

ME 411 / ME 511

Biological Frameworks for Engineers

Class Organization

- Exam 1 due on Fri
- *Tiny Workhorse* Project:

Motor Protein	Grad Student
	Morgan
	Nathan Lee
	Nathan Pepin
	Praveen
	Alex (Joseph)



ME 411 / ME 511

Cell Signaling



Cell Signaling

- How do G-Protein Linked Receptors Work?

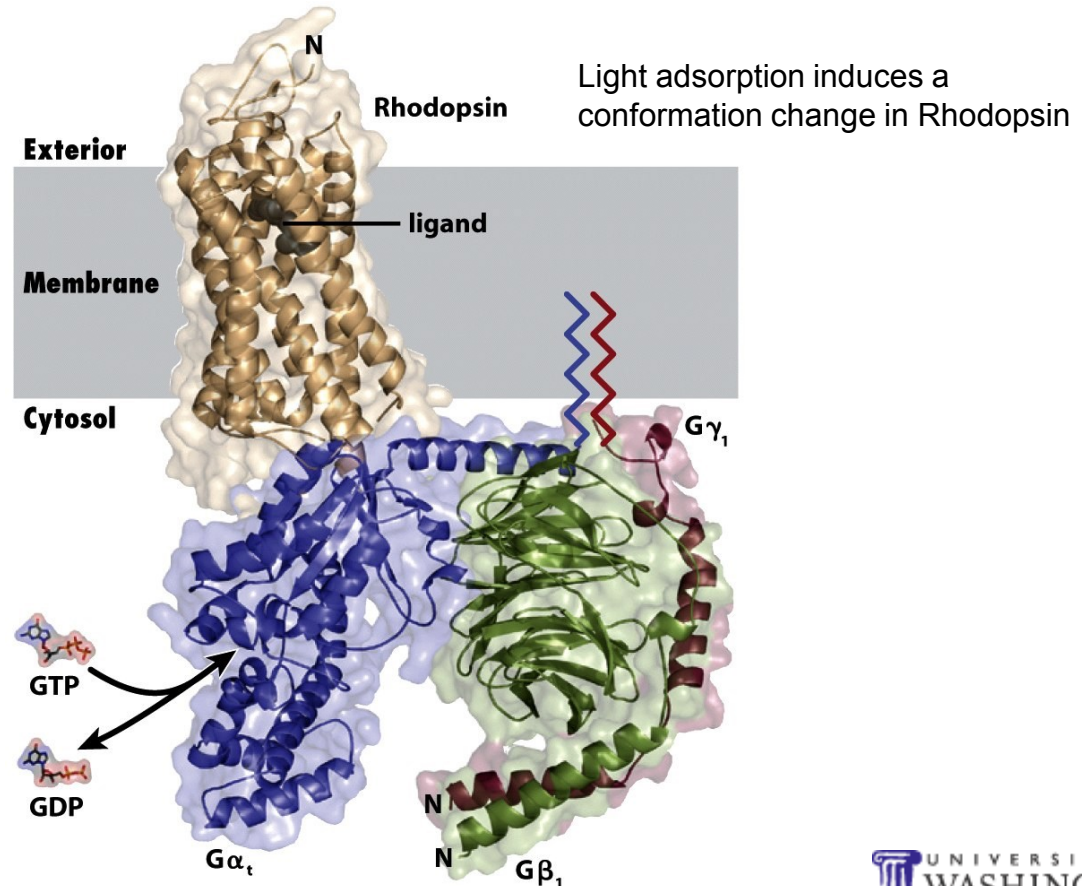


Figure 15-19
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G Protein & Effectors

TABLE 15-1 Major Classes of Mammalian Trimeric G Proteins and Their Effectors*

G _α CLASS	ASSOCIATED EFFECTOR	2ND MESSENGER	RECEPTOR EXAMPLES
G _{αs}	Adenylyl cyclase	cAMP (increased)	β-Adrenergic (epinephrine) receptor; receptors for glucagon, serotonin, vasopressin
G _{αi}	Adenylyl cyclase K ⁺ channel (G _{βγ} activates effector)	cAMP (decreased) Change in membrane potential	α ₂ -Adrenergic receptor Muscarinic acetylcholine receptor
G _{αolf}	Adenylyl cyclase	cAMP (increased)	Odorant receptors in nose
G _{αq}	Phospholipase C	IP ₃ , DAG (increased)	α ₁ -Adrenergic receptor
G _{αo}	Phospholipase C	IP ₃ , DAG (increased)	Acetylcholine receptor in endothelial cells
G _{αt}	cGMP phosphodiesterase	cGMP (decreased)	Rhodopsin (light receptor) in rod cells

*A given G_α subclass may be associated with more than one effector protein. To date, only one major G_{αs} has been identified, but multiple G_{αq} and G_{αi} proteins have been described. Effector proteins commonly are regulated by G_α but in some cases by G_{βγ} or the combined action of G_α and G_{βγ}.

IP₃ = inositol 1,4,5-trisphosphate; DAG = 1,2-diacylglycerol.

SOURCES: See L. Birnbaumer, 1992, *Cell* **71**:1069; Z. Farfel et al., 1999, *New Eng. J. Med.* **340**:1012; and K. Pierce et al., 2002, *Nature Rev. Mol. Cell Biol.* **3**:639.

Table 15-1

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Cell Signaling

- How do G-proteins work?

