

# Mekanisme Kerja Hormon

Blok 1.4

Biokimia FK-Unad

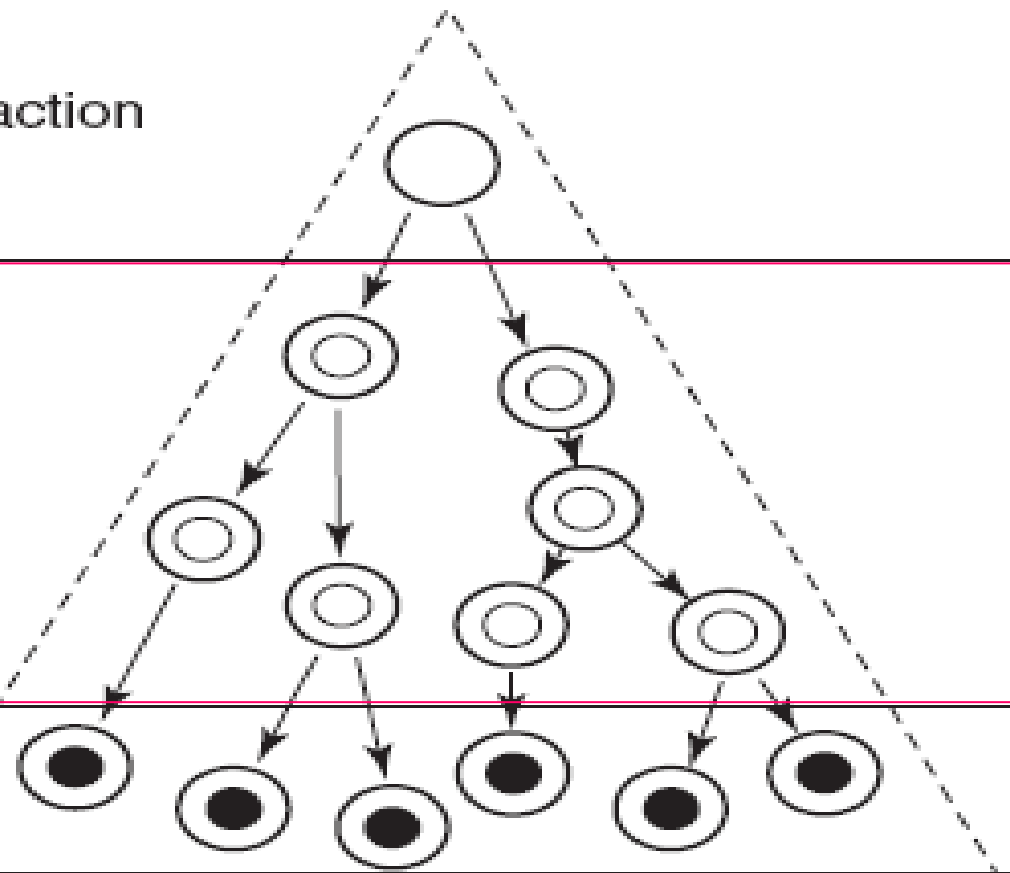
# Hormone Action

- Efek primer pada sel ( ikatan hormon – reseptor spesifik): **hormone–receptor complex**
- H-R complex → effector system → **signal transducing mechanism** → biochemical process(es) pada sel

