

# MULTI-DONOR FMT REVERSES DYSBIOSIS AND INDUCES CLINICAL REMISSION IN A RAT MODEL OF COLITIS

Petra Adamkova<sup>1</sup>, Petra Hradicka<sup>1</sup>, Sona Gancarcikova<sup>2</sup> and Vlasta Demeckova<sup>1\*</sup>

<sup>1</sup> Department of Animal Physiology, Faculty of Science, Pavol Jozef Safarik University in Kosice, Slovakia; \*vlasta.demeckova@upjs.sk

<sup>2</sup> Department of microbiology and immunology, University of Veterinary Medicine and Pharmacy in Kosice, Slovakia

Keywords: microbiome-based therapy, ulcerative colitis, colon inflammation

## Objectives

Growing evidence indicates that gut dysbiosis is a key factor in the pathogenesis of ulcerative colitis. Multi-donor faecal microbiota transplant (FMT) appears to be a promising treatment strategy to induce remission while minimizing the super-donor phenomenon typical for single-donor FMT. Therefore, the aim of our study was to assess the therapeutic potential of multi-donor FMT in experimental colitis.

## Methods

Sprague Dawley rats (♂, 5w, Velaz, Czech Republic) were divided into colitis group (DSS; n=16) and FMT-treated group (FMT; n=16) and control group (C; n=6). Colitis was induced by administering 5% dextran sodium sulphate (DSS; 40 kD; TdB Labs, Sweden) for 7 days in water. FMT was prepared from healthy rat faecal samples (n=16) and administered orally during 5 days after colitis induction. To evaluate the colitis severity, a disease activity index (DAI) score was determined daily. Animals were then sacrificed, colon tissues were collected for histopathological examination and for detection of cytokines by 22-Plex Rat ProcartaPlex™ Panel (Invitrogen, France). Microbiota profiling of faecal samples was performed by 16S rRNA sequencing (Novogene Europe, UK).

## Results

The evaluation of the health status of experimental animals showed gradual colitis remission in the FMT group, which was reflected in a significant decrease of DAI score ( $p < 0.01$  vs. DSS). The histopathological score for intestinal inflammation was significantly reduced after FMT treatment ( $p < 0.001$ ) supported also by the significant reduction of lymphoid aggregates ( $p < 0.01$ ). The levels of chemokines (monocyte chemoattractant protein-1, macrophage inflammatory protein-1 $\alpha$ ) and pro-inflammatory cytokines (interleukin (IL)-1 $\beta$ , IL-17A) were significantly decreased in the FMT group ( $p < 0.01$  and  $p < 0.05$ , respectively) compared to DSS. After FMT treatment, an increased abundance of anti-inflammatory *Bacteroides uniformis* and *B. vulgatus* was observed ( $p < 0.05$ ). Moreover, abundance of opportunistic pathogen *B. thetaiotaomicron*, which is able to cause severe colitis, was decreased after FMT ( $p = 0.004$ ).

## Conclusion

Our study confirmed, that FMT has evident restorative effect on microbial composition as well as on colon inflammation. However, the mechanisms by which it exerts its therapeutic effects have not yet been fully elucidated.

The work was supported by APVV-16-0176 and VEGA1/0015/21.