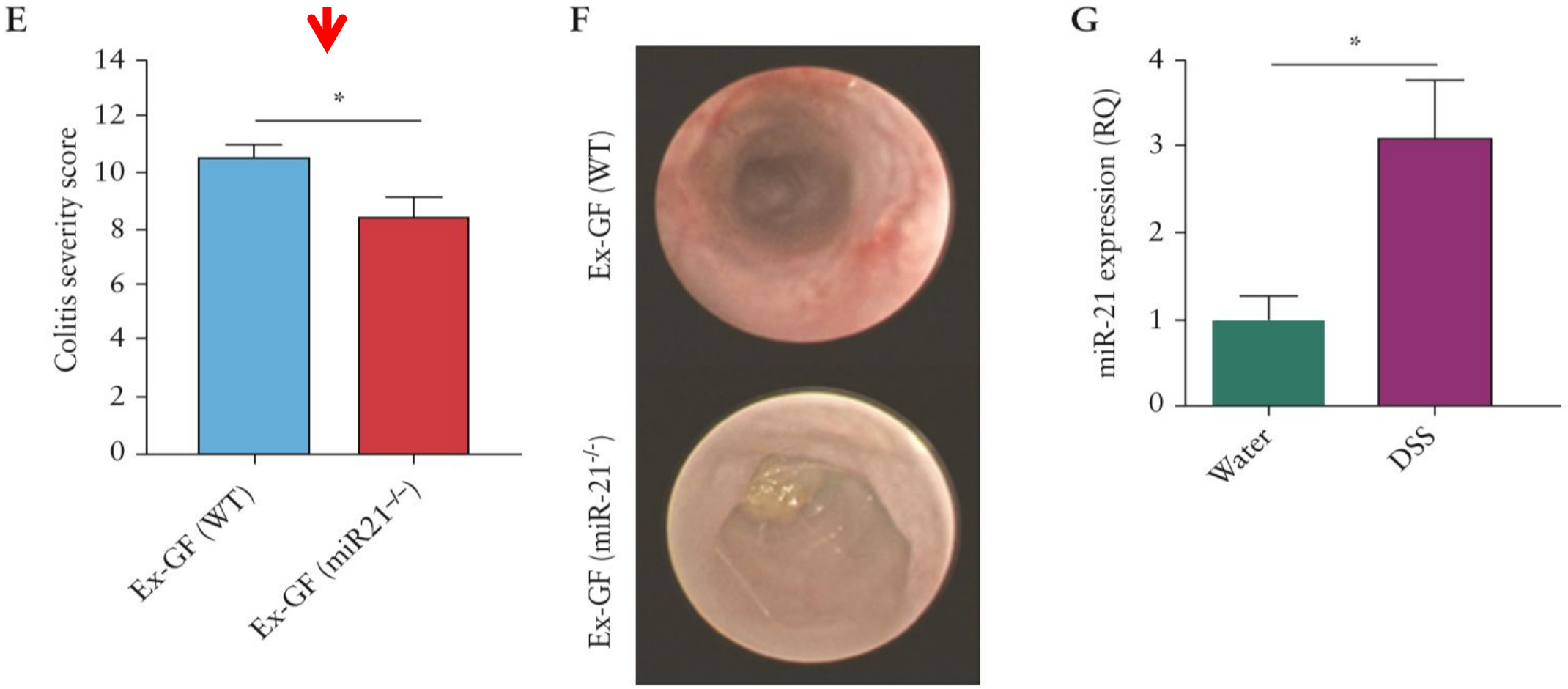


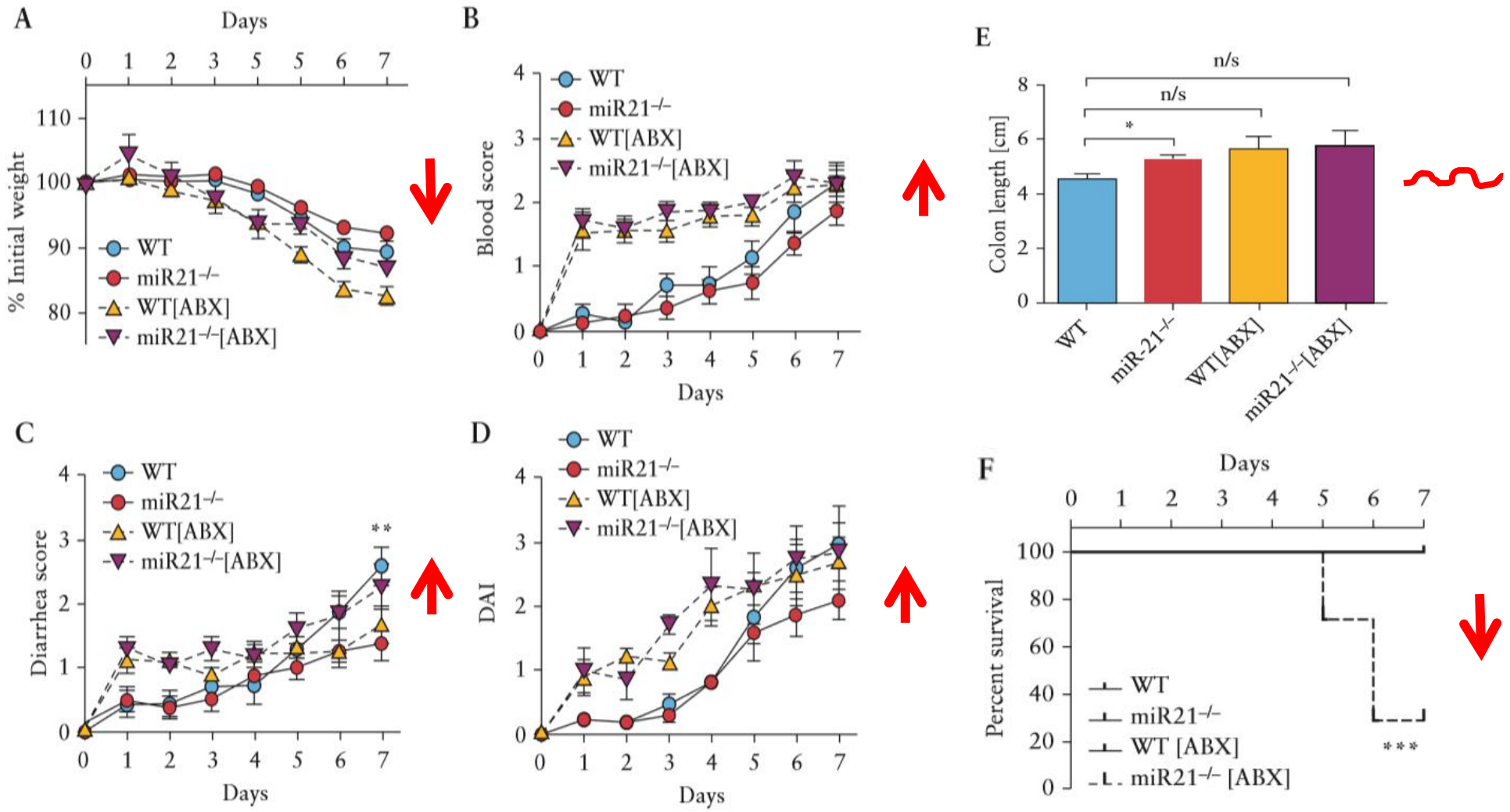
结果与讨论