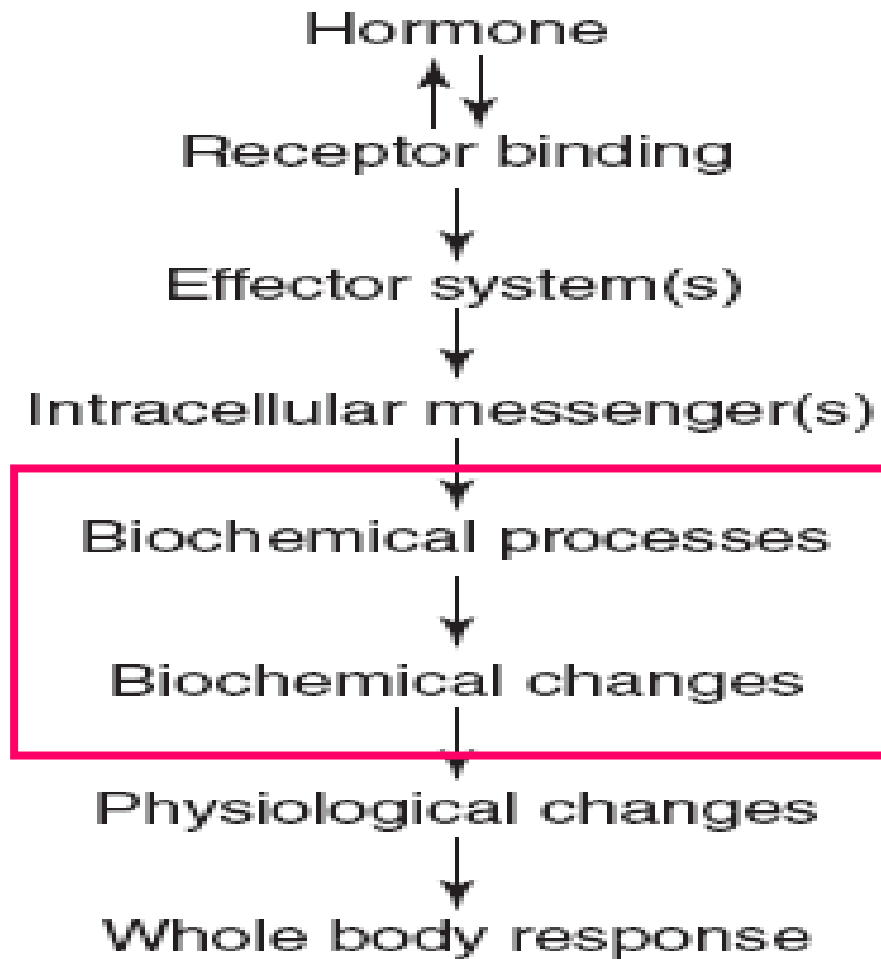
Mechanism of action

Biochemical effects

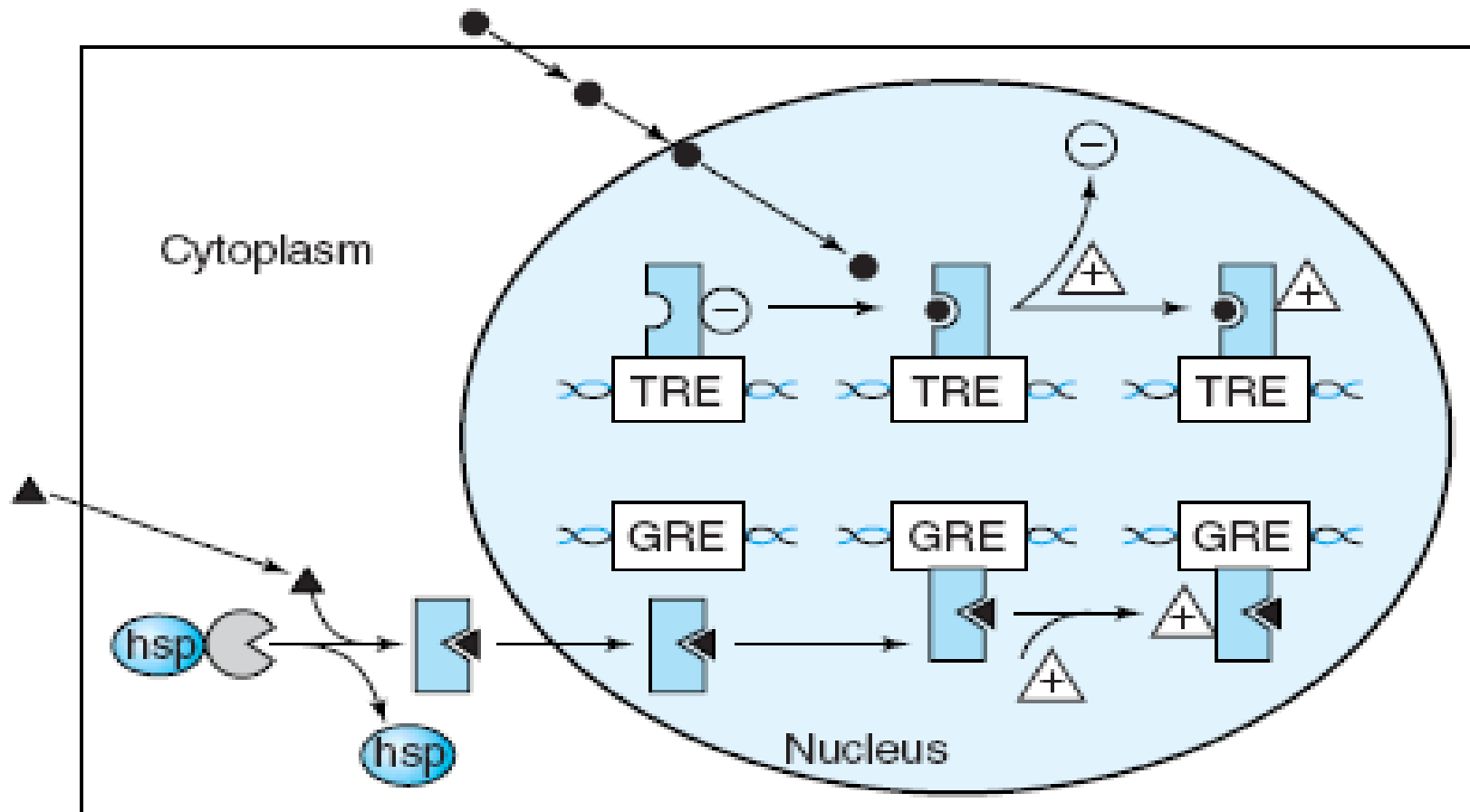
Physiological effects



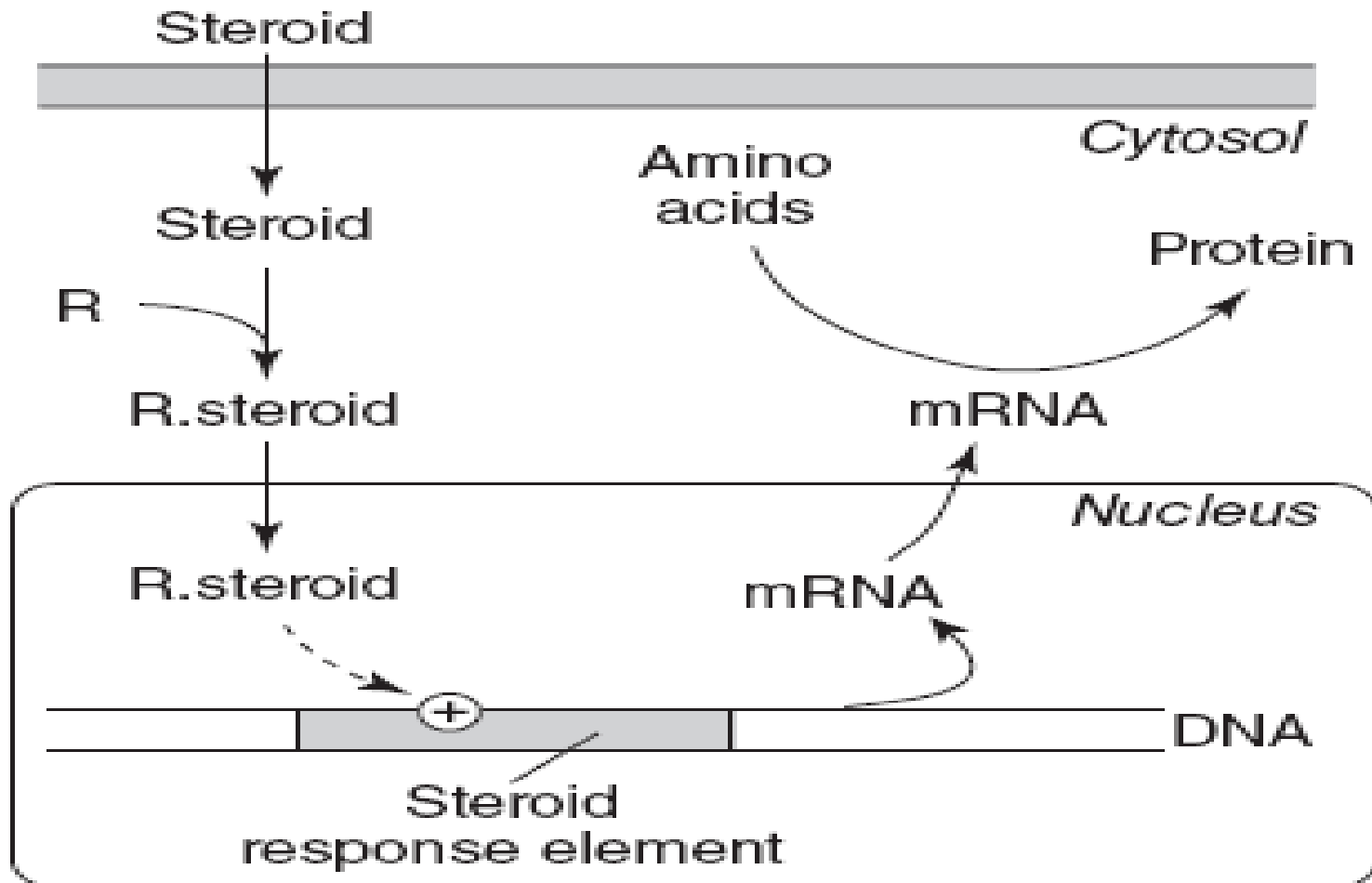
Function



# *Hormon: intracellular receptor*



# Complex activates a gene (transcription factor)



# The DNA sequences of several hormone response elements (HREs)

Hormone or Effector	HRE	DNA Sequence
Glucocorticoids	GRE	
Progestins	PRE	GGTACA NNN TGTTCT
Mineralocorticoids	MRE	← GGTACA NNN TGTTCT →
Androgens	ARE	
Estrogens	ERE	AGGTCA --- TGA/TCCT
Thyroid hormone	TRE	← AGGTCA --- TGA/TCCT →
Retinoic acid	RARE	AGGTCA <sub>n3,4,5</sub> AGGTCA
Vitamin D	VDRE	→ AGGTCA <sub>n3,4,5</sub> AGGTCA →
cAMP	CRE	TGACGTCA

# Hormon: *Transmembrane Receptors*

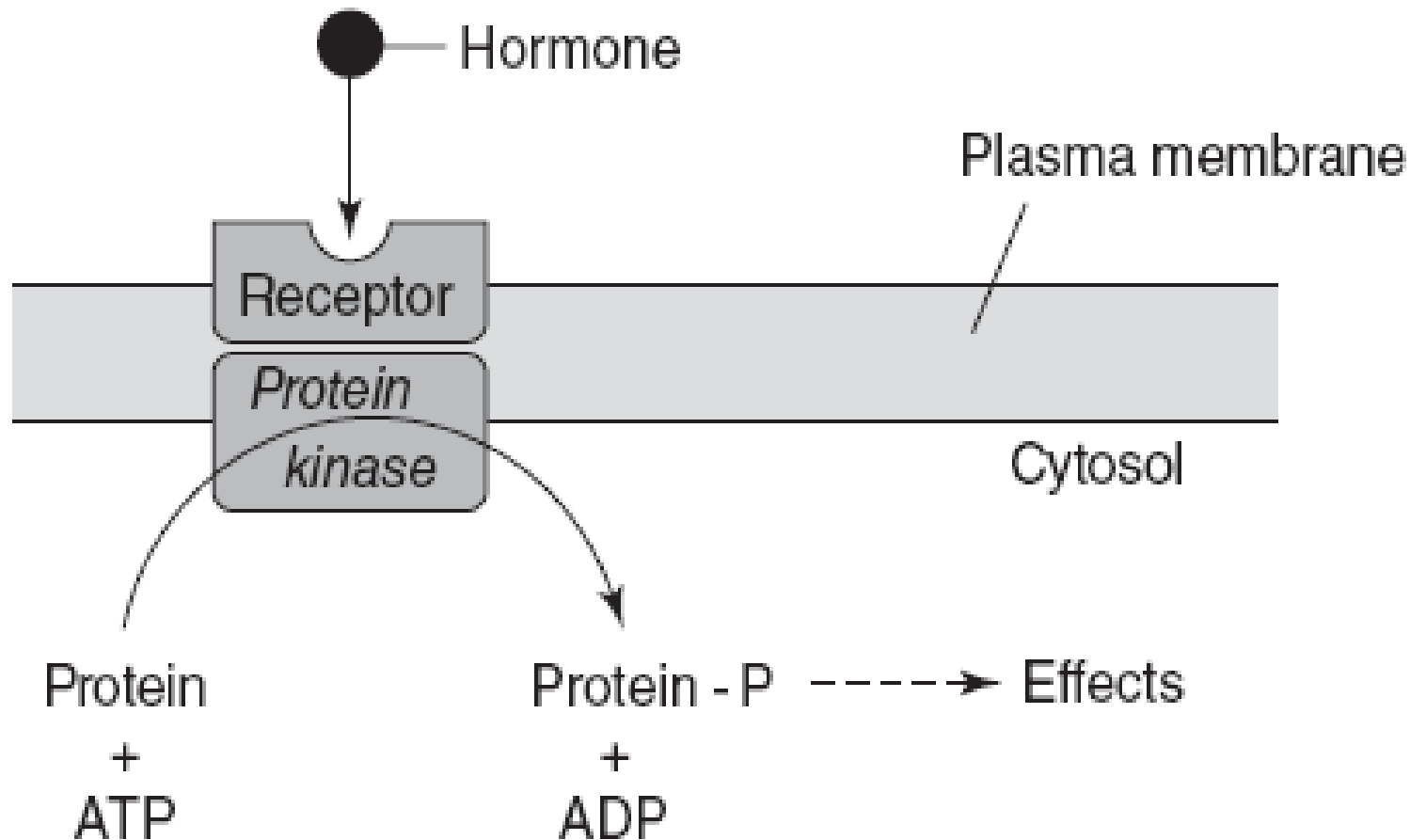
- **Enzyme coupled receptors:** Signal activates an enzyme activity of the receptor itself— tyrosine kinases, phospholipase C.
- **G-protein coupled receptors:** Signal activates a G-protein that activates downstream enzymes—makes second messenger(cAMP or Ca<sup>2</sup>).
- **Ion-channel coupled receptors:** Signal activates an ion channel



