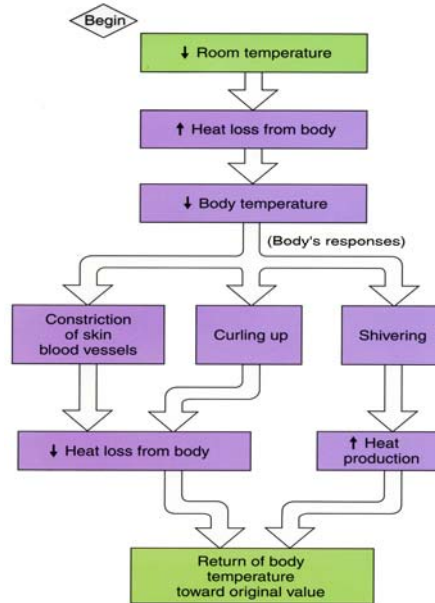
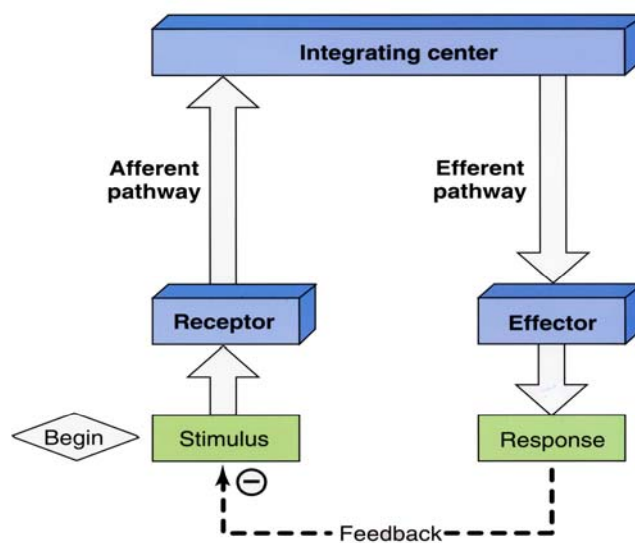


Negative Feedback System



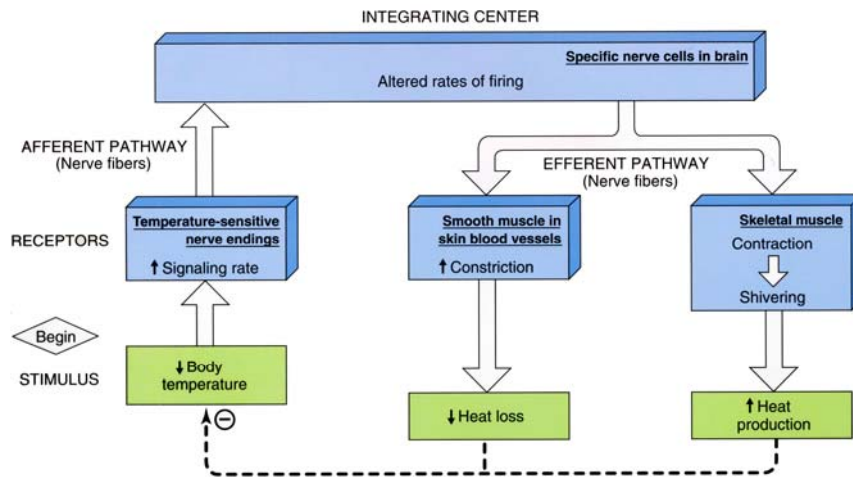
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Negative-Feedback Reflex Arc



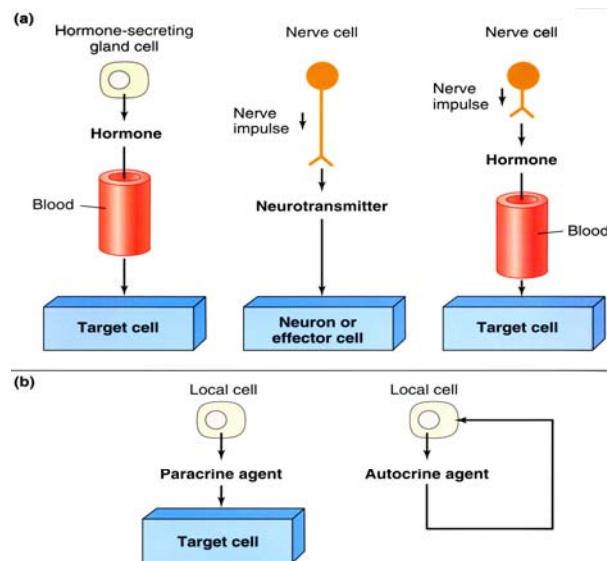
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Negative-Feedback Reflex Arc



