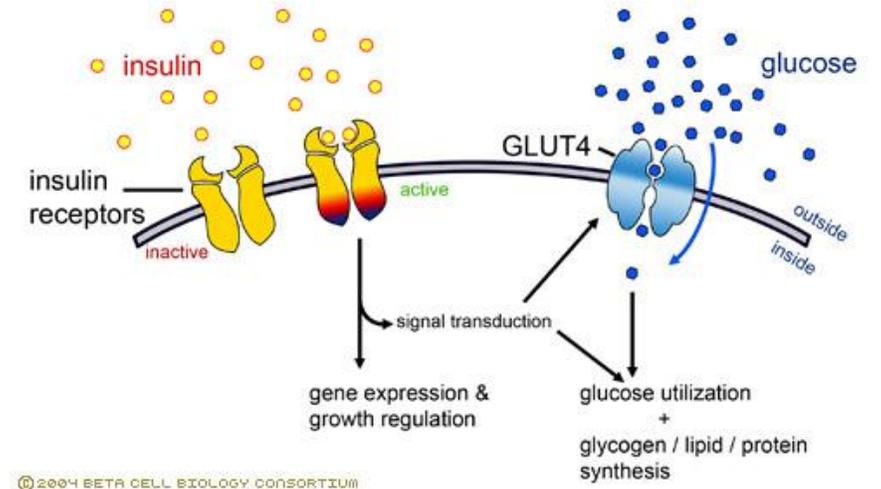


Insulin Increases the GLUT 4

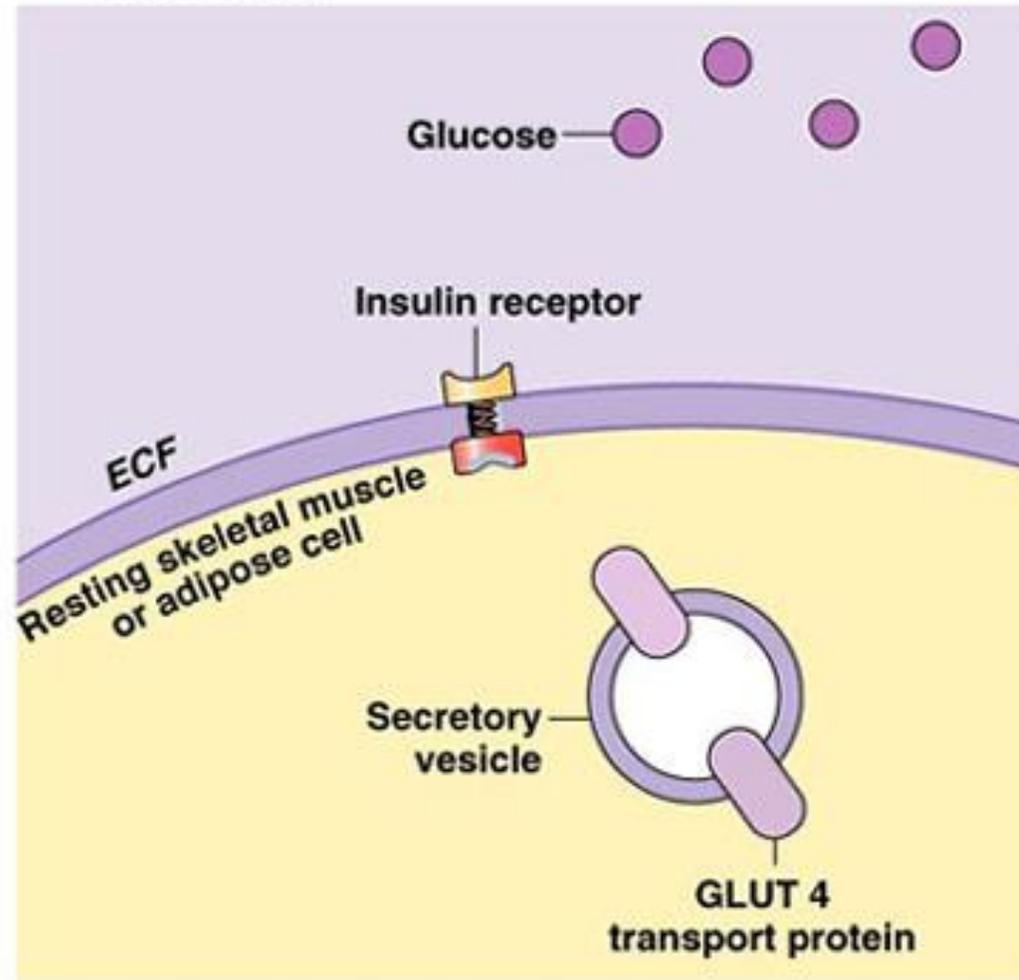
Ryan Salour

- Glucose molecules are relatively large and polar. Therefore, they can not just simply diffuse into the cells.
- The need for Glucose transporter (GLUT) arises.
- The primary glucose transporters on adipose and muscle tissues are GLUT4
- Glut 4 allows the shuttling of glucose across the membrane via facilitated diffusion.