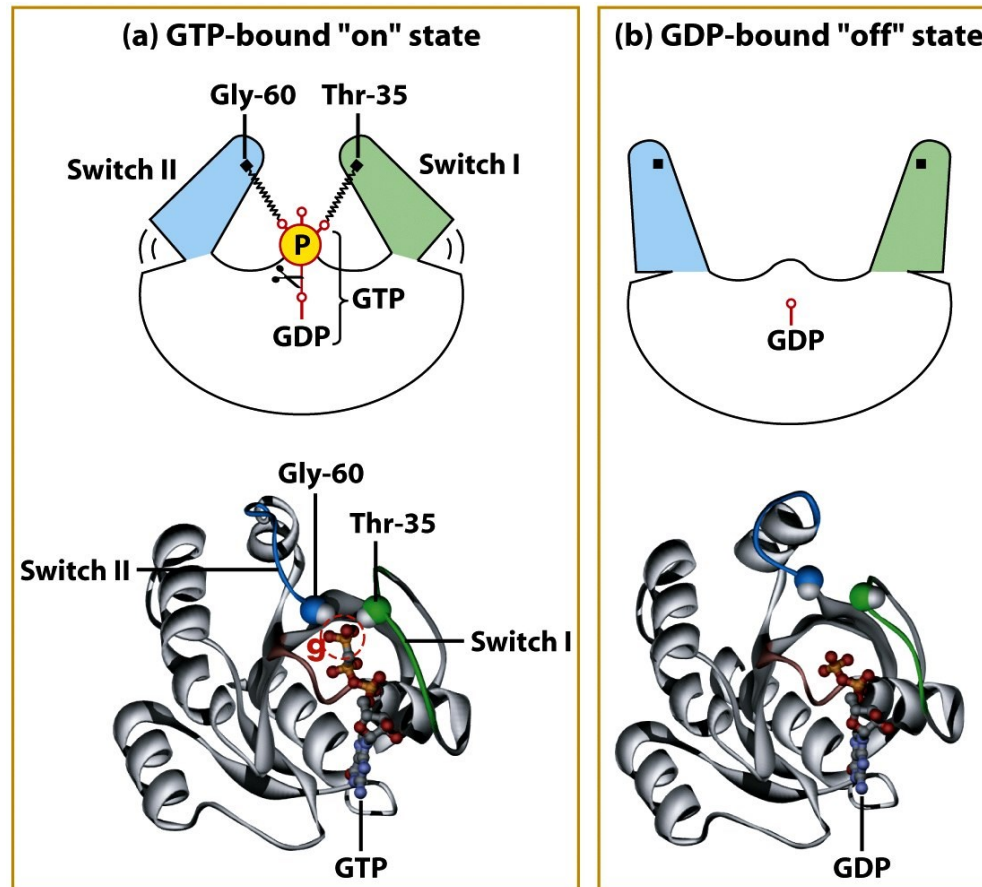


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Cell Signaling

- How do secondary messengers work?

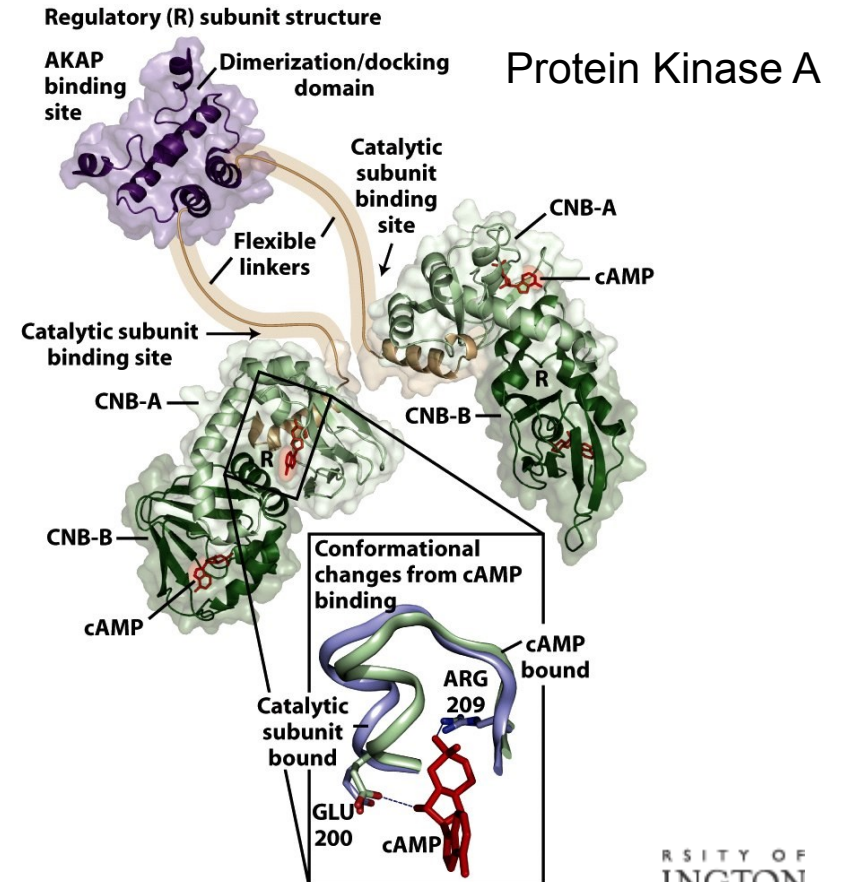
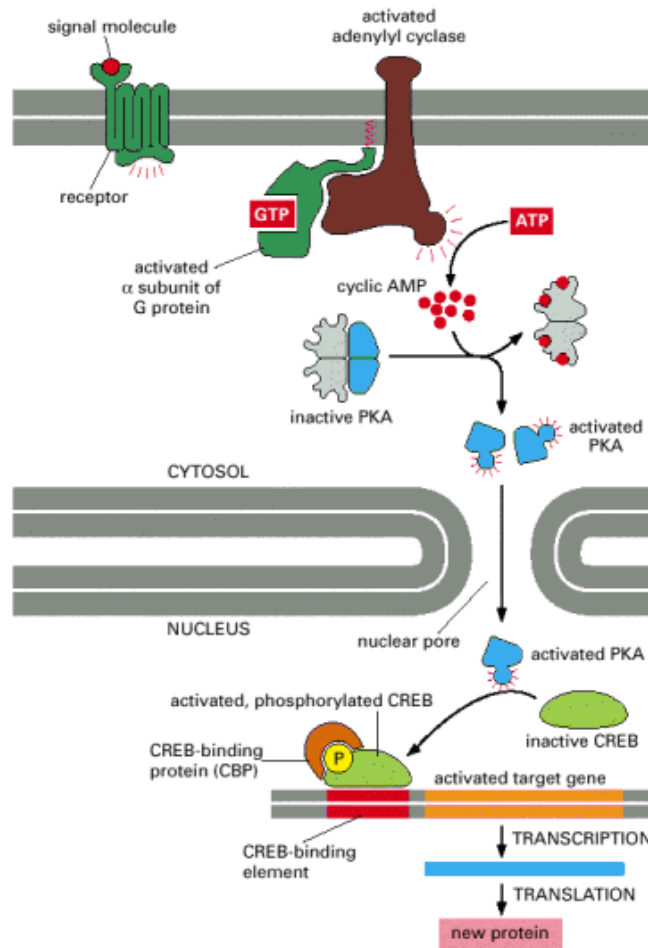