Fig-5

抗生素干扰后mir -21–/–对DSS诱导结肠炎的保护丧失

given a 4-way antibiotics mix ad libitum for 2 weeks

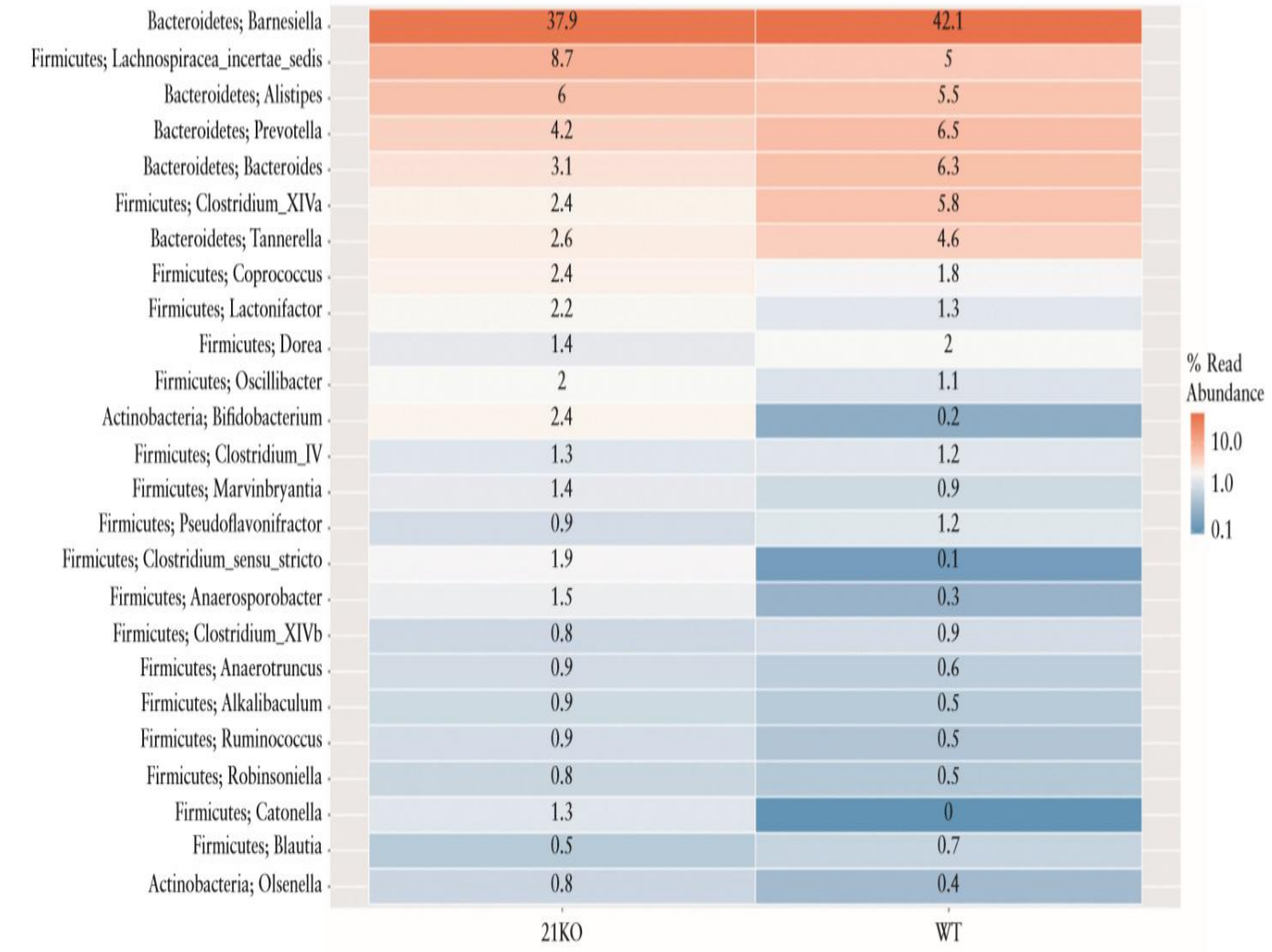
given 2.5% DSS [w/v] ad libitum for 7 days



