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| **GLUT2 and its role in blood glucose regulation** |
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**GLUT2 and its role in blood glucose regulation**

Regulation of glucose in organism’s body is one of important subject that studied by biologists since long time ago, because of the important role of glucose in metabolic energy in organism’s body, and the relationship between glucose level in blood and many diseases such as Diabetes. Organisms need a certain amount of glucose in their blood, for example; the normal blood glucose level in human is ∼5 mmol/l. So, organisms have specific mechanisms that detect blood glucose level called “glucose sensing mechanisms”, and other specific mechanisms that regulate blood glucose level called “glucose homeostasis mechanisms”. A lot of proteins contribute to the above mechanisms. One of these proteins is Glucose transporter 2 (GLUT2). ***(1) (2)***

Glucose transporter 2 (GLUT2) is a type of facilitative glucose transporters (GLUTs) that encoded by the SLC2A genes. GLUT2 is located in the plasma membrane of the liver, kidney, intestine, pancreas, and brain. And consists of distinct amino acid sequences, which give GLUT2 the ability to link with specific ligands, in which GLUT2 has a low affinity and high capacity for glucose (Km∼17 mmol/l), and a high affinity for glucosamine (Km∼0.8 mmol/l). In other words, GLUT2 cannot transport glucose inside a cell if the concentration of glucose in outside of a cell very low, and vice versa with glucosamine. In addition to, GLUT2 doesn't need insulin to transport glucose. ***(3)***

In cell biology, the types of protein which exist in specialized cells must to be relevance with functions of these cells. One of the important functions of the liver and pancreas is the regulation of blood glucose level, either by secretion of insulin and glucagon hormones from beta and alpha cells of the pancreas or by producing glycogen and glucose inside the liver (hepatocytes). So, the presence of GLUT2 in the plasma membrane of both organs indicates that GLUT2 may be associated with the regulation of blood glucose level especially that is the main function of GLUT2 is the transport of glucose across the membrane. ***(4) (5)***

When blood glucose level is increased (hyperglycemia state), GLUT2 transports glucose into the inside of beta cells of the pancreas, then the molecules of glucose are oxidized by the glycolysis pathway in the cytosol. This process stimulates beta cells to encode the insulin gene by a certain mechanism, in which the rate of glucose metabolism controls the rate of produce insulin. Thereafter, beta cells secrete insulin hormone, which binds with a specific receptor in body cells and allows glucose to transport inside these cells. As a result, blood glucose levels are decreased. ***(6)***

Hepatocytes (liver cells) can also contribute to decreasing blood glucose levels. In which when glucose is transported into the inside Hepatocytes by GLUT2 and because of hyperglycemia state, hepatocytes reduce these molecules to producing glycogen by glycogenesis process, which is (glycogen) a carbohydrate form of energy storage in the body. As a result, blood glucose levels are decreased. ***(7)***

Active beta cells of the pancreas work as an inhibitor to alpha cells by secretion of insulin. When blood glucose level is decreased (hypoglycemia state), GLUT2 cannot transport glucose into the inside beta cells because of its low affinity to glucose. So, beta cells become inactive and cannot secrete insulin hormone, which allows alpha cells of the pancreas to be active cells. As a result, alpha cells secrete glucagon hormone. Glucagon hormone can bind with a specific receptor in hepatocytes, this binding stimulates hepatocytes to oxidize stored glycogen by glycogenolysis and oxidize amino acid and lipid molecules by gluconeogenesis to producing glucose again. As a result, blood glucose levels are increased. ***(8)***

Several gene mutations occur in GLUT2, such as the "Fanconi-Bickle Syndrome" mutation, which causes the liver and kidneys to enlarge. These effects were observed in both humans and affected mice that were studied and tested, causing increased liver weight and glycogen accumulation in patients with this syndrome, and it was found that in the absence of the role of GLUT 2, other protein transporters such as GLUT1 and GLUT3 help maintain a moderate concentration .Other GLUT2-related diseases have been discovered, such as preserved kidney syndrome, and other GLUT2-related diseases such as neonatal diabetes, a disease that resolves 18 months after birth***. (9) (10)***

In conclusion, GLUT2 has an important role in blood glucose regulation. In which it contributes to glucose sensing and glucose homeostasis in an indirect way. And any defect that happens to it may lead to health problems. Scientists use mice to understand the mechanism of this protein, but the extent of its impact on blood glucose regulation was not very clear until now. So, we need more experiments to make GLUT2 and its roles clearer.

**References**:

1. Aronoff SL, Berkowitz K, Shreiner B, Want L (2004). "Glucose metabolism and regulation: Beyond insulin and glucagon". Diabetes Spectrum. 17 (3): 183–90. doi:10.2337/diaspect.17.3.183. Archived from the original on 2019-12-17. Retrieved 2016-12-07.
2. Mueckler M, Thorens B (2013) The SLC2 (GLUT) family of membrane transporters. Mol Asp Med 34:121–138
3. Uldry M, Ibberson M, Hosokawa M, Thorens B (2002) GLUT2 is a high affinity glucosamine transporter. FEBS Lett 524:199–203
4. Ebey Soman, [Scienceray](https://en.wikipedia.org/w/index.php?title=Scienceray&action=edit&redlink=1), [Regulation of Glucose by Insulin](http://scienceray.com/biology/human-biology/regulation-of-glucose-by-insulin) [Archived](https://web.archive.org/web/20110716022545/http:/scienceray.com/biology/human-biology/regulation-of-glucose-by-insulin) July 16, 2011, at the [Wayback Machine](https://en.wikipedia.org/wiki/Wayback_Machine), May 4, 2009. Retrieved November 1, 2009.
5. Romere C, Duerrschmid C, Bournat J, Constable P, Jain M, Xia F, Saha PK, Del Solar M, Zhu B, York B, Sarkar P, Rendon DA, Gaber MW, LeMaire SA, Coselli JS, Milewicz DM, Sutton VR, Butte NF, Moore DD, Chopra AR (April 2016). ["Asprosin, a Fasting-Induced Glucogenic Protein Hormone"](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4852710). *Cell*. **165** (3): 566–79. [doi](https://en.wikipedia.org/wiki/Doi_(identifier)):[10.1016/j.cell.2016.02.063](https://doi.org/10.1016%2Fj.cell.2016.02.063). [PMC](https://en.wikipedia.org/wiki/PMC_(identifier)) [4852710](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4852710). [PMID](https://en.wikipedia.org/wiki/PMID_(identifier)) [27087445](https://pubmed.ncbi.nlm.nih.gov/27087445).
6. Meglasson MD, Matschinsky FM 1986 Pancreatic islet glucose metabolism and regulation of insulin secretion. Diabetes Metab Rev 2:163–214
7. Rémy Burcelin, Wanda Dolci, and Bernard Thorens. Glucose Sensing by the Hepatoportal Sensor Is GLUT2-Dependent In Vivo Analysis in GLUT2-Null Mice. DIABETES, VOL. 49, OCTOBER 2000.
8. AnnaWendt,LenaEliasson. Pancreatic α-cells – The unsung heroes in islet function. Seminars in Cell & Developmental Biology, Volume 103, July 2020, Pages 41-50
9. Fanconi G, Bickel H (1949) Die chronische Aminoacidurie bei der Glykogenose und der Cystinkrankheit. Helv Paediatr Acta 4:359–396, article in German
10. Santer R, Schneppenheim R, Suter D, Schaub J, Steinmann B (1998) Fanconi-Bickel syndrome - the original patient and his natural history, historical steps leading to the primary defect, and a review of the literature. Eur J Pediatr 157:783–797