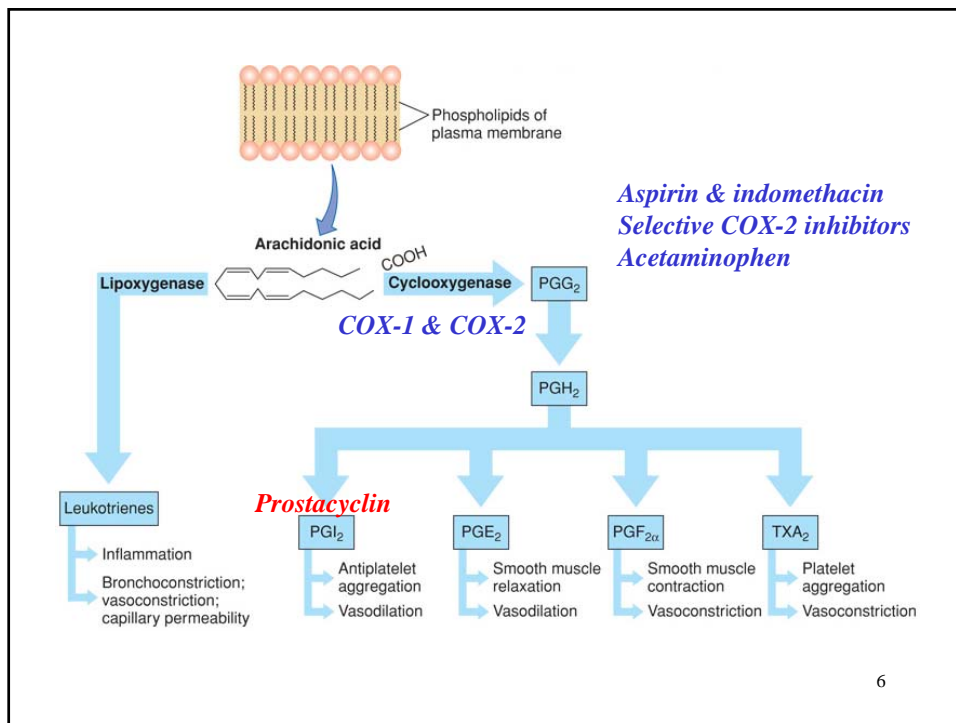
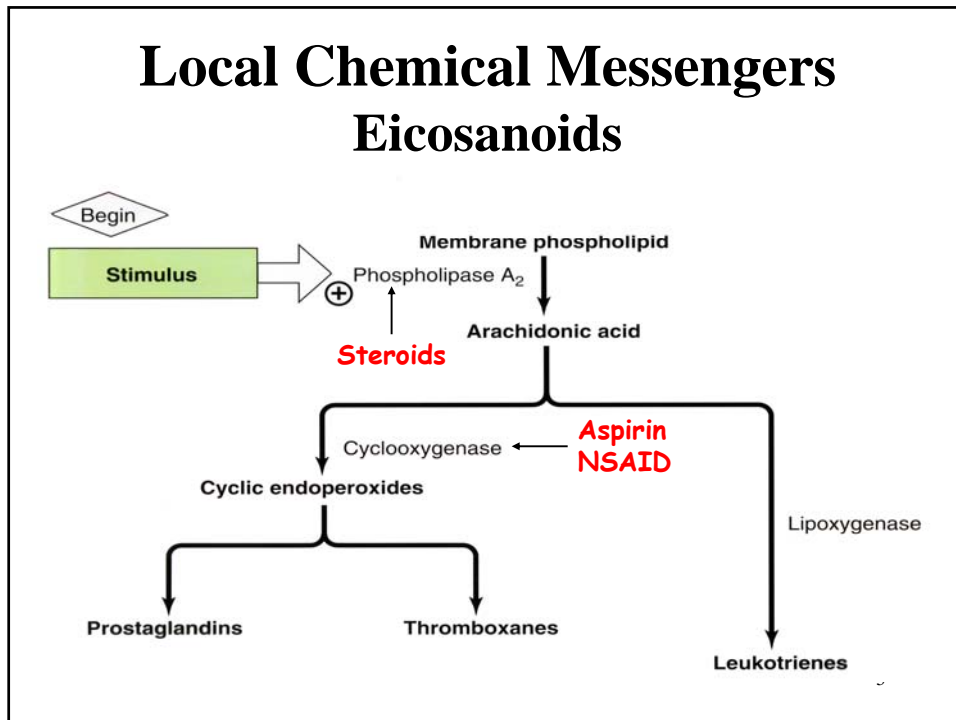
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Intercellular Communication Chemical Messengers

