

## Altered cellular metabolism in diabetes

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Diabetes is a leading metabolic disorder that occurs due to high blood glucose levels. According to the world health organisation, about 422 million people worldwide suffer from diabetes. There are 2 types of diabetes that include type 1 and type 2 diabetes mellitus. Type 1 diabetes mellitus is an autoimmune disease in which the body is unable to produce insulin in response to high blood glucose levels due to the destruction of pancreatic beta cells. Therefore, cells lose the ability to take up glucose. In type 2 diabetes, beta cells secrete insulin but the body cannot respond to insulin. This is because of a continuous elevated amount of insulin due to a bad diet and sedentary lifestyle. Over time the sensitivity of insulin goes down. Therefore, insulin resistance builds up. Type 2 diabetes is the most common type of diabetes but both types affect glucose metabolism and promote the progression of diabetes mellitus through impaired glucose regulation and lipid metabolism. Even though the blood glucose levels are found to be high, cells are unable to take up and utilise glucose. As a result of this, false starvation conditions occur. The increase in starvation triggers glucagon and cortisol hormones to mimic starvation. Therefore, the catabolic mechanisms get activated.

Glucagon promotes gluconeogenesis (glucose synthesis from non-sugar precursors) that increases the blood glucose levels which triggers the breakdown of proteins in the muscle tissues to glucogenic amino acids, such as alanine, glutamine and so on that can be used for gluconeogenesis to produce glucose. Glucagon activates hormone-sensitive lipase in adipose tissues and triacylglycerol hydrolysis in an uncontrolled manner which produces fatty acids and glycerol. Glycerol transports into the liver and carries out gluconeogenesis to produce glucose. Fatty acids transport into the liver and convert to acetyl CoA by beta-oxidation. Acetyl CoA cannot enter into gluconeogenesis since acetyl CoA cannot directly convert into pyruvate. Therefore, acetyl CoA is used for ketone body formation which leads to ketoacidosis and results in increased blood acidity. Ketone body formation does not occur in type 2 diabetes mellitus due to the presence of insulin but it is one of the characteristics of type 1 diabetes mellitus. Thus, the elevated levels of glucose is due to enhanced gluconeogenesis, which promotes diabetes mellitus. However, the knowledge of dysregulation of glucose homeostasis is less. Hence, it can be concluded that it is important to understand the altered cellular mechanisms in diabetes for disease management.

*Keywords: Diabetes, Cortisol, Glucagon, Gluconeogenesis, Insulin, Glucose*

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