# Effector systems

- Hormone–receptor complex: meningkatkan aktivitas
  - enzim
  - G-protein
  - ion channel
  - gene

# Hormone–receptor complex: meningkatkan aktivitas enzim protein kinase



# PROTEIN KINASES

## 1. Transmembrane receptor kinases : **tyrosine kinase**

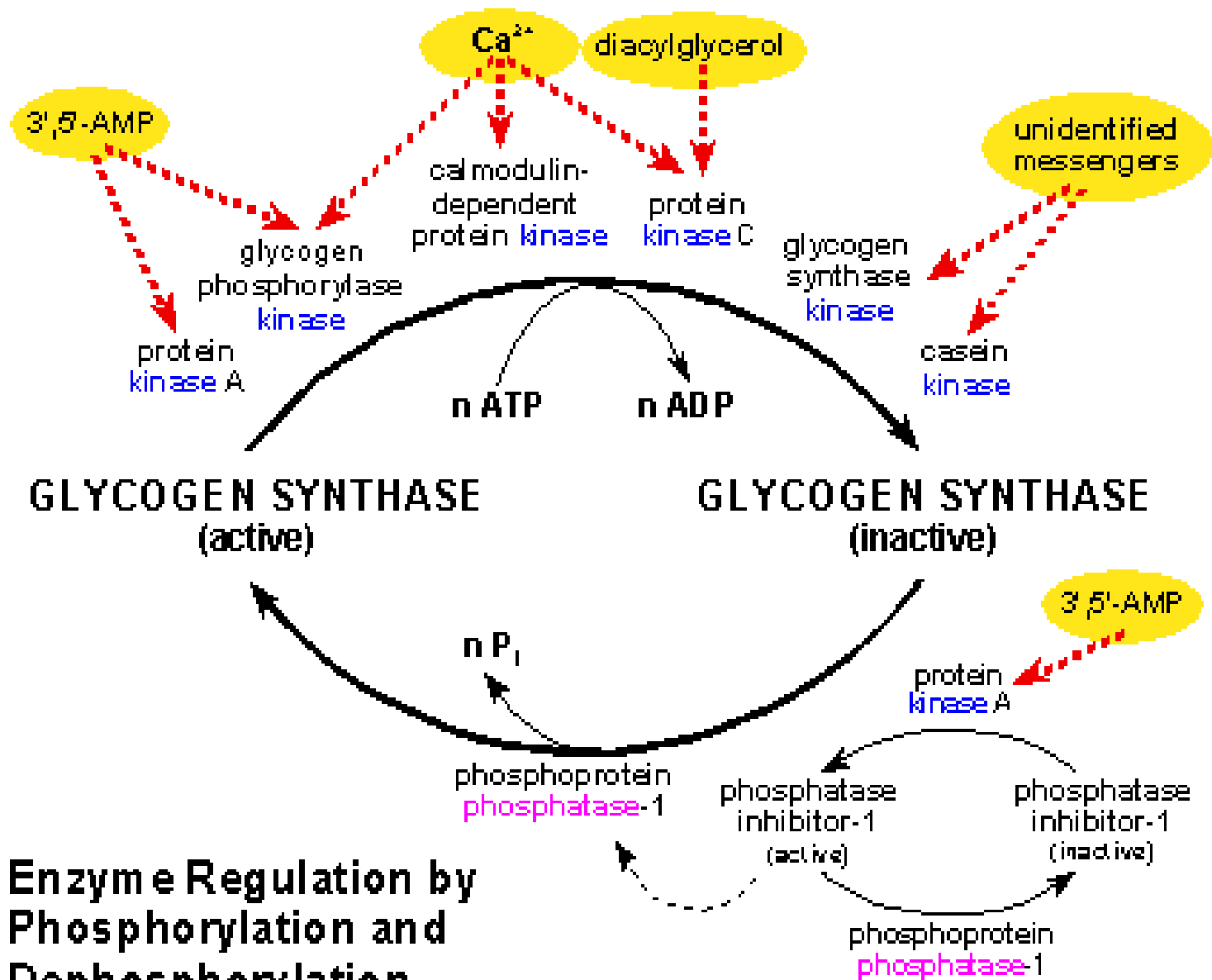
ATP : phosphorylate specific tyrosine enzymatic  
(amplification step).

## 2. **serine/ threonine** protein kinases

**ATP to phosphorylate specific serine or threonine.**

- phosphorylation cascades :

*one kinase phosphorylates another → MAP kinase  
kinase kinase. (mitogen-activated protein  
kinase that phosphorylates MAP kinase  
kinase)*

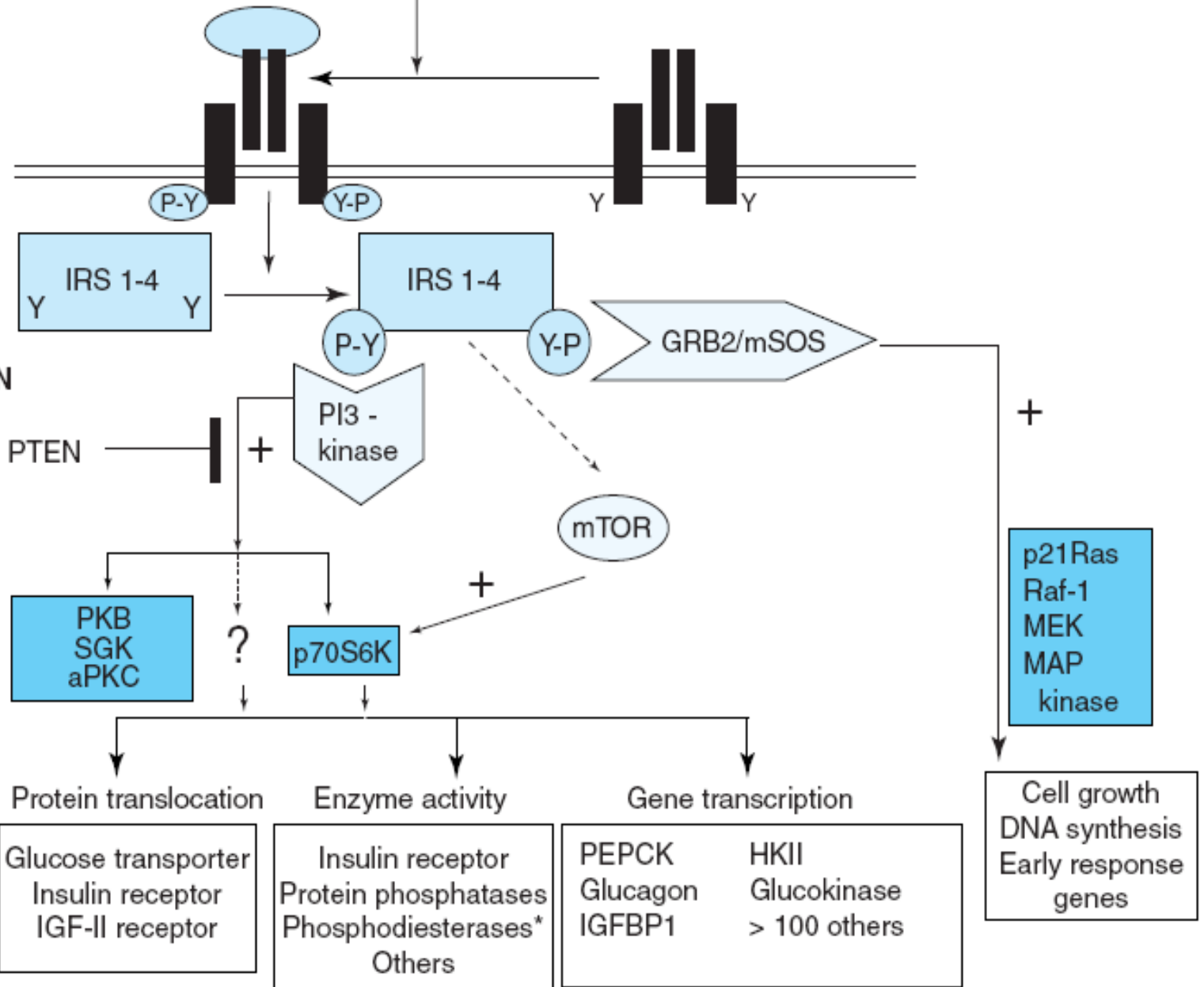


## Enzyme Regulation by Phosphorylation and Dephosphorylation

RECOGNITION  
(HYPERGLYCEMIA)

