Gpr17 signaling decreases GLP-1 secretion in GLUTag cells

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Background and Hypothesis: The incidence of obesity and diabetes continues to rise in devastatingly high proportions, making the need for safe, affordable, and effective treatment increasingly apparent. We discovered that the orphan G protein-coupled receptor 17 (Gpr17) is expressed in endocrine cells in the brain and gut and may have an important role in metabolic regulation. Glucagon-like peptide 1 (GLP-1), an incretin hormone secreted from enteroendocrine cells, is a strong insulin secretagogue and suppresses appetite. We hypothesized that Gpr17 signaling decreases GLP-1 secretion in gut enteroendocrine cells.

Experimental Design or Project Methods: In order to investigate the role of Gpr17 in GLP-1 secretion, we measured GLP-1 secretion in a murine enteroendocrine cell line (GLUTag cells) that expresses Gpr17 and the proglucagon gene and secretes GLP-1 in a regulated manner. GLUTag cells were stimulated with glucose or lipid, oleoyl-lysophosphatidylcholine (LPC), in the presence or absence of MDL29,951, a synthetic Gpr17 agonist. After a 2-hour incubation, we measured GLP-1 in the media and cell lysates to determine the percentage of secreted GLP-1.

Results: Cells treated with glucose and MDL29,951 had decreased GLP-1 secretion compared to glucose alone, however, the difference was not significant. Cells treated with LPC and MDL29,951 had a significant decrease in GLP-1 secretion compared to LPC alone.

Conclusion and Potential Impact: Gpr17 activation by MDL29,951 decreased GLP-1 secretion in GLUTag cells stimulated by both glucose and lipid, which supports our hypothesis that Gpr17 signaling regulates GLP-1 secretion. Therefore, Gpr17 may be a potential pharmacological target for combating obesity and diabetes.