Title: EVALUATION OF PROBIOTIC EFFECT OF *Escherichia coli* STRAIN NISSLE 1917 IN A CHRONIC MODEL OF ULCERATIVE COLITIS IN MICE

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Abstract:

Ulcerative colitis (UC) is a chronic inflammatory condition that affects the lining of the colon, with periods of remission and relapse. The etiology is unknown, although it is believed to be a dysregulated immune response against intestinal microbiota, being genetically triggered and influenced by environmental factors. The treatment typically involves the use of anti-inflammatory drugs and corticosteroids, probiotics being the latest alternative therapy, among which *Escherichia coli* Nissle 1917 (EcN) is noteworthy. The aim of this study was to evaluate the probiotic effect of EcN in a model of chronic ulcerative colitis in mice. For this purpose, 6-8 weeks female mice were used (CEUA/UFMG, protocol no. 046/2011), with UC induced by oral administration of three alternating cycles of a 3.0% Dextran Sodium Sulphate (DSS) solution. The probiotic was administered daily (10^8 cells) intragastrically. The treatment showed significant improvement in clinical signs of disease, on the shortening of the colon, characteristic of UC disease, as well as the macroscopic damage score of the mucosa. Histology revealed similar patterns between sick and treated groups, despite the obvious hyperplasia of Peyer's patches in the treated group, suggesting a stimulation of regulatory immune response by EcN. The analysis of bacterial translocation showed a recently discovered profile of this probiotic, which has great ability to translocate. When administered in colitis, EcN translocation reduces and it comes to play a local effect. The IgA production, important in the control of microbial density, was reestablished after EcN treatment, since colitis significantly reduces their concentrations in the intestinal fluid. To evaluate the modulating effect of EcN probiotic on the intestinal microbiota, germ-free mice were used, undergoing fecal transplantation with samples from mice treated or not with EcN, being UC induced after the conventionalization period. It was observed significant difference in the first two UC cycles, profile not maintained in the last one. This allows to conclude that the modulating effect of probiotic on the microbiota is not maintained unless it remains in the intestinal environment. Thus, the analyzes support the conclusion that EcN has beneficial effect on the improvement of symptoms of chronic ulcerative colitis, requiring further analysis aimed to identify the mechanisms by which this effect is being generated.

Keywords: Inflammatory Bowel Disease (IBD), Ulcerative Colitis (UC), Dextran Sodium Sulfate (DSS), probiotic, *Escherichia coli* strain Nissle 1917 (EcN).

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