结果与讨论

Fig-6 mir -21-/-使肠道菌群结构发生改变

A



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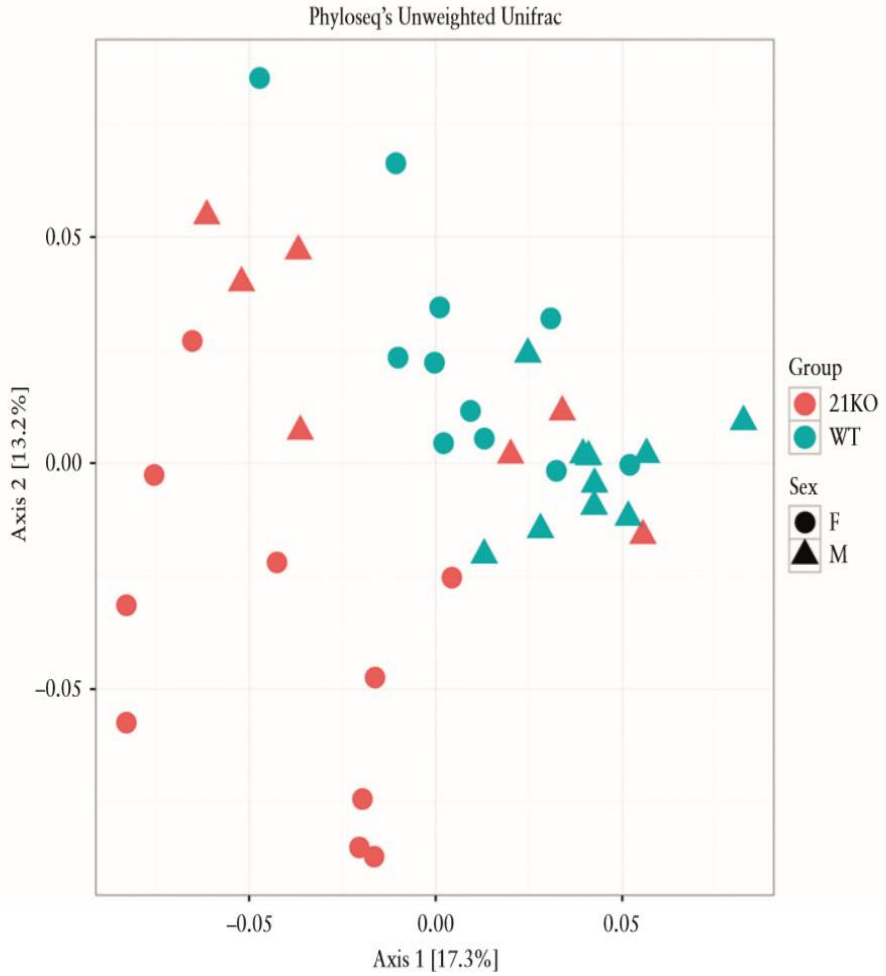
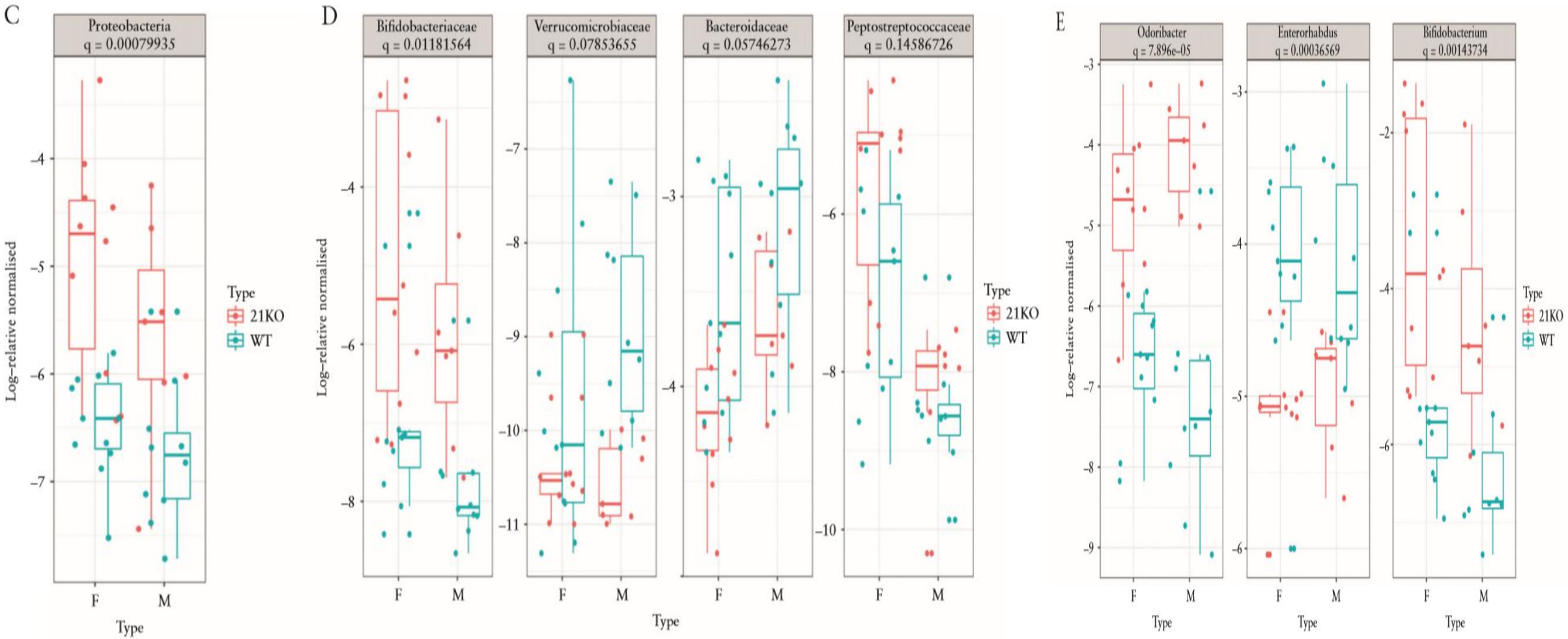


