FFAR CASCADE STIMULATES CCK AND GLP-1:

IMPLICATIONS FOR

DIABETES

GPR 40, 41, 119 and 120 are G-protein receptors that have been proven to respond to free fatty acids, thus earning the title free fatty acid receptors (FFARs). FFAs stimulate a cascade involving these receptors to release CCK and GLP-1 to play a role in Type 2 Diabetes. Phoenix now offers cDNAs for these receptors as well as their corresponding fatty-acid agonists.

Receptor	Receptor cDNA Cat. No., size, price	Effects in addition to insulin stimulation	Sites in addition to Islets
GPR40	G40, 100ug, $400	Stimulation of incretin hormone secretion	Brain, liver, muscle, enteroendocrine cells, omental adipocytes, islet alpha-cells
GPR119	G119, 100ug, $400	Stimulation of incretin hormone secretion	Enteroendocrine cells, brain
GPR41	G41, 100ug, $400	Anti-inflammation	Brain, lung, adipose tissue, immune cells
GPR43	G43, 100ug, $400	Inhibition of lipolysis, immune function	Immune cells, spleen, bone marrow, adipose tissue
GPR120	G120, 100ug, $400	Stimulation of GLP1 secretion	Enteroendocrine cells

Receptor	Ligands	Ligand Cat No., Size, Price
GPR40	OEA (Oleoylethanolamide); GW9508 4-[[(3-phoxyphenyl) methyl] amino]-benze-nepropanoic acid	032-51, 1mg, $50; 032-60, 5mg, $70
GPR120	DHA (Docosahexaenoic acid); EPA (Eicosa-pantaenoic acid)	032-54, 5mg, $50; 032-55, 5mg, $50

PHOENIX PHARMACEUTICALS, INC.
330 BEACH ROAD, BURLINGAME CA, 94010, USA
PHONE: (650) 558-8898 EMAIL: info@phoenixpeptide.com
WWW.PHOENIXPEPTIDE.COM

PHOENIX EUROPE GMBH
VIKTORIASTRASSE 3-5, D-76133 KARLSRUHE, GERMANY
PHONE: +49-721-1611950 EMAIL: germany@phoenixpeptide.com
WWW.PHOENIXPEPTIDE.COM

The G-Protein−Coupled Receptor GPR40 Directly Mediates Long-Chain Fatty Acid−Induced Secretion of Cholecystokinin

Background & Aims:
Long-chain fatty acid receptors G-protein−coupled receptor 40 (GPR40) (FFAR1) and GPR120 have been implicated in the chemosensation of dietary fats. I cells in the intestine secrete cholecystokinin (CCK), a peptide hormone that stimulates digestion of fat and protein, but these cells are rare and hard to identify. We sought to determine whether dietary fat-induced secretion of CCK is directly mediated by GPR40 expressed on I cells.
Methods:
We used fluorescence-activated cell sorting to isolate a pure population of I cells from duodenal mucosa in transgenic mice that expressed green fluorescent protein under the control of the CCK promoter (CCK−enhanced green fluorescent protein [eGFP] bacterial artificial chromosome mice). CCK-eGFP cells were evaluated for GPR40 expression by quantitative reverse transcription polymerase chain reaction and immunostaining. GPR40−/− mice were bred with CCK-eGFP mice to evaluate functional relevance of GPR40 on long-chain fatty acid−stimulated increases in [Ca2+]i and CCK secretion in isolated CCK-eGFP cells. Plasma levels of CCK after olive oil gavage were compared between GPR40+/+ and GPR40−/− mice.
Results:
Cells that expressed eGFP also expressed GPR40; expression of GPR40 was 100-fold greater than that of cells that did not express eGFP. In vitro, linoleic, oleic, and linolenic acids increased [Ca2+]i; linolenic acid increased CCK secretion by 53% in isolated GPR40+/+ cells that expressed eGFP. In contrast, in GPR40−/− that expressed eGFP, [Ca2+]i response to linoleic acid was reduced by 50% and there was no significant CCK secretion in response to linolenic acid. In mice, olive oil gavage significantly increased plasma levels of CCK compared with pregavage levels: 5.7-fold in GPR40+/+ mice and 3.1-fold in GPR40−/− mice.
Conclusions:
Long-chain fatty acid receptor GPR40 induces secretion of CCK by I cells in response to dietary fat.
Alice P. Liou Gastronterology published online 18 October 2010.

GPR120 Is an Omega-3 Fatty Acid Receptor Mediating Potent Anti-inflammatory and Insulin-Sensitizing Effects

Omega-3 fatty acids (ω-3 FAs), DHA and EPA, exert anti-inflammatory effects, but the mechanisms are poorly understood. Here, we show that the G protein-coupled receptor 120 (GPR120) functions as an ω-3 FA receptor/sensor. Stimulation of GPR120 with ω-3 FAs or a chemical agonist causes broad anti-inflammatory effects in monocytic RAW 264.7 cells and in primary intraperitoneal macrophages. All of these effects are abrogated by GPR120 knockdown. Since chronic macrophage-mediated tissue inflammation is a key mechanism for insulin resistance in obesity, we fed obese WT and GPR120 knockout mice a high-fat diet with or without ω-3 FA supplementation. The ω-3 FA treatment inhibited inflammation and enhanced systemic insulin sensitivity in WT mice, but was without effect in GPR120 knockout mice. In conclusion, GPR120 is a functional ω-3 FA receptor/sensor and mediates potent insulin sensitizing and antidiabetic effects in vivo by repressing macrophage-induced tissue inflammation.
Da Young Oh, Saswata Talukdar Cell, Volume 142, Issue 5, 687-698, 3 September 2010

- Other GPR-related products -

Catalog No.	Product Name	Standard Size
001-68	GPR-40 (280-300) (Human)	100 µg
001-39	GPR-41 (320-346) (Human)	100 µg
001-98	GPR-41 (292-319) (Rat, Mouse)	100 µg
032-53	GPR-119 (300-335) (Human)	100 µg
032-52	GPR-119 (312-335) (Human)	100 µg
032-51	OEA (Oleoylethanolamide)	1 mg