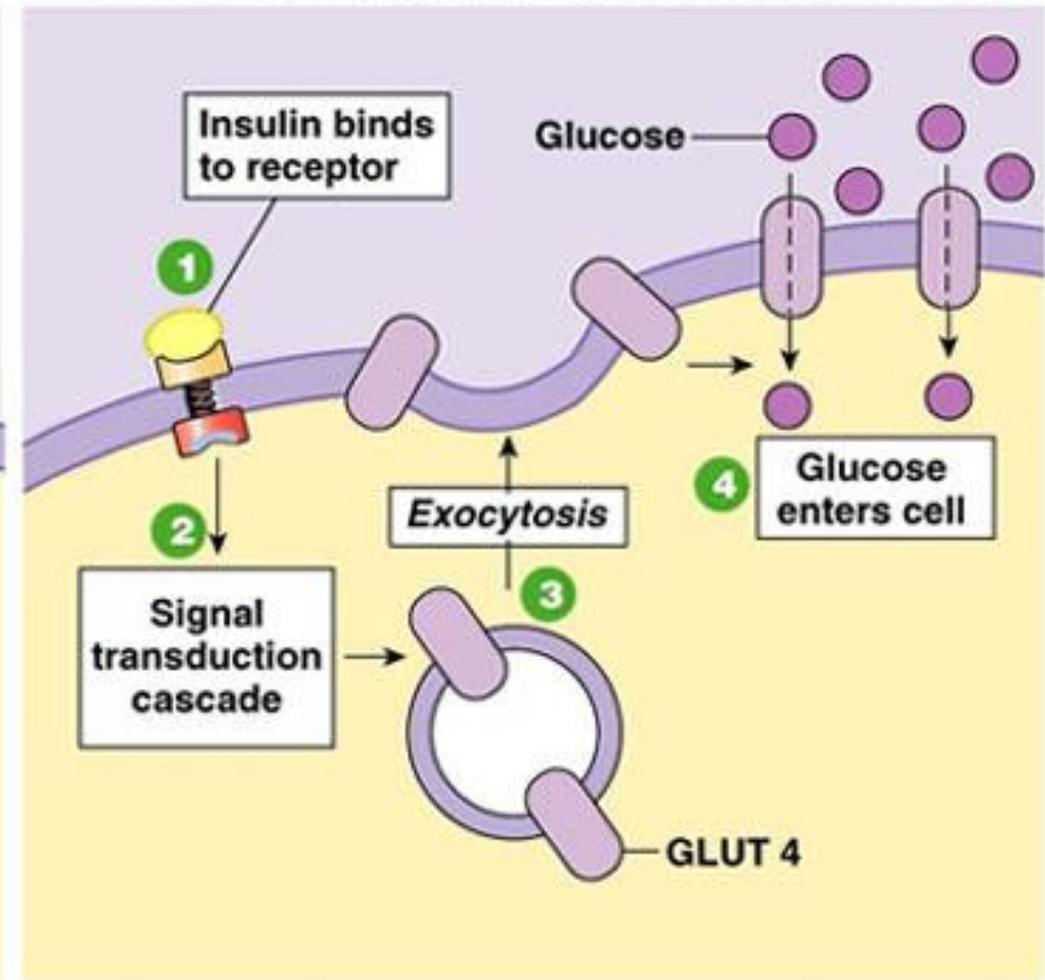


- For 3-5 hours after a meal, our blood glucose increases significantly.
- Higher blood glucose levels causes higher insulin secretion by pancreatic Beta cells
- Muscle and Fat Cells, in response, show increased GLUT 4 transporters on the membrane. This allows the glucose to diffuse from the bloodstream into the cell
- In muscle and fat tissues, the insulin receptor's activation, signals the cell to bring more GLUT4 to the membrane.

