Lecture title: Pancreas

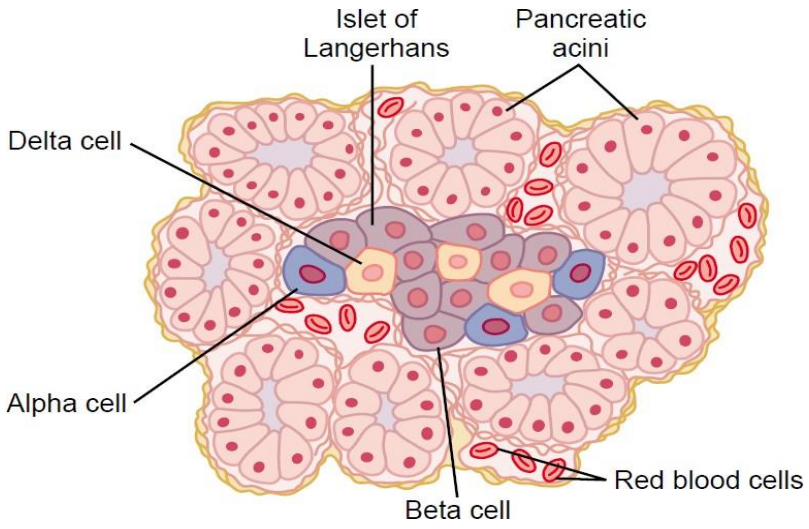
Lecturer Affiliation: University of Mosul / College of Veterinary Medicine /

Department of Physiology, Biochemistry and Pharmacology

Summary: Pancreas

It is a glandular organ or mixed gland of endocrine and digestive system of vertebrates. 2% of pancreas are consists of islets of Langerhans (about 3 million cell clusters); are clumps of cells with a specific endocrine function,four kinds of cells are identified in the islets of Langerhans (fig.):

1. Alpha cells secreted glucagon.
2. Beta cells secreted insulin.
3. Delta cells secreted somatostatin.
4. Gamma cells secreted pancreatic polypeptide (PP).

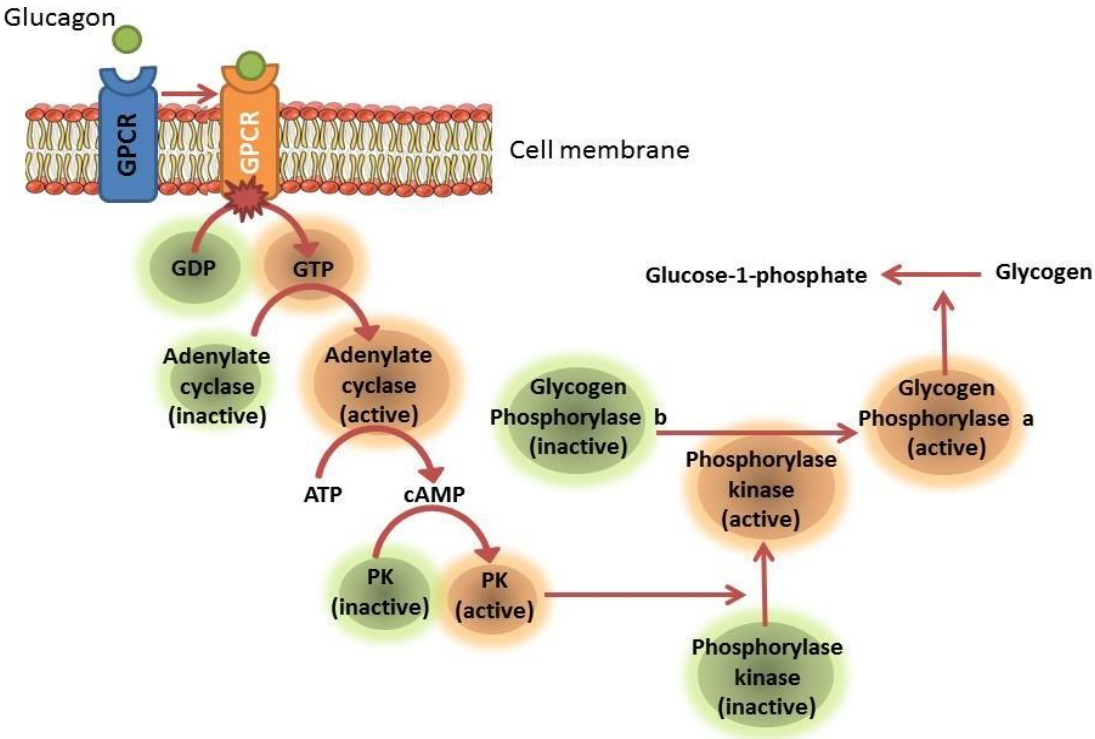


Glucagon

The name is due to "**gluc**ose **agon**ist". It is a 25 amino acid polypeptide hormone, act in opposite to insulin by elevating blood glucose level.

