

Properties of Glucose Transport Proteins

First one must remember the kinetics of transport. Glucose will not cross the membrane lipid by layer and is a facilitated, structure specific movement. This is a passive, concentration dependent transport mechanism that give a hyperbolic curve of transport vs. glucose concentration. This of course indicates that transport is receptor mediated and is saturated by high concentrations of glucose.

These transport proteins mediate facilitated transport, that is, they can only transport glucose (or fructose) from areas of high concentration to areas of lower concentration. The sugar is bound by the protein, a flip-flop mechanism reverses the membrane direction of the sugar-protein complex, the sugar is released and the protein flips around once more to initiate a new cycle. Transport activity is dependent upon the sugar concentrations and the number of transport proteins in the outer cell membrane. In principle the GLUT family can transport glucose both into and out of cells. In most tissues the internal glucose concentration is quite low; transport can only proceed from the extracellular area into the cell. Thus the very important role that phosphorylation plays in both metabolism and transport. REMEMBER that once glucose is covalently modified by glucokinase or hexokinase, it is not longer recognized (very low K_m) by the transporter.

Transporter	Tissue distribution	Special properties
GLUT 1 (492 aa)	Most cells. Placenta, erythrocytes, brain, blood brain barrier, adipose, muscle (low conc)	High capacity, relatively low K_m (2-3mM). Acts as a basal glucose uptake.
GLUT 2 (524 aa)	Liver, pancreatic beta cells, hypothalamus, basolateral membrane small intestine.	High capacity but low affinity [high K_m (ca. 5mM)]; part of "the glucose sensor". Involved in Glucose Regulation.
GLUT 3 (496 aa)	Neurons, placenta, testes	Lowest K_m (ca. 1mM) high capacity
GLUT 4 (509 aa)	Skeletal muscle, cardiac muscle, and adipose tissue	Activated by insulin
GLUT 5 (501 aa)	Mucosal surface in small intestine, sperm and adipose (high conc)	Fructose specific.
GLUT 6 (664 aa) also known as: SGLT-1	Small Intestines (apical membranes) and kidney	This is a sodium coupled secondary active transport that is involved in the active (vs the other transporters) uptake of glucose.

In gluconeogenic tissues (liver and kidney), intracellular glucose concentration can exceed blood glucose concentration in the post-absorptive or fasting states. Export of glucose from liver and kidney occurs through GLUT1.

The insulin-sensitive glucose transporter, GLUT4, is found bound to internal cellular membranes where it is inactive. Most researchers agree that GLUT4 is bound to the Golgi apparatus. GLUT4 is brought to the plasma membrane by an ATP requiring process. The transport protein molecules that arrive at the surface membrane contribute to glucose transport. Another ATP-dependent mechanism transports GLUT4 back to the Golgi apparatus where these molecules are once more inactive. Insulin shifts the balance between exocytosis and endocytosis such that the number of functional GLUT4 molecules in the plasma membrane increases, thereby activating glucose uptake

Muscle activity can increase the number of GLUT4 molecules in the plasma membrane through the same mechanism. Muscle activity and depletion of intracellular glucose alone (without increased insulin levels) activates glucose uptake. Exhaustive physical work can lead to hypoglycemia and loss of consciousness. Evolution gave us a way to activate maximum speed to run from lions tigers and bears as well as a simultaneous route to unconsciousness before being eaten.

Adapted from Dr. Horn, Department of Medical Biochemistry University of Oslo