(a) In the absence of insulin, glucose cannot enter the cell.

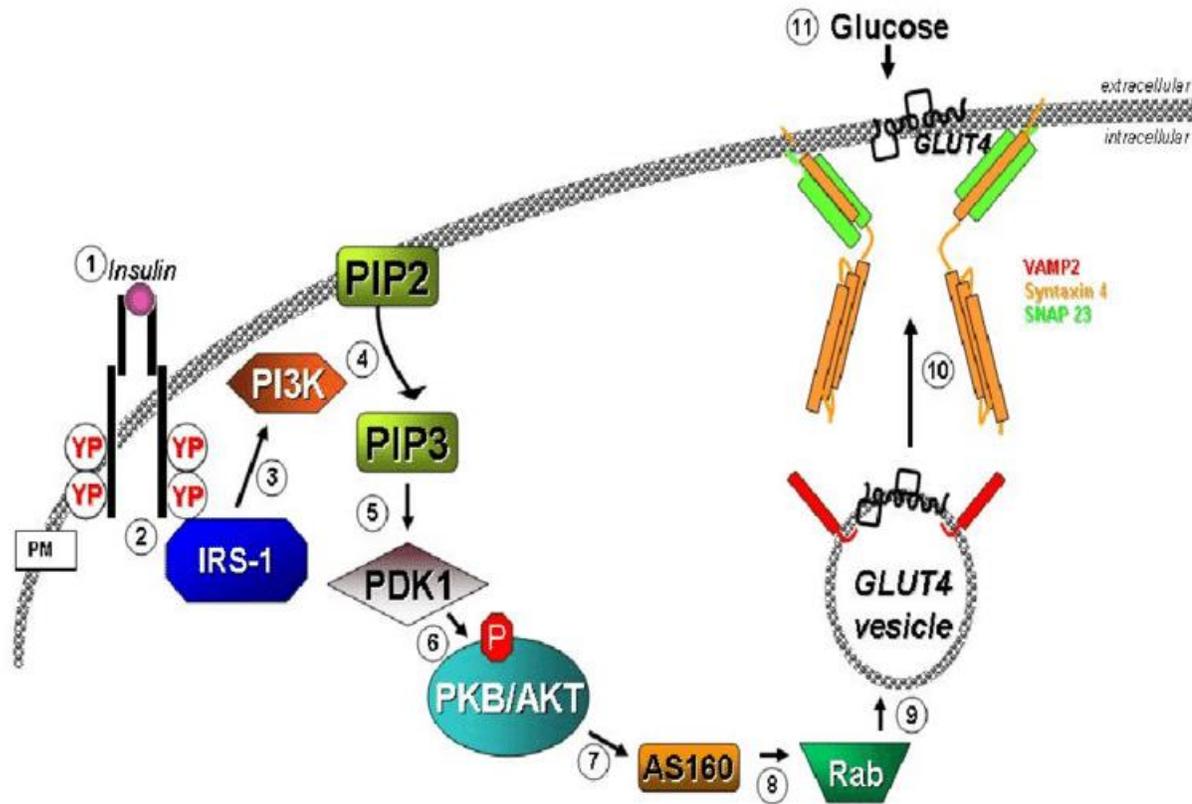


(b) Insulin signals the cell to insert GLUT 4 transporters into the membrane, allowing glucose to enter cell.