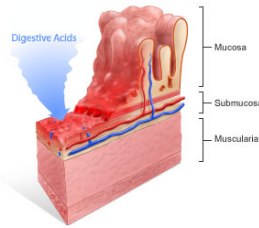
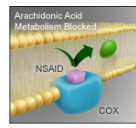


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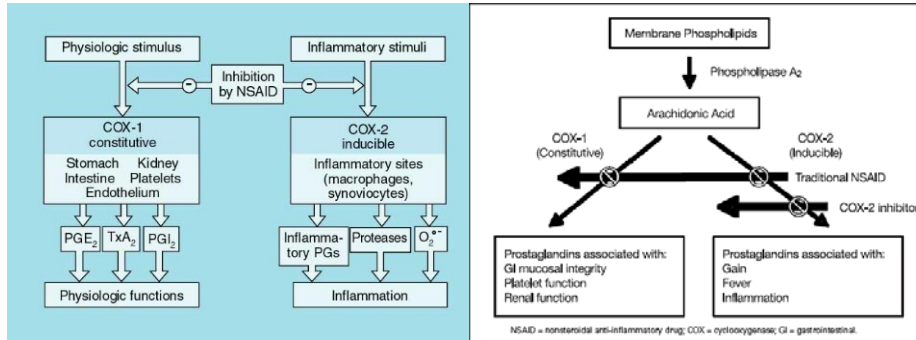
Local Chemical Messengers Eicosanoids



NSAIDs



Acid penetrates impaired mucosa causing ulceration

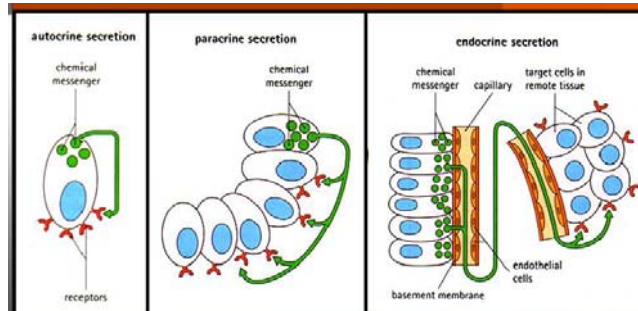


7

Autocrine & Paracrine Regulators

Table 11.9 Examples of Autocrine and Paracrine Regulators

Autocrine or Paracrine Regulator	Major Sites of Production	Major Actions
Insulin-like growth factors (somatomedins)	Many organs, particularly the liver and cartilages	Growth and cell division
Nitric oxide	Endothelium of blood vessels; neurons; macrophages	Dilation of blood vessels; neural messenger; antibacterial agent
Endothelins	Endothelium of blood vessels; other organs	Constriction of blood vessels; other effects
Platelet-derived growth factor	Platelets; macrophages; vascular smooth muscle cells	Cell division within blood vessels
Epidermal growth factors	Epidermal tissues	Cell division in wound healing
Neurotrophins	Schwann cells; neurons	Regeneration of peripheral nerves
Bradykinin	Endothelium of blood vessels	Dilation of blood vessels
Interleukins (cytokines)	Macrophages; lymphocytes	Regulation of immune system
Prostaglandins	Many tissues	Wide variety (see text)
TNF α (tumor necrosis factor alpha)	Macrophages; adipocytes	Wide variety