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cAMP is essential

TABLE 15-2 Cellular Responses to Hormone-Induced Rise in cAMP in Various Tissues*

TISSUE	HORMONE INDUCING RISE IN cAMP	CELLULAR RESPONSE
Adipose	Epinephrine; ACTH; glucagon	Increase in hydrolysis of triglyceride; decrease in amino acid uptake
Liver	Epinephrine; norepinephrine; glucagon	Increase in conversion of glycogen to glucose; inhibition of glycogen synthesis; increase in amino acid uptake; increase in gluconeogenesis (synthesis of glucose from amino acids)
Ovarian follicle	FSH; LH	Increase in synthesis of estrogen, progesterone
Adrenal cortex	ACTH	Increase in synthesis of aldosterone, cortisol
Cardiac muscle	Epinephrine	Increase in contraction rate
Thyroid gland	TSH	Secretion of thyroxine
Bone	Parathyroid hormone	Increase in resorption of calcium from bone
Skeletal muscle	Epinephrine	Conversion of glycogen to glucose
Intestine	Epinephrine	Fluid secretion
Kidney	Vasopressin	Resorption of water
Blood platelets	Prostaglandin I	Inhibition of aggregation and secretion

*Nearly all the effects of cAMP are mediated through protein kinase A (PKA), which is activated by binding of cAMP.

SOURCE: E. W. Sutherland, 1972, *Science* **177**:401.

Table 15-2

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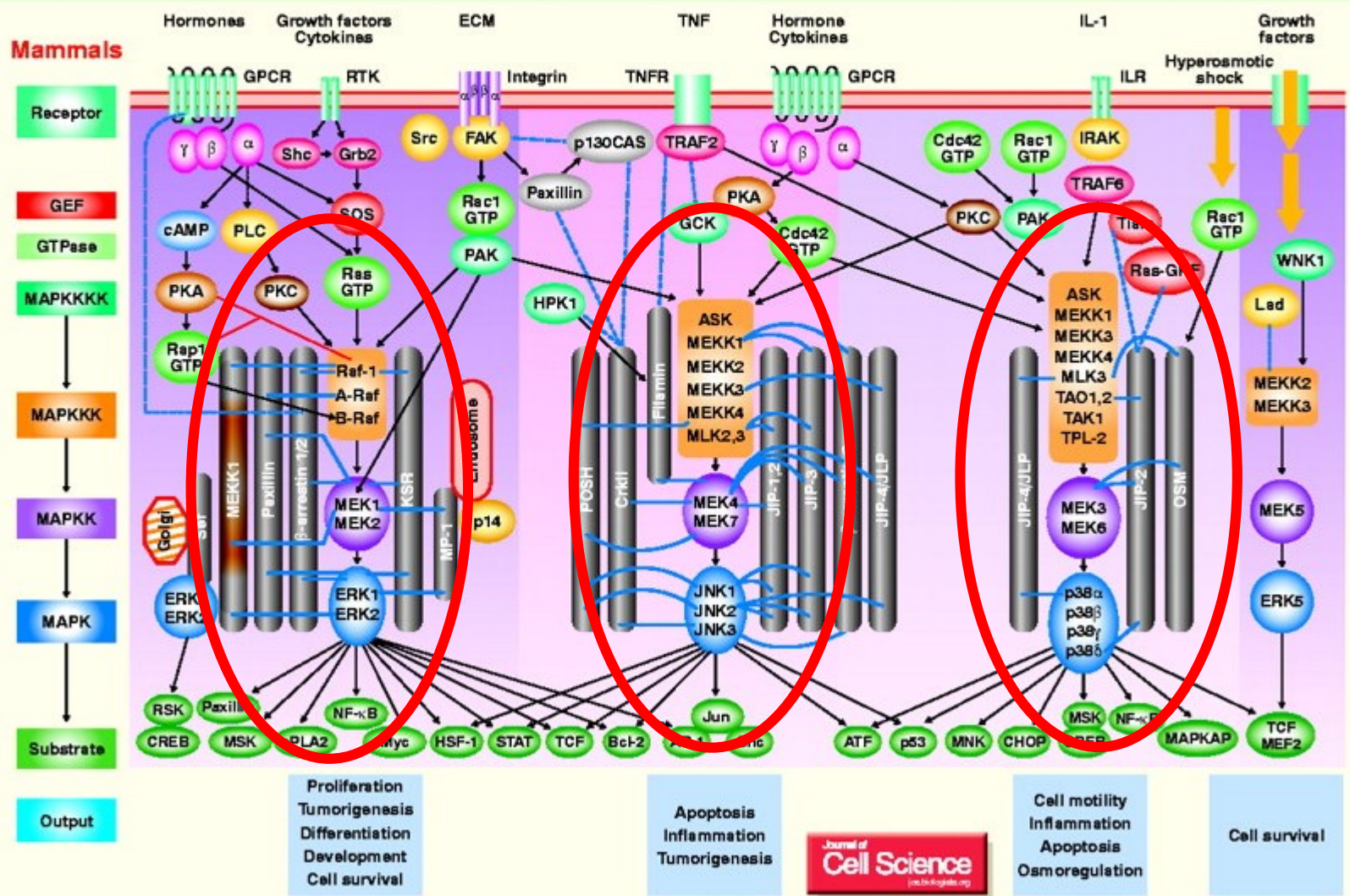
Signaling Cascades?



