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Oleoyl-lysophosphatidylinositol enhances glucagon-like peptide-1 secretion from enteroendocrine L-cells through GPR119 (Article)

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Abstract

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The gastrointestinal tract is increasingly viewed as critical in controlling glucose metabolism, because of its role in secreting multiple glucoregulatory hormones, such as glucagon like peptide-1 (GLP-1). Here we investigate the molecular pathways behind the GLP-1- and insulin-secreting capabilities of a novel GPR119 agonist, Oleoyl-lysophosphatidylinositol (Oleoyl-LPI). Oleoyl-LPI is the only LPI species able to potently stimulate the release of GLP-1 in vitro, from murine and human L-cells, and ex-vivo from murine colonic primary cell preparations. Here we show that Oleoyl-LPI mediates GLP-1 secretion through GPR119 as this activity is ablated in cells lacking GPR119 and in colonic primary cell preparation from GPR119^{-/-} mice. Similarly, Oleoyl-LPI-mediated insulin secretion is impaired in islets isolated from GPR119^{-/-} mice. On the other hand, GLP-1 secretion is not impaired in cells lacking GPR55 in vitro or in colonic primary cell preparation from GPR55^{-/-} mice. We therefore conclude that GPR119 is the Oleoyl-LPI receptor, upstream of ERK1/2 and cAMP/PKA/CREB pathways, where primarily ERK1/2 is required for GLP-1 secretion, while CREB activation appears dispensable. © 2018

Author keywords

[Glucagon-like peptide-1 \(GLP-1\)](#) [GPR119](#) [GPR55](#) [L-cells](#) [Lysophosphatidylinositol \(LPI\)](#) [Mixed colonic preparation](#)

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organized the literature and figures and performed statistical analyses. TM reviewed/edited the manuscript and provided intellectual contribution to the study. J.H.E., P.N. and M.M.R. reviewed/edited the manuscript. R.C. contributed to discussion and reviewed/edited manuscript. I.C. performed experiments and contributed to discussion. M.F. conceived the project, led and supervised the study, performed experiments and wrote ... View All 



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