growth factor 19 (FGF19) in sera (Figure 1A-C. The association of clostridia rich microbiota with BA synthesis and excretion in IBS-D patients a the histogram of the distribution of total fecal BA level in recruited subjects b c concentrations of C4). Their fecal metagenomes showed increased abundances of *Clostridia* and BA-transforming genomes (*bdhA* and *bais*). The increase of *Clostridia* (e.g. *Clostridium*) was positively associated with the levels of fecal BAs and serum C4, while being negatively correlated with serum FGF19 (Figure 1D, E). However, there is no big difference in BA profile and BA-transforming microbiome found in other IBS-D patients with normal BA excretion (grouped as BA-IBS-D) relative to controls. Further, transplantation of *Clostridia*-rich microbiota from IBS-D donors and introduction of a BA-transforming *Clostridium* species both enhanced levels of serum C4 and hepatic conjugated BAs in mice and reduced ileal FGF19 expression. Inhibition of *Clostridium* species by vancomycin yielded opposite findings. Moreover, *Clostridia*-derived BAs, like conjugated and free ursodeoxycholic acid, were also found to be significantly suppressed intestinal FGF19 expression *in vitro* and *in vivo*.

Conclusions The *Clostridia*-rich microbiota contributes to excessive BA excretion in IBS-D patients. This study provided the basis for more precise clinical diagnosis and management for IBS-D.

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ROLE OF ADHERENT-INVASIVE E. COLI IN INFLAMMATORY BOWEL DISEASE – EPIDEMIOLOGY, GENETICS AND THERAPEUTICS

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Background Adherent-invasive *Escherichia Coli* (AIEC) colonizes mucosa of patients with Crohn's disease (CD). Fecal microbiota transplantation (FMT) has been reported to be effective in treating CD but the response rates are variable. We investigated the prevalence of AIEC in Chinese population and explored the impact of AIEC on FMT efficacy.

Methods AIEC strains were isolated from ileal tissues of Chinese Crohn's disease patients (n=64) and healthy subjects (n=53) by selection culture and protection assay in Intestine-407 cell lines and their genomes analysed. Effect of AIEC on FMT was assessed in C57BL/6 wild type DSS-colitis model. Level of AIEC colonization was assessed by selective culture and Fluorescence in situ hybridization. Human ileal tissue and mice feces were collected for 16S rRNA sequencing.

Results Prevalence of AIEC was significantly higher in mucosa of CD subjects than healthy controls (p<0.05). Significant loss of *Megamonas* and *Veillonella* was observed in AIEC-positive ileal tissues, compared with AIEC-negative and healthy tissues. The majority of AIEC isolates belonged to B2 phylogroup. 43.9% of AIEC isolates were multi-drug-resistant. The Chinese AIEC isolates possessed a significantly higher prevalence of Quinolone-, Macrolide-, Sulphonamide-, Trimethoprim-, and Tetracycline- resistant

genes, compared with previously reported strains. These antibiotics resistant strains possessed significantly higher invasion properties than did non-resistant strains. In mice, FMT was not able to eradicate AIEC from the colon. After FMT, K12 (a noninvasive *E. coli* strain) - colonised mice, but not AIEC-infected mice, showed ameliorated colitis with elongated colon, improved colonic histology and decreased fecal Lcn-2 levels. FMT increased microbial diversity in K12-colonised mice but not in AIEC-infected mice. The proportion of donor-derived microbes in K12-colonised mice was significantly higher than in AIEC-infected mice, where a lack of engraftment of *Fecalibacterium prausnitzii*, *Akkermansia muciniphila* and *Allobaculum* was seen in AIEC-infected mice.

Conclusions AIEC is a risk factor for CD in the Chinese population. The presence of AIEC was sufficient to compromise the efficacy of FMT by hindering the engraftment of beneficial bacteria, leading to incomplete recovery of inflammation.

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GUT MICROBIOTA MODULATES THE CHEMOPREVENTIVE EFFICACY OF ASPIRIN ON COLORECTAL CANCER THROUGH IMPACT ON ASPIRIN BIOAVAILABILITY

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Background The gut microbiota, a pivotal regulator in colorectal cancer (CRC) development, is profoundly involved in drug metabolism. This study aims to decipher the role of the gut microbiota in aspirin-mediated chemoprevention of CRC in mice.

Methods Two models, azoxymethane (AOM, 10 mg/kg) and dextran sulfate sodium (DSS, 2.0%) induced CRC and APC^{min/+} induced CRC, were used in this study. Mice were orally administered aspirin (400 mg/L) with or without periodical antibiotics cocktail (0.1 g/L of vancomycin, 0.2 g/L of ampicillin, metronidazole and neomycin). AOM/DSS-treated germ-free mice and conventionally reared germ-free mice (conventionalized mice) were used for validation. Aspirin concentration was estimated by ultra-high performance liquid chromatography (UHPLC). Aspirin-degrading microbes were identified by UHPLC and 16S rRNA gene sequencing.

Results The tumor number and load were significantly reduced after aspirin treatment in antibiotics-treated mice in both AOM/DSS-treated and APC^{min/+} models, but not significantly changed in non-antibiotics-treated mice. Consistently, aspirin-treated germ-free mice exhibited significantly less tumor number and load compared to those not receiving aspirin, which was not seen in conventionalized mice, suggesting that gut microbiota impairs the chemopreventive efficacy of aspirin on CRC. UHPLC analysis revealed that plasma levels of aspirin were significantly higher in microbiota-depleted mice compared to microbiota-intact mice, indicating that gut microbiota limits aspirin bioavailability. Co-incubation of aspirin-containing medium and bacteria showed that aspirin levels in medium were significantly reduced when incubated with the fecal commensal bacteria from microbiota-intact mice compared to those from microbiota-depleted mice. Screening 1,093 bacterial colonies isolated from the feces of microbiota-intact mice