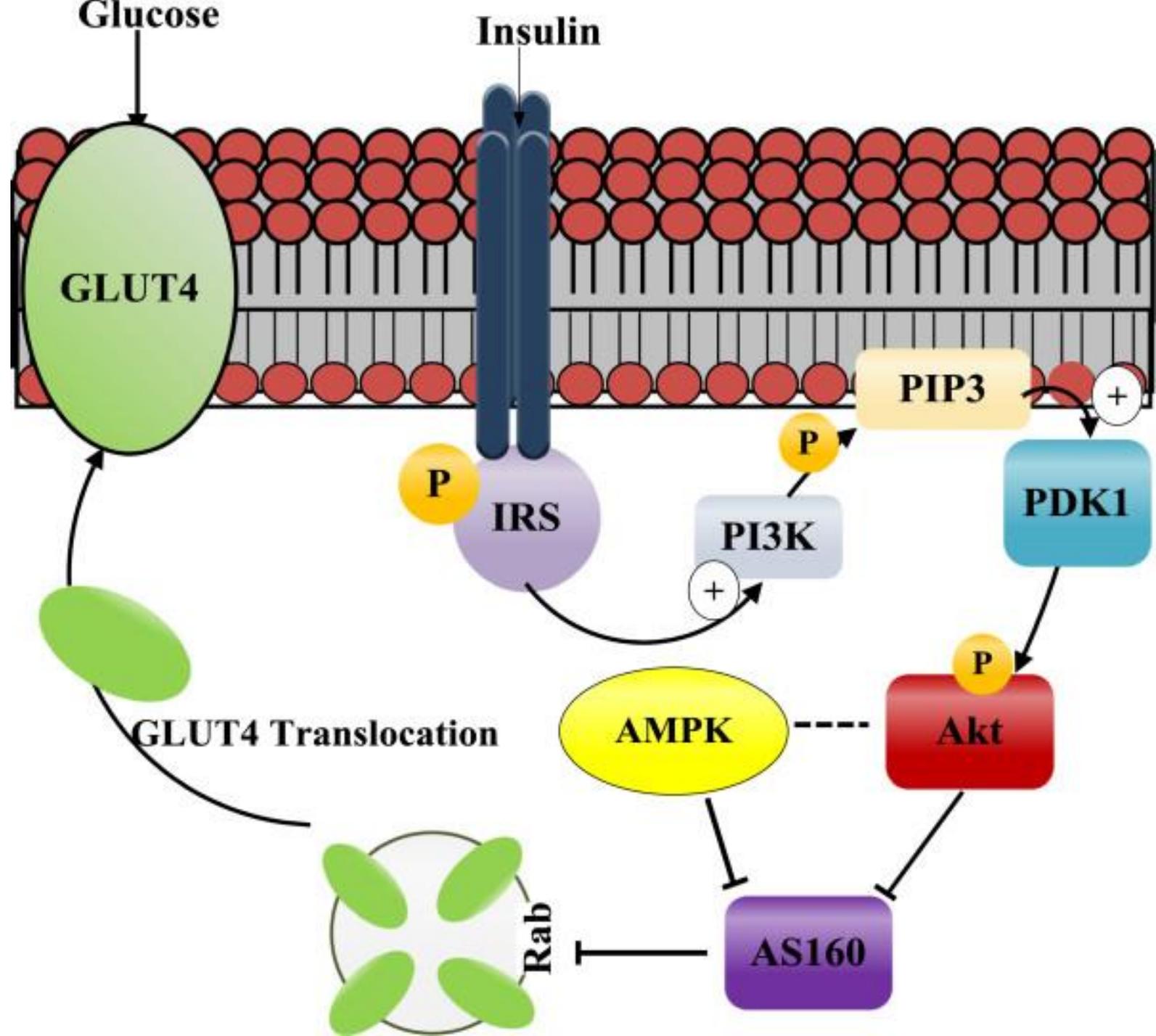


- Pancreatic Beta Cells are responsible for secretion of Insulin, when the blood glucose levels increase.
- For it to be activated, Glucose must first enter Beta cells and be metabolized.
- Metabolism of glucose => higher intracellular [ATP]:[ADP] ratio => larger calcium release into the cell
- The larger [Ca²⁺] would cause the exocytosis of Insulin Vesicles.

