

GIP at a Glance

- GIP stimulates postprandially insulin secretion in the glucose-dependent manner
- GIP receptors expressed on adipocytes may play role in the regulation of body weight
- Gastric bypass may rapidly cure diabetes as the result of surgical bypass of GIP-secreting K-cells in the upper small intestine
- GIP and GLP-1 both cause expansion of β cell mass and resistance to β cell apoptosis
- As with the other incretin hormones, dipeptidyl peptidase 4 (DPP-4) cleaves and rapidly inactivates GIP
- Immediate addition of DPP is required during collection of samples for potential future assay of active GIP; inhibition of serine and cysteine proteases help provide long-term storage stability

Related Information

GIP analysis is a useful biomarker for monitoring:

- GLP-1 mimetic therapies
- DPP inhibitor/therapies
- Gastric bypass outcomes
- SGLT2 inhibitor therapies
- Appetite suppressant therapies
- α -glucosidase inhibitor therapies

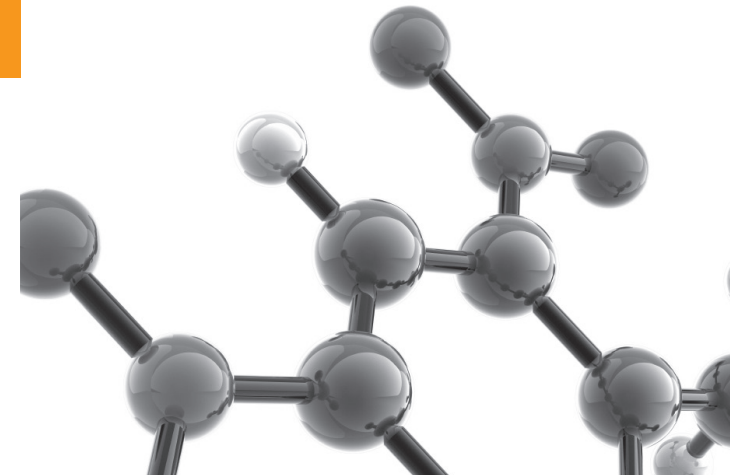
GIP is frequently requested in conjunction with:

- GLP-1
- PYY
- Glucagon
- Insulin
- C-peptide

Frequently Requested Assays

- Adiponectin
- Apolipoproteins (i.e. AI, B, B48, E, etc.)
- CETP (Cholesterol Ester Transfer Protein: Activity and Mass)
- Cholesterol (Total, Esterified, and Free)
- C-Peptide
- C-Reactive Protein
- E-Selectin
- Fibrinogen
- Glycerol, Free
- Ghrelin, Acylated and Total
- GLP-1, Active and Total
- Glucagon
- GIP (Glucose-dependent insulinotropic polypeptide)
- HDL Subclasses by ppt. or GGE
- HDL Cholesterol
 - Chemical Precipitation (e.g. Hep Mn, DS)
 - Direct Homogeneous Methods
- ICAM and VCAM
- IL-6
- LDL Subclasses by GGE
- LDL Cholesterol
 - Beta Quantification
 - Direct Homogeneous Methods
 - Friedewald Estimation
 - small dense LDL
- Lp (a) [Lipoprotein (a)]
- LpPLA2
- Myeloperoxidase
- Non-Esterified Fatty Acids (NEFA or FFA)
- Oxidized LDL (antigen)
- PAI-1 (plasminogen activator inhibitor)
- Paraoxonase
- Phospholipids, Total
- Pre beta-1 HDL
- Proinsulin
- PYY
- RLP-C and RLP-TG
- TNF α
- Triglycerides, Glycerol Blanked and Total
- Ultracentrifugation for chylo, VLDL, IDL, LDL & HDL

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FEATURED ASSAY:

GIP

(Gastric Inhibitory Peptide)

Gut hormone inducing post prandial insulin release and lipoprotein lipase activity.

SAMPLE REQUIREMENTS

Optimum Volume: 0.5 mL

Sample Type: EDTA Plasma with the appropriate preservative

Method: ELISA

PBI

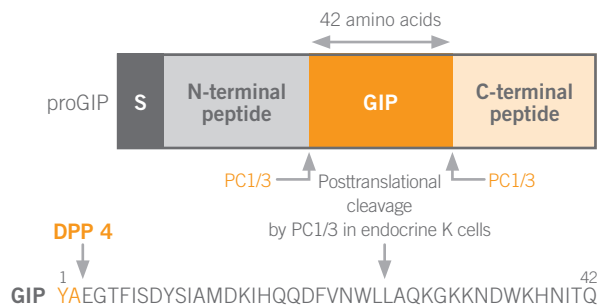
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Background Information

GIP, also known as glucose-dependent insulinotropic polypeptide or gastric inhibitory polypeptide, is a 42 amino acid peptide (Fig. 1) hormone secreted by K cells in the intestinal epithelium. The K cells sense nutrient intake and secrete GIP following ingestion of the nutrients, notably fats. GIP is a potent stimulator of insulin secretion (incretin activity), but unlike glucagon-like peptide-1 (GLP-1), which exerts multiple non-incretin activities in the regulation of blood glucose, the primary action of GIP is the stimulation of glucose-dependent insulin secretion. Preclinical studies indicate that both GIP and GLP-1 cause expansion of β cell mass and resistance to β cell apoptosis (1).

