Product Data Sheet

Product Name: [Pro3]-GIP (Mouse)
Cat. No.: GC50278

Chemical Properties

Cas. No.			
Formula	$C_{225}H_{342}N_{62}O_{64}S$	M.Wt	4971.62
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	[Pro3]-GIP (Mouse)		

Protocol

Cell experiment [1]:

Cell lines	CHL cells

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Preparation Method	The CHL cells that have been stably transfected with the human GIP receptor were cultured in DMEM medium containing 10% (v/v) fetal bovine serum and 1% (v/v) antibiotics (100U/ml penicillin, 0.1mg/ml streptomycin), and were maintained at 37°C in a culture environment with 5% CO_2 and 95% air. The cells were cultured for a further 48h before being loaded at 37°C for 6h with 2μCi of tritiated adenine. Then, the cells were washed twice with HBS buffer (130mM NaCl, 20mM HEPES, 0.9mM $NaHPO_4$, 0.8mM $MgSO_4$, 5.4mM KCl, 1.8mM $CaCl_2$, 25mM glucose and 25μM phenol red; pH 7.4). Subsequently, the cells were exposed to different concentrations (0.001, 0.01, 0.1, 1, 10, 100, and 1000nM) of [Pro3]-GIP at 37°C for 10 minutes. After that, the culture medium was removed and the cells were lysed with 1ml of 5% (v/v) trichloroacetic acid (containing 0.1mM unlabeled cAMP and 0.1mM unlabeled ATP). Finally, the intracellular cAMP was analyzed.
Reaction Conditions	0.001, 0.01, 0.1, 1, 10, 100, and 1000nM; 10min
Applications	[Pro3]-GIP treatment significantly inhibited cAMP generation in CHL cells in a dose-dependent manner.

Animal experiment [2]:

Animal models	Obese diabetic (ob/ob) mice

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Preparation Method	The ob/ob mice were housed in an air-conditioned room at 22±2°C, with a 12-hour light:12-hour dark cycle (08:00-20:00). Ob/ob mice were intraperitoneally injected with a 0.9% [w/v] NaCl saline vehicle or [Pro3]-GIP (25nmol/kg/day) once daily at 17:00 for 60 days. Food intake and body weight were recorded daily, and blood glucose and insulin concentrations were monitored every 3-7 days.
Dosage form	25nmol/kg/day for 60 days; i.p.
Applications	[Pro3]-GIP treatment significantly improved non-fasting glucose and insulin sensitivity in ob/ob mice.

References:

[1] Gault V A, O'harte F P M, Harriott P, et al. Effects of the novel (Pro3) GIP antagonist and exendin (9–39) amide on GIP-and GLP-1-induced cyclic AMP generation, insulin secretion and postprandial insulin release in obese diabetic (ob/ob) mice: evidence that GIP is the major physiological incretin[J]. Diabetologia, 2003, 46(2): 222-230.

[2] Irwin N, McClean P L, O’harte F P M, et al.

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Early administration of the glucose-dependent insulinotropic polypeptide receptor antagonist (Pro3) GIP prevents the development of diabetes and related metabolic abnormalities associated with genetically inherited obesity in ob/ob mice[J]. Diabetologia, 2007, 50(7): 1532-1540.

Background

[Pro3]-GIP (Mouse) is potent enzyme-resistant gastric inhibitory polypeptide (GIP) receptor antagonist, with an IC_{50} value of 2.6μM[1]. [Pro3]-GIP can block the ability of native GIP to increase cAMP and stimulate insulin secretion[2]. [Pro3]-GIP has been widely used in diabetes mouse and obesity mouse models to improve the obesity phenotype and β-cell function[3].

In vitro, [Pro3]-GIP treatment at 1μM for 10min significantly inhibited cAMP generation in GIP receptor-transfected CHL cells[4]. Treatment of BRIN-BD11 cells with 1μM [Pro3]-GIP for 20 minutes significantly inhibited the release of insulin induced by natural GIP (0.1μM)[5].

In vivo, [Pro3]-GIP treatment via intraperitoneally injection at a dose of 25nmol/kg/day for 60 days significantly improved non-fasting glucose and insulin sensitivity in ob/ob mice[6]. Continuous intraperitoneal injection of 25nmol/kg/day dose of [Pro3]-GIP for 20

consecutive days aggravated hyperglycemia and glycosylated hemoglobin in the streptozotocin-induced diabetic mouse model, reduced glucose tolerance, and impaired insulin sensitivity[7]. [Pro3]-GIP (25nmol/kg/day) combined with AM251 (6mg/kg/day) was administered intraperitoneally for 22 consecutive days, which reduced the blood glucose levels and glucose tolerance in high-fat-fed mice and decreased the body weight[8].

References:

[1] Gault V A, O'Harte F P M, Harriott P, et al. Characterization of the cellular and metabolic effects of a novel enzyme-resistant antagonist of glucose-dependent insulinotropic polypeptide[J]. Biochemical and biophysical research communications, 2002, 290(5): 1420-1426.
[2] Koefoed-Hansen F, Helsted M M, Kizilkaya H S, et al. The evolution of the therapeutic concept ‘GIP receptor antagonism’[J]. Frontiers in Endocrinology, 2025, 16: 1570603.
[3] Gault V A, Irwin N, Green B D, et al. Chemical ablation of gastric inhibitory polypeptide receptor action by daily (Pro3) GIP administration improves glucose tolerance and ameliorates insulin resistance and abnormalities of islet structure in obesity-related diabetes[J]. Diabetes, 2005, 54(8): 2436-2446.
[4] Gault V A, O'harte F P M, Harriott P, et al. Effects of the novel (Pro3) GIP antagonist and exendin (9–39) amide on GIP-and GLP-1-induced cyclic AMP generation, insulin secretion and postprandial insulin release in obese diabetic (ob/ob) mice: evidence that GIP is the major physiological incretin[J]. Diabetologia, 2003, 46(2): 222-230.
[5] McClean P L, Irwin N, Hunter K, et al. (Pro3) GIP [mPEG]: novel, long-acting, mPEGylated antagonist of gastric inhibitory polypeptide for obesity-diabetes (diabesity) therapy[J]. British journal of pharmacology, 2008, 155(5): 690-701.
[6] Irwin N, McClean P L, O’harte F P M, et al. Early administration of the glucose-dependent insulinotropic polypeptide receptor antagonist (Pro3) GIP prevents the development of diabetes and related metabolic abnormalities associated with genetically inherited obesity in ob/ob mice[J]. Diabetologia, 2007, 50(7): 1532-1540.
[7] McClean P L, Gault V A, Irwin N, et al. Daily administration of the GIP-R antagonist (Pro3) GIP in streptozotocin-induced diabetes suggests that insulin-dependent mechanisms are critical to anti–obesity-diabetes actions of (Pro3) GIP[J]. Diabetes, Obesity and Metabolism, 2008, 10(4): 336-342.
[8] Irwin N, Hunter K, Flatt P R. Comparison of independent and combined chronic metabolic effects of GIP and CB1 receptor blockade in high-fat fed mice[J]. Peptides,

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