REGULATORY T CELLS

A helping hand from *Bacteroides fragilis*

To maintain intestinal homeostasis and avoid the development of inflammatory bowel disease (IBD), the immune system must develop tolerance towards the intestinal microbiota. This can be achieved, in part, through the action of inducible $CD4^+CD25^+FOXP3^+$ regulatory T (T_{Reg}) cells, which produce the anti-inflammatory cytokine interleukin-10 (IL-10) and are induced in peripheral tissues, such as the colon. This study reveals that *Bacteroides fragilis* has an active role in promoting the development of inducible T_{Reg} cells and, consequently, inhibiting intestinal inflammation.

B. fragilis produces polysaccharide A (PSA), which is known to protect from inflammation by suppressing the production of the pro-inflammatory cytokine IL-17, so the authors assessed the effect of PSA on T_{Reg} cell induction in mice *in vivo*. PSA was required for the induction of IL-10-producing T_{Reg} cells in the colon; this depended on Toll-like receptor 2 (TLR2), as — following PSA treatment — *Tlr2*$^{-/-}$ mice produced similar levels of IL-10 to germ-free mice. Furthermore, T_{Reg} cells isolated from the mesenteric lymph nodes of mice treated with PSA showed increased suppressive capacity towards naive T cells *in vitro* compared with T_{Reg} cells isolated from control mice, and had enhanced expression of several genes, including *Il10*.

So what is the effect of PSA on colitis development? Mice with trinitrobenzene sulphonic acid (TNBS)-induced colitis that were treated with PSA had significantly more T_{Reg} cells in the mesenteric lymph nodes and higher expression of *Foxp3* mRNA than non-colitic mice or colitic mice treated with saline. T_{Reg} cells isolated from colitic PSA-treated mice also showed an increased suppressive capacity towards effector T cells *in vitro*. PSA-mediated protection depended on TLR2, as *Tlr2*$^{-/-}$ mice were not protected from inflammation by PSA treatment.

> *Bacteroides fragilis* has an active role in promoting the development of inducible T_{Reg} cells

Together, these findings suggest that *B. fragilis* PSA promotes the induction of IL-10-producing T_{Reg} cells in a TLR2-dependent manner, and that these cells mediate tolerance towards the intestinal microbiota. As this study found that PSA treatment both before and after TNBS-mediated colitis induction markedly prevented colitis development *in vivo*, future work on the immunomodulatory properties of this polysaccharide could lead to the development of treatments for IBD.

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ORIGINAL RESEARCH PAPER Round, J. L. & Mazmanian, S. K. Inducible $Foxp3^+$ regulatory T-cell development by a commensal bacterium of the intestinal microbiota. *Proc. Natl Acad. Sci. USA* 21 Jun 2010 (doi:10.1073/pnas.0909122107)