INSULIN

SIGNAL  
GENERATION



EFFECTS

Protein translocation

Glucose transporter  
Insulin receptor  
IGF-II receptor

Enzyme activity

Insulin receptor  
Protein phosphatases  
Phosphodiesterases\*  
Others

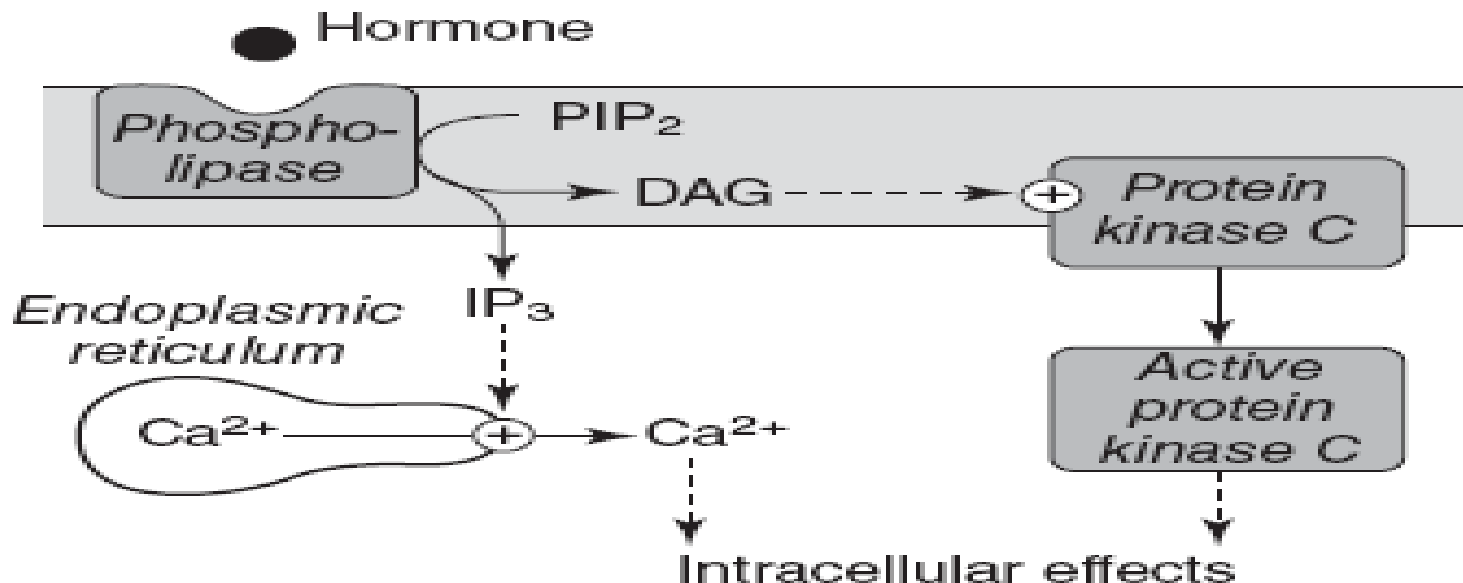
Gene transcription

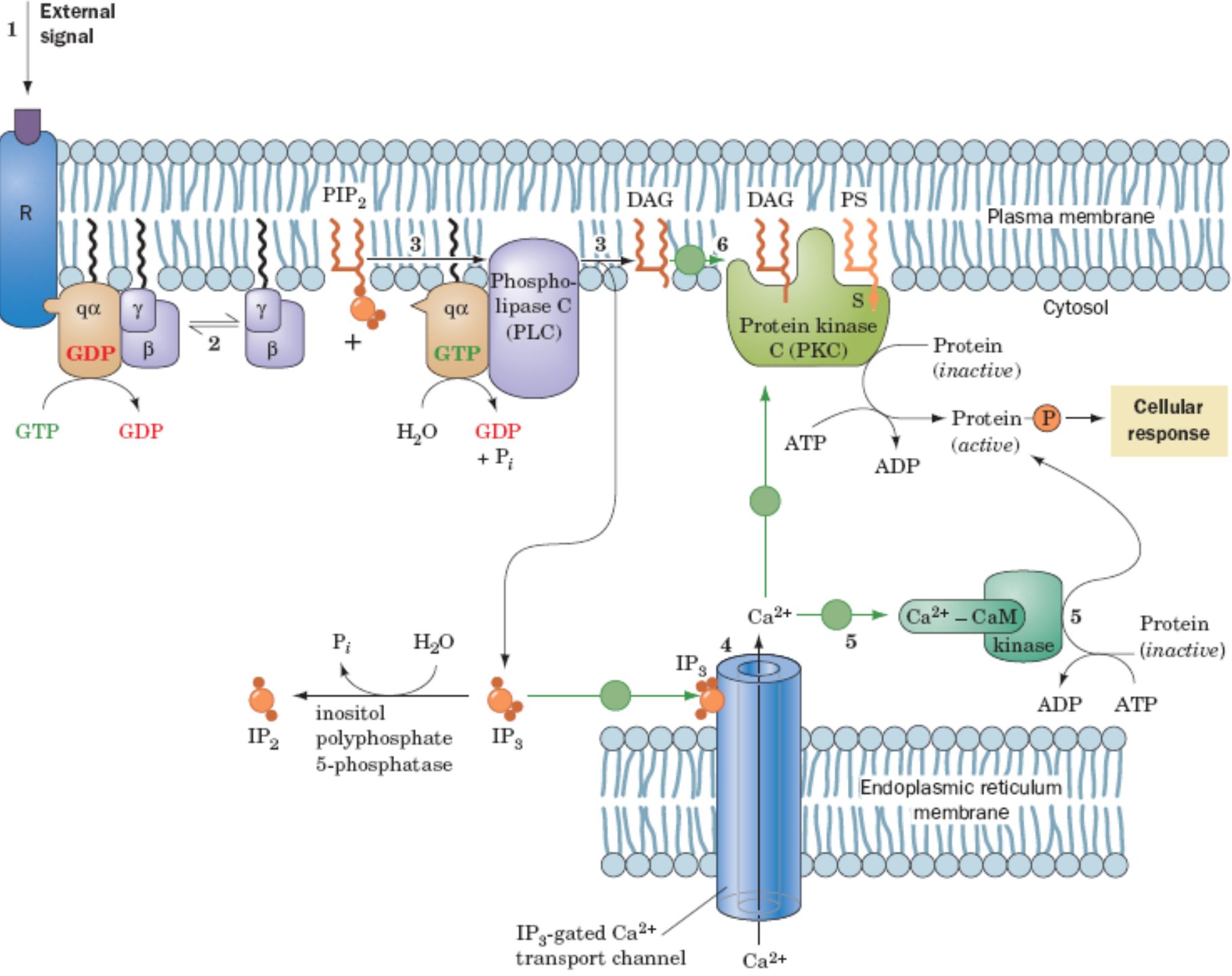
PEPCK  
Glucagon  
IGFBP1  
HKII  
Glucokinase  
> 100 others