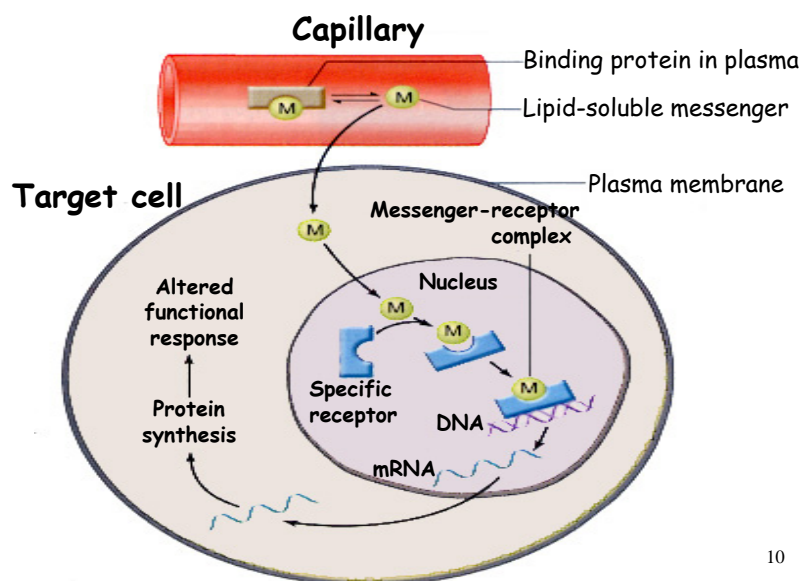
8

Classification of Receptors

1. **INTRACELLULAR RECEPTORS** (for lipid-soluble messengers)
Function in the nucleus as transcription factors to alter the rate of transcription of particular genes.
2. **PLASMA-MEMBRANE RECEPTORS** (for lipid-insoluble messengers)
 - A. Receptors that themselves function as **ion channels**.
 - B. Receptors that themselves function as **enzymes**.
 - C. Receptors that are bound to and activate cytoplasmic **JAK kinases**.
 - D. Receptors that activate **G proteins**, which in turn act upon effector proteins – either ion channels or enzymes – in the plasma membrane.

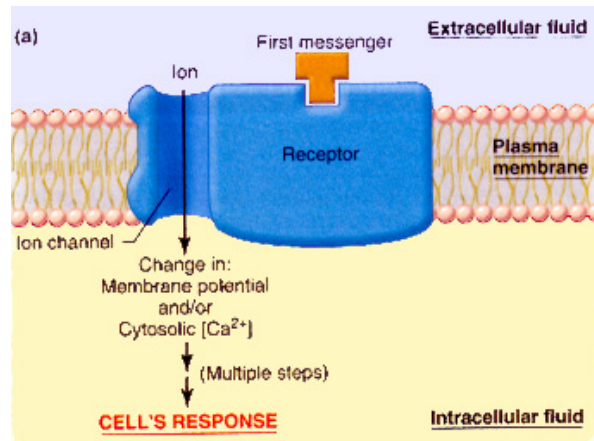
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Intracellular Receptors