Insulin Receptor pathway



- The Insulin is a peptide hormone and binds to a membrane bound receptor on Muscle and adipose tissues.
- Insulin receptor functions as a receptor tyrosine kinase. Upon binding, it will activate the insulin receptor substrate-1 (IRS-1)
- IRS-1 then activates the Phosphoinositide Kinase proteins

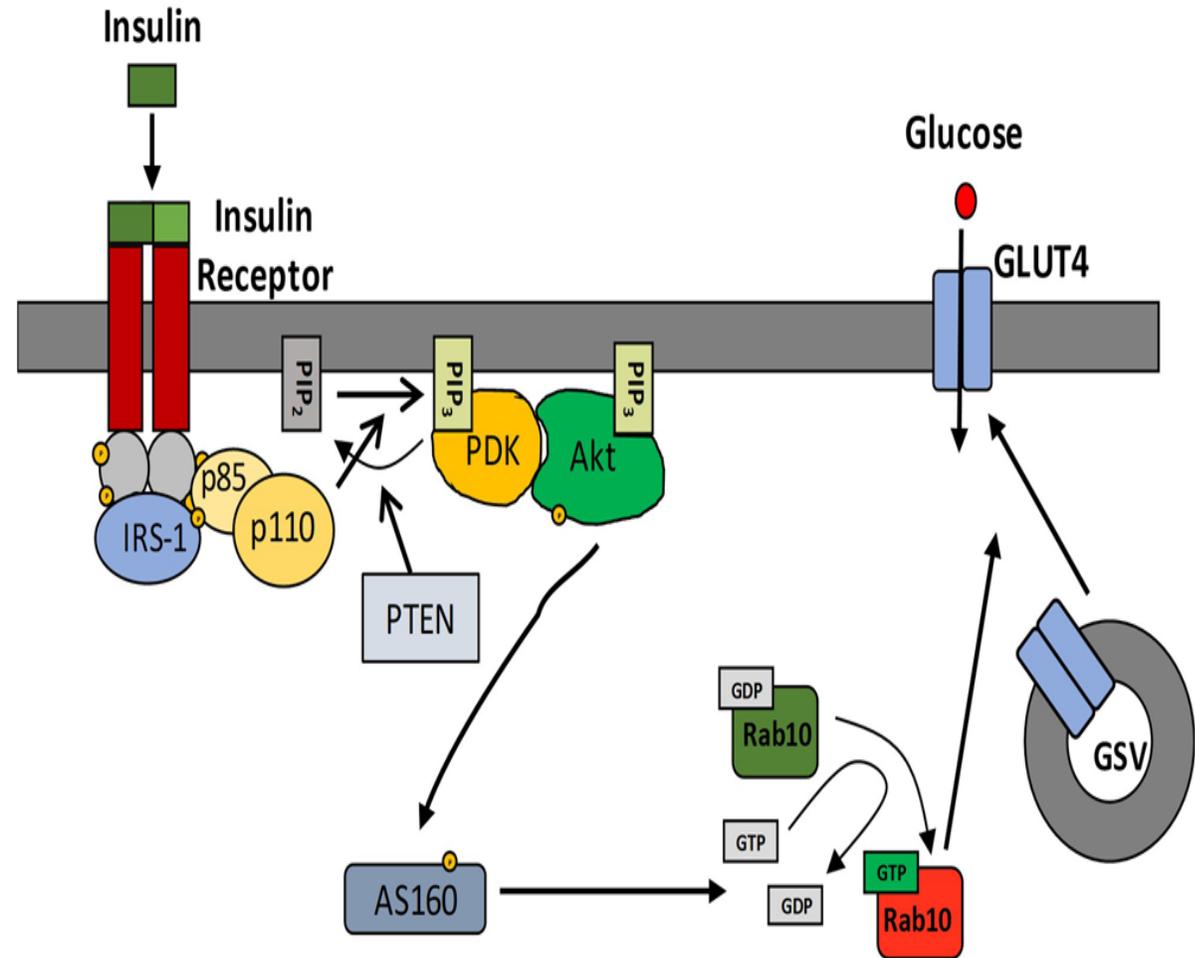


Phosphoinositide 3 Kinase enzyme, as the name implies, Phosphorylates and activates membrane bound PIP2 to form PIP3.

PIP3 serves as the ligand for the Phosphoinositide dependent Kinase 1.

Activated PDK phosphorylates AKT (Protein Kinase B)

- Protein Kinase B goes on to phosphorylate AS160.
- AS160 donates a phosphate to the Rab10 protein's GDP, converting it to GTP
- GTP-Rab10 then pushes the GLUT4 storage vesicle to go to the membrane
- GLUT4 acts as transport protein and a path that brings in the Glucose out of the blood into the cells for storage or metabolism
- More GLUT4 levels= more glucose metabolism and storage within the cell



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