Cell growth  
DNA synthesis  
Early response  
genes

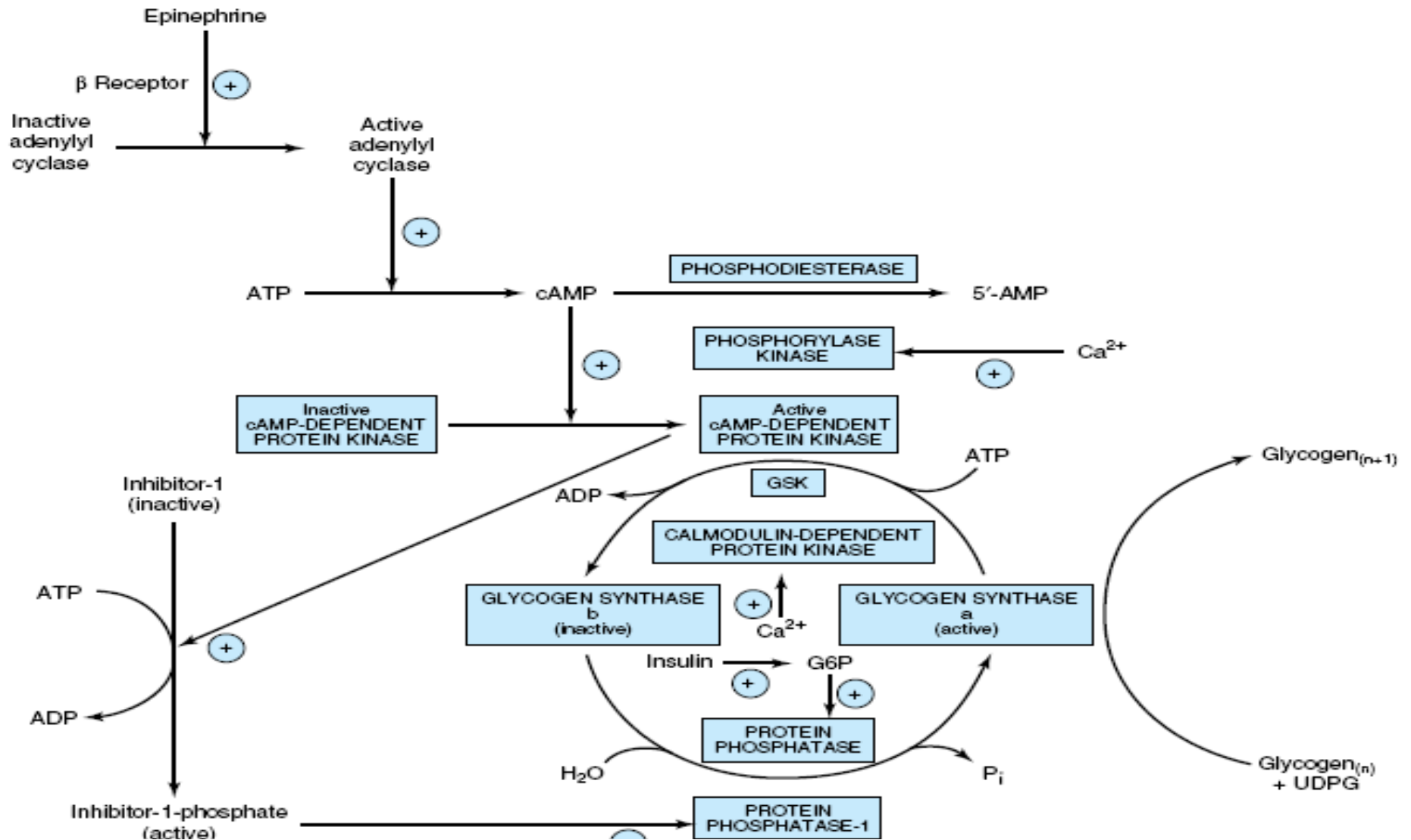
# Hormon: Membrane-bound *phospholipase*

- Hydrolisa: *phosphatidylinositol bisphosphate* (PIP<sub>2</sub>)  
→ dua *messenger* ,
  - inositol trisphosphate (IP<sub>3</sub>)
  - diacylglycerol (DAG)
- example: adrenaline binding to the  $\alpha$ -receptor in the liver: Ca<sup>2+</sup> ions stimulate glycogenolysis





# Glycogen synthase: Otot Rangka



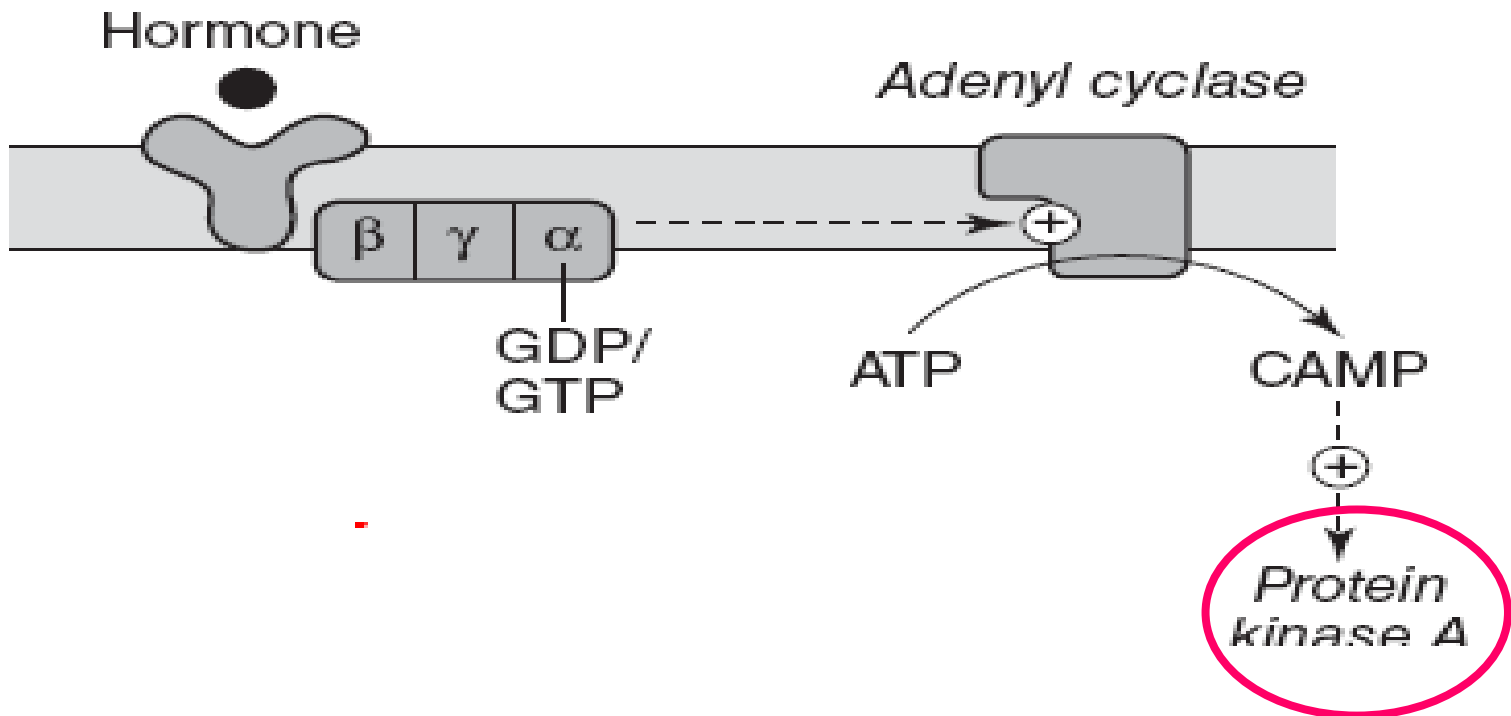


# Pengaturan Enzym & protein: calcium atau calmodulin.

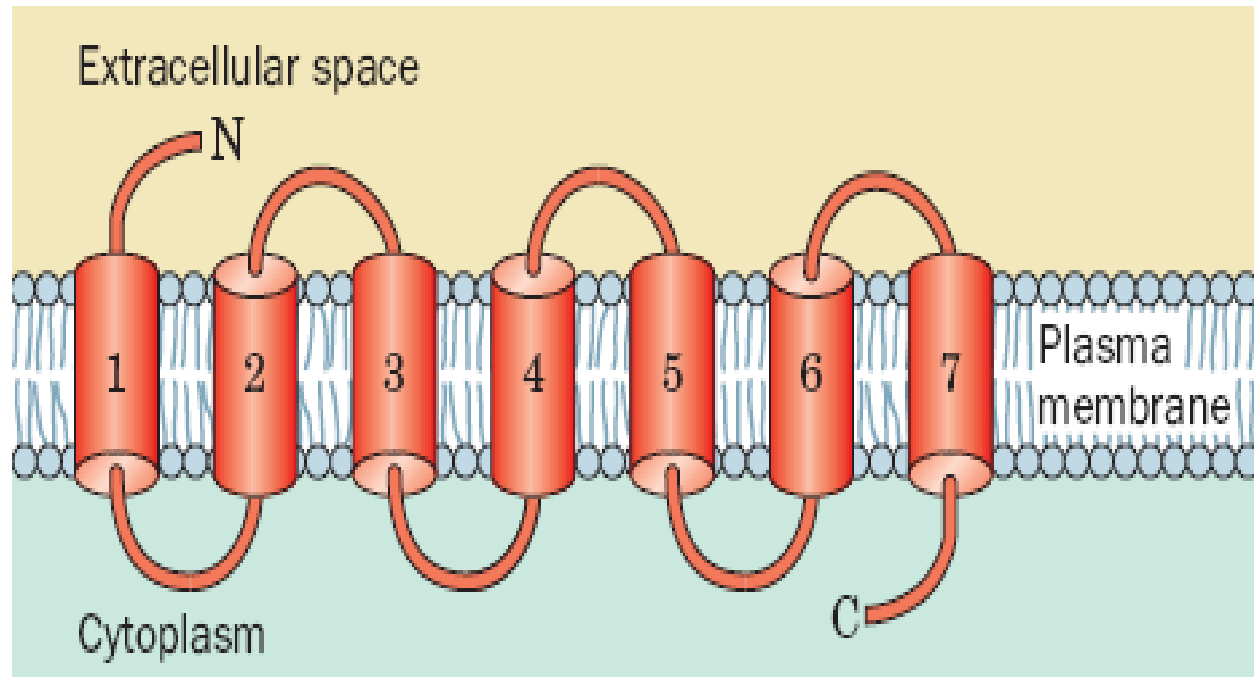
- Adenylyl cyclase
- Ca<sup>2+</sup>-dependent protein kinases
- Ca<sup>2+</sup>-Mg<sup>2+</sup> ATPase
- Ca<sup>2+</sup>-phospholipid-dependent protein kinase
- Cyclic nucleotide phosphodiesterase
- Some cytoskeletal proteins
- Some ion channels (eg, L-type calcium channels)
- Nitric oxide synthase
- Phosphorylase kinase
- Phosphoprotein phosphatase 2B
- Some receptors (eg, NMDA-type glutamate recept

