

Free Fatty Acid Receptor GPR120 Is Highly Expressed in Enteroendocrine K Cells of the Upper Small Intestine and Has a Critical Role in GIP Secretion After Fat Ingestion

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Abstract

Gastric inhibitory polypeptide (GIP) is an incretin secreted from enteroendocrine K cells in response to meal ingestion^{1), 2), 3)}. Recently free fatty acid receptor G protein-coupled receptor (GPR) 120 was identified as a lipid sensor involved in glucagon-like peptide-1 secretion^{4), 5)}. However, *Gpr 120* gene expression and its role in K cells remain unclear, partly due to difficulties in separation of K cells from other intestinal epithelial cells. In this study, we purified K cells using GIP-green fluorescent protein (GFP) knock-in mice, in which K cells can be visualized by GFP fluorescence⁶⁾. GFP-positive cells (K cells) were observed in the small intestine but not in the stomach and colon. K cell number and GIP content in K cells were significantly higher in the upper small intestine than those in the lower small intestine. We also examined the expression levels of several free fatty acid receptors in K cells. Among free fatty acid receptors, GPR120 was highly expressed in the K cells of the upper small intestine compared with the lower small intestine. To clarify the role of GPR120 on K cells in vivo, we used GPR120-deficient mice (GPR120^{-/-}). GPR120^{-/-} exhibited significantly lower GIP secretion (75% reduction, $p < 0.01$) after lard oil ingestion compared with that in wild-type mice. Consistently, pharmacological inhibition of GPR120 with grifolic acid methyl ether in wild-type mice significantly attenuated lard oil-induced GIP secretion. In conclusion, GPR120 is expressed abundantly in K cells of the upper small intestine and plays a critical role in lipid-induced GIP secretion. (Endocrinology 156: 837– 846, 2015)

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