

# Anti-TNF- $\alpha$ Therapy Exerts Intestinal Anti-inflammatory and Anti-apoptotic Effects After Massive Bowel Resection in a Rat

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## Background

Recent evidence has demonstrated that treatment of children with anti-TNF- $\alpha$  agents after major intestinal surgery results in a dramatic improvement in anastomotic ulcerations and Crohn's disease like symptoms. The aim of this study was to examine the effect of massive small bowel resection on proinflammatory cytokine intestinal expression and the effect of anti-TNF- $\alpha$  antibodies (ATA, Remicade) on intestinal inflammation, epithelial cell turnover and intestinal adaptation in a rat model of short bowel syndrome (SBS).

## Methods

Male Sprague-Dawley rats were divided into 4 experimental groups:

Group A: Sham-rats underwent bowel transection

Group B: Sham-ATA rats underwent bowel transection and were treated with ATA given SC at a dose of 15 mg/kg from day 4 to day 14

Group C: SBS-animals underwent 75% bowel resection

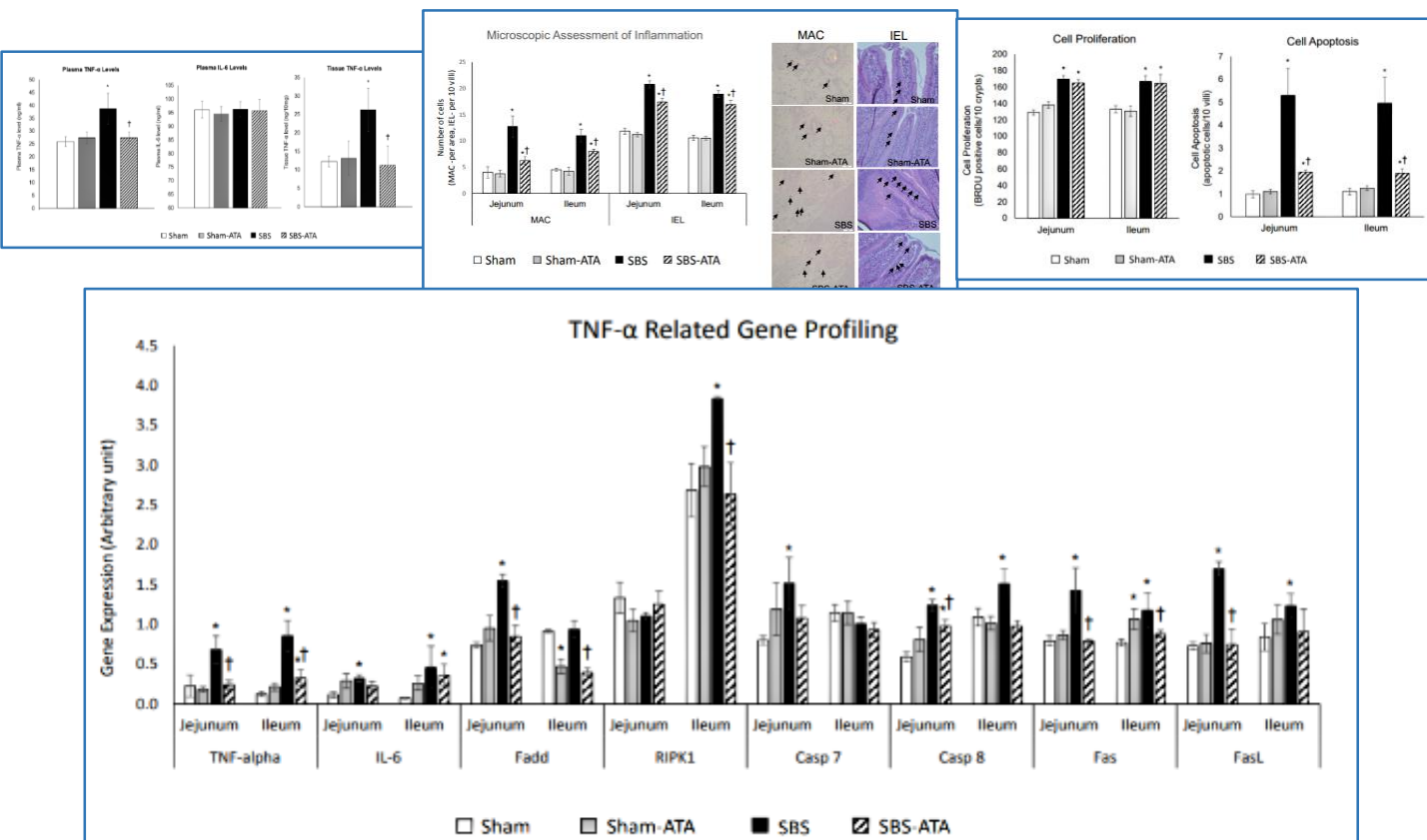
Group D: SBS-ATA rats underwent bowel resection and were treated with ATA similarly to Group B

Parameters of intestinal adaptation, enterocyte proliferation and apoptosis were determined at sacrifice.

Illumina's Digital Gene Expression (DGE) analysis was used to determine TNF- $\alpha$  related gene expression profiling.

TNF- $\alpha$  and apoptosis related gene and protein levels were determined by Real Time PCR, Western blotting and immunohistochemistry.

## Results



## Conclusion

- Microarray expression profiling demonstrates that most of the TNF- $\alpha$  signaling related genes are up-regulated in resected rats compared to control animals.
- Treatment with anti-TNF- $\alpha$  agent (Infliximab) results in a significant decrease in plasma and intestinal IL-6 and TNF- $\alpha$  levels with concomitant lowering the proinflammatory intestinal markers.
- Anti-TNF- $\alpha$  therapy enhances intestinal adaptation mainly by inhibiting cell apoptosis. Extrinsic rather than intrinsic apoptotic pathway is responsible for antiapoptotic effects of ATA on intestinal mucosa.