We wish!

MAP Kinase Pathways

Maosong Qi and Elaine A. Elion



Cell Signaling

- How does phosphorylation work?

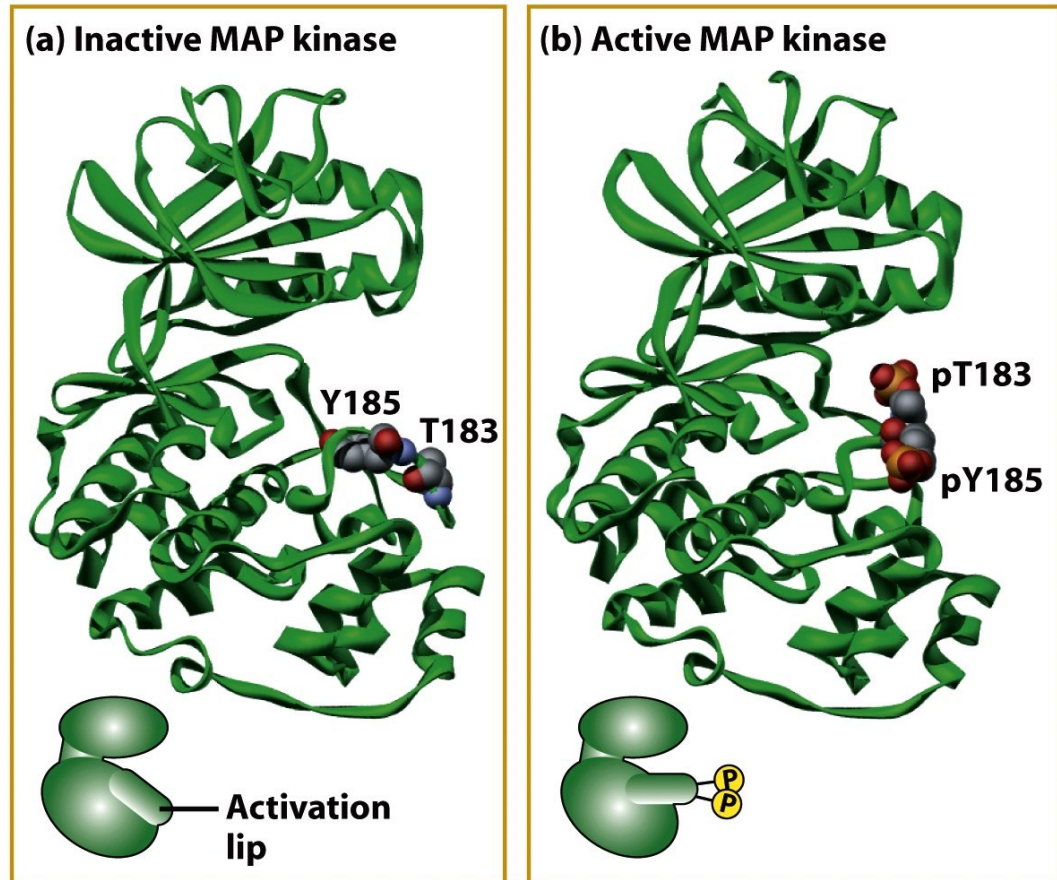
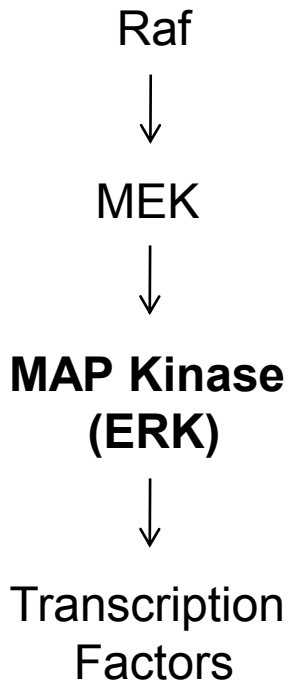


Figure 16-26
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Cell Signaling

- How do Receptor Tyrosine Kinases work?