结果与讨论

Fig-6

mir -21-/-使肠道菌群结构发生改变

变形菌　　双歧杆菌　　疣微菌　　拟杆菌　　消化链球菌



门水平　　科水平　　属水平

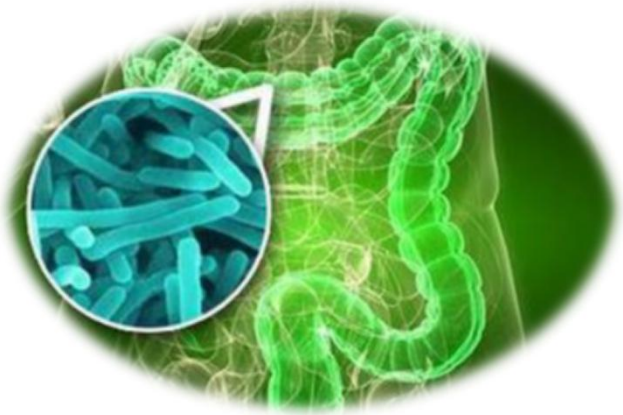
总结

1 .炎症性肠病[IBD]与microRNA-21表达改变有关，缺乏miR-21 可使机体对DSS诱导的结肠炎易感度降低----具有保护作用。

2 . microRNA-21对机体结肠炎的影响，是借由肠道微生物来实现的。缺乏miR-21 可使肠道菌群结构发生改变。

思考

miR-21



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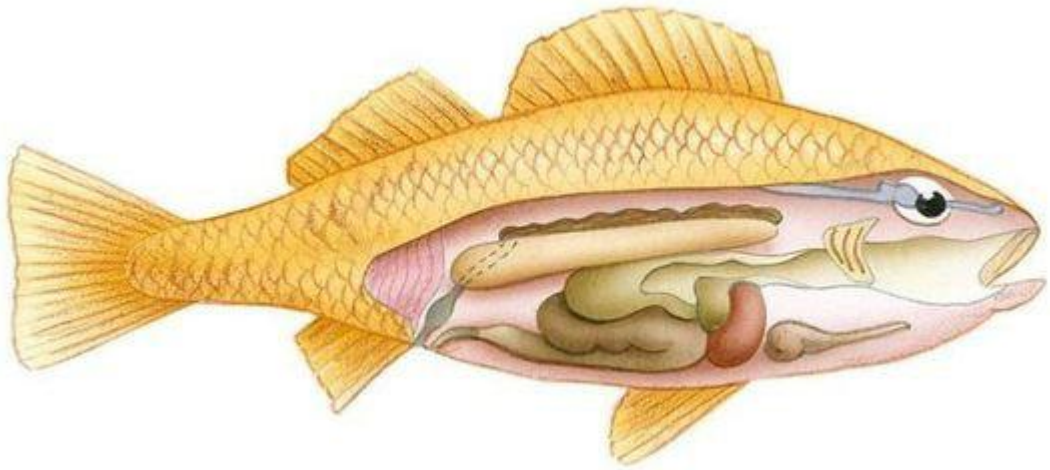

THANKS