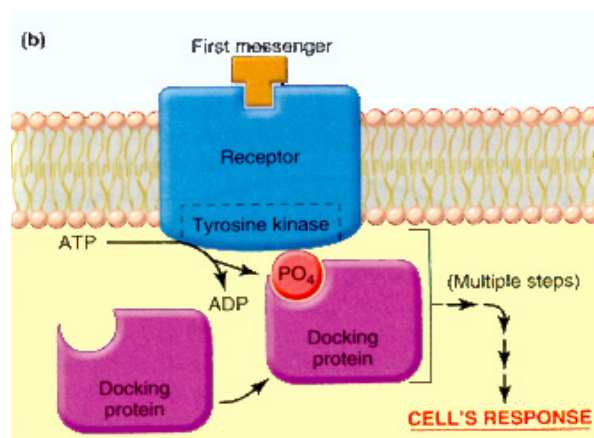
10

Plasma-Membrane Receptors Ion Channels



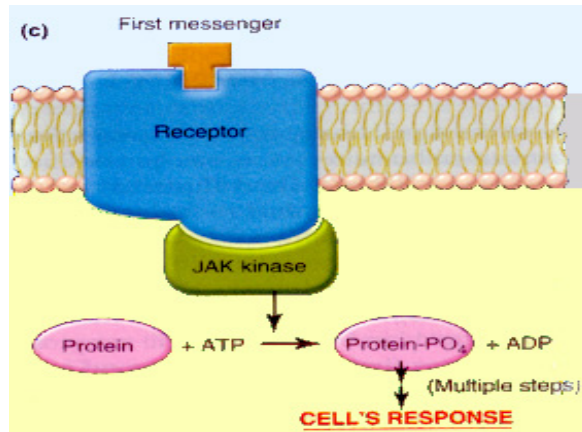
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Plasma-Membrane Receptors Enzymes-Tyrosine Kinase



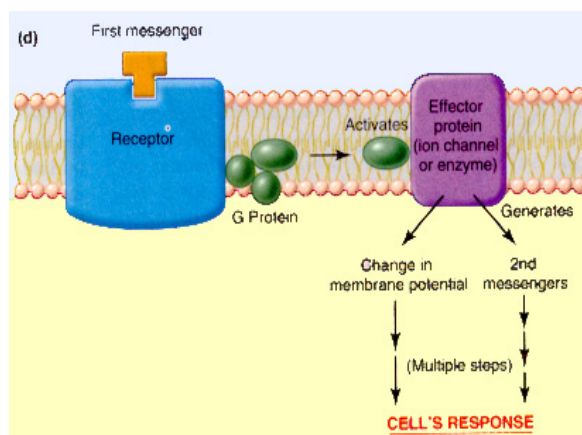
12

Plasma-Membrane Receptors Enzymes-JAK Kinase



13

Plasma-Membrane Receptors G Proteins



14

Plasma-Membrane Receptors G Proteins Adenylyl Cyclase - cAMP

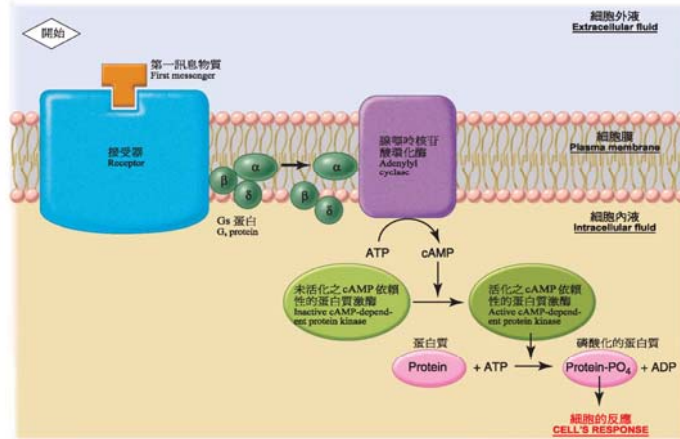
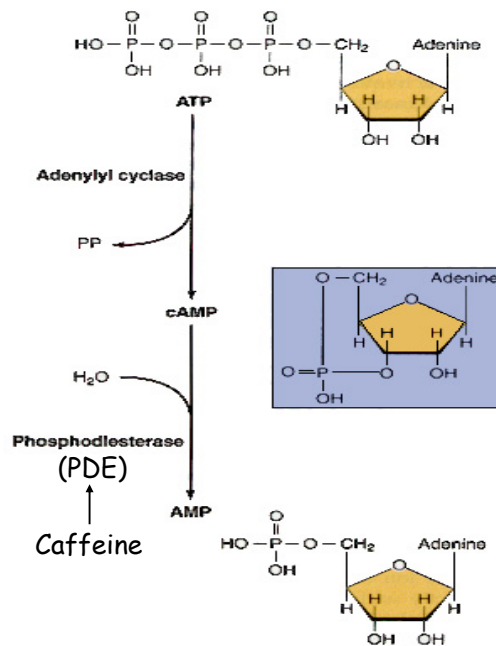


圖 3-5

環單磷酸腺嘌呤 (cAMP) 作為第二訊息物質之系統圖。圖中展示的是 G_s 蛋白，它的調節作用為增加細胞的反應。而另一種圖中沒有顯示的調節蛋白，稱為 G_i 蛋白，它與某些接受器產生反應而抑制腺嘌呤核苷酸環化酶，來降低細胞的反應。

