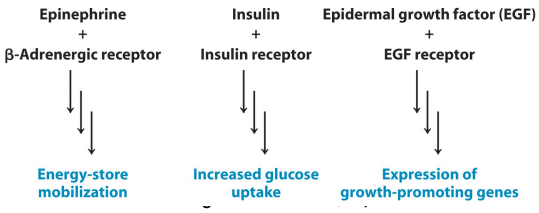
Chem 452 – Lecture 10
Signal Transduction & Sensory Systems
Part 2

Questions of the Day: How does the hormone insulin trigger the uptake of glucose in the cells that it targets.

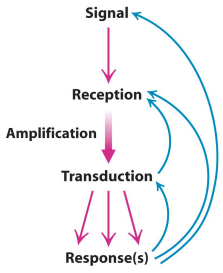
Introduction

- Signal transduction involves the changing of a cell's metabolism or gene expression in response to an external stimulus.



Introduction

- All three examples will present a common theme



Introduction

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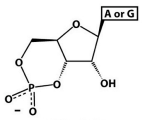
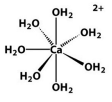
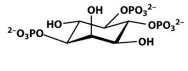


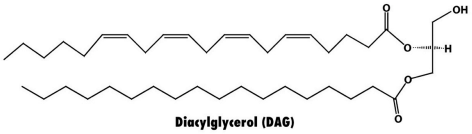
cAMP, cGMP



Calcium ion



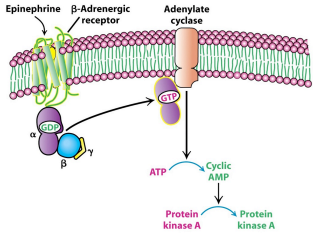
Inositol 1,4,5-trisphosphate (IP_3)

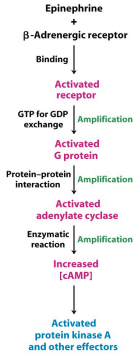


Diacylglycerol (DAG)

G-Protein Receptors

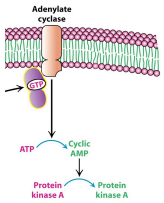
- Epinephrine binding activates $G_{\alpha s}$ by promoting GDP⇔GTP exchange.

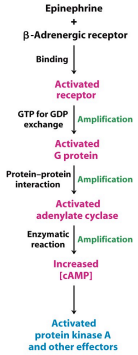




G-Protein Receptors

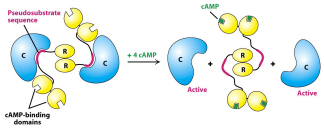
- $G_{\alpha s}$ binds to activates Adenylate cyclase, which catalyzes the formation of the secondary messenger, cAMP.

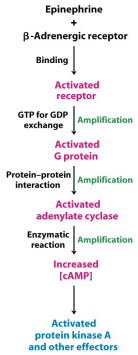




G-Protein Receptors

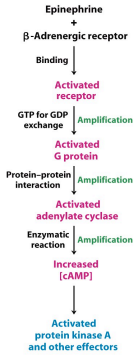
- cAMP binds to the regulatory subunit of Protein Kinase A (PKA) and activates it.





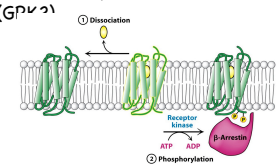
G-Protein Receptors

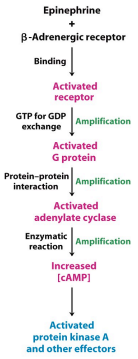
- PKA then phosphorylates and array of cellular proteins (at Ser & Thr), which are leads to
  - Degradation of stored fuels
  - Secretion of acid by gastric mucosa
  - Dispersion of melanin granules
  - Opening of chloride channels



G-Protein Receptors

- To turn off the pathway
  - $G\alpha_s$ catalyzes the hydrolysis of GTP back to GDP.
  - The β-adrenergic receptor can by inactivated by a G-protein receptor kinases (GRK's)





G-Protein Receptors

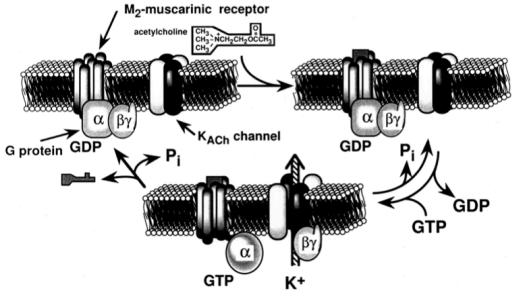
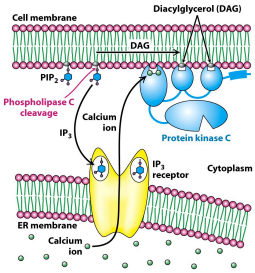


FIG. 2. Schematic representation of the G protein cycle involved in the activation of the muscarinic K^+ channel in response to acetylcholine.

The Phosphoinositide Cascade

- The phosphoinositide cascade also involved 7TM receptors that bind hormones.