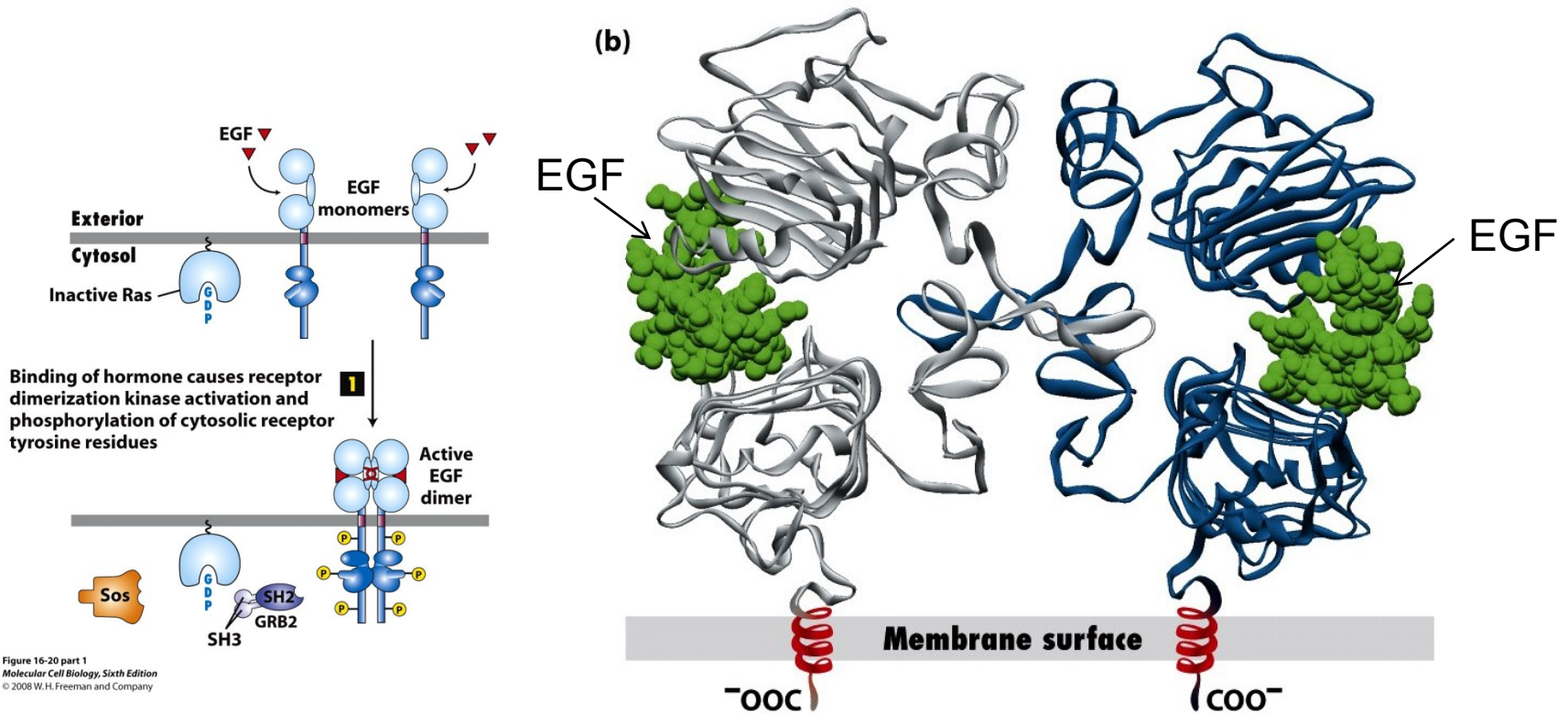
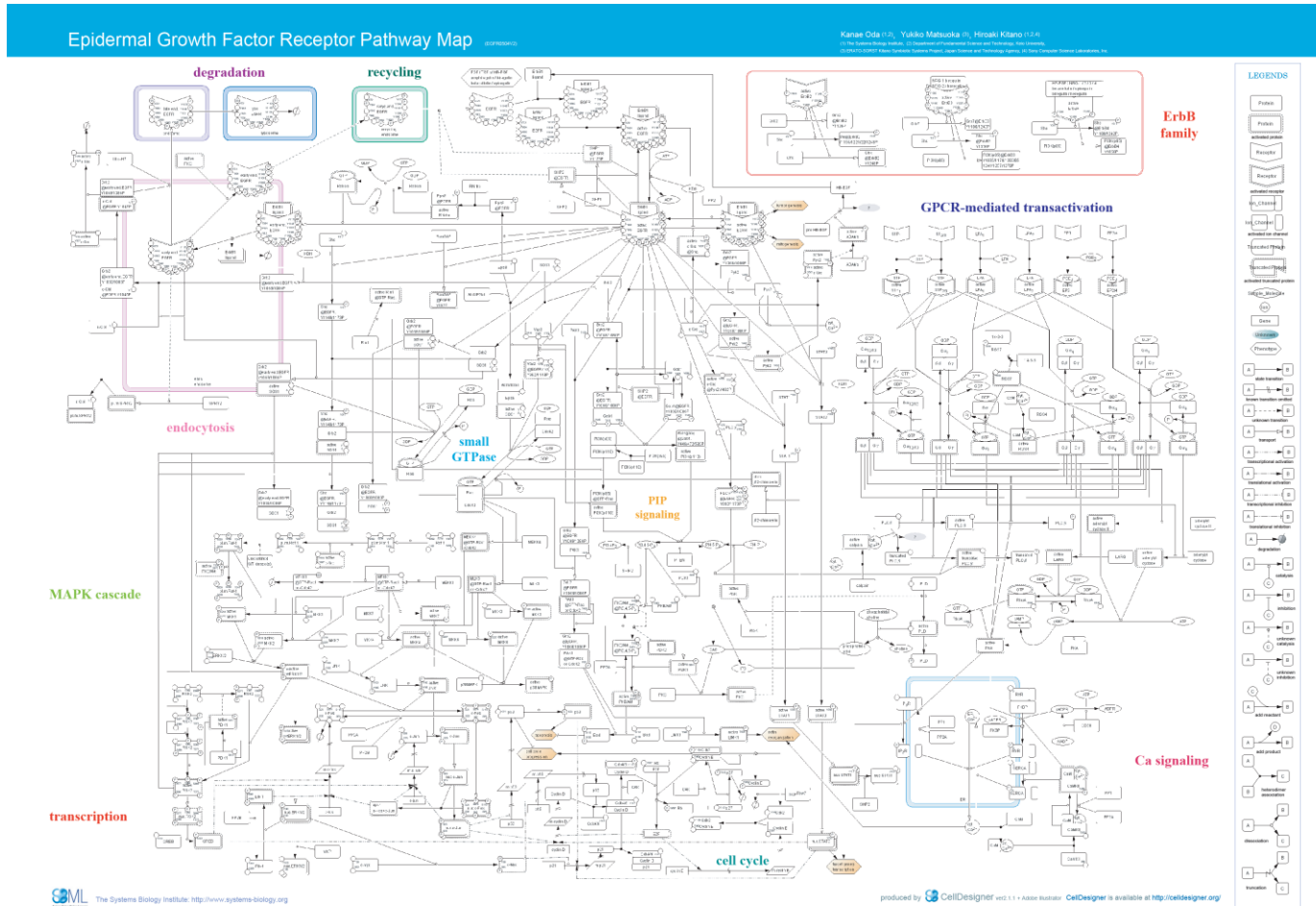