15



16

Plasma-Membrane Receptors G Proteins Phospholipase C - IP₃ & DAG

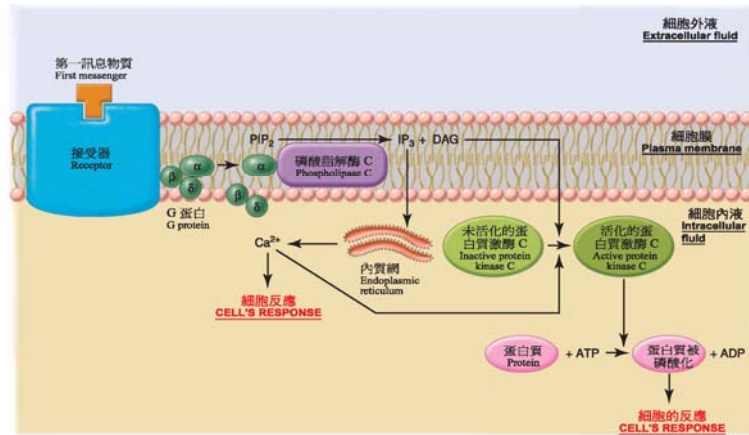


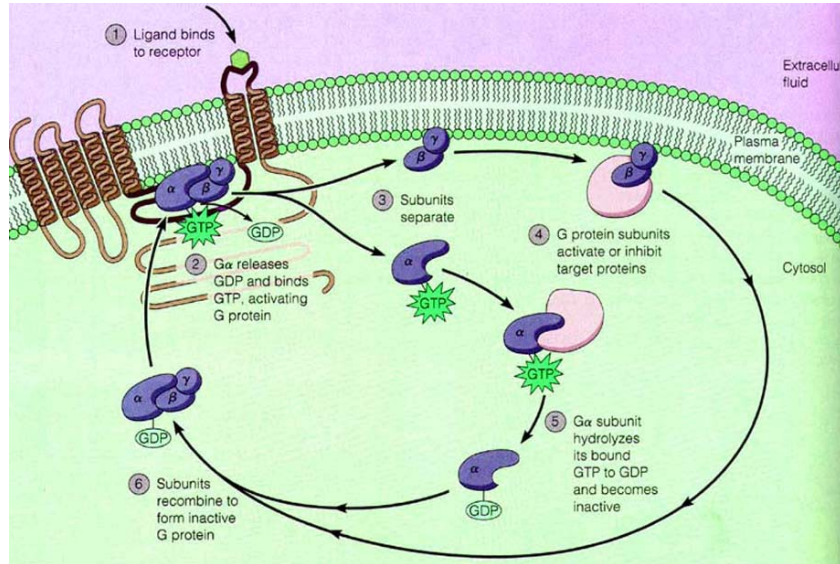
圖 3-9 活化之接受器刺激酶素將 PIP₂ 分解成 IP₃ 與 DAG 之機制圖。接著，IP₃ 促使內質網釋放鈣離子，再跟 DAG 一同活化蛋白質激酶 C。

