

GLP-1 at a Glance

- Insulin is stimulated by postprandial glucose elevation and a direct prandial effect called the incretin effect
- GLP-1 and GIP are the best characterized incretin hormones and are primarily responsible for the incretin effect
- GLP-1 and GIP affect glucose metabolism by stimulating insulin release and β -cell proliferation
- GLP-1, but not GIP, stimulates insulin biosynthesis, produces satiety, affects gastrointestinal motility, stimulates insulin biosynthesis, and has beneficial effects in a variety of other tissues
- Active GLP-1 in plasma is degraded (inactivated) by DPP-IV ($t_{1/2} = 2$ min), and measurement of GLP-1 activity requires immediate DPP-IV inhibition
- For longer-term storage of plasma samples for measurement of GLP-1, stabilization with serine-, metallo-, and cysteine-protease inhibitors is required.
- For clinical studies, GLP-1 measurement requires an assay with enough sensitivity to measure normal plasma levels, and an ELISA with an electrochemiluminescent detection has been validated at PBI

Related Information

Active GLP-1 is frequently requested in conjunction with:

- Total GLP-1
- Glucagon
- GIP
- 1,5-Anhydroglucitol (Glycomark™)
- PYY
- Ghrelin
- Glucose
- Insulin
- C-peptide

GLP-1 analysis is a useful efficacy biomarker in the following clinical studies:

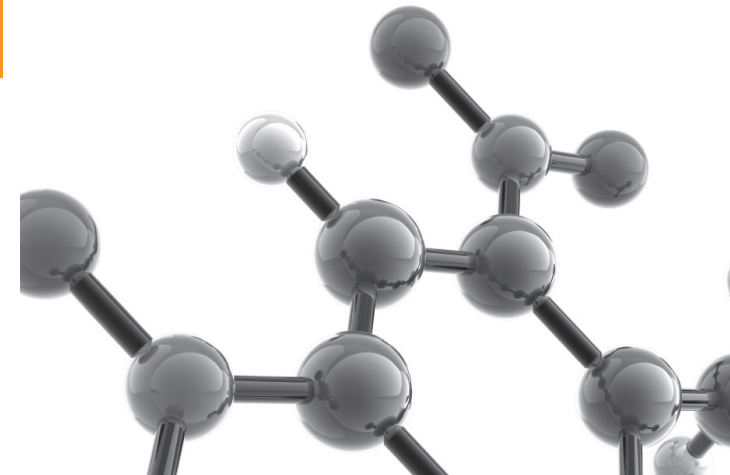
- GLP-1 mimetic therapy
- DPP-IV inhibitor therapy
- Gastric bypass outcomes
- SGLT2 inhibitor therapy
- Appetite suppressant therapy
- Alpha-glucosidase inhibitor therapy
- Pancreatic islet dysfunction

Available at PBI Lab

Cardiovascular Risk – Diabetes, Dyslipidemia, Metabolic Syndrome & Obesity

- Adiponectin
- Apolipoproteins (i.e. AI, B48, CIII, etc.)
- CETP (Cholesterol Ester Transfer Protein: Activity and Mass)
- Cholesterol (Total, Esterified, and Free)
- E – Selectin
- Fibrinogen
- Fructosamine
- Glycerol, Free
- Glycomark™
- HDL Cholesterol Subclasses by ppt or GGE
- HDL Cholesterol
 - CDC Designated Comparison Method
 - CDC Reference Method
 - Chemical Precipitation (Hep Mg or DS)
 - Direct Homogeneous Method
- HDL Particle Assay, LpAI:All
- Homocysteine
- ICAM and VCAM
- Leptin
- LDL Cholesterol
 - β – Quantification
 - Direct Homogeneous Method
 - Friedewald Estimation
- LDL Cholesterol Subclasses by GGE
- Lp (a)
- LpPLA2
- Myeloperoxidase
- Non-Esterified Fatty Acids (NEFA or FFA)
- Oxidized LDL (antigen and autoantibody)
- PAI – 1 (plasminogen activator inhibitor)
- Paraoxonase
- RLP-C & RLP-Tg
- sdLDL
- Triglycerides
- VLDL

Go to www.pacbio.com for more information or call us at 800.767.9151



FEATURED ASSAY:

