Glucagon – ELISA

Analyte: Glucagon

Specimen Type: Plasma from BD P700 or P800, EDTA Plasma with preservatives; contact nexelis for collection instructions

Optimum Volume: 0.5 mL

2-8°C	-20°C	-70°C
6 days	1 month	1 year

Reporting units: pg/mL

Method: ELISA

Biological or Clinical Significance:

Glucagon is a 29 amino acid peptide produced by the pancreas that plays a critical role in glucose metabolism and homeostasis. The glucagon precursor mRNA is expressed by alpha cells (a-cells) of the pancreas, L cells of the intestine, and in the brain. Only the pancreatic a-cells express the prohormone convertase PC2, also called PCSK2, which is required to produce glucagon. Intestinal L cells instead express the prohormone convertase PC1, which processes the precursor to the glucagon-overlapping peptides glicentin and oxyntomodulin. L cells also produce two glucagon-like peptides, GLP-1 and GLP-2, that are derived from the same glucagon precursor and influence glucose metabolism but do not share any common sequence with glucagon. The amino acid sequence of the mature glucagon peptide is identical in human, mouse, rat, pig, dog, horse, cow, sheep, and Xenopus.

In normal metabolism, glucagon is secreted in response to low blood glucose (hypoglycemia) and downregulated in response to high blood glucose (hyperglycemia). Although glucagon binding sites are found in liver, brain, pancreas, kidney, intestine, and adipose tissue, the main activity of glucagon receptors occurs in the liver, where glucagon stimulates gluconeogenesis and glycogenolysis, thereby increasing blood glucose. It is particularly important that the brain receive sufficient glucose, since it is unable to store more than a minute quantity. Therefore the release of glucagon from a-cells is under control by both hormones and neurotransmitters, and is very responsive to circulating glucose concentration. Insulin, and/or the zinc that islet b cells secrete with it, downregulates glucagon secretion in intact islets. Glucagon secretion is also downregulated by the neurotransmitter g-aminobutyric acid (GABA), somatostatin produced by islet d-cells, and GLP-1 but is enhanced by the neurotransmitter L-glutamate, amino acids (especially arginine), and glucagon itself. Through receptors on the a-cells, these substances affect potassium, sodium, and calcium channel activity and alter intracellular calcium concentration. Glucose suppression of glucagon secretion is probably indirect, acting

through paracrine signals from other islet cells.

Like insulin, glucagon is dysregulated in type 2 diabetes (T2D) and contributes to its pathology. Glucagon secretion is less responsive to insulin-mediated suppression in times of high circulating glucose, causing glucagonemia, and increasing the risk of hyperglycemia. Glucagon is also regulated by some of the same messengers that regulate insulin. Leptin inhibits a-cell glucagon secretion and stimulates b-cell insulin secretion, but glucagon blunts the leptin-mediated insulin secretion. Islet a-cells express ghrelin receptors and respond to ghrelin by increasing glucagon secretion. Glucocorticoids, activated by 11b-HSD1, depress glucagon secretion in hypoglycemia and insulin secretion in hyperglycemia. Although genetic polymorphisms of the glucagon receptor are associated with T2D, downregulation of glucagon secretion or deletion of the glucagon receptor in mice that are susceptible to T2D actually improves glycemic control.

Principle of Test Method:

The glucagon immunoassay is a solid-phase ELISA designed to measure human glucagon in EDTA plasma, serum and cell culture medium. This assay employs the quantitative sandwich enzyme immunoassay technique.