Heterotrimeric G Proteins

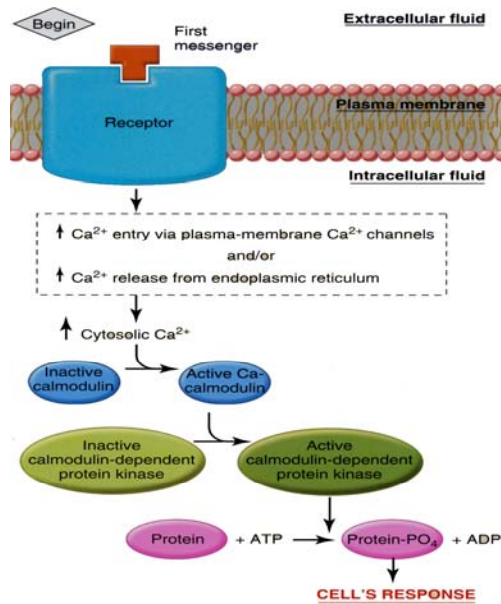
TABLE 5-1. SELECTED MAMMALIAN HETEROTRIMERIC G PROTEINS CLASSIFIED ON THE BASIS OF THEIR α SUBUNITS*			
G Protein	Activated by Receptors for	Effectors	Signaling Pathways
G _s	Epinephrine, norepinephrine, histamine, glucagon, adrenocorticotrophic hormone, luteinizing hormone, follicle-stimulating hormone, thyroid-stimulating hormone, others	Adenylyl cyclase Ca ²⁺ channels	↑ cAMP ↑ Ca ²⁺ influx
G _{olf}	Odorants	Adenylyl cyclase	↑ AMP (olfaction)
G _{α1} (rods)	Photons	cGMP phosphodiesterase	↓ cGMP (vision)
G _{α2} (cones)	Photons	cGMP phosphodiesterase	↓ cGMP (color vision)
G _{α1} , G _{α2} , G _{α3}	Norepinephrine, prostaglandins, opiates, angiotensin, many peptides	Adenylyl cyclase Phospholipase C Phospholipase A ₂ K ⁺ channels	↓ cAMP ↑ InsP ₃ , diacylglycerol, Ca ²⁺
G _q	Acetylcholine, epinephrine	Phospholipase C β	Membrane polarization ↑ InsP ₃ , diacylglycerol, Ca ²⁺

*There is more than one isoform of each class of α subunit; more than 20 distinct α subunits have been identified.

G Protein Cycle



Ca²⁺ as a Second Messenger



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Second Messengers

Table 5-5 Reference Table of Important Second Messengers

Substance	Source	Effects
Arachidonic acid	Converted into eicosanoids by cytoplasmic enzymes	Eicosanoids exert paracrine and autocrine effects, such as smooth muscle relaxation
Calcium	Enters cell through plasma membrane ion channels or is released from endoplasmic reticulum	Activates calmodulin and other calcium-binding proteins; calcium-calmodulin activates calmodulin-dependent protein kinases. Also activates protein kinase C
Cyclic AMP (cAMP)	A G protein activates plasma membrane adenylyl cyclase, which catalyzes the formation of cAMP from ATP	Activates cAMP-dependent protein kinase (protein kinase A)
Cyclic GMP (cGMP)	Generated from guanosine triphosphate in a reaction catalyzed by a plasma membrane receptor with guanylyl cyclase activity	Activates cGMP-dependent protein kinase (protein kinase G)
Diacylglycerol (DAG)	A G protein activates plasma membrane phospholipase C, which catalyzes the generation of DAG and IP ₃ from plasma membrane phosphatidylinositol bisphosphate (PIP ₂)	Activates protein kinase C
Inositol trisphosphate (IP ₃)	See DAG above	Releases calcium from endoplasmic reticulum

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名稱	定義
Receptor	A specific protein in either the plasma membrane or interior of a target cell with which a chemical messenger combines.
Specificity	The ability of a receptor to bind only one type or a limited number of structurally related types of chemical messengers.
Saturation	The degree to which receptors are occupied by a messengers. If all are occupied, the receptors are fully saturated; if half are occupied, the saturation is 50 percent, and so on.
Affinity	The strength with a chemical messenger binds to its receptor.
Competition	The ability of different molecules very similar in structure to its receptor.
Antagonist	A molecule that competes for a receptor with a chemical messenger normally present in the body. The antagonist binds to the receptor but does not trigger the cell's response.
Agonist	A chemical messenger that binds to a receptor and triggers the cell's response; often refers to a drug that mimics a normal messenger's action.
Down-regulation	A decrease in the total number of target-cell receptors for a given messenger in response to chronic high extracellular concentration of the messenger.
Up-regulation	An increase in the total number of target-cell receptors for a given messenger in response to a chronic low extracellular concentration of the messenger.
Supersensitivity	The increased responsiveness of a target cell to a given messenger, resulting from up-regulation.

22

自己

當你能飛的時候就不要放棄飛

當你能夢的時候就不要放棄夢

當你能愛的時候就不要放棄愛

用最少的悔恨面對過去

用最少的浪費面對現在

用最多的夢面對未來

你不能左右天氣，但你能轉變你的心情

好好扮演自己的角色，做自己該做的事，

活出你的生命，作自己的主角