FIGURE 1. Schematic representation of proGIP



GIP apparently plays a role in adipocyte biology; however, the physiological significance of GIP action in the adipocyte is not well defined. GIP receptors are expressed on adipocytes. Experimental data strongly implicate a role for the GIP receptor in the regulation of body weight.

GIP may, in addition to its insulinotropic effects, promote fat storage and obesity, either by direct insulin-mimetic effects in adipose tissue (1) or via enhancement of resistin-mediated stimulation of lipoprotein lipase activity (2). Thus, blocking these effects pharmacologically could be a strategy for treatment of obesity. (Fig. 2)

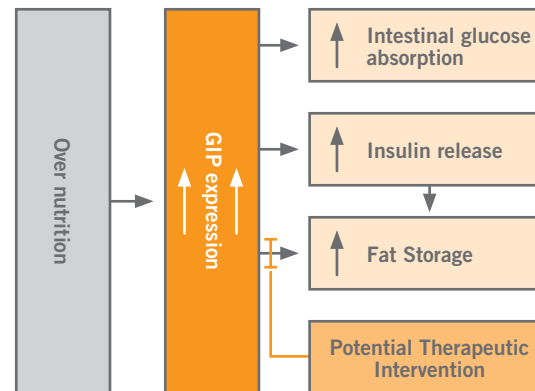
An important determinant of GIP action is the N-terminal cleavage of the peptide to the inactive GIP (3-42). The enzyme dipeptidyl peptidase 4 (DPP-4), which also cleaves GLP-1 and GLP-2, rapidly inactivates GIP. The majority of circulating GIP immunoreactivity

in both the fasting and postprandial states corresponds to the biologically inactive GIP (3-42). GIP infused into human subjects is rapidly degraded, with a $t_{1/2}$ of ~7min.

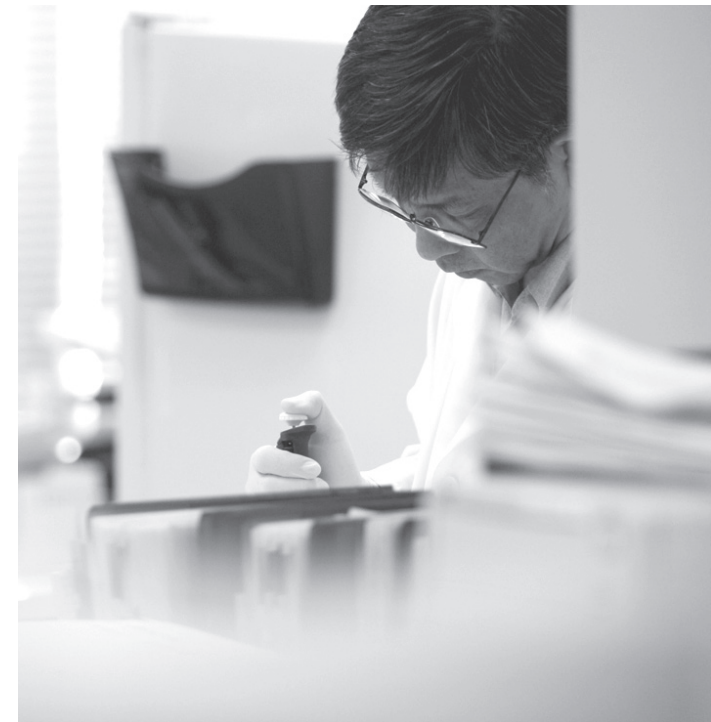
Accurate measurement of circulating GIP requires prompt addition of broad spectrum protease inhibitors to the blood sample during blood collection in order to prevent its degradation, particularly if the GIP is not assayed immediately. Blood should be drawn into tubes containing EDTA, which inhibits metalloproteinases. In addition the collection tube should contain a combination of inhibitors of serine proteases (e.g. aprotinin, AEBSF) and cysteine proteases (e.g. E-64).

A DPP inhibitor does not need to be added to human samples if only total GIP is assayed. However, addition of DPP inhibitor to the samples during the blood collection is generally recommended to allow the same sample to be used for the future measurement of intact GIP (1-42) (assays for the latter are currently under development). If collection of blood in a tube containing a DPP inhibitor is not feasible, the inhibitor must be added to the blood within 30 seconds of collection.

FIGURE 2. GIP actions and potential therapeutic targets



Currently at PBI, GIP is quantified by an ELISA that measures both the biologically inactive GIP (3-42) and intact GIP (1-42). This assay employs an anti-GIP monoclonal antibody to capture human GIP, and a biotinylated anti-GIP polyclonal detection antibody that contains a streptavidin-horseradish peroxidase conjugate.



References:

- McIntosh CH, Widenmasier S, Kim SJ. Glucose-dependent insulinotropic polypeptide (gastric inhibitory polypeptide: GIP). *Vitam Horm.* 2009; 80:409-471.
- Song DH, Getty-Kaushik L, Tseng E, et. al. Glucose-dependent insulinotropic polypeptide enhances adipocyte development and glucose uptake in part through Akt activation. *Gastroenterology* 2007; 133:1796-1805.
- Kim S-J, Nian C, McIntosh CH. Resistin is a key mediator of glucose-dependent insulinotropic polypeptide (GIP) stimulation of lipoprotein lipase (LPL) activity in adipocytes. *J Biol Chem.* 2007; 282:34139-34147.