# Gomplex activates G-protein

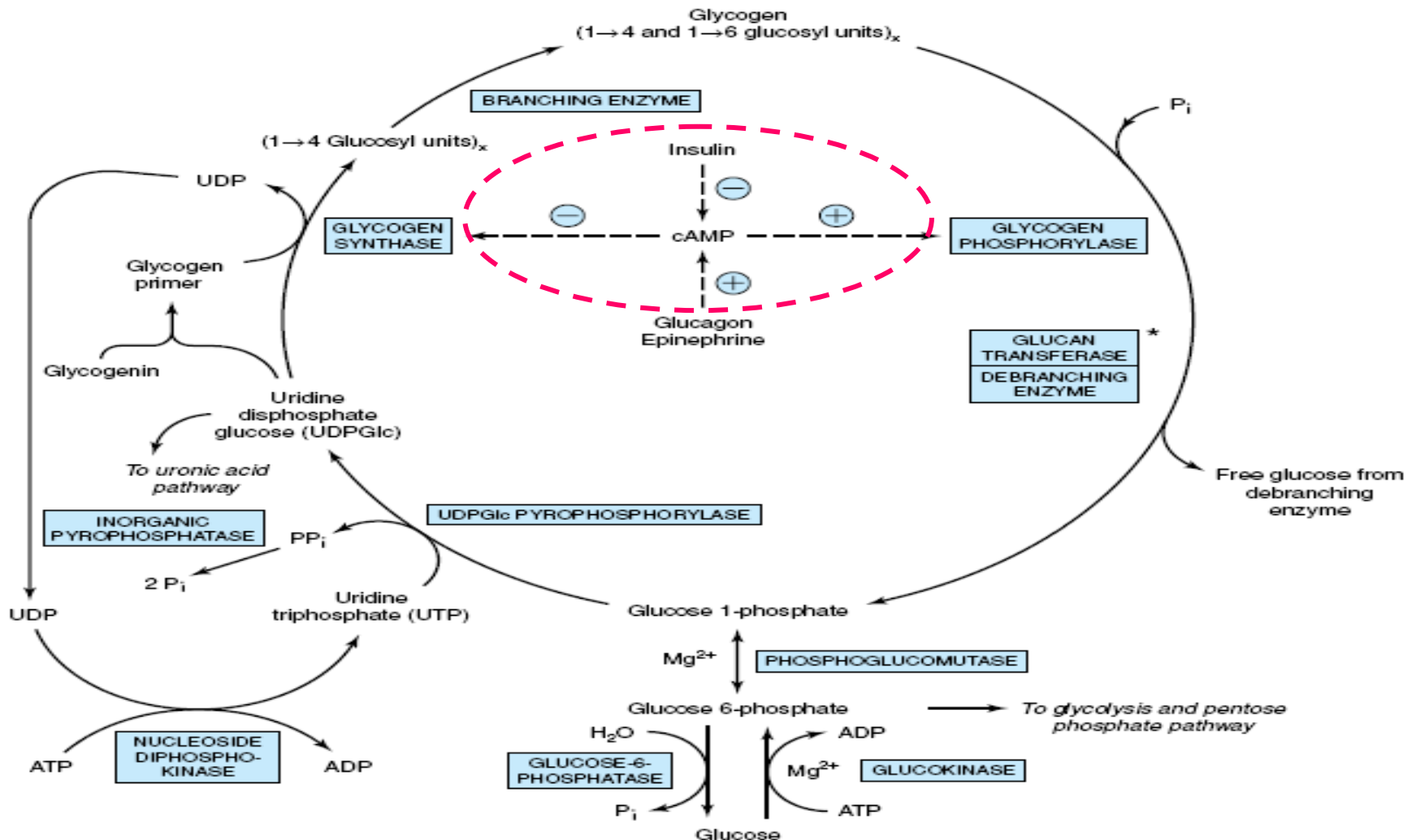
- H-R complex: activates G-protein → activates a *membrane-bound enzyme* (e.g. **adenyl cyclase**, which converts ATP to cyclic AMP).