Figure 16-20 part 1
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Figure 16-17
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A comprehensive pathway map of epidermal growth factor receptor signaling

K Oda, Y Matsuoka, A Funahashi & H Kitano
Molecular Systems Biology (2005) doi:10.1038/msb4100014



Signal Manipulations



Gene Inactivation

- Replacing a normal gene with another sequence
- Introducing an allele whose encoded protein inhibits functioning of the target protein
- Promoting destruction of the mRNA expressed from a gene

Replacements

- **Dominant Negative:** altered gene product that acts antagonistically to the wild-type allele. These mutations usually result in an altered molecular function (often inactive).
- **Constitutively Active:** altered gene product that renders protein that is locked in the active state. Kinase domain active regardless of state of upstream signals

Transfections

Transient transfection

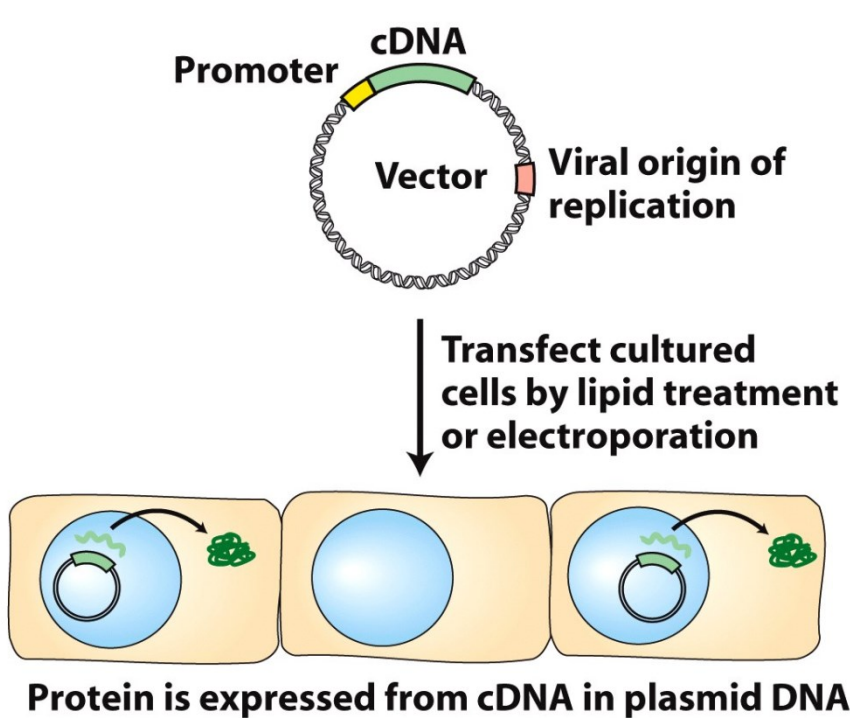


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Origin of replication: viral DNA sequence that hijacks a host's genetic machinery

Stable transfection (transformation)

