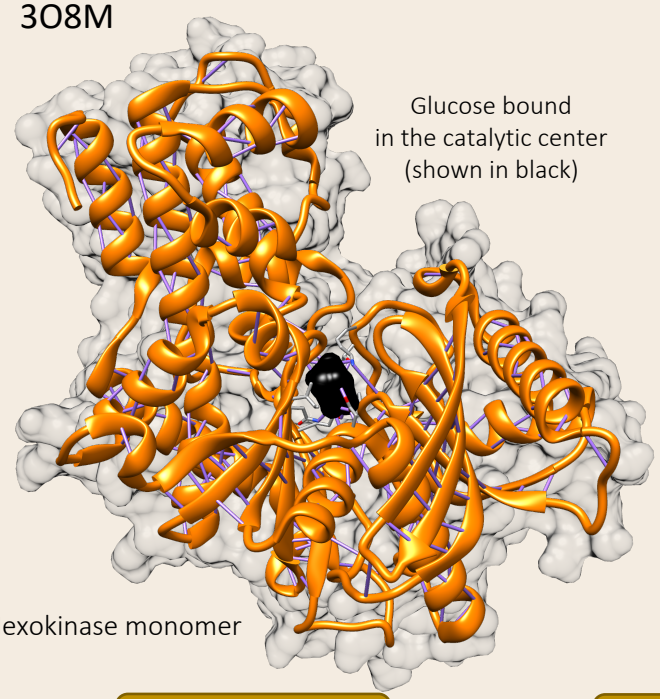
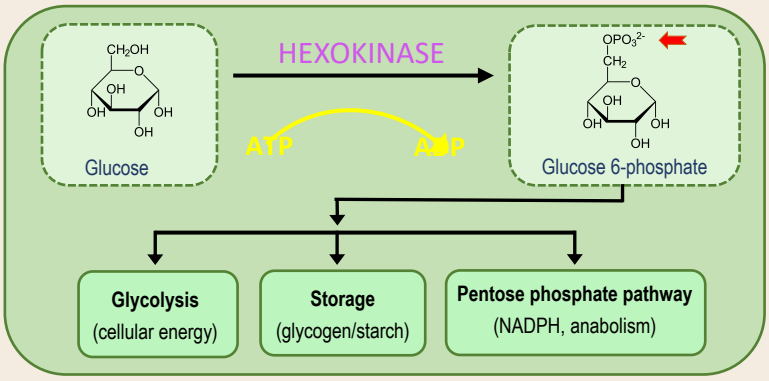
GLUCOSE TRAPPER

3O8M



Hexokinase

- an enzyme involved in energy metabolism
- phosphorylates the six-carbon sugar hexose, forming hexose phosphate (G6P)



STRUCTURE

- **large homodimer** made of 920 amino acids in each chain
- each monomer folds into **alpha helices** and **beta sheets**
- when it binds glucose, it undergoes **shape change** (induced-fit conformation change)
- Mammals have **4 isoforms**[1]:
  - Type I primarily involved in catabolism (glycolysis) – ”housekeeping enzyme”
  - Type II, III and IV serve in anabolism (glycogen and starch synthesis)

LOCATION

- essential enzymes in bacteria, fungi, plants, and animals
- expressed in **most tissues**, especially in those **with high energy demands**, such as heart, skeletal muscle, and adipose tissues
- Type I and Type II attached to mitochondria with access to ATP generated by oxidative phosphorylation
- Type III localized to cytosol
- Type IV translocates between cytosol and nucleus

FUNCTION

- carries out the **rate-limiting step** (1st step) of glycolysis
- **catalyzes** the transfer of phosphate group from **ATP to glucose**, forming **glucose-6-phosphate (G6P)**, “trapping” glucose in the cell for alternative metabolic pathways
- **allosterically inhibited** by its product (G6P)
- essential in tissues dependent on glucose as a source of energy (brain)

Disorders and Medicine:

- **Hexokinase deficiency**[2] is a rare autosomal recessive disorder characterized by hemolytic anemia, a condition in which red blood cells are destroyed at a faster rate then they are made
- **HK serves in innate immunity**[3] – in macrophages and dendritic cells it detects cytosolic N-acetylglucosamine (NAG), a component of the bacterial cell wall, and facilitates activation of the inflammatory response.
- **HK is a target of cancer therapies**[4] since high levels of hexokinase (HK-II) expressed in cancer cells allow for high levels of energy metabolism supporting tumor growth

[1] Wilson (2003), J Exp Biol 206:2049-2057; [2] NIH NCATS; [3] Wolf et al. (2016), Cell 166(3):624-636; [4]Mathupala et al. (2012), Oncogene 25(34):4777-4786;
Model made in UCSF Chimera