Administration of the colostrum extract IMM-124E ameliorates colitis

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Background

Inflammatory bowel disease (IBD) is accompanied by lesions in the epithelial barrier, which allow translocation of bacterial products from the gut lumen to the host's circulation. Systemic exposure to certain bacterial products, including lipopolysaccharide (LPS) elicits strong immune responses, and thereby contributes to the pathogenesis and perpetuation of IBD. LPS exposure in particular, promotes production of pro-inflammatory cytokines, and affects immune cell activation. Colostrum contains high levels of immunglobulins (Ig), which neutralize bacteria-derived antigens in the intestine, and thereby prevent systemic translocation of bacterial products. IMM-124E is a colostrum-based product, containing high levels of anti-LPS IgG, and therefore prevents systemic exposure to LPS. Since LPS is involved in IBD pathogenesis, we here investigated whether IMM-124E can ameliorate symptoms of intestinal inflammation.

Methods

Acute colitis was induced in WT C57Bl/6 mice by administration of 2% DSS in the drinking water for 7 days. T cell transfer colitis was induced via transfer of $0.25x10^6$ naïve T cells into $RAG2^{-/-}$ C57Bl/6 mice. IMM-124E was administered daily by oral gavages throughout the experiment (acute DSS colitis) or upon onset of colitis symptoms, namely weight loss and macroscopically inflamed colon as visible by colonoscopy (T cell transfer colitis).

IMM-124E administration ameliorates DSS colitis

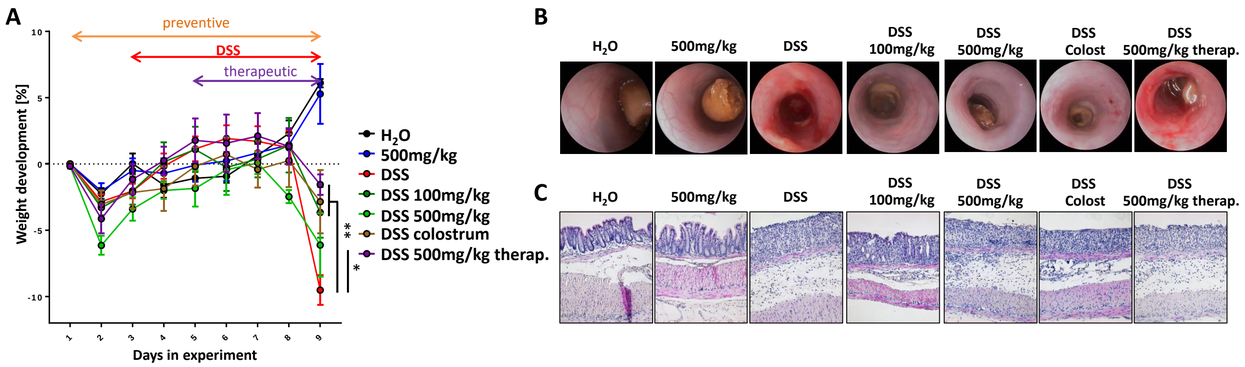

Figure 1. IMM-124E administration reduces DSS colitis. During induction of acute DSS colitis (2% DSS in the drinking water for 7 days), mice were treated with IMM-124E or colostrum either in a preventive (starting 2 days before DSS administration) or a therapeutic (the last 5 days of the experiment) setting. Depicted are **A)** weight development, **B)** representative pictures from colonoscopy, and **C)** representative pictures from H&E stained sections of the terminal colon. *p<0.05, **p<0.01

Decreased colitis in the T cell transfer model

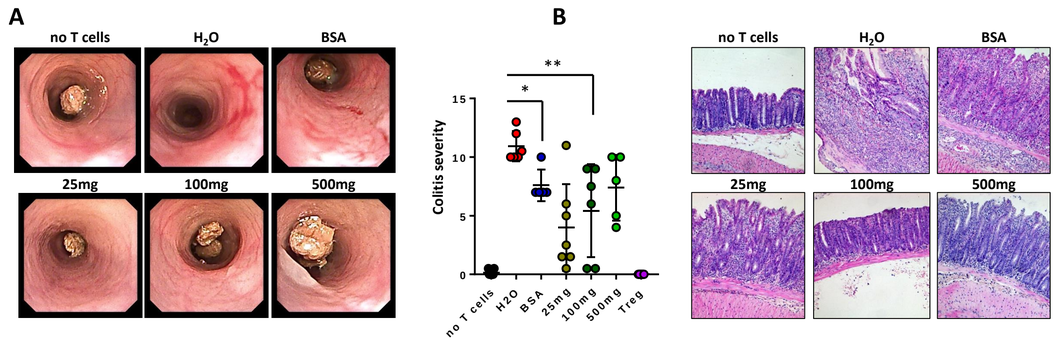

Figure 2. Decreased intestinal inflammation in the immune cell mediated naïve T cell transfer model of colitis. Rag-/- mice were injected with 0.5*10^6 naïve T cells. After 21 days, mice were randomized and administered IMM-124E in the indicated doses or 100 mg/kg BSA. Depicted are **A)** representative pictures from colonoscopy, **B)** scores of colitis severity, and **C)** representative pictures from H&E stained sections of the terminal colon. *p<0.05, **p<0.01, ***p<0.001

Reduced systemic exposure to LPS

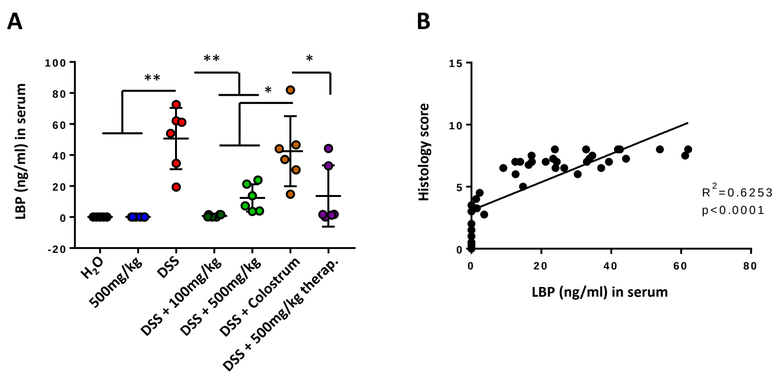

Figure 3. IMM-124E results in reduced levels of LPS binding protein (LBP) in the serum. A) During induction of acute DSS colitis via administration of 2% DSS, mice were administered IMM-124E or colostrum either preventive (starting 2 days before DSS administration) or therapeutically (the last 5 days of the experiment). LBP levels as an indicator for systemic LPS exposure were analysed by ELISA. **B)** Correlation of histology scores and LBP levels. *=p<0.05, **= p<0.001

Conclusions

Our results demonstrate that treatment with IMM-124E significantly reduces intestinal inflammation via reducing systemic exposure to LPS and preventing the accumulation and differentiation of pathogenic T cells, while concomitantly enhancing the induction of regulatory cells. This may suggest that inhibiting LPS-mediated effects on the mucosal immune system ameliorates colitis. Summarized, our findings indicate that IMM-124E administration might represent a novel therapeutic strategy to induce or maintain remission in IBD patients.

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The authors declare no financial conflict of interest

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