GLP-1

*(Glucagon-Like Peptide-1)
An Established Incretin Target*

SAMPLE REQUIREMENTS

Optimum volume: 0.5 mL

Sample Type: EDTA Plasma

Method: Electrochemiluminescent

PBI

Pacific **Biomarkers**

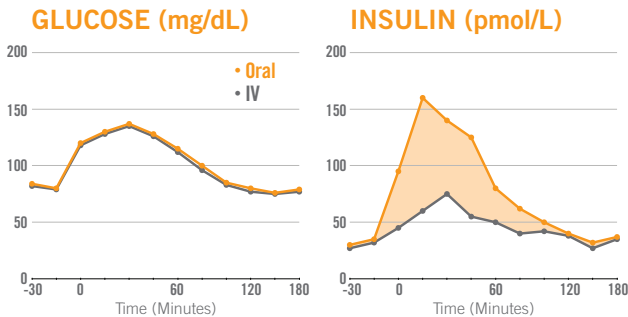
The Value of Expertise

Background Information

Although the term ‘incretin’ was introduced almost 80 years ago, the first incretin, glucose-dependent insulinotropic peptide (GIP; previously called gastric inhibitory peptide), was not isolated until 1969. In 1983, the proglucagon transcript – from which GLP-1 and GLP-2 are derived – was cloned, and shortly thereafter it was shown that GLP-1 stimulates insulin secretion.

Oral and intravenous glucose producing the same increases in plasma glucose concentration generate different insulin responses (see Fig. 1). Thus, there are multiple signals acting on the β -cell, a result known as the “incretin effect”. The non-glucose insulinotropic effect is the result of the actions of the incretin hormones, GIP and GLP-1. This effect accounts for about 50% of the total insulin secretion, but is greatly diminished or absent in type II diabetic (T2DM) subjects.

Figure 1. Measurement of the Incretin Effect:
OGTT and Matched IV Infusion



Secretion of GLP-1, but not GIP, appears to be reduced in T2DM. In contrast to GLP-1, GIP resistance parallels the development of insulin resistance. In addition to its insulinotropic effects, GLP-1 inhibits glucagon secretion, produces satiety, affects gastrointestinal motility, stimulates insulin biosynthesis, and has beneficial effects in a variety of other tissues (see Table 1).

GLP-1 is produced in the distal intestine from the proglucagon transcript, which also gives rise to GLP-2, glycentin (enteroglucagon), and other peptides. In the pancreas, the proglucagon transcript is processed to produce glucagon.

GLP-1 is secreted in two equally potent forms GLP-1 (7-37) and GLP-1 (7-36) amide. Circulating active GLP-1 moieties have a half-life of 1-2 minutes as the result of cleavage of GLP-1 peptide at the alanine at position 2 by dipeptidyl peptidase IV (DPP-IV), producing an essentially inactive fragment.

The primary tools for monitoring the level of circulating levels of GLP-1 during pharmacologic intervention have been immunoassays that include RIA and ELISA procedures.

Because of the ubiquitous nature of DPP-IV, unusual blood collection conditions must be observed to allow analysis of active GLP-1. To inhibit DPP-IV activity, blood should be collected in tubes containing a DPP-IV inhibitor, or it must be added to the blood within 30 seconds of collection.

In addition to a DPP-IV inhibitor, the collection tube should contain EDTA, and general protease inhibitors should be present or quickly added to blood if the GLP-1 is not assayed immediately. EDTA inhibits metalloproteinases, and aprotinin has often been used to protect against serine protease enzymes. Inhibition by these two inhibitors allows samples to be frozen for longer periods before assay. To further lengthen the period of GLP-1 stability during storage, additional serine-protease and cysteine-protease (cathespin) inhibitors must be added to the plasma at the time of collection. A broad spectrum of inhibitors will prevent degradation of both total and active GLP-1. As with other peptides, GLP-1 is likely to be most vulnerable to degradation during transition of the specimen from a solid to the liquid state, and inhibition of the variety of proteases that may form during storage is critically important to obtaining results that reflect circulating GLP-1 levels at the time of specimen collection.

At PBI, GLP-1 is measured by ELISA using visible or electrochemiluminescence (ECL) detection systems. The latter has the advantage of being more precise and sensitive. Because normal fasting levels of GLP-1 are <1.5 pmol/L in plasma, sensitivity is critically important.

References: Host JJ. The physiology of glucagon-like peptide
1. *Physiol Rev.* 2007; 87:1409-1439.



TABLE 1. EFFECTS OF GLP-1 ON SEVERAL TISSUES	
TISSUE	EFFECT
Stomach	Delays gastric emptying
Small intestine	Slows gut motility
Liver / Skeletal muscle	Stimulates glycogen synthesis
Fat	Stimulates glycogen synthesis Inhibits lipogenesis
Exocrine pancreas	Inhibits enzyme release
Endocrine pancreas	Stimulates insulin & somatostatin release Stimulates β -cell proliferation & proinsulin Inhibits glucagon synthesis & apoptosis β -cell
Central nervous system	Inhibits food intake Stimulates satiety Increases body temperature Stimulates TSH, LH & vasopressin secretion
Kidney	Stimulates sodium excretion Inhibits H ⁺ excretion & glomerular hyperfiltration
Heart	Increases blood and heart rate