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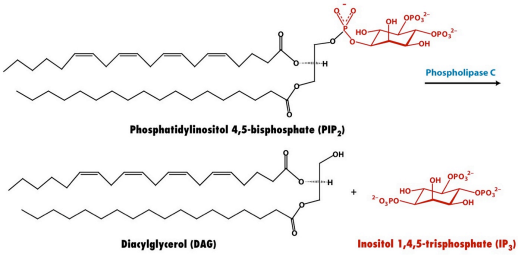
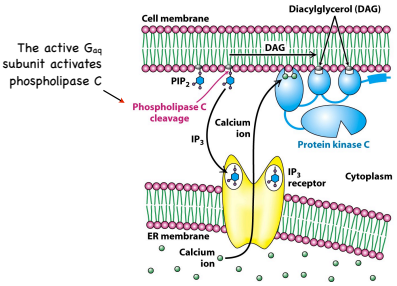


The Phosphoinositide Cascade

- IP_3 stimulates the release of yet another secondary messenger, Ca^{2+}, into the cytosol.



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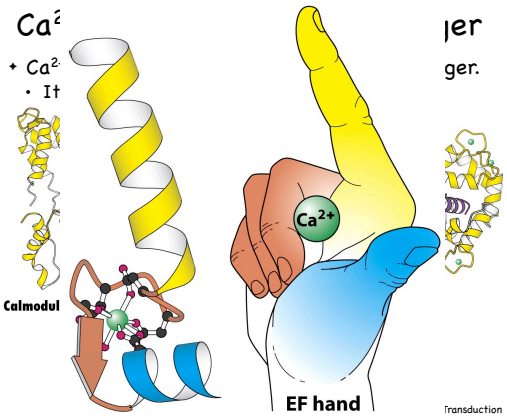

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The Insulin Signaling Pathway

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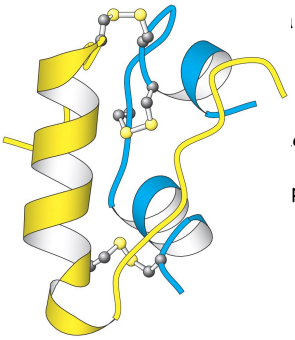

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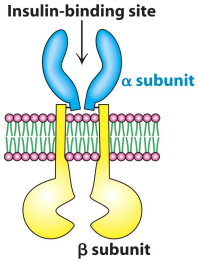
pathway

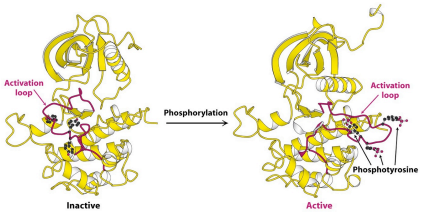
The Insulin Signaling Pathway

- The binding of insulin to its receptor activates a protein kinase activity within the receptor itself.



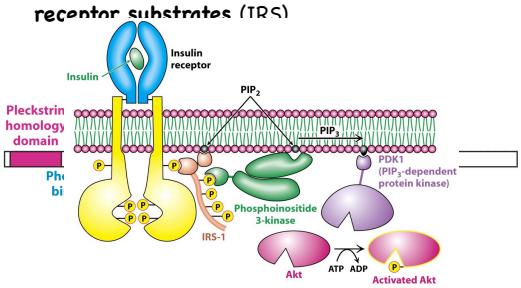
The Insulin Signaling Pathway

- The substrate for the kinase is the kinase itself.
  - Which in turn, is activated to phosphorylate other substrates



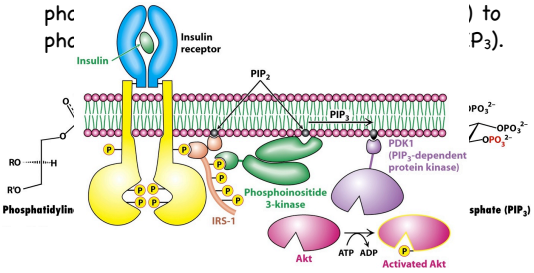
The Insulin Signaling Pathway

- These other substrates include the **insulin receptor substrates** (IRS)



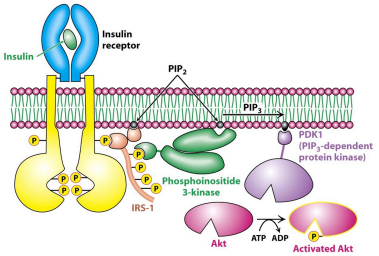
The Insulin Signaling Pathway

- The phosphorylated IRS activates a phosphoinositide 3-kinase, which converts phc) to phc P_3).



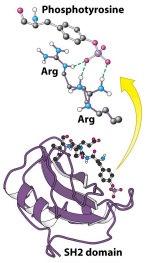
The Insulin Signaling Pathway

- The PIP_3 then activates a PIP_3-dependent protein kinase (PDK-1), which then phosphorylates and activates the Akt kinase.

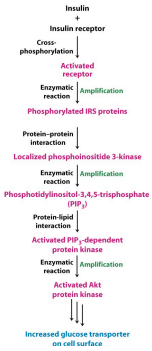


The Insulin Signaling Pathway

- The IRS has and example of the Src Homology 2 (SH2) domain, which bind to phosphorylated tyrosines.



The Insulin Signaling Pathway



Next up

- Lecture 10, Signal Transduction (con'd). (Chapter 14)