Insulin Function

PLAY PICMONIC

Receptors

Tyrosine Kinase Receptor

Tire Kite-ace

The insulin receptor (IR) is a transmembrane receptor that belongs to a class of receptor tyrosine kinase. The RTK has alpha and beta subunits. The extracellular alpha subunits are the site of insulin binding. The beta subunits span the cell membrane and, on their intracellular portion, contain tyrosine kinase domains. Insulin binding to the alpha subunit causes autophosphorylation of the beta subunit tyrosine kinase. The tyrosine kinase, in turn, activates two major intracellular pathways: the phosphatidylinositol 3-kinase (PI3K) pathway, which mostly mediates the metabolic effects of insulin, and the mitogen-activated protein kinase (MAPK) pathway, which is involved in mitogenesis and growth.

Growth Factor

Grow-factory

Growth factors (GFs) are signaling molecules, often proteins, that bind to specific receptors on the surface of target cells and, in doing so, initiate downstream signaling. Insulin, a peptide hormone, is one such GF. Insulin binds to a receptor tyrosine kinase and induces downstream signaling pathways (MAPK and PI3K). Other GFs include both cytokines and hormones. GFs regulate several cell processes, such as proliferation, differentiation, and migration. There are many families of GFs. Some examples include the epidermal growth factor (EGF) family, Vascular endothelial growth factors (VEGFs) family, Tumor necrosis factor (TNF) superfamily, platelet-derived growth factor (PDGF) family, and others.

Stimulates IGF-1

Grow-factory Releasing Insulin-like-insects

Insulin-like growth factor (IGF), formerly called somatomedin C, is a peptide hormone that primarily functions to stimulate growth. There are two IGFs: IGF-1 and IGF-2. Despite the similarity of their names, these two peptides have different, specific actions on tissues. IGF-2 is primarily involved in fetal growth. IGF-1, however, is active postnatally. IGF-1 acts on almost every tissue in the body to promote hypertrophy and hyperplasia via the upregulation of anabolic processes. Both insulin and pituitary growth hormone (GH) stimulate hepatic IGF-1 synthesis and secretion. IGF-1 can activate both its own IGF receptor and the insulin receptor and, thus, has some ability to decrease blood glucose levels as well. However, IGF-1 is far less potent than insulin in decreasing blood glucose concentrations.

Anabolic Effects

Glucose Uptake in Skeletal Muscle and Adipose

Glue-bottle on Muscle-man and A-fatty-dip

When insulin binds to insulin receptors, it induces glucose uptake. Glucose uptake is done via carrier-mediated transport into insulin-dependent tissue. Insulin binding to insulin receptors also induces gene transcription. One such insulin receptor is GLUT4, which facilitates insulin-stimulated glucose uptake into adipose tissue and striated muscle (skeletal muscle). Exercise can also induce GLUT4 expression. Of note, some tissues do not require insulin to uptake glucose (insulin-independent glucose uptake). These can be remembered by the pneumonic BRICK LIPS: Brain, RBCs, Intestines, Cornea, Kidneys, Liver, Islet cells, Placenta, and Spermatocytes. These cells don't use GLUT4 for importing glucose, but rather, another transporter that is not insulin-dependent.

Inhibits Glucagon Release

Glue-king-kong in Inhibiting-chains

Insulin inhibits glucagon release. Glucagon is a hormone released from alpha cells of the pancreas in response to hypoglycemia. Insulin and glucagon counterbalance each other to stabilize blood glucose – generally speaking, glucagon raises blood sugar while insulin decreases it. Insulin and glucagon also generally have opposite functions: glucagon promotes glycogenolysis, gluconeogenesis, lipolysis, and ketogenesis, while insulin inhibits these functions.

Glycogenesis

Glycogen-glider-genie

Glycogenesis is the formation of glycogen. Glycogen is the primary carbohydrate stored in the liver and muscle and is synthesized from glucose. Insulin promotes glycogenesis by affecting the enzyme glycogen synthase. Glycogen synthase is the rate-limiting enzyme in the conversion of glucose to glycogen. It does this by activating glycogen synthase phosphatase (PP-1). PP-1 then dephosphorylates glycogen synthase, which activates it. Activation of glycogen synthase increases the conversion of glucose to glycogen. PP-1 also dephosphorylates two enzymes (phosphorylase kinase and glycogen phosphorylase), which slows the reverse process known as glycogenolysis, or the breakdown of glycogen back into glucose.

Triglyceride Synthesis

Tag-triceratops

The liver and adipose tissue are the primary sites for the lipogenesis of fatty acids and triglycerides. Adipose tissue also serves to store triglycerides. Insulin both stimulates triglyceride synthesis and potently suppresses triglyceride breakdown (inhibits lipolysis) within adipocytes. It does this by facilitating rapid, potent glucose uptake by adipocytes. Within adipocytes, glucose is utilized to synthesize glycerol. Glycerol, along with fatty acids from the liver, is then used to synthesize triglyceride. Note that fatty acid transport into adipocytes is also increased by insulin.

Cellular Uptake of Potassium and Amino Acids

Cellular-phone Uptake-tube with Bananas and Amigo Acidic-lemon

Insulin stimulates the uptake of amino acids into cells. It also increases the permeability of many cells to potassium, which is of clinical relevance. Insulin activates sodium-potassium ATPases, causing an influx of potassium into cells. Under certain circumstances, injection of insulin can aid a patient with hyperkalemia or could kill a patient by causing hypokalemia.

Sodium Retention

Salt-shaker Retained

The acute effect of insulin is to stimulate renal tubular sodium transport. This stimulation promotes sodium retention by the kidney. Insulin stimulates sodium reabsorption along the nephron, in the proximal tubule, thick ascending limb, and distal tubule/collecting duct.

Protein Synthesis (Muscles)

Mr. Protein Assembly

While protein is formed in the absence of insulin, the net formation of protein in muscle is accelerated by insulin. Insulin promotes muscle anabolism. However, the mechanism by which insulin promotes protein synthesis is still controversial.