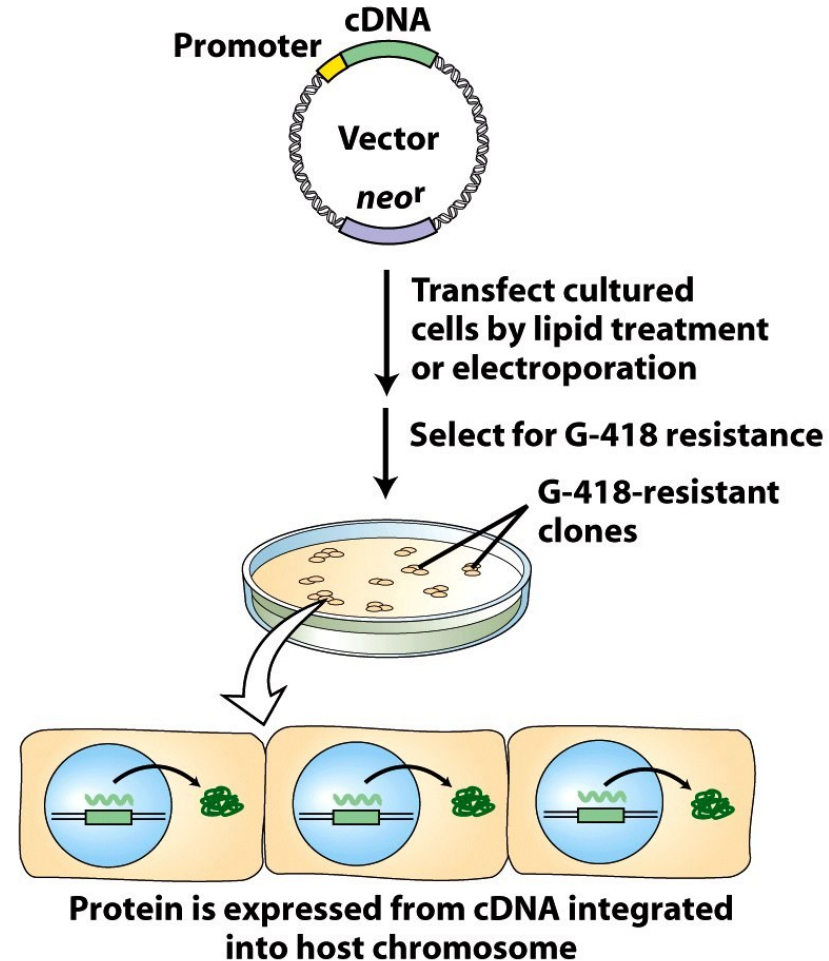


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Infections

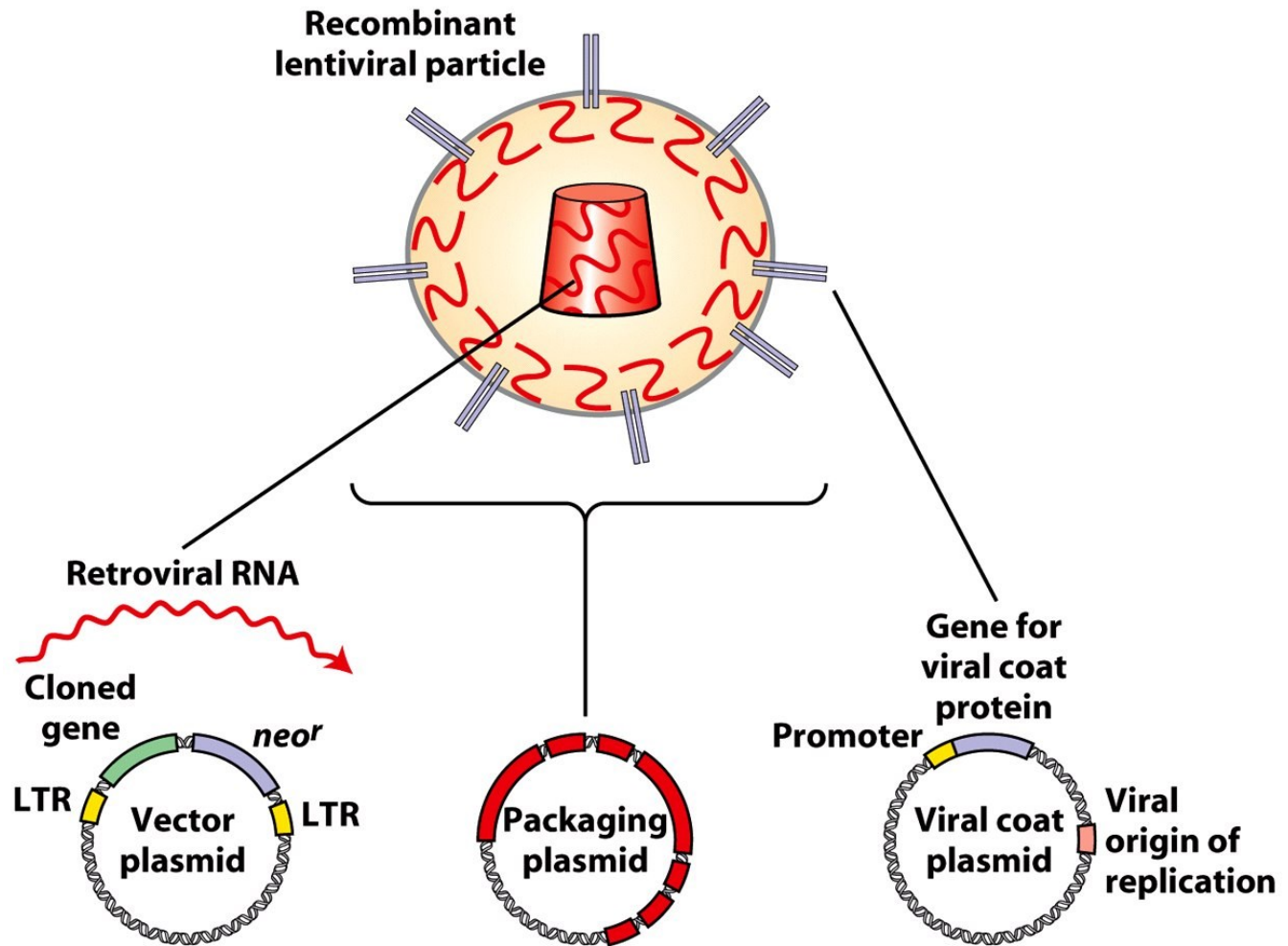
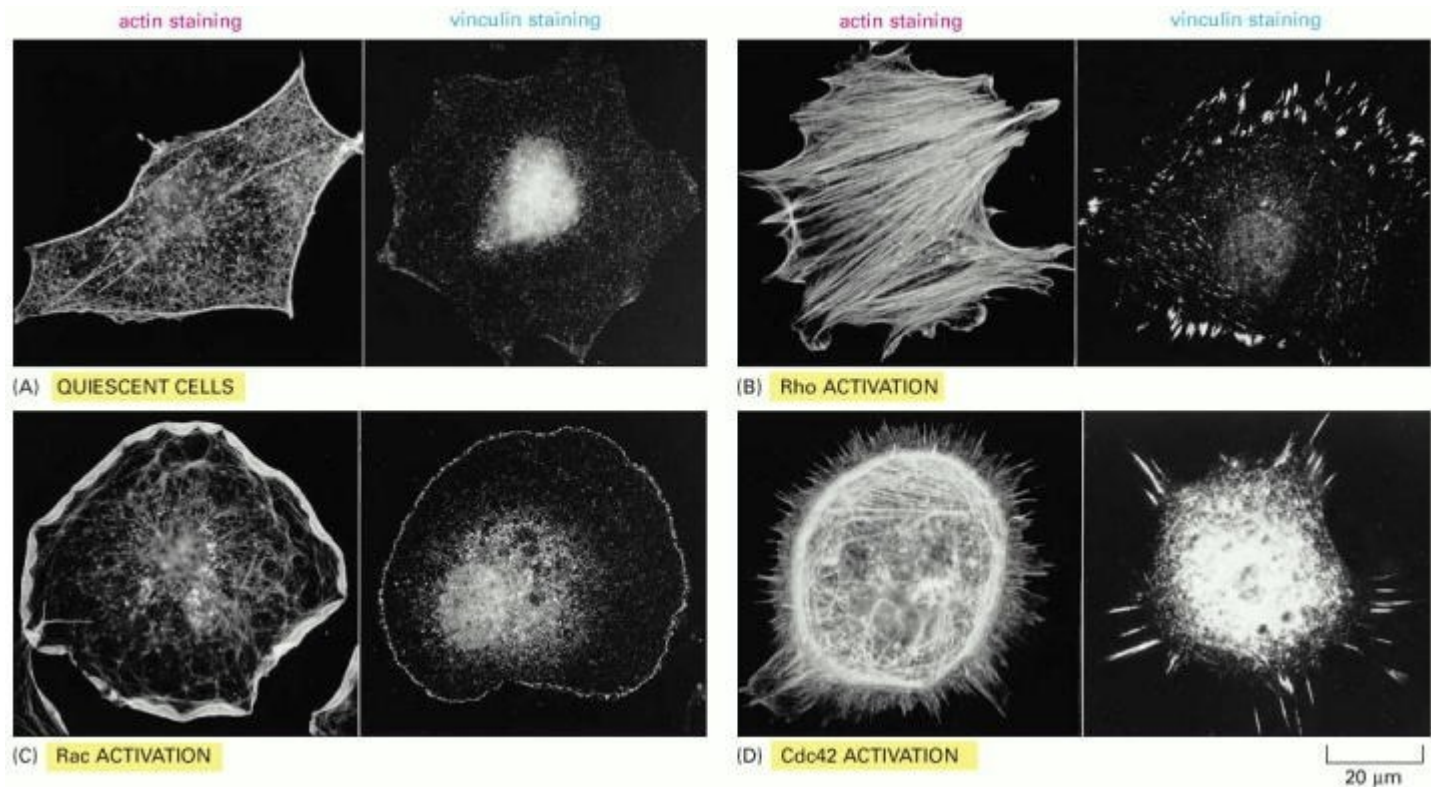