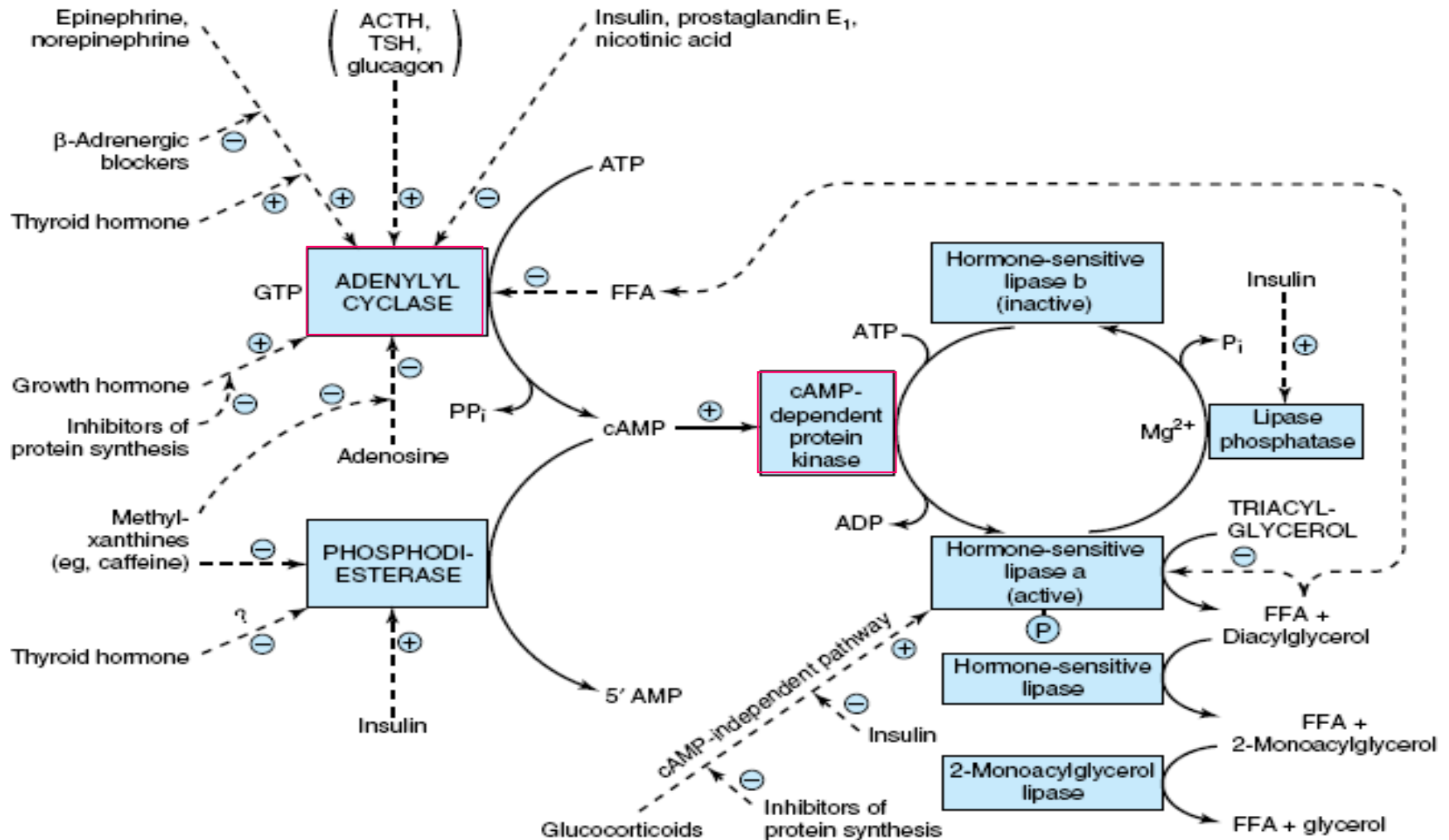
# G-Protein

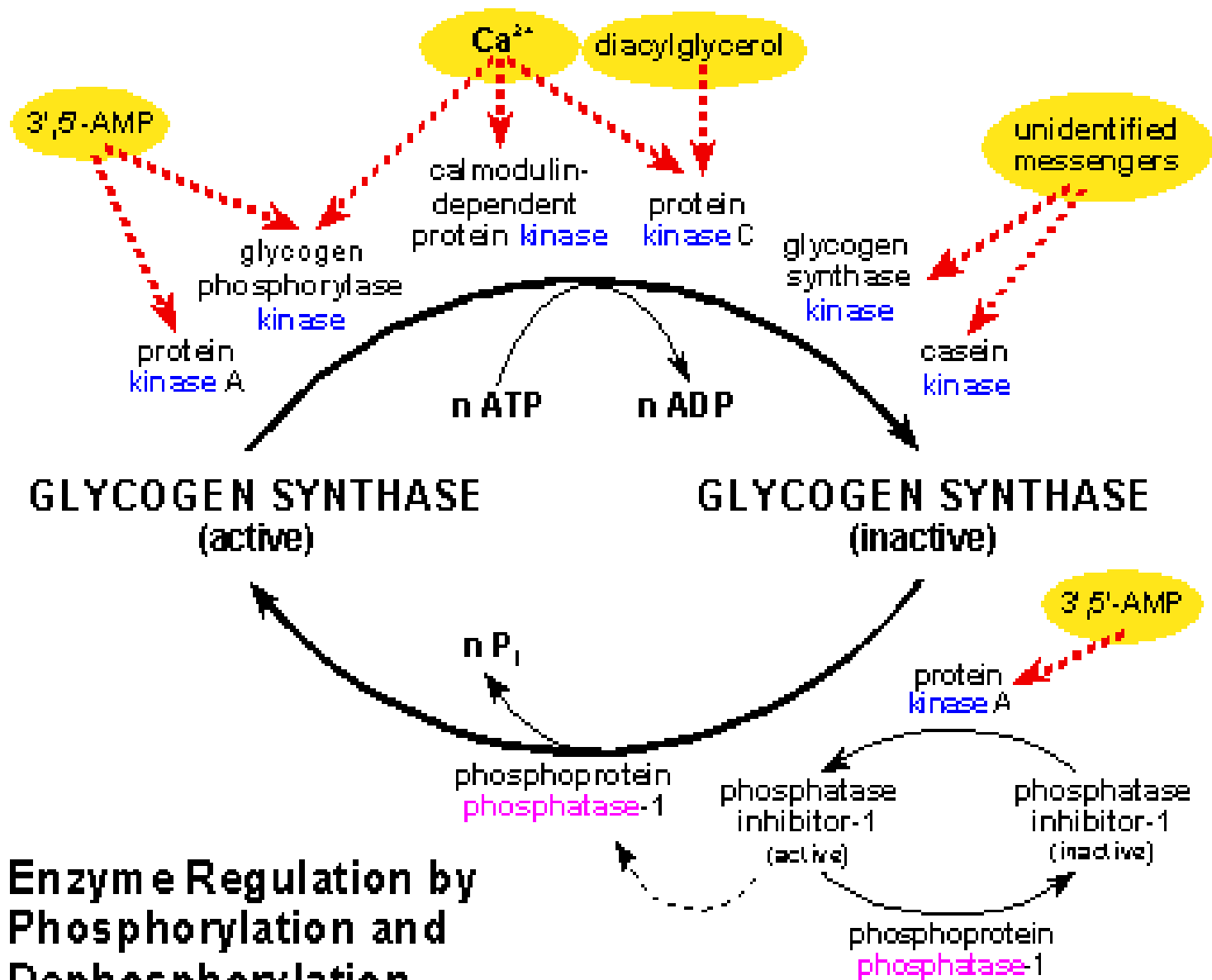


# Pathway of glycogenesis and of glycogenolysis in the liver



# Control of adipose tissue lipolysis.





## Enzyme Regulation by Phosphorylation and Dephosphorylation

# MEMBRANE RECEPTOR FAMILIES AND SIGNALING PATHWAYS

## RECEPTORS

## EFFECTORS

## SIGNALING PATHWAYS

### G Protein-Coupled Seven-Transmembrane (GPCR)

$\beta$ -Adrenergic  
LH, FSH, TSH

$G_s\alpha$ , adenylate cyclase

Stimulation of cyclic AMP production, protein kinase A

Glucagon

PTH, PTHrP

$Ca^{2+}$  channels

Calmodulin,  $Ca^{2+}$ -dependent kinases

ACTH, MSH

GHRH, CRH

$\alpha$ -Adrenergic

$G_i\alpha$

Inhibition of cyclic AMP production

Somatostatin

Activation of  $K^+$ ,  $Ca^{2+}$  channels

TRH, GnRH

$G_q$ ,  $G_{11}$

Phospholipase C, diacylglycerol,  $IP_3$ , protein kinase C, voltage-dependent  $Ca^{2+}$  channels

