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Mucosal delivery of IL-27 attenuates murine enterocolitis via T cell-derived IL-10

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Treatment of inflammatory bowel disease (IBD) would benefit by local delivery of therapeutics, avoiding systemic effects. *Lactococcus lactis* is a food grade bacterium that has been engineered to deliver experimental protein therapeutics to the bowel following oral administration. It has been shown to be safe in clinical trials. IL-27 is a cytokine that has been shown to inhibit development of pro-inflammatory Th17 cells and induce development of suppressor Tr1 cells that act by producing immunosuppressive IL-10. IL-27 was engineered into Lactococcus lactis (LL-IL-27) and used to treat, by gavaging, several mouse models of IBD. T cell transfer IBD was treated with LL-IL-27 at the time symptoms developed 7.5wk after transfer, and treatment was performed daily for two weeks. LL-IL-27 treatment showed a substantial therapeutic benefit in enterocolitis, improving survival, decreasing disease activity index, reducing inflammatory cytokine levels and eliminating pathology in the colon and small intestine. The therapeutic benefit required induction of IL-10 in the transferred T cell population which was primarily expressed by intraepithelial CD4+CD8∝+ T cells. LL-IL-27 was much more effective in reducing DAI and colon pathology than either LL-IL-10 or systemic administration of recombinant mouse IL-27. LL-IL-27 was also very effective in acute colitis induced by DSS in drinking water or TNBS installation. Since LL-IL-27 was highly effective in three different murine IBD models that differ substantially in mechanism it offers promise in human IBD.

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