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Case Study: RhoGTPases

- Ann Ridley & Alan Hall



RhoGTPase Cross-talk

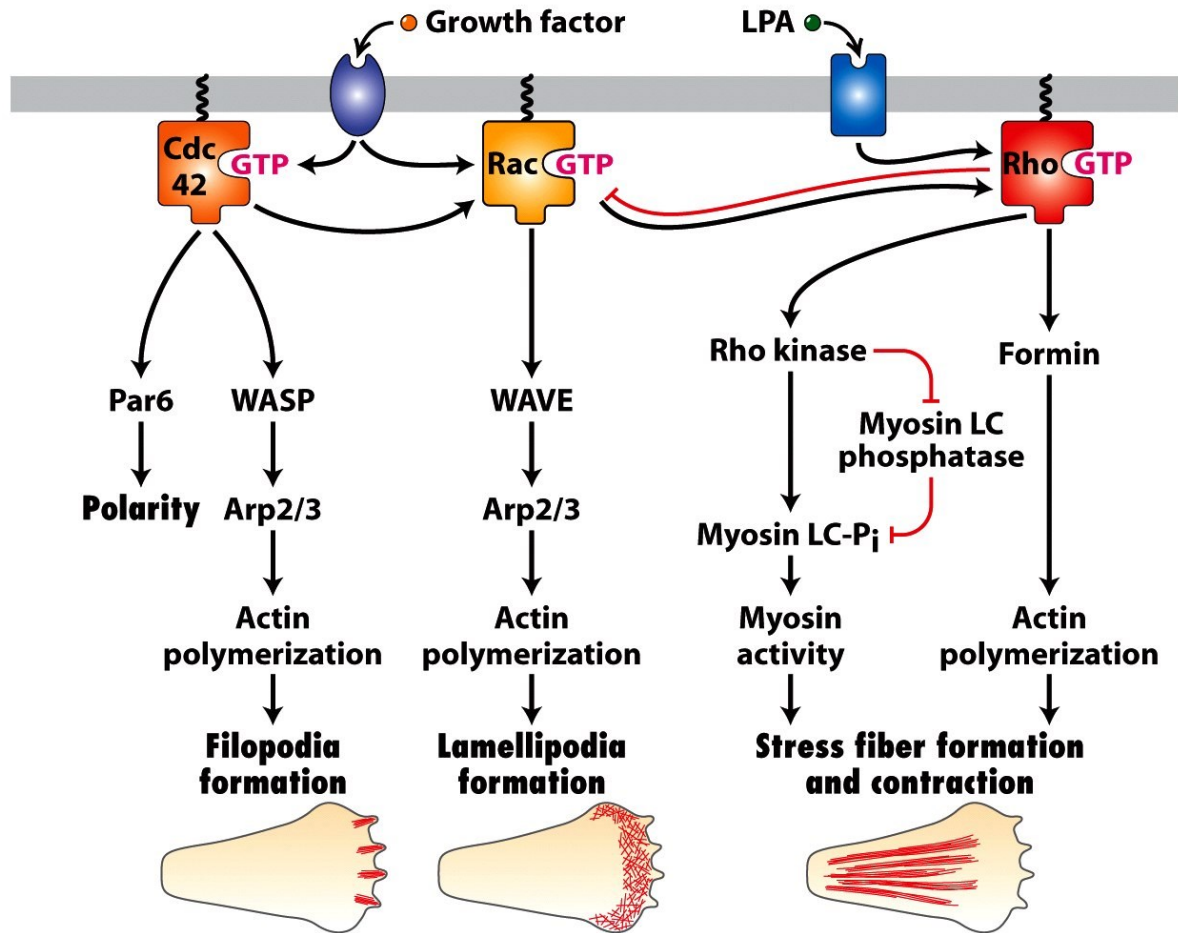


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Questions?