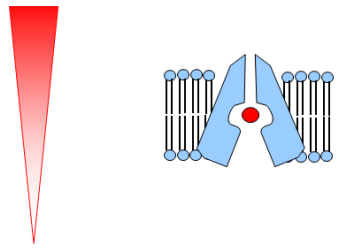
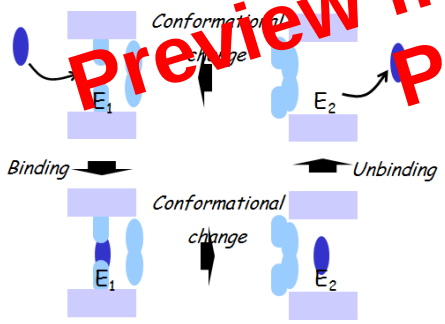
- GLUT protein family is part of the major facilitator superfamily – largest superfamily of proteins involved in membrane transport and are ubiquitous
- Integral membrane proteins of all eukaryotic cells
- Isoforms differ in kinetic properties, sugar specificity, tissue localisation and regulation
- Some transport other substrates such as galactose, water and painkiller glycopeptides
- Entry of glucose through GLUT is often the rate-limiting step for the performance of cells with high energy metabolism
- Abundant in epithelial cells lining the walls of small blood vessels, particularly on blood-brain barrier – high metabolic demand for glucose utilisation
- GLUT1 expressed in endothelial cell membrane at its interfaces with the blood and intercellular space, as well as astrocyte PM (important for function of blood-brain barrier)
- GLUT1 transports glucose from blood into the endothelial cells and then into the astrocytes – convert glucose into other energy sources that are transported into neurons

Facilitated transport

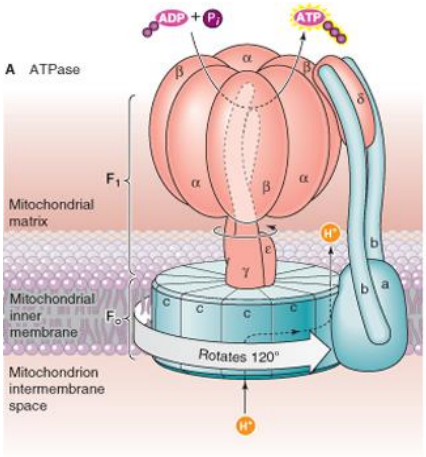


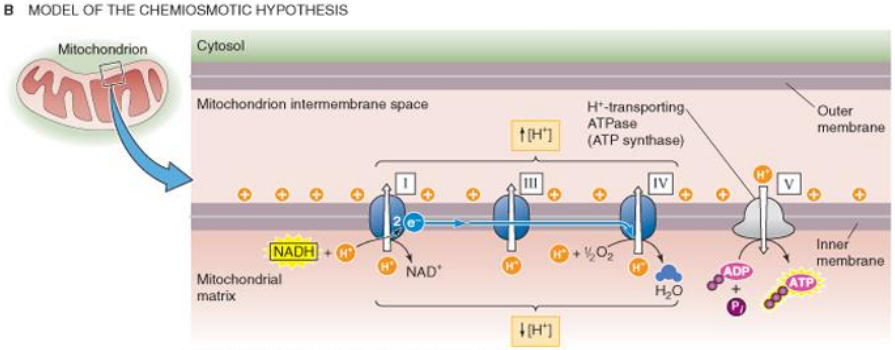
Mechanism



GLUT1 deficiency syndrome or De Vivo disease

- Rare autosomal dominant disease due to mutations in GLUT1
- In children, the brain glucose demand is 3-4 times higher than in adults and represents 80% of the glucose utilisation of the body
- Impaired glucose transport across the blood-brain barrier
- Characterised by seizures and developmental delay caused by impaired glucose transport into the brain
- Symptoms
    - Microcephaly (small head)
    - Mental and motor developmental delays
    - Infantile seizures refractory to anticonvulsants
    - Ataxia





Comparison of pores, channels and carriers

Table 5-5. Comparison of Properties of Pores, Channels, and Carriers

	Pores	Channels	Carriers
Example	Water channel (AQP1)	Shaker K+ channel	Glucose transporter (GLUT1)
Conduit through membrane	Always open	Alternately open	Never open
Unitary event	None (continuously open)	Opening	Cycle of conformational changes
Particles translocated per "event"	-	6×10^4*	1-5
Particles translocated per second	up to 10^9	10^6 to 10^8 when open	200-50,000

*Assuming 100-pS channel, driving force of 100 mV, and an opening time of 1 ms.

Cortical collecting duct showing V-ATPase staining of intercalated cells (yellow/green). The A-type intercalated cells have apical proton pumps (arrowheads) whereas B-type intercalated cells have basolateral proton pumps (arrows). This is an intriguing example of the same protein being targeted to different plasma membrane domains. The mechanism by which this opposing polarity of proton pumps is achieved in intercalated cells is unknown (bar = 10 µm).

The importance of V-ATPase activity in renal proton secretion is highlighted by the inherited disease distal renal tubular acidosis. In all cases, renal tubular acidosis results from a failure of the normal renal mechanisms that regulate systemic pH.