Actions of glucagon

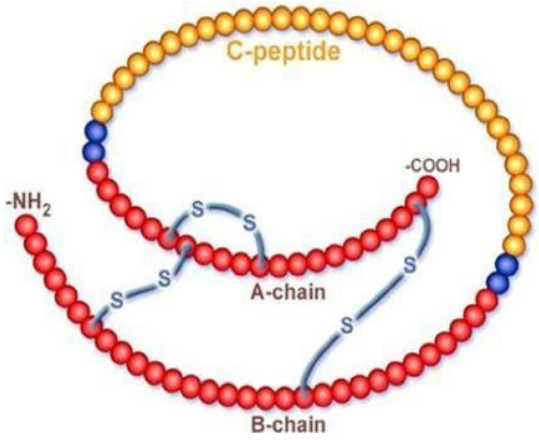
1. Increase blood glucose level.
2. Enhance gluconeogenesis and glycogenolysis.
3. Regulate glucose production rate by lipolysis.
4. Induce lipolysis under conditions of insulin suppression.
5. Increase amino acid transport into liver.


Glucagon
GPCR
GPCR
Cell membrane
GDP
GTP
Adenylate cyclase (inactive)
Adenylate cyclase (active)
ATP
cAMP
PK (inactive)
PK (active)
Phosphorylase kinase (inactive)
Phosphorylase kinase (active)
Glycogen Phosphorylase b
Glycogen Phosphorylase a
Glucose-1-phosphate
Glycogen

