FAECAL MICROBIOTA TRANSPLANTATION PROMOTES NORMOBIOSIS AND RESTORES EPITHELIAL BARRIER IN MOUSE MODEL OF ULCERATIVE COLITIS

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Objectives
Ulcerative colitis (UC) is a chronic inflammatory disease associated with gut dysbiosis and disrupted epithelial barrier which allows translocation of the bacteria into tissues and the subsequent inflammation. Our study aims to investigate whether faecal microbiota transplantation (FMT) can restore normobiosis and gut epithelial barrier.

Methods
Female BALB/c mice (Velaz, Prague, Czech Republic) underwent antibiotic treatment (5 days) and subsequent convalescence to obtain a pseudo germ-free status. Animals were divided into three groups: control group (INT, n=12), group with UC (UC, n=15) and FMT treated UC group (FMT, n=15). The UC was induced by simultaneous administration (5 days) of DSS (dextran sodium sulphate) in drinking water and orally administered FMT from an UC patient. Subsequently, FMT group was treated by oral administration of FMT from a healthy donor (5 days). Colon samples were homogenized, and total RNA was extracted. DNA was isolated from faecal samples. Both RNA and DNA samples were analysed by a commercial NGS provider (Novogene Europe, UK).

Results
Genomic analysis of faecal DNA showed a significant decrease in species richness (chao1 index) after the induction of UC ($p<0,01$). On the other hand, FMT treatment significantly increased species diversity (simson index) compared to the UC ($p<0,001$) and INT group ($p<0,001$). After the FMT treatment we observed an increased abundance of *Bacteroides uniformis* ($p<0.05$), *Lachnospiraceae bacterium* NK4A136 ($p<0.05$) and *Parabacteroides merdae* ($p<0.05$), which are decreased in patients with UC compared to healthy controls. Colitis induction significantly (padj<0,05) decreased the expression of several genes coding proteins of functional tight junctions (*Cldn3, Tjp2, Tjp3, Ocln, F11r, Igsf5, Marveld2*). Expression of these genes significantly increased (padj<0,05) after the FMT treatment along with *Cldn4* and *Cldn9*. Transcriptomic analysis revealed a significant decrease (padj<0,05) in expression of genes for inflammatory cytokines IL-4 and IL-6 whose role in disrupting

the epithelial barrier has been described. Levels of *Il4* and *Il6* transcripts significantly decreased (padj<0,05) after the FMT treatment.

Conclusion
Our study provides evidence that FMT treatment can restore gut epithelial barrier and normobiosis in a pseudo germ-free mice model of UC.
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