

Glossary

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Cytokines

Cytokines refer to a group of compounds that are produced under a variety of conditions, including the immune response and inflammatory reactions. Tumor necrosis factor- α and interleukin-1 are examples of two cytokines.

Free fatty acids

The majority of fatty acids in the blood are esterified to glycerol in the form of triacylglycerols or phospholipids in lipoproteins such as very low density lipoproteins or chylomicrons. However, some circulate as unesterified fatty acids. Because of the low solubility of fatty acids, these “free fatty acids” are bound to albumin, which facilitate the passage of the free fatty acids throughout the circulation.

Glucose oxidation

The metabolism of glucose in muscle first involves the uptake of glucose into the cell, following which most of the glucose is metabolized by the glycolytic pathway, with pyruvate being one of the metabolic byproducts of glycolysis. This pyruvate can be taken up into the mitochondria where it is used as a substrate of pyruvate dehydrogenase or pyruvate carboxylase, which provides carbons for the citric acid cycle. If glucose both passes through glycolysis and the pyruvate is subsequently oxidized by the mitochondria the process is called glucose oxidation.

Insulin resistance

Insulin resistance refers to a situation where the amounts of insulin are inadequate to produce a normal insulin response from fat, muscle and liver cells. Insulin resistance in fat cells results in hydrolysis of stored triacylglycerol, which blood free fatty acids in the levels. Insulin resistance in muscle decreases glucose uptake, whereas insulin resistance in liver reduces glucose storage. Both of these actions increase blood glucose levels. Insulin-resistance is often characterized by high plasma levels of insulin, since higher insulin levels are needed to evoke similar responses in adipocytes, muscle, and liver.

Lactate metabolism

Lactate is a carbohydrate used by various tissues, including muscle. Lactate can be taken up by muscle and converted to pyruvate (by lactate dehydrogenase), where the pyruvate is subsequently oxidized in the mitochondria. Lactate is also a product of muscle glycolysis, and if the pyruvate from glycolysis is not oxidized it is converted to lactate (also by lactate dehydrogenase), and the lactate is subsequently released from the muscle.

Pyruvate dehydrogenase

Pyruvate dehydrogenase (PDH) is an intramitochondrial complex that converts pyruvate (which primarily originates from glucose or lactate) into acetyl CoA. PDH is the rate-limiting enzyme for the mitochondrial metabolism of carbohydrates. Maintaining mitochondrial glucose metabolism is an important therapeutic strategy to protect the ischemic heart. Therefore, activating PDH is a potential therapeutic approach to treating heart disease.

Slow sodium current

During rhythmic firing, the action potential of cardiac cells involves different phases, all involving different ion fluxes across the membrane. In Phase 4 of the action potential there is a slow inward flow of sodium, called the funny current, as well as an inward flow of calcium. This all serves to make the cell more positive, and involves a relatively slow depolarization of the cell until a threshold potential is reached and the cells enter phase 0 of depolarization.

3 KAT

3-Ketoacyl-CoA-thiolase (3-KAT) is the last enzyme in the intramitochondrial pathway that is involved in the metabolism of fatty acids (fatty acid β -oxidation). 3-KAT inhibitors, such as trimetazidine, inhibit the activity of this enzyme, thereby inhibiting fatty acid oxidation. Recent interest has focused on 3-KAT inhibitors as a novel therapeutic approach to protecting the ischemic heart.