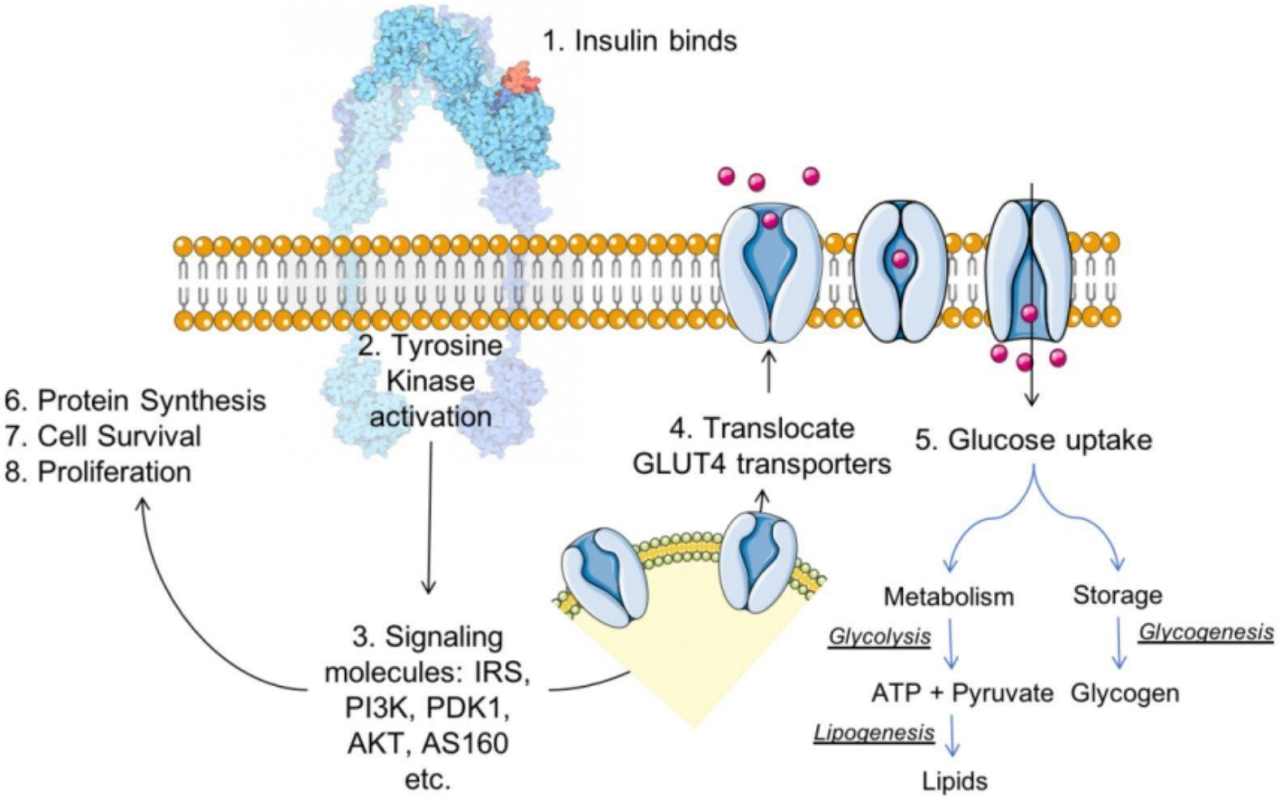
Insulin

- Insulin is the key hormone in the regulation of metabolism of carbohydrates, lipids, and proteins.
- Insulin consists of two polypeptide chains; A chain and B chain linked together by disulfide bonds.
- First insulin synthesized as a single polypeptide chain called preproinsulin (preprohormone).
- The single peptide is removed forming proinsulin molecule, the sequence of proinsulin starts from amino terminus (B chain), then connecting (C) peptide, and A chain (fig).

- Proinsulin undergo maturationinto active insulin through the action of endopeptidase (prohormone convertase (PC1 and PC2)), which act on two sites releasing a fragments called C- peptide, and leaving two chains of peptides (A and B) linked together by two disulfide bonds.



- The resulted mature insulin is packaged inside mature granules and remains waiting metabolic signals or vagal nerve stimulation to be exocytosed from the cell into the circulation.



Mechanism of insulin action

Functions of insulin

Insulin increases	Insulin decreases
1. Glycogenesis. 2. Cellular uptake of glucose, particularly muscles and adiposetissues. 3. Lipogenesis. 4. Fatty acids esterification. 5. K^+ uptake. 6. HCl secretion by stomach parietal cells. 7. Amino acid uptake. 8. Relax of atrial wall muscle leading toincrease blood flow. 9. DNA replication and protein synthesis.	1. Gluconeogenesis and glycogenolysis. 2. Lipolysis. 3. Proteolysis. 4. Autophagy. 5. Na^+ excretion by kidney.

Insulin is secreted in biphasic manner of secretion:

1. In the first phase stored insulin is released directly after meal.
2. In the second phase newly synthesized insulin is released over a coupleof hours, and increases food storage (glycogenesis).

Diabetes mellitus (DM)

DM comprises a group of metabolic disorders that share a common feature of hyperglycemia.

1. IDDM (Insulin dependent DM)

2. NIDDM (Non-insulin dependent DM)

IDDM	NIDDM
• Absolute insulin deficiency abnormal/lack of pancreatic function)	• Resistance resides in liver, muscles and adipose tissue
• Increased hepatic glucose output; releasing glucose and ketones into the blood	• Seen in terms of glucose metabolism, fat metabolism and lipoprotein metabolism
• Increased proteolysis; releasing amino acids which leads to weight loss	• Leads to increase in circulating non-esterified fatty acids (as a result of adipocytes breakingdown triglycerides)
• Increased lipolysis; releasing glycerol and fatty acids from adipocytes	• Increased hypertension
• Glycosuria with osmotic symptoms; increased glucose in urine lead to increased water in urine and dehydration with increased thirst	• Central adiposity; 60-80% of obese
• Ketonuria: presence of ketone bodies in urine	• Dyslipidaemia: A disorder of metabolism
• Treatment: insulin	• Life style changes • Diet • Hypoglycemic drugs (e.g. Metformin)

Somatostatin

Also known as growth hormone-inhibiting hormone (GHIH), it is apeptide hormone that regulates the endocrine system and affect neurotransmission and cell proliferation. Main somatostatin producing cell is the delta cells of islands of Langerhans in pancreas.

Functions of somatostatin

Somatostatin inhibit release of GH, TSH, prolactin, and adenylylcyclase.

1. Suppress the release of GIT hormones (gastrin, cholecystokinin (CCK), secretin, motilin, vasoactive intestinal peptide (VIP), gastric inhibiting peptide (GIP), pancreatic hormones.
2. Decrease rate of gastric emptying.

Pancreatic polypeptide

It is a polypeptide consists of 36 amino acids with molecular weight 4200, secreted by PP cells of pancreas. It is self-regulate pancreatic secretion activities (endocrine and exocrine), also it is regulates hepatic glycogen concentration and GIT secretions. Its secretion in humans is increased after a protein meal, fasting, exercise, and acute hypoglycemia, and is decreased by somatostatin and intravenous glucose.

Plasma PP has been shown to be reduced in conditions associated with increased food intake and elevated in anorexia nervosa. In addition, peripheral administration of PP has been shown to decrease food intake in rodents.