GLP-1 Induces Barrier Protective Expression in Brunner's Glands and Regulates Colonic Inflammation

Background: Beneficial roles for glucagon-like peptide 1 (GLP-1)/GLP-1R signaling have recently been described in diseases, where low-grade inflammation is a common phenomenon. We investigated the effects of GLP-1 in Brunner's glands and duodenum with abundant expression of GLP-1 receptors, as well as GLP-1 effect on colonic inflammation.

Methods: RNA from Brunner's glands of GLP-1R knockout and wild-type mice were subjected to full transcriptome profiling. Array results were validated by quantitative reverse transcription polymerase chain reaction in wild-type mice and compared with samples from inflammatory bowel disease (IBD) patients and controls. In addition, we performed a detailed investigation of the effects of exogenous liraglutide dosing in a T-cell driven adoptive transfer (AdTr) colitis mouse model.

Results: Analyses of the Brunner's gland transcriptomes of GLP-1R knockout and wild-type mice identified 722 differentially expressed genes. Uregulated transcripts after GLP-1 dosing included IL-33, chemokine ligand 20 (CCL20), and mucin 5b. Biopsies from IBD patients and controls, as well as data from the AdTr model, showed deregulated expression of GLP-1R, CCL20, and IL-33 in colon. Circulating levels of GLP-1 were found to be increased in mice with colitis. Finally, the colonic cytokine levels and disease scores of the AdTr model indicated reduced levels of colonic inflammation in liraglutide-dosed animals.

Conclusions: We demonstrate that IL-33, GLP-1R, and CCL20 are deregulated in human IBD, and that prophylactic treatment with 0.6 mg/kg liraglutide improves disease in AdTr colitis. In addition, GLP-1 receptor agonists upregulate IL-33, mucin 5b, and CCL20 in murine Brunner's glands. Taken together, our data indicate that GLP-1 receptor agonists affect gut homeostasis in both proximal and distal parts of the gut.