### Receptor Tyrosine Kinase

Insulin, IGF-I

Tyrosine kinases, IRS

MAP kinases, PI 3-kinase; AKT, also known as protein kinase B, PKB

EGF, NGF

Tyrosine kinases, ras

Raf, MAP kinases, RSK

### Cytokine Receptor-Linked Kinase

GH, PRL

JAK, tyrosine kinases

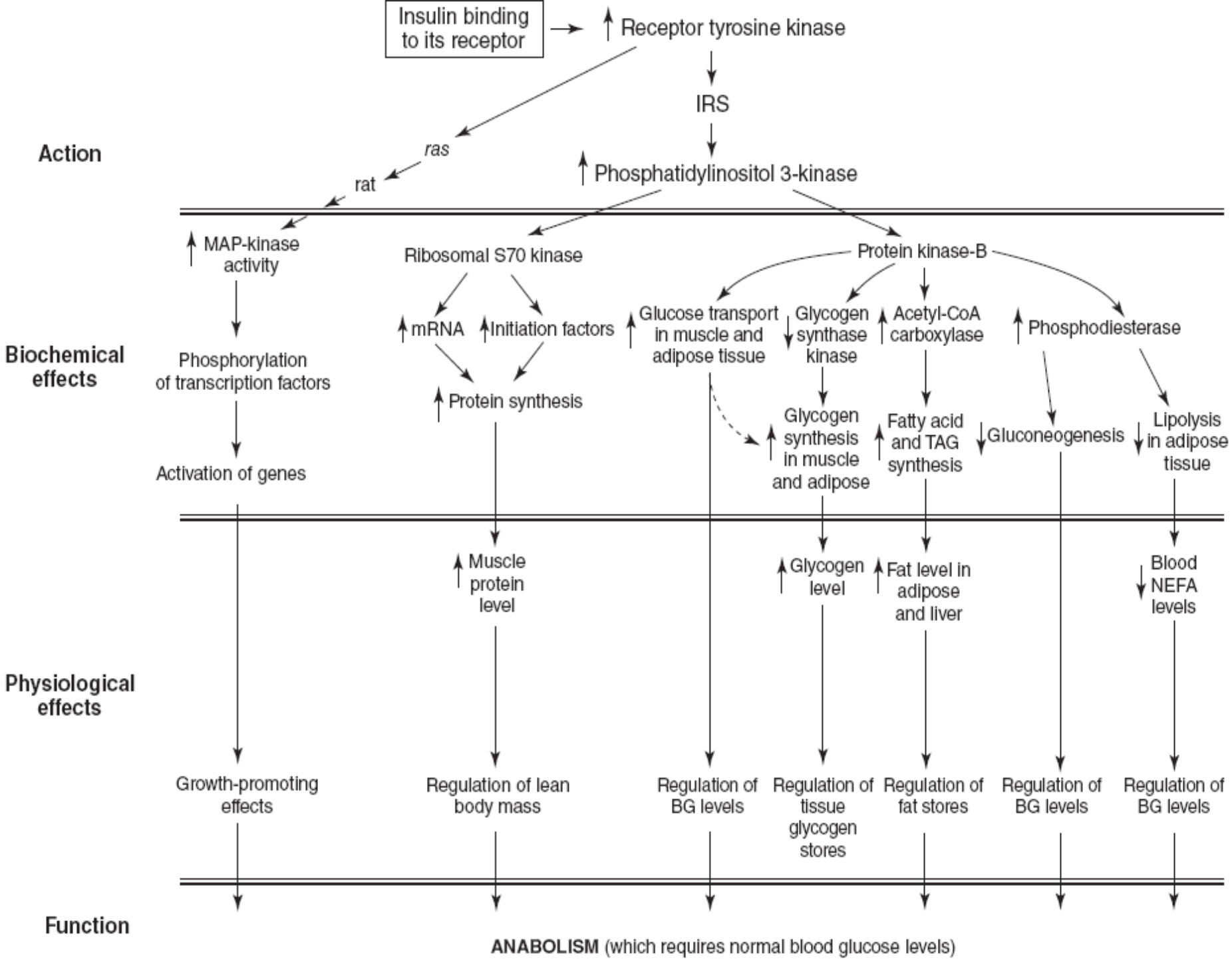
STAT, MAP kinase, PI 3-kinase, IRS-1

### Serine Kinase

Activin, TGF- $\beta$ , MIS

Serine kinase

Smads

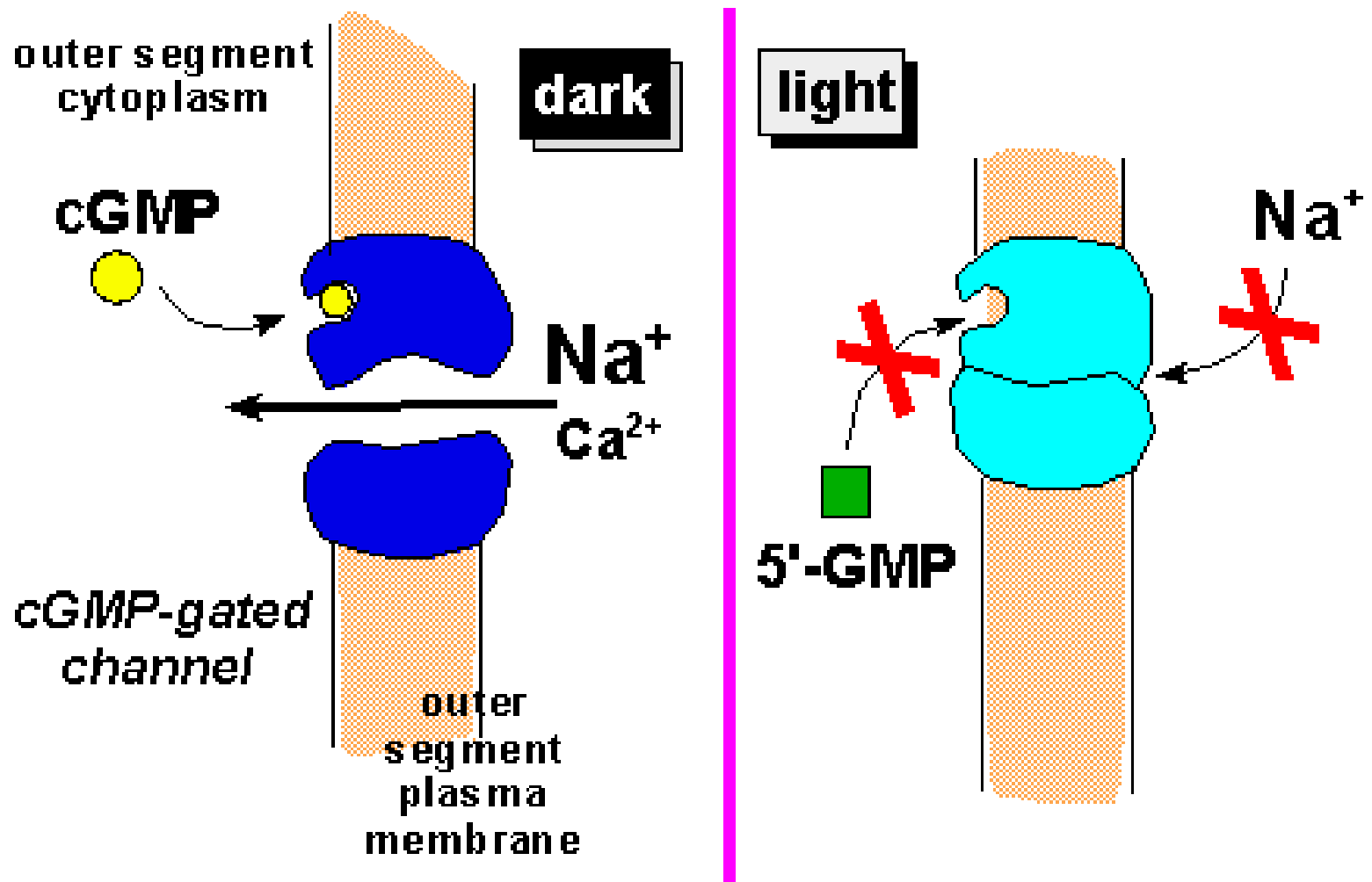




# Cyclic GMP

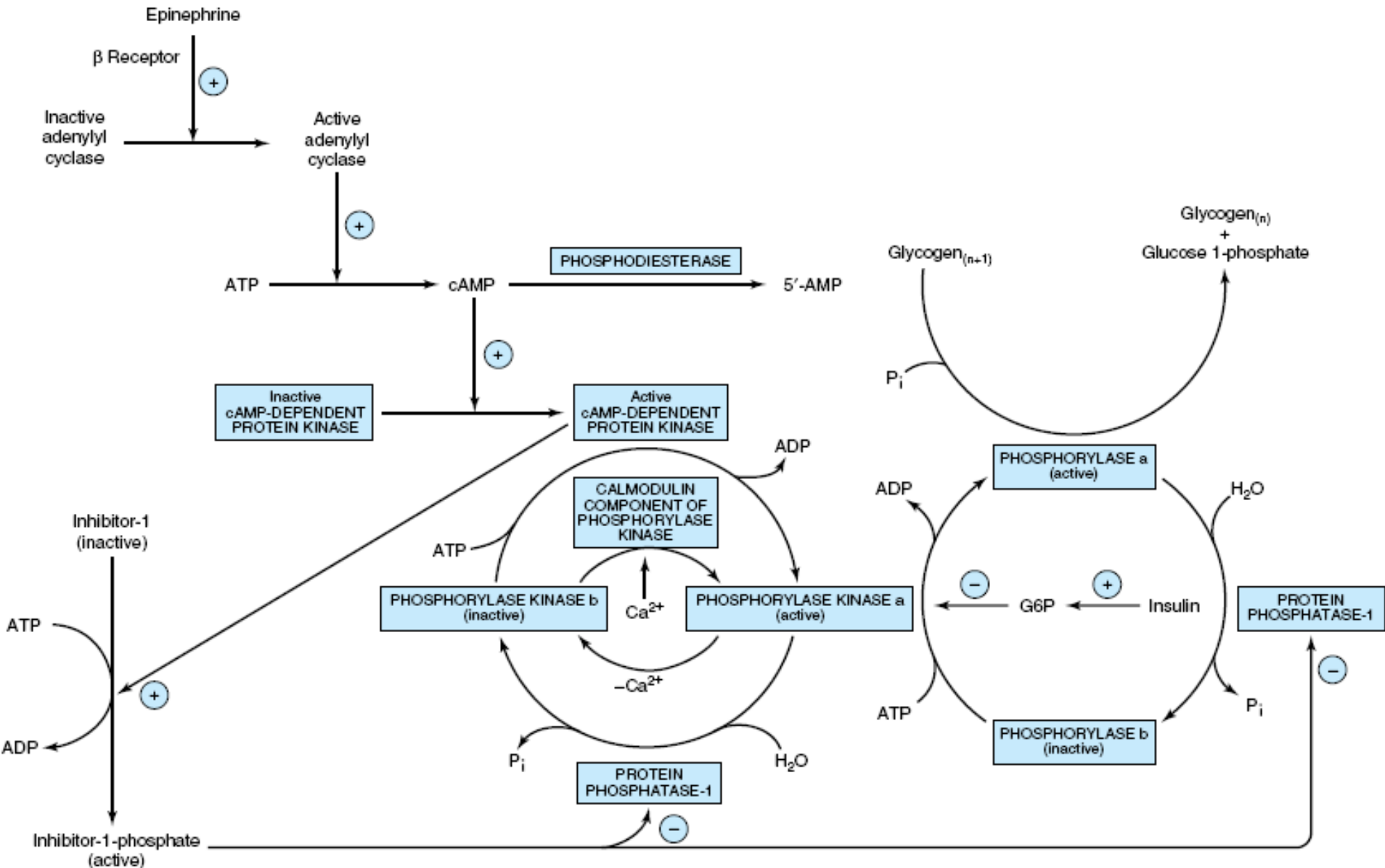
- Cyclic GMP: berasal dari GTP dengan bantuan enzim *guanylyl cyclase* (activated by atrial natriuretic factor)





**Regulation of Ligand-Gated Cation Channel**

# Control of phosphorylase in muscle.





# Referensi

- MURRAY, R. K., BENDER, D. A., BOTHAM, K. M., J, P., KENNELLY, RODWELL, V. W. & WEIL, P. A. (2009) *Harper's Illustrated Biochemistry*, The McGraw-Hill Companies, Inc
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